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BORRISTON
LABORATORIES, INC.

FINAL REPORT

THIRTEEN WEEK GAVAGE ADMINISTRATION OF
PET (MEHSL Sample No. 700811) TO RATS

Borriston Project No. 3401

RECEIVED

Sponsored by:
Mobil Environmental Health
Science Laboratory (MEHSL)
Mobil Oil Corporation
P.O. Box 1029
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INITIATION DATE: October 18, 1982
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Borriston Laboratories, Inc.
5050 Beech Place
Temple Hills, MD 20748

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THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET (MEHSL Sample No. 700811) TO RATS MEHSL

Borriston Project No. 3401

FEB 1 9 1991

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ADDENDUM I - Experimental Pathology Laboratories, Inc., Pathology Report

ADDENDUM II - Experimental Pathology Laboratories, Inc., Addendum Pathology Report

SPONSOR:	Mobil Oil Corporation	INITIATION DATE:	October 18, 1982
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ABSTRACT

Three groups of Fischer 344 rats received gavage doses of PET 700811 at 100, 300, and 900 milligrams per kilogram of body weight daily for 13 consecutive weeks to evaluate the toxic effects and to determine target organs.

The subchronic toxicity of PET (MEHSL Sample No. 700811) was assessed by evaluation of the following: mortality, pharmacotoxic signs, body weight, food consumption, physical condition, clinical pathology, gross pathologic findings, and absolute and relative weights of selected organs. Selected data were analyzed by appropriate statistical procedures. Complete histopathologic evaluations were conducted on all control and high-dose animals; the liver kidneys, and testes of the low- and mid-dose animals also were examined.

Dose-related mortality was observed for the mid-(300 mg/kg) and high-dose (900 mg/kg) males and females.

Significant ($p \leq 0.05$) body weight depression and lowered body weight gains were noted for the mid- and high-dose males throughout the course of the study.

Body weights of the mid- and high-dose females were significantly lower than controls during the first four weeks of study.

Noteworthy differences in food consumption between control and treated groups were not observed.

No treatment-related pharmacotoxic signs were observed in either sex at any dose level.

Hematology data indicated hematoconcentration in the male mid- and high-dose groups during Week 5 with complete abatement by Week 13. No similar findings were observed in female treated groups. A leukocyte differential shift was evident in all treated male and female groups during Weeks 5, 13, and 14 and consisted of increased numbers of segmented neutrophils with corresponding decreases in lymphocyte numbers in the treated male groups and increased numbers of both segmented neutrophils and lymphocytes in the treated female groups; the shift appeared to be treatment related in the mid- and high-dose males and high-dose females. Dose-related reductions in platelet cell number were observed in all treated male and female groups by Week 13.

Treatment-related elevations in SGPT, ALP and albumin levels were present in the male and female mid- and high-dose groups during Week 5, as well as significant reductions in total cholesterol levels (mid- and high-dose males and high-dose females) and glucose levels (high-dose males). Total protein levels for the high-dose males and females also were elevated at Week 5. Treatment-related elevations in SGPT, ALP, total protein, and albumin levels were confined to the high-dose males and females during Week 13, as well as treatment-related reductions in total cholesterol and glucose levels in the mid- and high-dose males.

Results of the urinalyses were unremarkable.

No consistent treatment-related trends in gross necropsy data were evident.

The absolute and relative liver weights of the 300 and 900 mg/kg male and female groups were increased and a dose-related pattern was observed. No corresponding liver lesions were seen upon histopathologic evaluation.

Dose-related reductions in absolute and relative testes/epididymides weights of the mid- and high-dose males were observed. Microscopically, administration of PET was associated with testicular atrophy and hypospermatogenesis of the testes and hypospermia or aspermia of the epididymides in the high-dose males; a number of these animals had sperm granulomas in the epididymides. No microscopic indication of atrophy was seen in the sections of testicles from the mid-dose rats; however, two of the animals showed minimal hypospermatogenesis. Testicle sections from all low-dose male rats appeared normal.

Based on the results of this study, the no effect level for PET 700811 is 100 mg/kg day. As discussed above, definitive effects on survival, body weight gains, clinical pathology parameters, liver and testicular weights and testicular histopathology were seen at both the 300 and 900 mg/kg/day dose levels.

INTRODUCTION

This study was designed to evaluate the toxic effects of PET when administered daily by gavage to rats for 13 weeks and to determine target organs. A previous study[a] indicated that when PET was administered by gavage to young rats for two weeks, a slight decrease in body weight and a slight increase (16%) in liver weight was observed in rats receiving 800 mg/kg/day; at 400 mg/kg/day a liver weight increase of 8% was noted. The low- and mid-dose levels for this study, 100 and 300 mg/kg/day respectively, were selected for direct comparison to a 13-week study of paramethylstyrene (PMS) with dose levels of 100 and 300 mg/kg/day. The high-dose (900 mg/kg/day) was a multiple of the mid-dose and intended to show definite toxicity. The study was initiated on October 18, 1982, and was completed on January 20, 1983. Borriston Laboratories, Inc. was authorized to conduct Project 3401 by Mobil Order to Contractor, Number LPT 20028. Project 3401 was conducted according to an approved protocol and in compliance with FDA Standards (43 FR 12/22/78, 58.1-219).

MATERIALS AND METHODS

Test and Control Articles

Approximately 3.185 kg of the test substance, PET (MEHSL Sample No. 700811, Lot Number D580-328-70, BRL No. 540) and approximately 10 gallons of the vehicle for PET, The Original Pompeian Olive Oil (Lot Number 110173-70404, Batch Number 8226, BRL No. 541) were received from Mobil Environmental

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[a]Results supplied by sponsor.

and Health Science Laboratory (MEHSL) on October 8, 1982. The test substance was described as a clear volatile liquid having a density of 0.86 g/ml and an approximate purity of 99.7%[b]. The vehicle control was described as an oily liquid with a density of 0.91 g/ml. Both the test and control articles were received from MEHSL in drum type containers. The test article was stored under refrigeration and the vehicle control was kept at room temperature.

Information on the methods of synthesis, stability under the conditions of use, as well as data on composition or other characteristics which define the test article, are on file with the sponsor.

Test Animals and Husbandry

One-hundred male and 100 female CDF Fischer 344 rats were received from Charles River Breeding Laboratories, Inc., Kingston, New York, on October 6, 1982. The date of birth of all rats was September 7, 1982; all rats were 40 days of age on the first day of dosing. Following receipt of the animals, 10% of their number were weighed and all animals were observed for their general physical appearance. Body weights of the males ranged from 44.1 to 60.0 g and from 36.6 to 49.4 g for the females. The physical appearances of all animals were good.

All animals were housed individually in hanging wire stainless steel cages. Non-contact paper bedding (Shur-Lab Products, Gaithersburg, Maryland) was placed in the pans below the cages and was changed at least three times per week. Racks and cages were sanitized in a commercial rack washer once during the study, during Week 9. Water was provided via an automatic watering system and was available ad libitum. The water supplied to the animal colony was analyzed for total coliforms, pesticides, heavy metals, and halogens. Results of these analyses are presented in Appendix 12. Purina Certified Rodent Chow #5002 (Lot No. SEP 10 82 24) was available to the animals on an ad libitum basis (see Appendix 11 - Feed Analysis). No contaminants were reasonably expected to be present in the feed at levels sufficient to interfere with this study; contaminant assay results provided by Analytical

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[b]Dosage calculations were based on a purity of 100%.

Services of Ralston Purina Company did not exceed the levels set forth in the protocol.

The animals were housed in an air-conditioned room with a temperature range of 19 to 27°C and with relative humidity between 20 and 80%. The study room was maintained manually on a 12-hour light/dark cycle. Protocol accountability information is presented in Appendix 13.

The Fischer 344 rat was selected as the study system because of its survival rate, large amount of background data available on the incidence of diseases, and for direct comparison to a previous gavage study using paramethylstyrene (PMS).

Quarantine Period

All animals were maintained in quarantine from October 6 to October 18, 1982. Quarantine was conducted in the assigned study room. Each animal was examined daily for physical appearance and twice daily for mortality [except quarantine Days (-7), (-4), and (-1) when the animals were observed only once]. The body weight of each animal was recorded during October 11, 1982 and on October 18, 1982. Each animal assigned to the study was examined by a staff veterinarian to verify its physical condition and disease status.

Assignment to Groups

On October 12, 1982, 80 male and 80 female rats were randomly assigned to four groups of 20 males and 20 females each by a BLI computerized randomization procedure, which utilized body weight (weights from October 11, 1982), as the selection criterion. Any animal whose body weight exceeded the mean body weight of all same-sexed animals by ±2 standard deviations and/or had obvious physical abnormalities were not eligible for randomization. The following groups were established:

Group	Test Article	Dose Level (mg/kg/day)	Number Per Sex	Animal Numbers
1	Olive Oil	0	20M/20F	8210000-8210039
2	PET	100	20M/20F	8210040-8210079
3	PET	300	20M/20F	8210080-8210119
4	PET	900	20M/20F	8210120-8210159

Each animal was identified by its unique permanent animal number by ear punching. A cage card with the corresponding unique permanent animal number was affixed to each cage.

Preparation and Administration of Dosing Solutions

Dosing solutions were prepared on three occasions: on October 17, 1982, for dosing Weeks 1 through 4; on November 12, 1982, for dosing Weeks 5 through 8; and on December 9, 1982, for dosing Weeks 9 through study completion. Additional amounts of dosing solution were prepared on November 12, 1982, since the amount of dosing solutions prepared for Groups 2 and 3 were underestimated. An additional 40 ml was prepared for each dose level and used during the last three days of Week 4.

Dosing solutions were prepared by adding the correct amount of test article to the correct amount of Pompeian Olive Oil and thoroughly mixing on a magnetic stirrer for 10 to 20 minutes. The volume of dosing solution was equal to the sum of the volume of test article and olive oil. Dosing solutions based on each 100 ml of total solution prepared were as follows:

Group	Dose Level (mg/kg/day)	Dosing Solution[a] PET (g)	or (ml)	Olive Oil (ml)	Dosing[a] Factor (ml/kg)
1	0		0	100	0.55
2	100	15.05	17.5	82.5	0.67
3	300	33.39	38.8	61.5	0.90
4	900	56.33	65.5	34.5	1.60

The dosing solutions of each dose level prepared on October 17 and November 12, 1982, were divided into 32 aliquots. A larger volume of dosing solution was prepared during December 9, 1982, and each dose level was divided into 43 aliquots. Except for aliquots prepared for use during the first 4 weeks, each aliquot was sufficient for one day of dosing. During the first 4 weeks it was necessary to use more than one aliquot per day since the actual amount of dosing solution needed exceeded the amount prepared.

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[a]Dosing solutions and dosing factors as presented, reflect corrected values based on the specific gravity of both the test and control articles.

The aliquots were placed into glass containers with a minimum of head space to lessen evaporation of the test article. The glass containers had been rinsed in acetone and air dried prior to their use. The aliquots then were frozen (-10°C) until shortly before their use. At that time, they were removed from the freezer and allowed to warm to room temperature. The sponsor reported that, based on the chemical and physical properties of the test article and experiments with similar chemicals, the test article was stable in the dosing solution for the period of time that it was stored before study use.

Three aliquots from each of the PET treated groups and one aliquot from the control group were selected after preparation, frozen (-10°C), and sent to Analytical Chemistry for quantitation of PET in the olive oil. One aliquot each from the additional dosing solutions prepared for Groups 2 and 3 also was submitted for quantitative analysis. One final aliquot from each dose level prepared during December 9, 1982, was randomly selected, frozen (-10°C), and held as archive samples.

Dosing solutions were administered daily, 7 days/week by oral gavage; each animal received a volume of dosing solution calculated from its most recent body weight and the dosing factor for that treatment group. Dosing volumes were recorded and are part of the raw data for this study. A stainless steel feeding needle fitted to a 0.25 or 0.5 cc BD® syringe was used to administer daily gavage doses. Since the carrier, Pompeian Olive Oil, was a digestible oil that added to the caloric intake of the animals, each animal received 0.5 g of olive oil/kg body weight per day.

This study was designed for 91 consecutive days of gavage exposure to PET. Additional dosing was necessary to accomplish the objectives of the study; however, each terminally sacrificed animal was necropsied a minimum of 20 hours after the last dose[a].

The primary route of human exposure to PET is via the diet; however, since the test article was volatile, it was tested by gavage.

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[a]The final dosing took place on Day 94.

Quantitation of PET in Olive Oil

The frozen aliquots of PET/olive oil were allowed to thaw to ambient temperature. One ml of each aliquot was accurately pipetted into a 100 ml volumetric flask and q.s. with chromatographic grade hexane. Chromatographic runs were performed on a Perkin Elmer 3920B Gas Chromatograph and FID. Three level PET standards were run with each extraction set. A six foot glass column, 4 mm I.D., was packed with 10% Silar 10C. Column temperature was 100°C and the carrier gas was helium with a flow rate of 50 cc/min. Chart speed was set at 0.5 cm/min. Results of PET quantitation analyses are presented in Appendix 10. All dosing solutions were within 10% of the intended concentrations.

Mortality and Pharmacotoxic Signs

The animals were observed twice daily for mortality; at least 7 hours apart on weekdays and at least 4 hours apart on weekends and holidays (see Appendix 13 - Protocol Accountability, Section F). Animals not expected to survive to the next observation interval were sacrificed at that time. Each animal was observed in its cage at the beginning of each day for the presence of obvious pharmacotoxic or toxicologic signs. Any obvious clinical signs noted at this time, which had appeared since the previous physical examination interval, were recorded. Occasional or sporadic signs, typical of Fischer 344 rats, were not recorded at the daily observation intervals. These included chromodacryorrhea, swelling, discharge and/or opacity of the eye, crust around the nose, a thin or hunched appearance, rough hair coat, hair loss, soft feces, lethargy, and slowed breathing.

Physical Examinations

Each animal was examined by Borriston personnel for appearance, behavior, reaction to handling, reflexes, posture, gait, and body discharges on the first day of each study week. The presence or absence of obvious clinical signs were noted at this time.

Body Weight and Food Consumption

The body weight of each animal was recorded initially (first day of study), then weekly for the duration of the study, and at termination just prior to necropsy (fasting weights taken before terminal sacrifice). Food consumptions were measured for each animal over a 7-day period. Approximately 500 to 600 g of new food were offered to each animal at the start of each study week. At week's end, the weight of the feeder and remaining food was subtracted from the weight of the feeder and food offered to arrive at each weekly food consumption value.

Clinical Pathology

Clinical pathology analyses were performed during Weeks 5 and 13. Blood specimens were obtained from the orbital sinus of 10 animals/sex/group without anesthesia. The animals were fasted approximately 20 hours before blood collection and the blood samples were collected and analyzed in an order that rotated through the treatment groups and sexes. Blood samples were collected in blood tubes appropriate for the type of analysis required. Urine samples were collected in metabolism pan run-off into gauze filtered plastic urinalysis cups. The urine was analyzed when there was a sufficient quantity collected. All samples collected for the clinical pathology analyses were analyzed on the same working day that they were collected. The following clinical pathology tests were conducted at each analysis interval:

Hematology

- o hematocrit (HCT)
- o hemoglobin (HGB)
- o erythrocyte count (RBC)
- o erythrocyte morphology
- o leukocyte count (WBC)
- o leukocyte differential[a]
- o platelet count

[a]Blood samples were collected from all animals during Week 14 and analyzed for leukocyte differential when a cursory examination of WBC differentials showed a dose-related shift in the leukocyte differential counts during Weeks 5 and 13.

Clinical Chemistry

- o glucose
- o urea nitrogen (BUN)
- o total protein (T PROT)
- o albumin
- o albumin/globulin ratio (A/G)
- o alanine aminotransferase (SGPT)
- o alkaline phosphatase (ALP)
- o cholesterol (T CHOL)
- o calcium (Ca)
- o sodium (Na)
- o potassium (K)
- o chloride (Cl)

Urinalysis

- o pH
- o specific gravity
- o occult blood
- o glucose
- o protein
- o ketones
- o bilirubin
- o urobilinogen
- o color and clarity
- o microscopic sediment

Normal ranges observed in Fischer 344 rats in this laboratory for Hematology and Clinical Chemistry analyses are presented in Appendix 15.

Sacrifice and Necropsy

Animals that died were necropsied immediately after being found. Those animals sacrificed moribund also were necropsied immediately after euthanasia. In all cases necropsies were performed within 16 hours of death. At the study conclusion, all surviving rats were weighed, anesthetized by CO_2 asphyxiation, exsanguinated, and necropsied in an order that rotated through the treatment groups and sexes. Necropsy was performed over a three-day period during Week 14. Each animal received its final dose approximately 20 hours before necropsy. All necropsies were performed according to approved standard operating procedures under the supervision of a Board-certified veterinary pathologist. The following organs and tissues were removed following gross pathologic examination and preserved in 10% neutral buffered formalin:

- o brain (entire)
- o pituitary
- o spinal cord
- o rectum
- o mesenteric lymph node
- o mandibular lymph node

- o eyes (both)
- o salivary glands
- o thyroid
- o trachea
- o thymus
- o esophagus
- o heart and aorta
- o spleen
- o adrenals
- o pancreas
- o skin with mammary gland
- o tongue
- o head (entire)
- o duodenum
- o jejunum
- o ileum
- o colon
- o cecum
- o urinary bladder
- o testes/epididymides
- o prostate
- o seminal vesicle
- o ovaries
- o uterus (entire)
- o vagina
- o sciatic nerve
- o bone with marrow
- o lungs
- o liver
- o kidneys
- o stomach
- o skeletal muscle
- o gross lesions

The trachea was severed just below the thyroid. Fixative was injected into the trachea until the lungs were about 3/4 life size. A ligature was placed around the trachea near the cut end and closed. Samples of liver, kidney, mesenteric fat, and blood were taken from 10 rats/sex/group. All liver and kidney tissues not saved for histopathology, all available mesenteric fat (up to 10 g), and approximately 5-10 cc of blood (in K_3EDTA Vacutainer® tubes) were quickly frozen (-20°C) and sent to the sponsor for possible PET residue analysis.

In addition to terminal body weights, the following absolute organ weights were determined for each terminally sacrificed animal prior to fixation (paired organs or dual-lobed organs were weighed together): lungs, kidneys, adrenals, liver, heart, brain, spleen, gonads, and thymus. The thyroid/parathyroids were weighed following fixation. All organs were weighed to the nearest milligram. Relative organ/body weights were determined for each animal.

Tissue Processing and Histopathology

All tissues collected from all control and high-dose animals and liver and kidneys from the low- and mid-dose groups were processed for microscopic examination by Experimental Pathology Laboratories, Inc. (EPL). Additionally, testes from all male rats from the low- and mid-dose groups were examined

microscopically. Microscopic examination and interpretation of the histopathologic findings were the responsibility of EPL, P.O. Box 474, Herndon, Virginia 22070.

Statistical Analysis

Body weights and body weight changes (Initial through Week 13), food consumption values, hematology (except leukocyte differential counts), absolute leukocyte differential count parameters (segmented neutrophils and lymphocytes) (Weeks 13 and 14), and clinical chemistry values, terminal body weights, and absolute and relative organ weights of the control group (Group 1, 0 mg/kg/day) were statistically compared to the treated group data of the same sex using a two-tailed Student's t-test[a] at the 5% probability level. The following symbols were used to denote statistical differences:

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

[a]G.W. Snedecor and G.W. Cochran; Statistical Methods, Iowa University Press, Ames, Iowa, 10:258-268, 1967.

RESULTS

Mortality and Pharmacotoxic Signs

A summary of group mortality is presented in Table 1. Mortality data (date and day of death and type of death) for each animal are presented in Appendix 1. A summary of physical examination findings is presented in Table 2.

Dose-related mortality was observed for the mid- and high-dose[a] males and females. Eight (8 of 20) deaths or moribund sacrifices were recorded for each of the mid- and high-dose male groups compared to no deaths in the male control group. Two (2 of 20) low-dose, seven (7 of 20) mid-dose, and 18 (18 of 20) high-dose female deaths or moribund sacrifices were recorded compared to a single (1 of 20) female control death.

None of the deaths were attributed to dosing errors since no necropsy findings indicative of gavage-related complications were evident; however, a number of animals died or were sacrificed moribund immediately following blood collection for clinical pathology analyses during Weeks 5 and 13, as shown in the table below. Clinical pathologic changes (e.g., hematologic, leukocytic and liver enzyme changes, see Clinical Pathology) observed in the mid- and high-dose male and female animals may have contributed to a lowered physical resistance to stress in these animals subsequently resulting in a moribund condition or death.

Mortality Distribution By Type of Death

	Males				Females			
	Group				Group			
	1	2	3	4	1	2	3	4
Found Dead During Study	0	0	1	3	0	0	2	8
Sacrifice Moribund During Study	0	0	4	1	0	0	1	8
Died or Sacrificed after Bleeding	0	0	3	4	1	2	4	2
Total Deaths	0	0	8	8	1	2	7	18

[a]High-dose, 900 mg/kg; mid-dose, 300 mg/kg; low-dose, 100 mg/kg.

No consistent pattern suggestive of treatment-related pharmacotoxic signs were apparent from the weekly physical examination data. Clinical signs noted sporadically with equal distribution among treated and control groups were those which are normally associated with Fischer 344 rats; these included: chromodacryorrhea, swelling, discharge, and/or opacity of the eye, crust around the nose, a thin or hunched appearance, rough hair coat, hair loss, soft feces, soiled anal area, and lethargy and slowed breathing.

Body Weight and Food Consumption

Individual and mean body weights with body weight change (gain) are presented in Appendix 2 and Table 3, respectively. Graphic illustration of body weight is shown in Figure 1. Individual and mean food consumption are presented in Appendix 3 and Table 4, respectively and graphic illustration is shown in Figure 2.

Dose-related body weight depression was observed for the mid- and high-dose males; statistically significantly lower than control mean body weights were noted during all study weeks for both groups. The mean body weight gains (Weeks 1 through 13) of the mid- and high-dose males also were significantly lower than the control mean weight gain. Figure 1 clearly shows the body weight depression for the mid- and high-dose male groups throughout the duration of the study. An incidental statistical difference (lower than control) was noted in the low-dose male mean body weight during Week 1 only.

Statistically significantly lower than control mean body weights were noted for the mid- and high-dose female groups during Weeks 1 through 4; however, body weight parity was established in both groups by Week 5 and body weights remained comparable to controls for the remainder of the study. Figure 1 shows the initial body weight depression with subsequent recovery for the mid- and high-dose groups. Body weight gains for the mid- and high-dose female groups were similar to controls. An incidental statistical difference (lower than control) was noted in the mid-dose female mean body weight during Week 12.

No pattern or consistent trends were noted in the food consumption data for treated male or female groups. Sporadic instances of significantly higher or lower than control mean food consumption values were noted: males - mid-dose, lower than control during Weeks 1 and 3 and higher than control during Week 7; high-dose, lower than control during Weeks 1, 3, and 4 and higher than control during Weeks 11 and 12; females - mid-dose, lower than control during Week 1 and higher than control during Weeks 5, 8, and 11; high-dose, higher than control during Weeks 4, 7, 8, 9, and 10.

Clinical Pathology

Individual and mean clinical hematology data are presented in Appendix 4 and Table 5, respectively. Individual and mean clinical chemistry data are presented in Appendix 5 and Table 6, respectively. Clinical pathology methodology is presented in Appendix 14. Normal ranges for clinical pathology parameters are presented in Appendix 15.

Results of the hematology data were somewhat equivocal; data from the Weeks 5 and 13 analysis indicated variable erythropoietic changes in the mid- and high-dose male groups, decreased numbers of platelets in male and female treated groups, and differential leukocytic changes in all treated male and female groups.

Erythropoietic changes involved statistically significantly elevated mean RBC, HGB, and HCT values in the mid- and high-dose males during Week 5. No evidence of erythropoietic changes were observed in the treated female groups during the Week 5 interval; a significantly higher than control mean hematocrit level was noted in the high-dose group and was considered statistically incidental. By Week 13, all indications of hematoconcentration were absent from the mid- and high-dose males. Statistically significantly lower than control mean RBC and HGB levels were noted in the low-dose females during Week 13 and were considered incidental.

Leukocytic changes consisted of statistically significantly elevated mean total leukocyte counts (WBC) in the mid- and high-dose male and female groups during Week 5 and an apparent leukocyte differential shift in all treated male and female groups during Weeks 5 and 13 when compared to the control group.

When compared to historical controls, these data were generally outside of or at the lower or upper extreme of the normal ranges (see Appendix 15).

As with the erythropoietic changes observed in the mid- and high-dose males, elevations in WBC counts in the mid- and high-dose males and females were highest during Week 5 with a return to normal levels by Week 13.

A dose-related shift in the leukocytic differential count occurred in all treated male groups and consisted of increases in segmented neutrophils with decreases in lymphocytes at Weeks 5 and 13. The leukocytic shift appeared to be most evident at Week 5 with only minimal abatement by Week 13. In contrast, all treated female groups showed increases in segmented neutrophils with corresponding minimal increases in lymphocyte number as well; no dramatic differences were observed in the intensity of the differential shift between Weeks 5 and 13.

Absolute leukocyte differential counts were calculated for Week 13 and Week 14. Week 13 absolute leukocyte differential counts were calculated for 10 rats/sex/group. Week 14 absolute leukocyte differential counts were calculated for all surviving animals (in addition to the 10/sex/group) in order to increase the statistical and interpretive reliability of the leukocyte differential shift observed at Week 13. The percentages of increase or decrease in segmented neutrophils and lymphocytes in the treated groups compared with controls were as follows:

Week 13 - Absolute Differential Leukocyte Count
(%) Percent Increase (Decrease) Above (Below) Control

	Male			Female		
GROUP	(N)	SEGS.	LYMPHS.	(N)	SEGS.	LYMPHS.
2	9[a]	+37	-3	10	+3	+9
3	10	+46	-12	10	+21	+4
4	10	+112	-29	2	+119	+18

[a]Data from animal 8210046 excluded to lower standard error.

000021

Week 14 - Absolute Differential Leukocyte Count
(%) Percent Increase (Decrease) Above (Below) Control

	Male			Female		
GROUP	(N)	SEGS.	LYMPHS.	(N)	SEGS.	LYMPHS.
2	19[a]	+35	+1	19	+4	+7
3	12	+56	-20	16	+18	-1
4	14	+128	-27	2	+128	+10

Statistically significant elevations in the mean absolute segmented neutrophils of the mid- and high-dose male groups were noted during Weeks 13 and 14. Concomitantly, statistically significant decreases in the mean absolute lymphocytes were noted for the high-dose males during Week 13 and for the mid- and high-dose male groups during Week 14. These values were within the historical ranges of control, however the normal range is very broad (Appendix 15). When compared to the control group, the increased numbers of segmented neutrophils for all treated male groups with corresponding decreases in total lymphocytes in the mid- and high-dose males showed a treatment relationship. Segmented neutrophil and lymphocyte counts for the low- and mid-dose females were similar to those of the control group. A statistically significant increase in the mean absolute segmented neutrophil count was noted for the high-dose females during Weeks 13 and 14. Data for the high-dose females suggested a treatment-related increase in segmented neutrophils and possibly in lymphocytes. The shift in the differential counts may be related to stress inducement as a result of dosing with PET.

Statistically significantly lower than control mean platelet counts were noted for the high-dose males during Week 5 and for the mid- and high-dose male groups during Week 13. In addition, these values were lower than historical controls (Appendix 15). Mean platelet counts of the male low-dose group were numerically lower than control values during Weeks 5 and 13. Statistically significantly lower than control mean platelet counts were noted for the low- and mid-dose females during Week 13 and numerical decreases in mean platelet counts were noted in all other treated female groups at both intervals (except low-dose, Week 5). Decreases in platelet cell number appeared to be dose-related in both the male and female treated groups by Week 13.

Spleen; Absolute/Relative	4	M	Lower/Higher than Control
Lung; Relative	3	F	Higher than Control
Kidney; Relative	3/4	F	Higher than Control
Adrenal; Absolute/Relative	3	F	Higher than Control
Heart; Absolute	4	F	Lower than Control

Pathology

Results of the microscopic examination of all tissues from the control and high-dose treated groups, liver and kidney only from the low- and mid-dose groups, and abnormal appearing tissues from any group are presented as an addendum to this report (Addendum I), which follows in its entirety after Appendix 15. The Pathology Report for low- and mid-dose testes is presented as an addendum to the EPL Pathology Report (Addendum II).

Raw Data and Report Storage

All raw data, including tissue blocks and slides, and the original copy of the final report are stored indefinitely in the archives of Borriston Laboratories, Inc., 5050 Beech Place, Temple Hills, Maryland 20748.

TABLE 1

CUMULATIVE MORTALITY

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP NO. DOSE LEVEL	CUMULATIVE MORTALITY[a] WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13	TERMINAL SACRIFICE
MALES														
1 0 mg/kg/day	0	0	0	0	0	0	0	0	0	0	0	0	0	20
2 100 mg/kg/day	0	0	0	0	0	0	0	0	0	0	0	0	0	20
3 300 mg/kg/day	0	0	0	0	8	8	8	8	8	8	8	8	8	12
4 900 mg/kg/day	0	1	2	2	4	4	4	4	4	4	4	5	8	12
FEMALES														
1 0 mg/kg/day	0	0	0	0	0	0	0	0	0	0	0	0	1	19
2 100 mg/kg/day	0	0	0	0	1	1	1	1	1	1	1	1	2	18
3 300 mg/kg/day	0	0	0	1	3	3	3	4	4	4	4	4	7	13
4 900 mg/kg/day	2	4	10	11	13	13	13	13	15	15	18	18	18	2

[a]The number dead based on 20 animals/sex/group.

000026

TABLE 2

SUMMARY OF PHYSICAL EXAMINATION FINDINGS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

	INCIDENCE OF CLINICAL SIGNS							
	MALES				FEMALES			
Group No.:	1	2	3	4	1	2	3	4
Day 1								
Discharge, right or both eyes		1			2	1		
Discharge, nose		4	3	5	3	1		1
Day 8								
Discharge, right eye		1						
Discharge, nose		1						
Lethargic and slowed breathing								1
Day 15								
Discharge, right eye		1						
Injury to left hind leg							1	
Nasal discharge and thin								1
Day 22								
Discharge, right eye		1						
Soft feces		2	1					
Injury to left hind leg							1	
Soiled anal area, wheezing, nasal discharge, and slow breathing								1
Day 29								
Discharge, right eye		1						
Soft feces			1					
Day 36								
Discharge, right eye		1						
Chromodacryorrhea, right eye		1						
Right eye opacity						1		
Right eye swelling, opacity, and scab			1					
Right eye opacity, crust around nose							1	
Wheezing				1				
Swelling and scab, right eye				1				
Crust around nose								1
Swelling and opacity, right eye								1

000027

TABLE 2 (Continued)

SUMMARY OF PHYSICAL EXAMINATION FINDINGS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

	INCIDENCE OF CLINICAL SIGNS							
	MALES				FEMALES			
Group No.:	1	2	3	4	1	2	3	4
Day 43								
Thin appearance					1			
Right eye opacity						1		
Scab and swelling, right eye			1	1				
Crust around nose								1
Swelling and opacity, right eye								1
Day 50								
Hunched, thin, rough haircoat, discharge right eye					1			
Discharge, partial closure and opacity right eye						1		
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Right eye opacity and swelling; crust on nose								1
Day 57								
Hunched, thin, rough haircoat, discharge right eye					1			
Discharge, partial closure and opacity right eye						1		
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Right eye opacity and swelling								1
Day 64								
Chromodacryorrhea, right eye	1							
Thin appearance					1			
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Hairloss on abdomen				1				
Discharge, partial closure and opacity right eye						1		
Discharge and opacity right eye								1

000028

TABLE 2 (Continued)

SUMMARY OF PHYSICAL EXAMINATION FINDINGS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

	INCIDENCE OF CLINICAL SIGNS							
	MALES				FEMALES			
Group No.:	1	2	3	4	1	2	3	4
Day 71								
Chromodacryorrhea, right eye	1							
Thin appearance					1			
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Hairloss on abdomen				1				
Discharge, partial closure and opacity right eye						1		
Discharge and opacity right eye								1
Day 78								
Chromodacryorrhea, right eye	1							
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Hairloss on abdomen				1				
Discharge, partial closure and opacity right eye						1		
Day 85								
Chromodacryorrhea, right eye		1						
Hairloss and ulceration, partial closure and discharge right eye			1	1				
Hairloss on abdomen				1				
Discharge, partial closure and opacity right eye						1		
Hunched and thin, soiled anal area, and chromodacryorrhea of both eyes							1	
Day 92								
Chromodacryorrhea, right eye		1	1					
Hairloss and ulceration, partial closure and discharge right eye			1					
Hairloss on abdomen				1				
Protrusion and chromodacryorrhea right eye					2			
Right eye totally closed						1		
Hunched and thin, soiled anal area and chromodacryorrhea of both eyes							1	

000029

TABLE 3

MEAN BODY WEIGHTS AND BODY WEIGHT GAIN

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP NO. DOSE LEVEL		MEAN BODY WEIGHT (g) WEEK														WEIGHT GAIN (g) WEEKS
		INITIAL	1	2	3	4	5	6	7	8	9	10	11	12	13	1 - 13
MALES																
1	MEAN	112.2	145.9	173.2	186.8	210.9	221.4	239.4	250.0	263.3	274.3	280.5	286.9	294.4	288.2	176.1
0	S.D.	5.3	7.5	11.6	20.9	17.8	20.5	21.0	20.6	21.6	22.0	22.1	22.6	23.2	35.0	31.2
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	109.2	140.4^{S-}	169.8	188.9	209.9	222.4	239.1	250.6	263.5	274.1	280.2	287.0	295.1	291.1	181.9
100	S.D.	5.1	7.3	8.6	11.6	11.5	12.9	14.2	15.1	15.1	16.8	16.8	17.4	19.8	19.6	17.8
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
3	MEAN	110.6	130.1^{S-}	152.5^{S-}	175.4^{S-}	195.8^{S-}	201.9^{S-}	220.7^{S-}	233.4^{S-}	243.3^{S-}	253.0^{S-}	256.3^{S-}	262.9^{S-}	265.8^{S-}	255.6^{S-}	145.2^{S-}
300	S.D.	6.3	10.9	10.7	12.9	16.4	12.8	12.5	13.4	13.4	14.2	14.1	14.9	15.4	16.0	13.9
mg/kg/day	N	20	20	20	20	20	12	12	12	12	12	12	12	12	12	12
4	MEAN	110.0	120.7^{S-}	134.3^{S-}	150.3^{S-}	167.5^{S-}	172.6^{S-}	186.3^{S-}	202.4^{S-}	209.5^{S-}	215.4^{S-}	220.7^{S-}	225.9^{S-}	222.6^{S-}	215.4^{S-}	104.6^{S-}
900	S.D.	4.4	6.8	10.8	9.7	10.9	13.7	14.2	14.4	14.7	17.3	15.0	18.0	15.7	22.8	19.6
mg/kg/day	N	20	20	19	18	18	16	16	16	16	16	16	15	15	12	12
FEMALES																
1	MEAN	87.6	104.6	120.1	129.5	138.6	139.0	148.7	152.8	155.8	161.4	164.7	168.1	172.8	166.9	78.9
0	S.D.	3.3	4.2	4.5	5.4	6.2	14.3	9.8	11.5	10.8	9.1	9.2	9.7	9.5	18.0	17.5
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	20	19	19
2	MEAN	87.4	104.0	118.5	129.9	137.7	142.6	150.7	154.7	159.1	161.5	164.8	170.1	173.7	171.5	83.8
100	S.D.	3.3	4.4	5.1	4.8	4.6	4.4	5.1	5.9	5.8	9.3	6.7	6.0	6.1	6.6	4.7
mg/kg/day	N	20	20	20	20	20	19	19	19	19	19	19	19	19	18	18
3	MEAN	87.3	99.6^{S-}	111.1^{S-}	121.7^{S-}	130.7^{S-}	136.7	144.9	150.8	154.2	159.5	160.7	164.4	164.7^{S-}	165.8	78.7
300	S.D.	3.7	6.2	7.0	6.4	6.3	6.9	6.6	7.1	7.4	8.1	7.9	7.5	12.3	8.8	7.4
mg/kg/day	N	20	20	20	20	18	17	17	17	16	16	16	16	16	14	14
4	MEAN	86.6	94.6^{S-}	100.7^{S-}	112.9^{S-}	125.9^{S-}	128.6	140.0	147.3	153.9	163.0	163.4	164.9	162.3	159.0	69.7
900	S.D.	5.0	8.5	12.8	13.8	9.2	10.9	11.4	10.0	11.2	9.3	10.2	5.0	11.1	3.0	4.0
mg/kg/day	N	20	18	16	10	9	7	7	7	7	5	5	2	2	2	2

s- = Statistically significantly lower than control at $p \leq 0.05$.

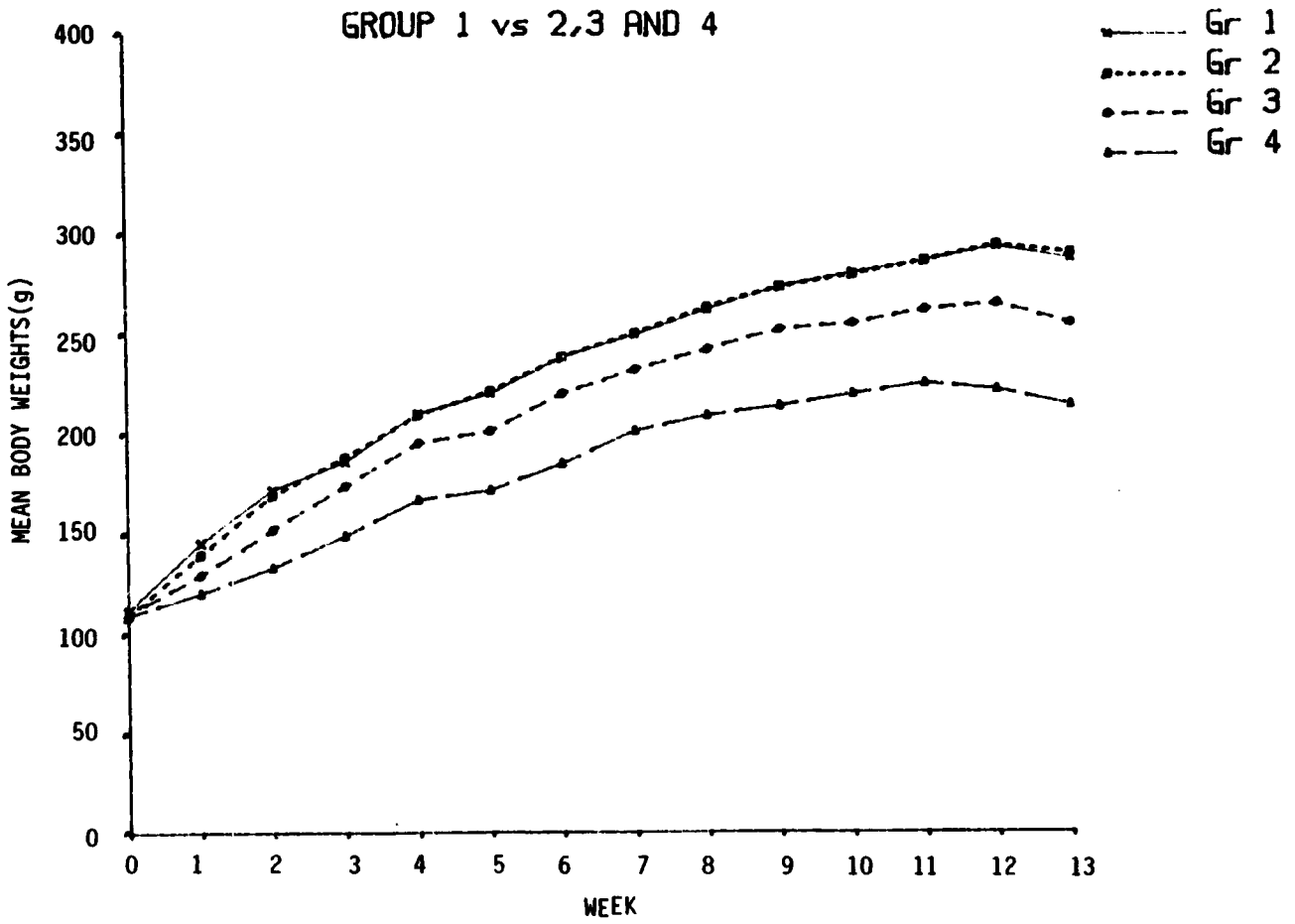
000030

FIGURE 1

MEAN BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES



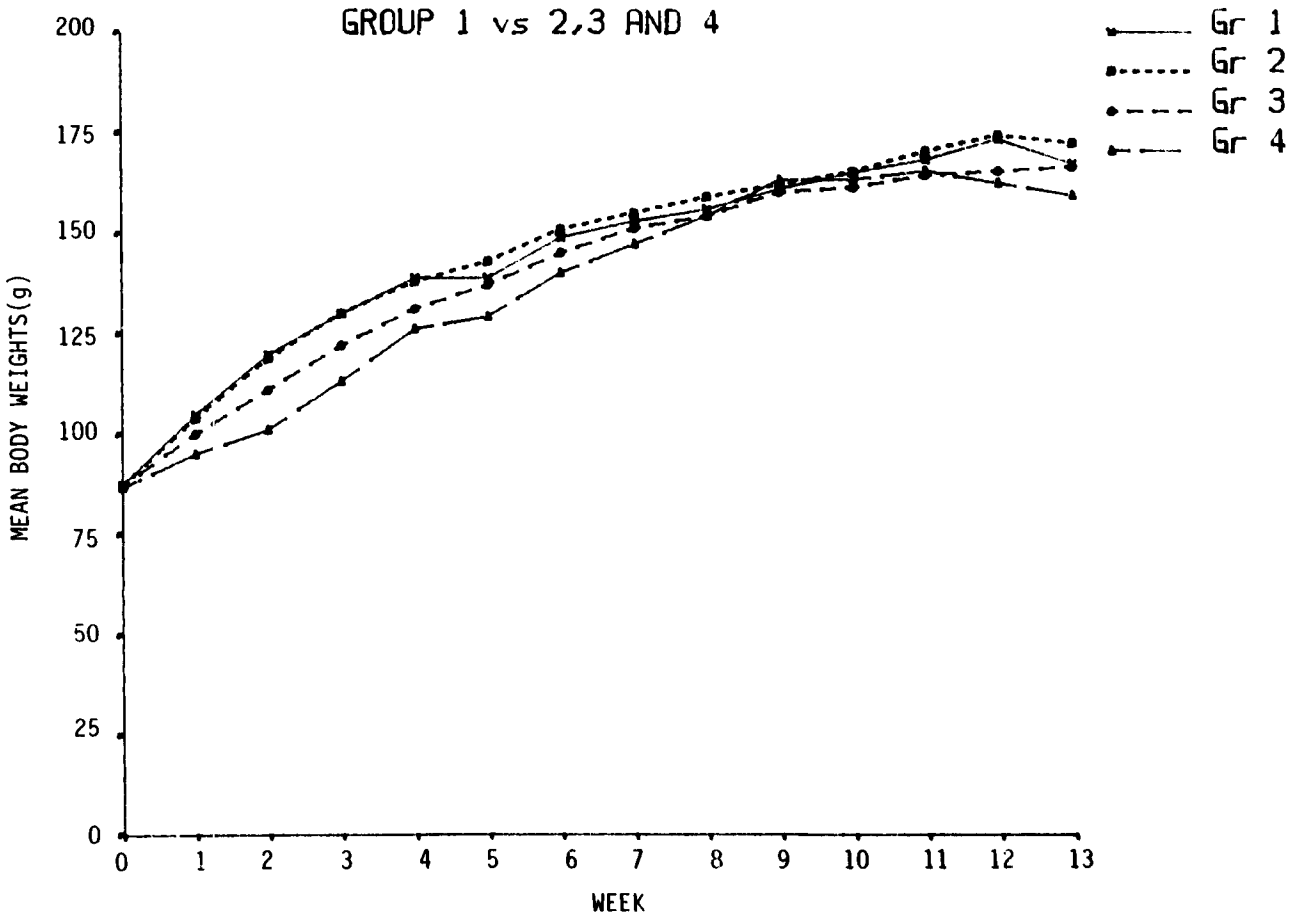
000031

FIGURE 1 (Continued)

MEAN BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES



000032

TABLE 4

MEAN FOOD CONSUMPTIONS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP NO. DOSE LEVEL		MEAN FOOD CONSUMPTION (g) WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13
MALES														
1	MEAN	111.4	119.2	158.6	128.8	124.3	134.6	114.2	123.8	115.0	117.4	112.2	114.8	112.4
0	S.D.	6.9	19.4	68.1	11.8	37.0	39.5	10.6	12.8	8.9	9.0	8.8	7.8	22.7
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	106.9^{S-}	124.8	141.0	126.3	118.9	130.9	114.6	121.4	115.6	119.9	114.2	114.5	107.4
100	S.D.	4.6	41.2	46.8	11.2	25.1	32.2	7.2	7.2	7.8	7.8	7.1	6.8	24.7
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	20
3	MEAN	98.7^{S-}	103.1	105.8^{S-}	123.4	115.8	141.8	121.9^{S+}	124.7	116.3	122.1	124.7	117.9	99.6
300	S.D.	12.0	40.3	21.8	10.3	27.6	34.1	7.3	8.5	17.0	8.0	28.2	10.4	23.3
mg/kg/day	N	20	20	20	20	12	12	12	12	12	12	12	12	12
4	MEAN	94.2^{S-}	110.7	116.5^{S-}	109.1^{S-}	112.4	136.7	115.9	127.5	115.7	124.2	126.3^{S+}	124.0^{S+}	124.0
900	S.D.	7.4	42.8	33.1	6.7	47.2	41.0	8.3	10.9	14.4	21.2	15.3	14.0	52.1
mg/kg/day	N	20	19	18	18	16	16	16	16	16	16	15	15	12
FEMALES														
1	MEAN	95.5	122.6	114.3	95.3	86.8	115.9	81.9	91.8	84.7	84.3	81.1	88.5	86.8
0	S.D.	6.9	60.5	52.7	6.2	17.1	48.6	9.2	14.2	7.6	9.2	6.5	12.3	28.0
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20	20	19
2	MEAN	94.7	103.2	96.0	100.4	86.3	108.2	81.5	91.8	82.7	83.4	83.5	85.4	97.0
100	S.D.	6.4	31.7	43.0	20.8	19.4	36.6	4.8	10.6	8.7	4.9	5.4	4.3	48.7
mg/kg/day	N	20	20	20	20	19	19	19	19	19	19	19	19	18
3	MEAN	84.5^{S-}	95.7	96.4	98.8	109.4^{S+}	104.4	95.7	107.6^{S+}	95.8	96.3	90.1^{S+}	87.5	103.7
300	S.D.	18.2	45.0	27.2	15.7	38.1	22.7	31.9	25.2	35.8	26.2	10.9	20.5	34.4
mg/kg/day	N	20	20	20	17	17	17	17	16	16	16	16	16	14
4	MEAN	93.1	107.2	114.8	127.3^{S+}	95.6	124.3	99.1^{S+}	106.5^{S+}	96.1^{S+}	101.1^{S+}	88.8	85.4	72.4
900	S.D.	23.5	71.5	34.6	55.9	22.6	44.4	19.9	12.5	4.2	6.9	13.5	0.5	2.8
mg/kg/day	N	18	16	10	9	7	7	7	7	5	5	2	2	2

s- = Statistically significantly lower than control at $p \leq 0.05$.

s+ = Statistically significantly higher than control at $p \leq 0.05$.

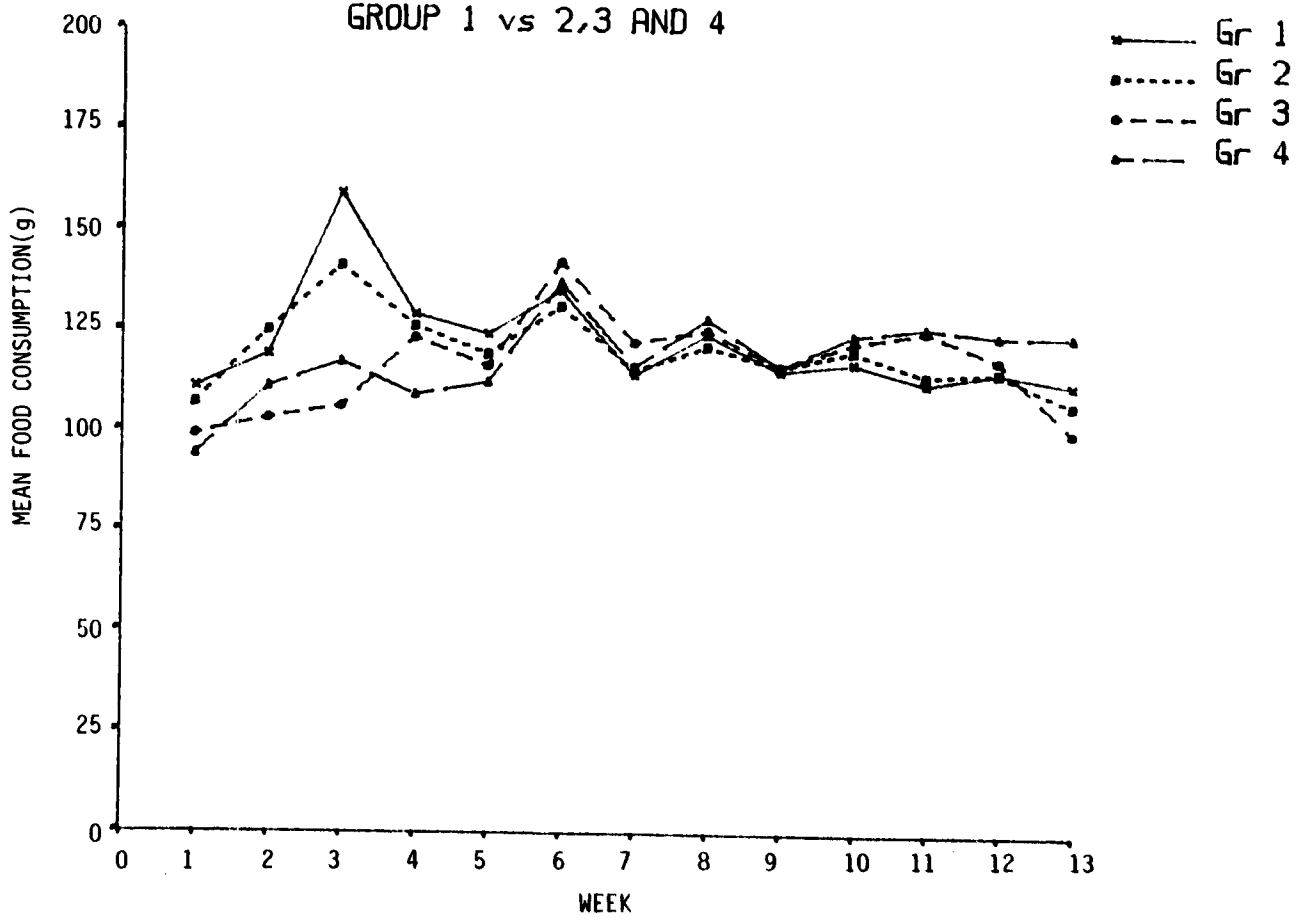
000033

FIGURE 2

MEAN FOOD CONSUMPTION

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES



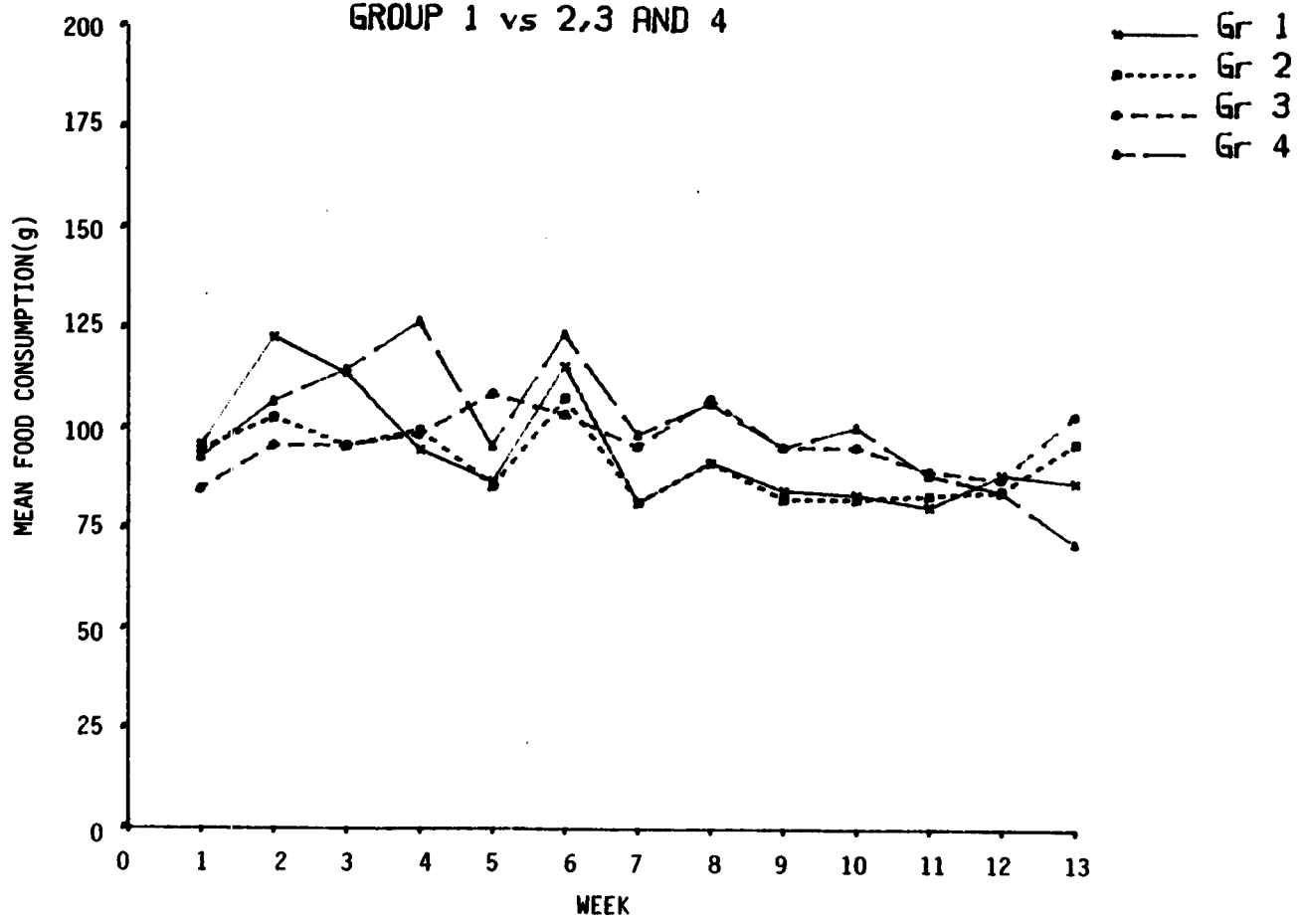
000034

FIGURE 2 (Continued)

MEAN FOOD CONSUMPTION

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES



000035

TABLE 5
MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL		RBC 10^6/cmm	WBC 10^3/cmm	HGB G/DL	HCT %	PLATELET 10^3/cmm
1	MEAN	8.56	7.7	17.3	48.6	346
0	S.D.	0.25	0.9	0.8	2.0	47
mg/kg/day	N	10	10	10	10	10
2	MEAN	8.54	8.6	17.4	49.2	307
100	S.D.	0.46	1.2	0.9	2.3	51
mg/kg/day	N	10	10	10	10	10
3	MEAN	9.62 S+	8.7 S+	19.3 S+	52.8 S+	289
300	S.D.	0.40	1.1	1.0	2.1	99
mg/kg/day	N	10	10	10	10	10
4	MEAN	9.34 S+	9.5 S+	18.3 S+	51.1 S+	266 S-
900	S.D.	0.70	1.6	0.8	2.2	96
mg/kg/day	N	10	10	10	10	10

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000036

TABLE 5 (Continued)

MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL		RBC 10^6/cmm	WBC 10^3/cmm	HGB G/DL	HCT %	PLATELET 10^3/cmm
1	MEAN	8.45	8.5	17.2	48.3	325
0	S.D.	0.26	1.4	0.4	1.2	20
mg/kg/day	N	10	10	10	10	10
2	MEAN	8.49	9.4	17.3	47.5	298
100	S.D.	0.66	1.1	1.1	3.3	41
mg/kg/day	N	10	10	10	10	10
3	MEAN	8.71	8.3	16.9	48.1	262 S-
300	S.D.	0.62	1.1	0.8	1.5	74
mg/kg/day	N	10	10	10	10	9
4	MEAN	8.70	8.1	17.2	49.6	284 S-
900	S.D.	0.67	1.3	1.4	3.3	72
mg/kg/day	N	10	10	10	10	10

S- = Statistically significantly lower than control at $p \leq 0.05$.

000037

TABLE 5 (Continued)
MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF FET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL		RBC 10^6/cmm	WBC 10^3/cmm	HGB G/DL	HCT %	PLATELET 10^3/cmm
1	MEAN	8.04	6.6	17.1	47.2	351
0	S.D.	0.30	0.8	1.0	1.8	89
mg/kg/day	N	10	10	10	10	10
2	MEAN	8.24	7.1	17.3	47.9	354
100	S.D.	0.39	0.8	0.8	1.4	28
mg/kg/day	N	10	10	10	10	9
3	MEAN	8.43	7.5 S+	17.7	48.7	318
300	S.D.	0.69	0.9	1.4	2.6	38
mg/kg/day	N	10	10	10	10	10
4	MEAN	8.32	9.0 S+	17.8	49.5 S+	308
900	S.D.	0.59	2.3	0.6	1.0	43
mg/kg/day	N	9	9	9	9	9

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000038

TABLE 5 (Continued)

MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL		RBC 10^6/cmm	WBC 10^3/cmm	HGB G/DL	HCT %	PLATELET 10^3/cmm
1	MEAN	7.55	6.9	17.0	46.6	333
0	S.D.	0.43	1.5	0.5	1.5	36
mg/kg/day	N	10	10	10	10	9
2	MEAN	7.02 S-	7.5	16.3 S-	47.3	294 S-
100	S.D.	0.50	0.8	0.4	1.1	27
mg/kg/day	N	10	10	10	10	10
3	MEAN	7.53	7.4	16.9	47.5	236 S-
300	S.D.	0.55	1.2	0.7	1.4	33
mg/kg/day	N	10	10	10	10	10
4	MEAN	7.78	9.1	16.9	47.3	303
900	S.D.	1.08	2.3	0.6	1.8	32
mg/kg/day	N	2	2	2	2	2

S- = Statistically significantly lower than control at $p \leq 0.05$.

000039

TABLE 5 (Continued)

MEAN CLINICAL HEMATOLOGY DATA-ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700011 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST	NRBC/ 100 WBC
1	MEAN	1300	7	6830	0	279	54	0	0	0	0	0	0
0	S.D.	386	23	1565	0	147	42	0	0	0	0	0	0
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
2	MEAN	2113	20	7004	0	265	19	0	0	0	0	0	0
100	S.D.	1170	63	1378	0	118	40	0	0	0	0	0	0
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
3	MEAN	1901 S+	0	6017	0	317	88	0	0	0	0	0	0
300	S.D.	477	24	970	0	226	78	0	0	0	0	0	0
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
4	MEAN	2754 S+	0	4978 S-	0	333	15	0	0	0	0	0	0
900	S.D.	809	0	973	0	123	32	0	0	0	0	0	0
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10

FEMALES

	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST	NRBC/ 100 WBC
1	MEAN	1023	0	5594	0	214	65	0	0	0	0	0	1
0	S.D.	428	0	1081	0	144	77	0	0	0	0	0	1
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
2	MEAN	1056	8	6072	0	294	70	0	0	0	0	0	1
100	S.D.	317	25	762	0	127	110	0	0	0	0	0	1
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
3	MEAN	1242	0	5810	0	240	78	0	0	0	0	0	1
300	S.D.	385	0	1184	0	152	44	0	0	0	0	0	1
mg/kg/day	N	10	10	10	10	10	10	10	10	10	10	10	10
4	MEAN	2243 S+	107	6584	0	129	38	0	0	0	0	0	0
900	S.D.	308	151	1887	0	30	53	0	0	0	0	0	0
mg/kg/day	N	2	2	2	2	2	2	2	2	2	2	2	2

S+ = Statistically significantly higher than control at $p \leq 0.05$.
S- = Statistically significantly lower than control at $p \leq 0.05$.

000040

TABLE 5 (Continued)
MEAN CLINICAL HEMATOLOGY DATA - ABSOLUTE DIFFERENTAIL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 14 MALES

GROUP NO. DOSE LEVEL		SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
1	MEAN	1165	4	7458	0	341	51	0	0	0	0	0
0	S.D.	368	16	1414	0	175	64	0	0	0	0	0
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	1570	10	7347	0	319	23	0	0	0	0	0
100	S.D.	1004	44	1314	0	117	49	0	0	0	0	0
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
3	MEAN	1821 S+	6	5976 S-	0	335	86	0	0	0	0	0
300	S.D.	546	22	912	0	224	78	0	0	0	0	0
mg/kg/day	N	12	12	12	12	12	12	12	12	12	12	12
4	MEAN	2660 S+	0	5439 S-	0	331	19	0	0	0	0	0
900	S.D.	736	0	1163	0	149	39	0	0	0	0	0
mg/kg/day	N	14	14	14	14	14	14	14	14	14	14	14

FEMALES

		SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
1	MEAN	982	0	5969	0	243	45	0	0	0	0	0
0	S.D.	399	0	1066	0	190	61	0	0	0	0	0
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	1020	4	6374	0	297	51	0	0	0	0	0
100	S.D.	282	18	1175	0	137	86	0	0	0	0	0
mg/kg/day	N	19	19	19	19	19	19	19	19	19	19	19
3	MEAN	1162	0	5894	0	306	62	0	0	0	0	0
300	S.D.	383	0	1176	0	168	67	0	0	0	0	0
mg/kg/day	N	16	16	16	16	16	16	16	16	16	16	16
4	MEAN	2243 S+	107	6584	0	129	38	0	0	0	0	0
900	S.D.	308	151	1887	0	30	53	0	0	0	0	0
mg/kg/day	N	2	2	2	2	2	2	2	2	2	2	2

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000041

TABLE 6

MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL		GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO %	T.CHOL. MG/DL	CALCIUM MG/DL
1	MEAN	105	17	31	140	6.8	4.5	1.92	52	11.4
0	S.D.	7	1	3	16	0.3	0.1	0.14	6	0.4
mg/kg/day	N	10	10	10	10	10	10	10	10	10
2	MEAN	104	18	30	151	6.9	4.6	2.00	52	11.3
100	S.D.	10	2	5	15	0.4	0.3	0.14	14	0.8
mg/kg/day	N	10	10	10	10	10	10	10	10	10
3	MEAN	101	29	41 S+	224 S+	7.4	4.9 S+	1.99	40 S-	11.6
300	S.D.	18	21	10	109	0.9	0.5	0.23	10	0.5
mg/kg/day	N	10	10	10	10	10	10	10	10	10
4	MEAN	94 S-	19	40 S+	201 S+	7.7 S+	5.1 S+	1.98	37 S-	12.1 S+
900	S.D.	14	3	5	26	0.4	0.2	0.18	7	0.4
mg/kg/day	N	10	10	10	10	10	10	10	10	10

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000042

TABLE 6 (Continued)
MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL		Na MMOL/L	K MMOL/L	Cl[a] MMOL/L
1	MEAN	150	5.8	0
0	S.D.	6	0.4	0
mg/kg/day	N	10	10	0
2	MEAN	150	6.5 S+	0
100	S.D.	7	0.9	0
mg/kg/day	N	10	10	0
3	MEAN	119	5.2	0
300	S.D.	63	2.8	0
mg/kg/day	N	10	10	0
4	MEAN	135	5.7	0
900	S.D.	48	2.1	0
mg/kg/day	N	10	10	0

[a] Quantity of blood not sufficient for analysis.

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000043

TABLE 6 (Continued)
MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL		GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO %	T.CHOL. MG/DL	CALCIUM MG/DL
1	MEAN	86	16	42	109	7.5	4.6	1.61	79	11.1
0	S.D.	8	1	8	21	0.4	0.2	0.11	14	1.2
mg/kg/day	N	10	10	10	10	10	10	10	10	10
2	MEAN	85	17	44	119	7.7	4.8 S+	1.63	77	10.5
100	S.D.	8	2	7	18	0.4	0.2	0.11	14	2.6
mg/kg/day	N	10	10	10	10	10	10	10	10	10
3	MEAN	73 S-	15	42	117	7.5	4.7	1.70	59 S-	10.3
300	S.D.	8	2	8	11	0.4	0.2	0.09	12	2.0
mg/kg/day	N	10	10	10	10	10	10	10	10	10
4	MEAN	65 S-	19	55 S+	153 S+	8.4 S+	5.2 S+	1.63	68 S-	10.9
900	S.D.	11	8	12	34	0.6	0.3	0.11	9	2.8
mg/kg/day	N	10	10	10	10	10	10	10	10	10

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000044

TABLE 6 (Continued)

MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL		Na MMOL/L	K MMOL/L	Cl MMOL/L
1 0 mg/kg/day	MEAN S.D. N	148 2 10	5.3 0.4 10	103 1 9
2 100 mg/kg/day	MEAN S.D. N	149 2 10	5.6 0.5 10	104 2 9
3 300 mg/kg/day	MEAN S.D. N	148 1 9	5.5 0.4 9	104 2 9
4 900 mg/kg/day	MEAN S.D. N	148 2 9	5.7 0.4 8	103 3 7

000045

TABLE 6 (Continued)
MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF FET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL		GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO %	T.CHOL. MG/DL	CALCIUM MG/DL
1	MEAN	99	17	27	115	6.7	4.3	1.81	92	11.3
0	S.D.	5	3	2	9	0.3	0.2	0.10	4	0.3
mg/kg/day	N	10	10	10	10	10	10	10	10	10
2	MEAN	98	15	27	117	6.7	4.4	1.88	94	11.3
100	S.D.	9	2	4	11	0.2	0.1	0.16	6	0.4
mg/kg/day	N	10	10	10	10	10	10	10	10	10
3	MEAN	104	17	33 S+	139 S+	6.7	4.5 S+	1.95	86	11.0
300	S.D.	9	3	5	14	0.3	0.2	0.17	14	1.1
mg/kg/day	N	10	10	10	10	10	10	10	10	10
4	MEAN	95	16	39 S+	168 S+	7.2 S+	4.7 S+	1.86	78 S-	11.8 S+
900	S.D.	12	5	5	39	0.4	0.2	0.16	9	0.5
mg/kg/day	N	9	9	9	9	9	9	9	9	9

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000046

TABLE 6 (continued)

MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL		Na MMOL/L	K MMOL/L	Cl[a] MMOL/L
1	MEAN	150	6.0	0
0	S.D.	6	0.5	0
mg/kg/day	N	10	10	0
2	MEAN	150	6.2	0
100	S.D.	5	0.7	0
mg/kg/day	N	10	10	0
3	MEAN	150	6.1	0
300	S.D.	7	0.8	0
mg/kg/day	N	10	10	0
4	MEAN	133	5.8	0
900	S.D.	50	2.2	0
mg/kg/day	N	9	9	0

[a] Quantity of blood not sufficient for analysis.

000047

TABLE 6 (Continued)
MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL		GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO %	T.CHOL. MG/DL	CALCIUM MG/DL
1	MEAN	78	17	40	85	7.4	4.6	1.60	115	11.2
0	S.D.	7	2	7	10	0.5	0.3	0.08	14	1.0
mg/kg/day	N	10	10	10	10	10	10	10	10	10
2	MEAN	75	16	37	81	7.3	4.5	1.63	116	10.1
100	S.D.	10	1	4	13	0.5	0.3	0.08	12	2.8
mg/kg/day	N	10	10	10	10	9	10	9	10	10
3	MEAN	76	16	45	107 S+	7.2	4.5	1.72 S+	105	11.5
300	S.D.	9	3	9	19	0.4	0.2	0.15	10	1.1
mg/kg/day	N	10	10	10	10	10	10	10	10	9
4	MEAN	78	19	43	142 S+	8.3 S+	5.2 S+	1.66	95	11.5
900	S.D.	16	4	1	47	0.1	0.2	0.14	15	1.1
mg/kg/day	N	2	2	2	2	2	2	2	2	2

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000048

TABLE 6 (Continued)

MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. / DOSE LEVEL		Na MMOL/L	K MMOL/L	Cl MMOL/L
1 0 mg/kg/day	MEAN S.D. N	148 2 8	5.6 0.4 8	105 1 7
2 100 mg/kg/day	MEAN S.D. N	147 1 10	5.4 0.4 10	105 2 10
3 300 mg/kg/day	MEAN S.D. N	146 S- 1 8	5.5 0.4 9	106 2 8
4 900 mg/kg/day	MEAN S.D. N	147 7 2	5.1 1.1 2	106 6 2

S- = Statistically significantly lower than control at $p \leq 0.05$.

000049

TABLE 7

MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP NO. DOSE LEVEL		BODY WT. (g)	LUNG ABS (g)	LUNG REL (%)	KIDNEY [a] ABS (g)	KIDNEY [a] REL (%)	ADRENAL [a] ABS (g)	ADRENAL [a] REL (%)	LIVER ABS (g)	LIVER REL (%)	HEART ABS (g)	HEART REL (%)
MALES												
1	MEAN	272	1.327	0.489	2.213	0.813	0.119	0.043	8.083	2.965	0.973	0.358
0	S.D.	24	0.124	0.049	0.204	0.052	0.097	0.035	0.856	0.142	0.126	0.043
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	269	1.332	0.496	2.220	0.825	0.109	0.041	8.282	3.081 S+	0.983	0.366
100	S.D.	18	0.131	0.042	0.218	0.052	0.049	0.017	0.631	0.163	0.086	0.023
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
3	MEAN	238 S-	1.298	0.547 S+	2.016 S-	0.848	0.103	0.044	8.526	3.580 S+	0.972	0.409 S+
300	S.D.	14	0.130	0.065	0.129	0.055	0.030	0.013	0.912	0.322	0.191	0.085
mg/kg/day	N	12	12	12	12	12	12	12	12	12	12	12
4	MEAN	198 S-	1.170 S-	0.594 S+	2.002 S-	1.014 S+	0.087	0.043	7.480 S+	4.888 S+	0.914	0.465 S+
900	S.D.	18	0.167	0.094	0.208	0.124	0.038	0.018	1.242	0.460	0.276	0.139
mg/kg/day	N	12	12	12	12	12	12	12	12	12	12	12
FEMALES												
1	MEAN	159	0.991	0.621	1.345	0.845	0.079	0.050	4.640	2.926	0.682	0.428
0	S.D.	6	0.147	0.085	0.081	0.060	0.023	0.015	0.226	0.162	0.042	0.031
mg/kg/day	N	19	19	19	19	19	19	19	19	19	19	19
2	MEAN	157	0.957	0.610	1.341	0.855	0.082	0.052	4.881 S+	3.113 S+	0.677	0.432
100	S.D.	7	0.095	0.060	0.081	0.051	0.026	0.017	0.378	0.242	0.043	0.043
mg/kg/day	N	18	18	18	18	18	18	18	18	18	18	18
3	MEAN	151 S-	1.035	0.686 S+	1.369	0.904 S+	0.098 S+	0.065 S+	5.129 S+	3.389 S+	0.669	0.441
300	S.D.	8	0.114	0.082	0.122	0.064	0.023	0.015	0.471	0.250	0.051	0.025
mg/kg/day	N	13	13	13	13		13	13	13	13	13	13
4	MEAN	143 S-	0.948	0.663	1.348	0.942 S+	0.103	0.071	6.949 S+	4.856 S+	0.616 S-	0.430
900	S.D.	1	0.032	0.003	0.119	0.055	0.028	0.017	0.517	0.217	0.055	0.026
mg/kg/day	N	2	2	2	2	2	2	2	2	2	2	2

NOTE: All tissues weighed fresh except where noted.
[a]= Total weight of paired organs.
S- = Statistically significantly lower than control at $p \leq 0.05$.
S+ = Statistically significantly higher than control at $p \leq 0.05$.

000050

TABLE 7 (Continued)

MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP NO. DOSE LEVEL		BODY WT. (g)	BRAIN ABS (g)	BRAIN REL (%)	THYROID/PARA[a,b] ABS (g)	THYROID/PARA[a,b] REL (%)	SPLEEN ABS (g)	SPLEEN REL (%)	THYMUS ABS (g)	THYMUS REL (%)	TESTIS/EPID[a] OVARIES ABS (g)	TESTIS/EPID[a] OVARIES REL (%)
						MALES						
1	MEAN	272	1.842	0.679	0.020	0.007	0.633	0.234	0.316	0.118	4.095	1.511
0	S.D.	24	0.099	0.050	0.005	0.002	0.070	0.030	0.398	0.154	0.245	0.125
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
2	MEAN	269	1.845	0.688	0.022	0.008 S+	0.642	0.240	0.350	0.130	4.193	1.563
100	S.D.	18	0.076	0.040	0.003	0.001	0.074	0.033	0.555	0.204	0.196	0.073
mg/kg/day	N	20	20	20	20	20	20	20	20	20	20	20
3	MEAN	238 S-	1.824	0.768 S+	0.018	0.008	0.614	0.258 S+	0.210	0.088	3.803 S-	1.601
300	S.D.	14	0.098	0.059	0.002	0.001	0.087	0.035	0.056	0.021	0.227	0.118
mg/kg/day	N	12	12	12	12	12	12	12	12	12	12	12
4	MEAN	198 S-	1.630 S-	0.826 S+	0.022	0.011 S+	0.529 S-	0.270 S+	0.148	0.075	1.846 S-	0.931 S-
900	S.D.	18	0.111	0.054	0.003	0.002	0.111	0.061	0.037	0.017	0.267	0.093
mg/kg/day	N	12	12	12	12	12	12	12	12	12	12	12
						FEMALES						
1	MEAN	159	1.704	1.070	0.018	0.011	0.531	0.333	0.209	0.131	0.107	0.068
0	S.D.	6	0.105	0.070	0.004	0.002	0.143	0.092	0.058	0.034	0.028	0.018
mg/kg/day	N	19	19	19	19	19	19	19	19	19	19	19
2	MEAN	157	1.703	1.086	0.019	0.012	0.502	0.319	0.205	0.131	0.104	0.066
100	S.D.	7	0.082	0.064	0.015	0.010	0.107	0.063	0.033	0.021	0.023	0.015
mg/kg/day	N	18	18	18	18	18	18	18	18	18	18	18
3	MEAN	151 S-	1.656	1.098	0.017	0.011	0.505	0.334	0.200	0.132	0.101	0.067
300	S.D.	8	0.114	0.104	0.005	0.003	0.108	0.076	0.046	0.029	0.025	0.017
mg/kg/day	N	13	13	13	13	13	13	13	13	13	13	13
4	MEAN	143 S-	1.593	1.115	0.018	0.013	0.521	0.365	0.147	0.104	0.096	0.067
900	S.D.	4	0.018	0.046	0.000	0.000	0.035	0.036	0.079	0.058	0.023	0.018
mg/kg/day	N	2	2	2	2	2	2	2	2	2	2	2

NOTE: All tissues weighed fresh except where noted.
a= Total weight of paired organs.
b= Fixed weights.
S- = Statistically significantly lower than control at $p \leq 0.05$.
S+ = Statistically significantly higher than control at $p \leq 0.05$.

APPENDIX 1

INDIVIDUAL MORTALITY DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 1 - 0 mg/kg/day

MALE				FEMALE			
ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH	ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH
8210000	1/18/83	93	T	8210020	1/18/83	93	T
8210001	1/18/93	93	T	8210021	1/12/83	87	FD*
8210002	1/18/83	93	T	8210022	1/18/83	93	T
8210003	1/18/83	93	T	8210023	1/18/83	93	T
8210004	1/18/83	93	T	8210024	1/18/83	93	T
8210005	1/18/83	93	T	8210025	1/12/83	93	T
8210006	1/18/83	93	T	8210026	1/18/83	93	T
8210007	1/19/83	94	T	8210027	1/19/83	94	T
8210008	1/19/83	94	T	8210028	1/19/83	94	T
8210009	1/19/83	94	T	8210029	1/19/83	94	T
8210010	1/19/83	94	T	8210030	1/19/83	94	T
8210011	1/19/83	94	T	8210031	1/19/83	94	T
8210012	1/19/83	94	T	8210032	1/19/83	94	T
8210013	1/19/83	94	T	8210033	1/20/83	95	T
8210014	1/20/83	95	T	8210034	1/20/83	95	T
8210015	1/20/83	95	T	8210035	1/20/83	95	T
8210016	1/20/83	95	T	8210036	1/20/83	95	T
8210017	1/20/83	95	T	8210037	1/20/83	95	T
8210018	1/20/83	95	T	8210038	1/20/83	95	T
8210019	1/20/83	95	T	8210039	1/20/83	95	T

FD = Found dead.
MS = Moribund sacrifice.
T = Terminal sacrifice.
* = Died immediately following blood collection.

000052

APPENDIX 1 (Continued)

INDIVIDUAL MORTALITY DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 2 - 100 mg/kg/day

MALE				FEMALE			
ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH	ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH
8210040	1/18/83	93	T	8210060	11/17/82	31	FD*
8210041	1/18/83	93	T	8210061	1/12/83	87	FD*
8210042	1/18/83	93	T	8210062	1/18/83	93	T
8210043	1/18/83	93	T	8210063	1/18/83	93	T
8210044	1/18/83	93	T	8210064	1/18/83	93	T
8210045	1/18/83	93	T	8210065	1/18/83	93	T
8210046	1/19/83	94	T	8210066	1/18/83	93	T
8210047	1/19/83	94	T	8210067	1/18/83	93	T
8210048	1/19/83	94	T	8210068	1/19/83	94	T
8210049	1/19/83	94	T	8210069	1/19/83	94	T
8210050	1/19/83	94	T	8210070	1/19/83	94	T
8210051	1/19/83	94	T	8210071	1/19/83	94	T
8210052	1/19/83	94	T	8210072	1/19/83	94	T
8210053	1/20/83	95	T	8210073	1/19/83	94	T
8210054	1/20/83	95	T	8210074	1/20/83	95	T
8210055	1/20/83	95	T	8210075	1/20/83	95	T
8210056	1/20/83	95	T	8210076	1/20/83	95	T
8210057	1/20/83	95	T	8210077	1/20/83	95	T
8210058	1/20/83	95	T	8210078	1/20/83	95	T
8210059	1/20/83	95	T	8210079	1/20/83	95	T

FD = Found dead.
MS = Moribund sacrifice.
T = Terminal sacrifice.
* = Died immediately following blood collection.

000053

APPENDIX 1 (Continued)

INDIVIDUAL MORTALITY DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 3 - 300 mg/kg/day

MALE				FEMALE			
ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH	ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH
8210080	11/16/82	30	MS	8210100	11/17/82	31	FD*
8210081	11/17/82	31	FD	8210101	1/12/83	87	FD*
8210082	11/17/82	31	FD*	8210102	1/18/83	93	T
8210083	11/16/82	30	MS	8210103	1/12/83	87	FD*
8210084	11/18/82	32	MS**	8210104	1/18/83	93	T
8210085	11/16/82	30	MS	8210105	1/18/83	93	T
8210086	1/18/83	93	T	8210106	1/19/83	94	T
8210087	1/18/83	93	T	8210107	1/14/83	89	FD*
8210088	1/18/83	93	T	8210108	1/19/83	94	T
8210089	1/18/83	93	T	8210109	1/19/83	94	T
8210090	1/19/83	94	T	8210110	1/19/83	94	T
8210091	11/17/82	31	MS	8210111	12/9/82	53	FD
3210092	1/19/83	94	T	8210112	1/19/83	94	T
8210093	1/19/83	94	T	8210113	1/20/83	95	T
8210094	11/18/82	32	FD*	8210114	1/20/83	95	T
8210095	1/19/83	94	T	8210115	1/20/83	95	T
8210096	1/20/83	95	T	8210116	1/20/83	95	T
8210097	1/20/83	95	T	8210117	11/15/82	29	FD
8210098	1/20/83	95	T	8210118	1/20/83	95	T
8210099	1/20/83	95	T	8210119	11/10/82	24	MS

FD = Found dead.
MS = Moribund sacrifice.
T = Terminal sacrifice.
* = Killed immediately following blood collection.
** = Sacrificed moribund immediately following blood collection.

000054

APPENDIX 1 (Continued)

INDIVIDUAL MORTALITY DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 4 - 900 mg/kg/day

MALE				FEMALE			
ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH	ANIMAL NUMBER	DATE OF DEATH	DAY OF STUDY	TYPE OF DEATH
8210120	1/18/83	93	T	8210140	11/7/82	21	FD
8210121	11/5/82	19	MS	8210141	11/3/82	17	FD
8210122	1/18/83	93	T	8210142	10/25/82	8	MS
8210123	11/17/82	31	FD*	8210143	10/23/82	6	FD
8210124	1/12/83	87	FD*	8210144	11/2/82	16	FD
8210125	1/14/83	89	FD*	8210145	12/15/82	59	MS
8210126	1/18/83	93	T	8210146	10/29/82	12	MS
8210127	1/14/83	89	FD*	8210147	11/7/82	21	FD
8210128	1/19/83	94	T	8210148	10/20/82	3	FD
8210129	1/19/83	94	T	8210149	11/10/82	24	FD
8210130	11/19/83	33	FD	8210150	12/16/82	60	FD
8210131	1/19/83	94	T	8210151	11/17/82	31	FD*
8210132	1/19/83	94	T	8210152	1/18/83	93	T
8210133	1/20/83	95	T	8210153	1/19/83	94	T
8210134	1/20/83	95	T	8210154	11/17/82	31	FD*
8210135	10/28/82	11	FD	8210155	12/28/82	72	MS
8210136	1/3/83	78	FD	8210156	11/4/82	18	MS
8210137	1/20/83	95	T	8210157	12/28/82	72	MS
8210138	1/20/83	95	T	8210158	12/29/82	73	MS
8210139	1/20/83	95	T	8210159	11/3/82	17	MS

FD = Found dead.
MS = Moribund sacrifice.
T = Terminal sacrifice.
* Died immediately following blood collection.

000055

APPENDIX 2
INDIVIDUAL AND MEAN BODY WEIGHTS AND BODY WEIGHT CHANGES [a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 1 MALES
0 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210000	113.2	139.0	178.4	192.8	214.7	224.4	241.7	252.5	265.0	274.5	285.0	289.6	295.7	282.4	169.2
8210001	113.6	141.7	173.2	199.1	218.0	227.7	237.7	248.8	270.1	281.3	296.1	301.4	310.0	293.1	179.5
8210002	108.7	140.7	161.5	157.4	186.7	200.0	214.8	225.9	241.8	259.1	271.8	271.9	272.2	262.5	153.8
8210003	111.2	146.9	171.6	199.7	214.8	210.8	234.8	244.9	255.1	267.1	273.9	281.2	288.8	276.4	165.2
8210004	108.4	143.6	159.3	199.1	214.3	217.5	232.8	241.4	253.3	263.5	267.4	268.9	270.6	269.6	156.2
8210005	110.2	141.4	169.8	187.0	209.4	217.6	231.5	241.7	256.6	266.8	271.1	277.1	284.9	266.2	156.0
8210006	104.0	130.9	154.8	166.6	185.6	189.2	203.4	212.4	227.7	238.4	243.9	252.2	260.4	181.4	80.1
8210007	111.6	148.7	181.0	206.3	223.3	230.5	242.4	253.7	267.4	275.2	282.4	286.5	295.3	290.8	178.2
8210008	108.0	138.2	165.2	186.6	202.1	204.0	212.6	224.6	235.0	246.7	251.9	243.3	246.3	260.5	152.5
8210009	115.0	146.1	177.6	187.5	211.1	214.3	230.2	257.3	272.4	280.9	294.4	302.8	311.8	301.8	186.8
8210010	111.6	144.4	173.1	178.7	196.2	211.3	224.7	233.0	244.3	254.4	261.8	265.0	277.9	289.0	177.4
8210011	103.6	139.2	157.7	150.3	182.9	209.9	226.1	241.2	252.4	265.2	273.3	278.9	289.9	291.7	188.1
8210012	122.0	159.8	196.5	222.8	251.3	270.8	292.2	300.2	317.1	335.1	341.4	344.4	354.9	361.5	239.5
8210013	106.8	139.7	167.9	195.7	218.4	234.2	245.2	259.8	270.9	276.4	283.7	287.7	297.3	297.4	190.6
8210014	112.7	146.4	176.3	198.5	218.2	234.4	246.2	254.2	259.3	270.3	276.8	284.2	292.3	293.3	180.6
8210015	115.1	150.3	186.4	204.1	226.2	249.2	267.4	272.0	289.0	299.8	303.1	315.3	325.8	327.9	212.8
8210016	121.9	158.6	190.7	211.8	234.9	256.3	265.9	277.5	290.0	297.7	301.4	310.3	319.7	326.1	204.2
8210017	109.6	143.4	160.7	151.2	183.4	205.0	219.7	231.7	240.4	251.3	255.8	258.8	268.3	267.5	157.9
8210018	111.9	148.1	170.1	157.9	204.4	220.0	245.2	264.7	271.2	277.2	287.9	294.2	299.9	305.4	193.5
8210019	121.9	160.6	188.3	176.9	222.7	246.4	262.1	273.5	286.9	294.8	304.3	312.3	315.3	315.0	193.1
MEAN	112.2	145.9	173.2	186.8	210.9	221.4	239.4	250.9	263.3	274.3	280.5	284.9	294.4	288.2	176.1
S.D.	5.3	7.5	11.4	20.9	17.8	20.5	21.0	20.4	21.6	22.0	22.1	22.6	23.2	35.0	31.2
N	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20

GROUP 1 FEMALES
0 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210020	93.6	108.5	120.3	130.7	143.6	144.8	152.9	154.2	155.9	164.0	164.9	176.3	180.5	179.1	85.5
8210021	78.7	92.0	104.8	113.6	119.2	122.1	126.0	129.5	132.3	138.1	138.1	140.9	145.6	-----	-----
8210022	85.2	102.7	122.1	133.4	143.1	141.2	156.4	163.4	165.6	171.5	173.3	178.1	180.3	172.9	87.7
8210023	91.9	109.5	125.3	132.9	139.7	140.8	145.5	150.6	153.8	158.5	161.4	162.8	167.9	163.4	71.5
8210024	93.7	112.0	125.1	132.8	139.9	105.4	152.0	157.4	161.8	165.0	167.6	170.3	171.8	168.0	74.3
8210025	90.1	108.0	121.6	135.0	146.8	147.0	158.9	161.8	165.3	167.5	170.0	177.9	180.2	179.1	88.7
8210026	87.7	106.3	121.0	132.1	141.6	141.8	143.8	143.9	146.9	154.2	156.0	161.5	168.3	165.9	78.2
8210027	81.8	103.0	118.9	131.3	143.1	143.8	149.4	157.0	158.3	161.9	163.1	166.3	170.8	110.6	28.8
8210028	86.0	102.2	118.8	132.1	140.2	141.4	152.7	154.1	159.1	165.2	168.3	169.7	179.0	131.3	45.3
8210029	87.4	101.9	121.1	131.4	140.5	140.0	149.5	154.2	156.4	160.0	164.1	166.9	171.0	169.8	82.4
8210030	88.6	107.0	125.3	136.4	141.1	154.8	144.4	162.7	161.1	168.7	174.3	175.9	179.3	178.5	89.9
8210031	90.1	107.9	126.1	118.3	138.2	146.8	158.0	161.1	164.7	170.9	173.3	175.6	179.1	152.3	62.2
8210032	87.3	101.0	117.1	126.0	137.7	138.1	141.6	148.8	154.9	158.3	163.0	164.3	173.5	179.4	92.1
8210033	88.9	101.9	118.5	129.0	133.1	141.1	146.8	149.2	154.1	156.6	159.4	161.1	165.8	165.6	76.7
8210034	87.1	103.7	118.0	127.0	129.8	129.0	120.0	117.6	124.5	141.2	147.5	151.0	155.9	161.4	74.3
8210035	81.3	102.8	119.5	131.3	140.4	148.9	155.6	159.5	157.9	168.2	170.1	176.5	182.7	181.9	100.6
8210036	85.8	102.5	117.4	122.2	134.7	145.6	151.9	152.7	160.4	159.1	167.3	167.3	173.1	170.1	84.3
8210037	87.9	107.8	122.9	127.7	143.8	152.3	161.1	164.1	167.8	172.5	176.1	179.0	185.9	184.3	96.4
8210038	88.9	103.2	121.5	131.2	139.7	145.4	148.4	152.7	156.3	158.9	161.4	163.0	168.8	168.6	79.7
8210039	87.1	103.7	120.6	131.3	140.4	150.1	151.7	158.9	158.7	167.6	167.4	171.1	178.4	177.2	89.6
MEAN	87.6	104.6	120.1	129.5	138.6	139.0	148.7	152.8	156.8	161.1	161.7	168.1	172.8	166.9	78.9
S.D.	3.3	3.2	5.5	5.4	6.2	14.3	9.8	11.5	10.8	9.1	9.2	9.5	9.5	18.0	17.5
N	20	20	20	20	20	20	20	20	20	20	20	20	20	19	19

----- =No value due to death of the animal.

[a] Values in grams.

950006

APPENDIX 2 (Continued)

INDIVIDUAL AND MEAN BODY WEIGHTS AND BODY WEIGHT CHANGES[a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 2 MALES
100 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210050	114.1	146.2	177.8	203.6	224.1	239.9	252.5	265.9	277.5	288.7	292.5	295.4	310.9	308.1	192.0
8210051	114.2	152.2	183.2	203.8	219.8	233.9	242.5	244.9	254.7	267.1	272.5	302.9	310.2	311.2	197.0
8210052	113.0	146.8	178.6	199.7	215.8	230.7	238.4	244.8	248.7	277.1	288.8	292.6	299.3	296.3	183.3
8210053	102.9	131.5	157.4	168.8	184.9	212.1	232.4	241.0	256.3	262.3	268.9	278.3	285.5	287.9	185.0
8210055	114.3	142.7	174.9	177.5	205.0	229.7	250.1	263.1	270.8	281.3	288.4	294.8	308.9	309.3	195.0
8210056	101.1	135.3	160.6	177.2	202.5	226.1	242.5	255.8	268.9	281.7	292.2	301.6	307.8	312.8	211.7
8210057	114.9	147.0	173.0	187.1	205.2	222.7	240.8	247.4	261.4	267.2	273.6	284.5	292.8	287.9	173.0
8210058	103.9	135.7	157.0	172.5	186.2	198.0	204.2	214.7	224.8	232.2	239.6	243.7	248.3	253.7	149.8
8210059	108.9	142.0	161.5	182.8	205.6	223.3	238.2	245.9	258.3	270.2	271.7	281.3	286.5	287.9	179.0
MEAN	109.2	140.4 S-	169.8	188.9	209.9	222.4	237.1	250.6	263.5	274.1	280.2	287.0	295.1	291.1	181.9
S.D.	5.1	7.3	8.6	11.6	11.5	12.3	11.2	13.1	12.1	14.8	14.8	12.4	11.8	11.6	17.8
N	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20

GROUP 2 FEMALES
100 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210060	82.9	97.0	111.9	125.6	134.1	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210061	87.0	102.5	117.1	128.9	137.5	139.8	151.4	153.6	159.8	162.5	159.1	162.9	175.6	-----	-----
8210062	91.6	111.2	124.3	135.9	144.7	145.2	153.8	159.7	162.2	163.8	169.7	173.4	174.7	174.5	82.9
8210063	89.3	107.3	118.8	133.6	140.4	144.5	151.4	157.2	164.8	166.9	171.1	175.4	179.5	170.3	81.0
8210064	85.1	99.8	114.3	130.4	137.1	139.6	146.9	150.0	155.5	164.8	165.5	167.6	172.7	172.1	87.0
8210065	88.0	106.1	122.6	131.6	139.8	146.0	155.2	157.1	160.8	165.9	169.5	172.8	177.0	167.0	79.0
8210066	84.2	103.4	120.7	129.8	138.3	141.0	151.2	154.7	158.8	163.2	163.5	170.4	177.4	172.3	88.1
8210067	87.9	108.6	121.3	135.2	141.6	142.3	150.7	156.7	160.3	164.2	170.2	175.8	176.5	174.3	86.4
8210068	93.2	111.0	126.6	137.9	144.8	150.9	161.8	167.2	170.2	173.7	177.0	178.7	182.4	185.9	92.7
8210069	86.7	102.4	122.0	131.4	138.6	141.2	151.3	154.1	158.4	159.9	167.5	171.5	176.4	173.8	86.1
8210070	84.5	102.0	118.9	127.5	135.9	138.5	148.0	151.4	156.5	161.0	165.0	166.8	172.0	166.3	81.8
8210071	85.1	100.7	116.2	128.0	136.4	142.6	150.1	152.9	157.1	163.2	162.4	167.4	172.7	173.6	88.5
8210072	99.2	104.9	112.0	125.0	133.2	143.3	149.1	155.8	160.9	164.2	165.8	171.1	178.2	177.4	87.2
8210073	81.8	101.2	111.2	123.6	131.3	135.8	141.8	145.4	142.9	153.2	156.2	158.0	161.6	159.3	74.5
8210074	82.0	97.6	110.5	123.4	127.8	135.7	141.6	146.7	151.2	154.6	155.9	162.0	162.8	163.6	81.6
8210075	92.2	108.1	121.1	131.1	142.0	149.0	154.8	163.3	167.0	164.9	169.7	176.3	179.0	177.7	85.5
8210076	89.5	107.0	118.3	128.8	141.0	145.0	154.3	158.5	160.4	168.8	169.0	174.1	175.9	175.2	85.7
8210077	87.7	105.4	122.6	133.3	140.3	148.5	154.1	159.4	163.9	167.2	166.3	174.5	175.7	175.9	88.2
8210078	83.2	96.5	112.2	119.7	128.9	135.5	142.3	142.8	149.0	152.1	153.8	158.0	160.1	159.5	76.3
8210079	91.1	107.5	122.5	136.3	139.0	144.4	150.6	153.8	158.5	159.5	163.0	165.6	170.0	169.8	78.7
MEAN	87.1	104.0	118.5	129.9	137.7	142.4	150.7	154.7	159.1	161.5	164.8	170.1	173.7	171.5	83.8
S.D.	3.3	4.4	5.1	4.8	4.6	4.4	5.1	5.9	5.8	6.3	6.7	6.0	6.1	6.5	4.7
N	20	20	20	20	20	19	19	19	19	19	19	19	19	18	18

S- = Statistically significantly lower than control at P≤0.05.
----- = No value due to death of the animal.

[a] Values in grams.

000057

APPENDIX 2 (Continued)

INDIVIDUAL AND MEAN BODY WEIGHTS AND BODY WEIGHT CHANGES [a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 7008[1] TO RATS

GROUP 3 MALES
300 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210080	103.0	111.2	128.3	151.0	174.1	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210081	102.5	123.2	141.4	167.7	188.0	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210082	114.4	148.5	148.3	188.3	212.4	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210083	109.8	132.6	154.4	180.2	195.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210084	122.0	131.1	155.0	185.0	210.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210085	112.0	130.6	158.7	186.2	209.9	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210086	111.6	132.3	156.7	179.1	201.5	198.0	231.4	237.2	254.4	266.7	271.6	275.8	285.7	268.2	156.6
8210087	116.5	135.3	167.2	187.5	209.9	217.0	236.3	248.3	255.6	264.2	272.7	282.6	277.0	266.8	150.3
8210088	104.2	117.8	144.9	170.3	192.3	194.3	213.3	228.9	240.2	255.2	253.2	264.9	260.5	250.0	145.8
8210089	113.4	128.6	152.6	183.2	199.2	205.3	229.1	234.9	249.0	258.6	254.2	274.9	271.0	242.7	129.3
8210090	115.9	127.4	158.9	157.9	183.7	188.1	207.4	226.9	236.1	244.6	248.1	253.1	256.7	249.9	131.0
8210091	115.1	137.2	154.5	182.7	210.5	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210092	109.7	141.5	161.9	187.8	210.4	216.7	236.9	250.6	261.6	266.3	273.4	275.3	281.0	277.0	167.3
8210093	114.6	143.5	162.4	178.6	199.9	193.8	221.3	241.8	253.0	265.8	259.8	267.7	276.3	265.0	150.4
8210094	109.3	137.3	157.2	183.4	200.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210095	121.3	152.5	155.3	192.0	212.0	223.9	238.9	250.4	248.8	259.6	244.1	271.4	278.2	272.6	151.3
8210096	98.0	113.9	132.3	148.3	168.0	187.8	204.9	215.3	224.7	238.9	244.5	250.9	248.8	242.5	144.5
8210097	106.8	127.1	153.8	166.0	179.3	203.5	215.4	225.7	233.4	238.5	244.2	247.0	254.2	230.2	123.6
8210098	106.0	120.2	138.8	164.1	181.9	184.1	201.4	208.9	217.0	222.1	226.6	232.7	233.9	233.7	127.7
8210099	105.3	120.1	148.4	169.0	194.8	207.9	219.1	232.5	245.3	257.0	261.7	256.2	266.3	268.0	161.4
MEAN	110.6	130.1 S-	152.5 S-	175.4 S-	195.8 S-	201.9 S-	220.7 S-	233.4 S-	243.3 S-	253.0 S-	256.3 S-	262.9 S-	265.8 S-	255.6 S-	145.2 S-
S.D.	6.3	10.9	10.7	12.9	16.4	12.8	12.5	13.4	13.4	14.2	14.1	14.9	15.4	16.0	13.9
N	20	20	20	20	20	12	12	12	12	12	12	12	12	12	12

GROUP 3 FEMALES
300 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210100	85.1	102.2	117.9	127.4	135.1	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210101	92.0	100.6	112.0	120.3	127.1	135.9	148.8	152.2	158.7	165.0	167.4	168.3	170.2	-----	-----
8210102	86.1	90.5	105.0	116.4	128.5	138.5	137.3	145.9	148.9	154.2	158.6	160.2	160.2	157.9	71.8
8210103	90.3	99.7	112.1	123.6	132.7	138.2	148.2	154.0	157.3	163.9	164.0	168.8	161.0	177.2	86.9
8210104	89.7	108.4	120.5	130.5	138.0	142.4	156.6	163.7	164.5	173.2	176.0	177.8	181.9	176.5	86.8
8210105	88.6	105.2	121.4	124.6	131.7	137.1	147.7	150.4	155.8	162.5	160.3	158.7	168.3	163.9	75.3
8210106	91.9	102.6	107.6	124.6	129.2	133.3	143.7	147.0	152.9	157.9	158.8	163.4	166.6	162.4	70.5
8210107	89.9	107.9	118.4	128.4	140.2	139.0	146.5	154.3	160.3	162.2	163.2	167.7	171.1	-----	-----
8210108	86.1	100.4	104.8	119.5	124.8	130.2	140.3	147.8	152.9	156.7	157.9	161.9	163.6	159.0	72.9
8210109	79.9	94.8	99.9	110.5	121.1	123.6	135.4	142.8	145.3	150.0	150.3	155.3	159.4	155.1	75.2
8210110	91.3	102.7	116.3	129.0	140.2	149.9	159.6	162.8	168.1	170.5	173.4	177.1	180.3	178.7	87.4
8210111	87.0	93.8	112.8	121.9	131.4	142.1	145.5	151.9	-----	-----	-----	-----	-----	-----	-----
8210112	85.1	103.4	116.8	125.8	129.0	138.4	142.8	149.0	152.3	156.4	160.7	159.6	159.8	158.6	73.5
8210113	92.8	103.3	115.1	121.9	131.5	141.5	146.7	154.6	154.5	162.4	158.8	162.7	165.0	165.8	73.0
8210114	79.3	84.9	96.0	106.8	118.5	125.9	133.2	137.4	140.5	143.5	148.1	153.9	151.0	154.4	75.1
8210115	86.1	102.3	108.7	124.9	136.4	144.7	151.3	157.6	159.3	167.3	167.6	175.3	177.2	177.0	90.9
8210116	88.5	95.8	111.0	120.9	125.6	131.2	137.6	143.3	147.3	150.9	150.7	159.2	163.2	162.9	74.4
8210117	88.6	100.2	105.3	120.3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210118	83.3	90.3	108.8	120.0	131.6	140.7	145.5	152.7	151.5	159.5	159.7	163.0	165.8	171.1	88.1
8210119	88.3	98.9	101.3	110.1	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
MEAN	87.3	99.6 S-	111.1 S-	121.7 S-	130.7 S-	134.7	144.9	150.8	154.2	159.5	160.2	164.1	164.7 S-	165.8	78.7
S.D.	3.7	6.2	5.6	5.1	6.3	6.9	6.8	7.1	7.4	8.1	7.9	7.5	10.3	8.8	7.1
N	20	20	20	20	18	17	17	17	16	16	16	16	16	14	14

S- = Statistically significantly lower than control at p≤0.05.
----- = No value due to death of the animal.

a Values in grams.

000058

APPENDIX 2 (Continued)
INDIVIDUAL AND MEAN BODY WEIGHTS AND BODY WEIGHT CHANGES [a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 7008[1] TO RATS

GROUP 4 MALES
900 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210120	108.2	118.8	140.0	154.9	170.1	171.7	185.7	206.9	215.5	190.6	212.2	228.9	229.9	235.2	127.0
8210121	104.5	118.7	135.5	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210122	115.3	127.5	141.5	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210123	114.4	129.9	142.3	151.2	173.8	185.9	213.6	233.9	237.5	251.9	253.3	245.0	251.8	232.3	117.9
8210124	106.8	115.0	131.7	138.8	157.8	158.2	166.9	184.1	179.4	177.8	210.4	212.5	209.1	-----	-----
8210125	108.1	122.5	141.5	150.8	174.8	179.9	185.3	202.8	209.3	215.3	218.3	225.3	220.6	-----	-----
8210126	108.0	113.4	124.1	132.3	154.7	157.8	172.2	189.8	190.4	199.3	197.8	204.5	203.8	194.9	86.9
8210127	115.5	126.4	130.8	138.8	174.1	171.2	190.8	207.5	200.8	223.2	222.7	226.2	226.8	-----	-----
8210128	112.3	114.8	130.7	148.9	164.1	155.2	173.8	189.4	201.7	201.6	211.2	206.5	213.8	207.5	95.2
8210129	105.5	112.6	129.3	142.9	158.1	161.1	182.8	196.2	203.3	204.7	211.8	214.2	207.8	198.8	93.3
8210130	104.8	118.8	135.7	147.7	167.1	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210131	114.7	128.4	139.7	149.6	163.8	178.9	191.9	210.2	224.8	229.2	234.9	237.5	231.8	220.9	106.2
8210132	107.2	121.3	132.9	151.3	173.1	185.6	198.1	202.6	210.7	221.3	224.2	220.1	219.9	178.2	75.0
8210133	113.1	122.7	134.1	148.2	162.1	171.1	188.6	195.9	197.2	206.4	215.1	214.0	213.3	188.2	75.1
8210134	113.8	132.6	152.8	166.2	187.9	198.9	207.8	217.7	226.1	235.3	232.5	233.9	228.9	235.0	121.2
8210135	106.2	113.3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210136	106.4	106.8	134.1	156.7	162.9	174.2	188.2	196.2	204.1	206.7	234.9	-----	-----	-----	-----
8210137	116.8	129.7	143.4	156.6	174.1	169.8	189.5	200.1	213.2	218.5	197.1	242.6	238.6	250.0	133.2
8210138	107.5	118.9	119.7	129.4	141.1	150.3	168.3	179.8	195.2	193.2	237.9	193.2	194.2	198.4	90.9
8210139	112.4	125.4	102.0	142.3	177.9	192.3	198.7	217.7	229.7	233.3	214.9	243.5	241.8	246.7	134.1
MEAN	110.0	120.7 S-	134.3 S-	150.3 S-	167.5 S-	172.6 S-	184.3 S-	202.4 S-	209.5 S-	215.4 S-	220.7 S-	225.9 S-	222.6 S-	215.4 S-	104.4 S-
S.D.	4.4	6.8	10.8	9.7	10.9	13.7	14.3	14.4	14.7	17.3	15.0	18.0	15.7	22.8	17.4
N	20	20	19	18	18	14	14	14	14	14	14	15	15	12	12

GROUP 4 FEMALES
900 mg/kg/day

ANIMAL NUMBER	INIT.	1	2	3	4	5	6	7	8	9	10	11	12	13	CHANGE
8210140	87.7	99.9	97.7	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210141	95.6	102.9	110.6	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210142	78.9	75.2	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210143	76.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210144	85.3	92.3	65.5	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210145	85.4	85.5	93.2	103.3	111.9	108.0	118.6	128.8	134.4	-----	-----	-----	-----	-----	-----
8210146	91.6	93.3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210147	79.3	79.9	91.0	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210148	89.4	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210149	85.0	101.9	99.1	79.9	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210150	88.5	95.4	108.9	111.0	125.7	131.0	142.5	152.2	159.9	-----	-----	-----	-----	-----	-----
8210151	91.6	98.7	105.2	117.5	122.6	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210152	89.9	107.4	112.6	121.4	131.0	131.9	142.9	151.9	157.5	163.6	164.9	161.3	151.4	156.8	66.9
8210153	88.6	103.5	110.4	120.6	130.4	134.1	148.6	155.2	164.1	167.3	165.5	160.4	170.1	161.1	72.5
8210154	90.3	93.0	96.4	109.1	116.0	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210155	90.3	101.7	120.7	131.7	142.3	143.6	153.4	155.5	164.3	175.4	178.2	-----	-----	-----	-----
8210156	85.7	91.3	91.6	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210157	84.1	94.1	105.8	113.0	122.3	125.1	132.2	138.4	143.6	150.9	150.3	-----	-----	-----	-----
8210158	86.1	101.8	109.0	117.8	130.0	128.5	142.1	150.1	153.4	158.0	158.6	-----	-----	-----	-----
8210159	93.8	93.3	94.2	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
MEAN	85.4	91.6 S-	100.7 S-	112.9 S-	125.9 S-	128.6	140.0	147.3	153.9	163.0	163.1	164.9	162.3	159.0	89.7
S.D.	5.6	8.5	12.8	13.8	9.2	10.9	11.1	10.0	11.2	9.3	10.2	5.0	11.1	3.6	1.5
N	20	18	15	10	6	7	7	7	7	5	5	2	2	2	2

S- = Statistically significantly lower than control at $p \leq 0.05$.
----- = No value due to death of the animal.
[a] Values in grams.

000059

APPENDIX 3
INDIVIDUAL AND MEAN FOOD CONSUMPTION VALUES[a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 1 MALES
0 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210000	120.3	111.1	130.2	123.1	110.3	108.4	113.1	124.8	120.6	123.1	122.1	122.7	105.0
8210001	109.0	108.7	116.6	120.1	104.3	99.6	105.5	126.1	118.7	119.4	114.8	120.6	104.9
8210002	103.1	125.2	259.1	114.8	100.3	91.5	105.3	116.5	110.7	112.1	105.8	109.1	100.8
8210003	113.9	109.3	117.8	135.9	104.9	112.1	108.7	115.5	108.7	111.1	104.4	115.6	93.5
8210004	108.5	109.3	117.6	132.2	105.1	113.0	105.3	119.6	108.0	112.3	97.6	97.9	96.4
8210005	110.7	109.4	136.4	119.1	107.5	110.7	111.3	-----	110.8	116.7	107.1	111.7	90.5
8210006	102.1	97.8	107.2	122.9	94.1	113.1	97.1	-----	102.8	103.1	92.2	104.1	101.7
8210007	-----	112.1	125.8	128.6	111.6	122.2	116.5	117.4	107.9	-----	110.9	111.6	100.6
8210008	100.1	103.9	111.7	113.3	99.2	109.5	99.5	107.2	105.1	104.6	112.7	102.0	104.8
8210009	108.6	105.7	101.8	123.6	97.5	120.1	114.9	121.0	115.7	121.0	107.7	117.0	120.4
8210010	103.7	105.7	127.3	108.4	101.6	106.4	99.8	107.2	103.7	102.1	99.3	105.4	79.2
8210011	113.5	152.4	272.4	158.9	118.2	239.5	126.2	120.1	127.8	115.3	111.2	117.4	121.6
8210012	123.1	122.1	138.1	140.0	113.5	142.9	121.7	140.2	131.7	135.4	126.2	126.8	120.9
8210013	105.1	100.8	118.9	119.8	102.8	123.2	117.6	123.4	111.8	124.2	111.0	114.1	114.7
8210014	113.9	110.7	116.7	132.1	115.6	130.5	115.1	120.0	111.7	114.5	109.1	113.7	108.2
8210015	117.6	117.6	119.3	134.0	125.5	135.1	119.1	131.4	123.4	120.8	121.4	120.0	119.6
8210016	118.6	118.7	127.4	136.7	205.2	129.8	124.4	129.9	120.7	125.6	124.3	126.1	121.5
8210017	108.1	102.1	254.6	122.8	107.3	115.7	112.7	114.1	108.0	111.4	104.1	113.6	101.1
8210018	115.6	155.6	284.0	136.1	118.9	129.2	125.3	127.5	120.8	120.1	122.4	123.9	120.5
8210019	122.6	115.2	289.8	145.1	237.5	125.6	127.9	127.2	124.7	130.7	120.9	118.7	116.5
MEAN	111.9	119.2	158.6	128.8	124.3	134.4	114.2	123.8	115.0	117.4	112.2	114.8	112.9
S.D.	5.9	19.4	68.1	11.8	37.0	39.5	10.6	12.8	8.9	9.0	8.8	7.8	22.7
N	20	20	20	20	20	20	20	20	20	20	20	20	20

GROUP 1 FEMALES
0 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210020	90.1	92.5	84.7	101.7	77.9	91.7	85.9	83.7	82.4	85.3	83.5	91.9	82.9
8210021	108.3	74.3	79.5	80.1	68.2	73.5	69.2	77.9	69.9	68.6	62.2	72.2	-----
8210022	93.3	88.7	92.0	96.5	81.1	105.6	92.7	92.5	88.9	88.7	82.1	87.5	58.1
8210023	93.4	205.6	91.8	90.4	75.3	88.3	76.3	84.1	77.6	77.5	74.4	80.0	49.4
8210024	102.1	185.1	170.9	91.5	71.2	95.0	87.1	92.7	86.9	84.4	81.8	88.0	67.7
8210025	94.9	85.7	105.3	90.9	77.6	89.9	81.0	89.3	83.5	82.3	81.2	85.1	77.2
8210026	93.6	83.2	87.0	92.4	77.9	154.8	87.6	77.5	77.7	78.4	79.3	81.0	73.5
8210027	91.3	260.9	94.2	97.1	77.5	88.4	87.0	86.9	85.7	84.1	80.7	84.4	72.8
8210028	95.2	87.8	89.7	98.8	84.7	102.5	87.1	94.1	88.4	89.7	89.1	93.7	75.7
8210029	89.5	86.4	92.1	96.6	75.0	89.4	85.1	87.5	82.5	86.9	80.2	83.7	74.5
8210030	94.7	91.7	120.3	103.3	92.4	212.6	91.4	93.2	91.8	115.9	88.3	91.4	89.2
8210031	97.3	99.8	267.0	99.4	94.5	134.7	102.4	139.2	99.6	90.4	85.1	134.2	138.3
8210032	90.6	83.9	89.0	85.7	84.5	172.1	83.3	88.7	90.5	78.9	81.9	84.6	82.9
8210033	88.3	268.1	90.6	89.3	81.5	91.1	76.8	81.9	80.0	82.9	80.5	80.6	181.1
8210034	96.1	89.1	91.4	103.9	149.2	83.2	82.3	131.8	82.5	84.2	82.0	89.0	90.0
8210035	96.2	90.9	108.4	99.8	99.8	215.0	85.2	93.8	90.9	90.3	88.8	98.9	88.5
8210036	86.8	90.9	101.1	102.0	90.4	153.0	80.4	88.9	85.1	83.1	85.8	83.2	81.1
8210037	89.0	131.3	217.3	97.3	97.6	143.0	84.7	91.0	79.7	81.7	86.1	90.2	87.2
8210038	86.1	160.7	90.0	92.3	91.3	143.7	73.2	80.1	72.8	74.6	68.2	77.0	74.2
8210039	115.8	87.9	89.8	97.0	88.0	94.3	79.4	91.8	87.3	82.0	90.2	88.8	83.2
MEAN	95.6	122.6	111.3	95.3	86.8	115.9	81.9	91.8	84.7	84.1	81.1	88.5	86.8
S.D.	5.9	58.5	52.3	8.2	17.1	48.6	9.3	11.2	7.6	9.2	6.5	12.3	39.0
N	20	20	20	20	20	20	20	20	20	20	20	20	19

----- = No value due to death of the animal.

[a] Values in grams.

090060

APPENDIX 3 (Continued)
INDIVIDUAL AND MEAN FOOD CONSUMPTION VALUES [a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 7000[] TO RATS

GROUP 2 MALES
100 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210040	108.2	107.1	117.8	137.3	111.3	125.0	117.1	122.5	117.7	122.5	120.9	112.4	104.5
8210041	107.9	104.8	114.8	134.3	97.6	120.8	122.1	125.9	122.1	120.2	125.0	125.0	111.6
8210042	99.7	230.1	99.3	98.6	87.0	98.6	101.2	96.2	96.2	96.2	91.3	98.6	93.1
8210043	107.6	116.1	120.0	134.0	108.6	124.0	117.3	120.0	123.9	117.9	113.5	119.9	104.1
8210044	101.3	100.3	114.1	132.1	98.4	117.2	99.2	118.0	118.0	118.0	118.0	112.1	101.6
8210045	105.8	109.5	120.8	135.1	101.4	120.3	120.3	117.2	118.8	118.8	118.8	118.8	104.1
8210046	106.4	110.4	122.1	130.6	102.1	122.1	120.0	123.0	120.0	118.0	118.0	116.3	101.4
8210047	109.3	110.9	210.0	132.2	100.7	120.4	120.4	120.4	120.4	120.4	118.5	118.5	93.0
8210048	107.7	150.8	118.9	129.1	96.5	119.0	119.0	120.8	120.8	120.8	118.9	118.7	95.9
8210049	111.0	114.7	244.7	137.4	103.3	124.2	124.2	124.2	124.2	124.2	122.2	122.2	110.4
8210050	105.0	106.1	115.2	134.3	100.7	120.9	120.9	120.9	120.9	120.9	118.9	118.9	104.4
8210051	108.7	104.8	117.9	137.0	102.7	122.7	120.7	120.7	120.7	120.7	118.7	118.7	115.3
8210052	113.5	120.1	119.7	132.1	98.4	118.1	118.1	118.1	118.1	118.1	116.1	116.1	111.3
8210053	116.1	116.5	129.1	134.1	100.4	120.4	120.4	120.4	120.4	120.4	118.5	118.5	118.2
8210054	104.4	98.8	179.4	113.2	107.6	129.2	129.2	129.2	129.2	129.2	127.2	127.2	114.9
8210055	112.2	107.9	253.6	127.2	120.6	229.3	120.6	120.6	120.6	120.6	118.7	118.7	103.7
8210056	100.3	104.0	99.3	113.8	111.0	110.7	110.7	110.7	110.7	110.7	108.8	108.9	91.5
8210057	108.6	109.7	108.1	108.9	108.9	108.9	108.9	108.9	108.9	108.9	107.0	121.8	120.4
8210058	103.8	251.1	109.8	132.1	107.2	127.2	127.2	127.2	127.2	127.2	125.3	115.1	109.4
8210059	107.4	115.3	144.4	134.1	117.7	129.8	118.0	122.9	119.1	125.6	117.1	109.2	111.8
MEAN	106.9 S-	121.8	141.0	126.3	118.9	130.9	114.6	121.4	115.6	119.9	119.2	114.5	107.9
S.D.	4.6	41.2	46.8	11.2	25.1	32.2	7.2	7.2	7.8	7.8	7.1	6.8	24.7
N	20	20	20	20	20	20	20	20	20	20	20	20	20

GROUP 2 FEMALES
100 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210060	91.0	90.8	88.7	98.5	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210061	89.0	88.7	87.2	96.0	76.4	92.7	81.2	91.5	78.4	80.1	79.8	85.1	-----
8210062	100.1	91.9	91.4	95.5	74.8	101.7	81.4	80.2	79.6	84.4	83.9	84.4	82.3
8210063	107.7	103.2	89.1	93.9	76.1	127.9	84.8	94.1	84.8	86.9	86.5	88.4	84.8
8210064	89.1	72.0	90.6	89.9	70.2	152.9	74.1	82.9	56.8	79.2	72.4	81.8	72.1
8210065	91.5	88.1	89.8	95.7	80.5	90.7	78.9	84.2	82.4	83.5	81.2	82.5	84.8
8210066	93.2	92.0	98.0	97.9	83.4	91.8	80.7	95.8	84.4	88.5	88.8	92.5	74.5
8210067	98.8	91.3	92.0	92.9	74.4	90.5	88.9	91.4	92.2	89.4	92.0	87.4	81.2
8210068	101.6	90.3	91.2	97.5	98.7	102.2	91.6	99.0	89.3	92.2	91.4	88.5	234.2
8210069	91.0	92.1	101.7	93.3	81.5	27.1	84.6	88.4	100.5	86.3	86.6	93.0	77.8
8210070	89.8	88.2	83.3	120.8	74.9	159.2	80.8	92.1	79.4	83.0	81.4	81.8	84.3
8210071	88.9	84.2	94.1	93.0	83.1	101.2	82.5	87.0	85.3	81.1	83.4	86.5	84.0
8210072	101.3	158.7	244.3	98.6	87.6	97.4	84.9	92.5	84.5	82.5	82.1	89.2	84.9
8210073	85.5	78.8	85.2	85.8	76.7	141.4	73.2	79.9	78.8	74.1	74.3	78.3	74.3
8210074	108.2	93.9	93.3	89.9	79.8	87.8	81.1	85.7	79.8	80.3	80.4	82.7	80.1
8210075	95.6	169.9	88.7	182.2	152.7	97.4	86.4	93.2	81.2	85.0	87.2	83.6	191.4
8210076	91.7	137.9	95.2	95.5	83.5	93.1	74.9	83.3	83.3	77.1	81.2	83.0	80.8
8210077	89.5	89.5	89.1	95.2	85.5	98.7	77.8	93.9	87.6	85.9	88.9	81.6	82.8
8210078	96.8	89.2	81.4	112.2	117.1	107.5	77.8	81.4	83.4	93.3	87.8	92.1	77.9
8210079	91.2	94.3	90.4	93.2	79.3	90.1	78.3	129.2	80.9	79.5	76.3	80.0	138.9
MEAN	94.7	103.2	96.6	100.1	86.3	108.2	81.5	91.8	82.7	83.4	83.5	85.1	97.0
S.D.	6.1	31.3	33.0	20.8	19.4	36.6	4.8	10.6	8.7	4.9	5.1	4.3	48.3
N	20	20	20	20	19	19	19	19	19	19	19	19	18

S- = Statistically significantly lower than control at p≤0.05.
----- = No value due to death of the animal.
[a] Values in grams.

190000

APPENDIX 3 (Continued)
INDIVIDUAL AND MEAN FOOD CONSUMPTION VALUES [a]
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

GROUP 3 MALES
300 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210080	83.9	73.1	88.0	103.9	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210081	98.0	90.0	29.2	109.2	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210082	118.6	270.0	119.3	127.6	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210083	101.0	92.6	110.9	135.8	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210084	92.5	87.9	109.4	132.1	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210085	95.3	99.7	114.6	134.0	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210086	96.4	99.2	115.4	127.5	85.1	219.6	127.2	131.9	124.2	119.2	117.5	120.6	98.9
8210087	95.1	110.7	117.4	128.6	156.8	131.7	130.8	118.0	108.3	115.5	116.9	103.0	88.7
8210088	82.0	88.4	109.3	120.1	100.8	123.0	122.4	122.7	69.0	125.5	122.3	105.8	80.0
8210089	105.8	90.6	108.0	122.6	101.1	118.1	107.3	117.9	113.2	133.1	114.9	107.0	61.7
8210090	93.4	100.7	107.9	122.1	107.8	123.5	126.0	131.0	124.5	127.5	108.7	118.9	101.4
8210091	87.2	89.0	104.4	125.1	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210092	114.7	98.1	110.5	131.5	113.2	136.1	124.8	130.5	131.4	131.2	117.1	122.2	115.8
8210093	115.3	98.5	142.3	130.0	91.7	140.7	128.7	141.6	127.6	111.6	124.3	121.3	152.9
8210094	103.8	96.9	114.5	121.6	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210095	121.7	112.8	123.3	127.6	183.2	136.5	128.5	123.2	125.5	125.8	126.0	126.1	110.6
8210096	89.6	83.8	83.7	111.2	102.5	205.3	123.1	113.8	131.4	124.3	212.4	118.3	85.6
8210097	100.6	99.7	99.6	109.8	114.7	125.6	120.2	123.7	113.8	120.7	117.6	123.1	75.5
8210098	85.7	85.7	104.3	112.7	104.4	114.7	110.2	114.2	107.7	105.7	107.7	108.1	103.5
8210099	90.0	95.5	100.7	124.8	118.3	123.2	115.8	124.0	118.5	124.5	109.3	139.9	114.9
MEAN	98.7 S-	103.1	105.8 S-	123.4	115.8	141.8	121.9 St	124.7	116.3	122.1	121.7	117.9	99.6
S.D.	12.0	10.3	21.8	10.3	27.6	34.1	7.3	8.5	17.0	8.0	28.2	10.4	23.3
N	20	20	20	20	12	12	12	12	12	12	12	12	12

GROUP 3 FEMALES
300 mg/kg/day

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13
8210100	104.9	99.6	92.1	89.1	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210101	74.1	77.8	86.1	-----	166.5	97.5	143.2	96.8	87.4	93.3	81.9	81.0	-----
8210102	98.9	78.8	87.1	91.7	101.7	94.4	83.1	102.0	86.5	87.8	88.5	82.9	155.4
8210103	81.1	78.9	83.5	95.8	79.8	94.8	86.5	106.1	90.4	85.1	101.6	82.8	67.7
8210104	95.5	90.9	89.1	94.5	85.0	173.2	101.2	114.4	99.5	90.4	100.2	100.1	128.3
8210105	94.1	87.4	93.9	123.0	85.3	102.7	85.1	94.5	113.7	88.7	67.5	94.5	184.0
8210106	97.0	70.6	89.1	95.1	108.7	85.8	76.7	91.4	108.2	85.7	80.7	87.2	77.5
8210107	97.3	85.8	88.5	97.2	87.0	91.4	80.4	96.0	45.2	91.4	89.6	85.3	-----
8210108	92.3	191.9	192.6	118.1	77.8	110.8	204.8	168.3	218.0	174.0	112.2	79.6	80.1
8210109	83.1	64.4	78.2	84.3	66.8	91.9	78.9	87.1	77.3	75.5	82.6	78.2	68.5
8210110	86.6	87.8	89.5	100.7	173.2	104.7	90.9	150.2	91.6	148.3	100.9	146.5	102.7
8210111	30.4	83.0	81.6	93.5	89.5	89.8	85.0	-----	-----	-----	-----	-----	-----
8210112	96.9	88.2	86.7	84.9	144.9	105.0	87.7	91.1	85.0	88.2	78.7	83.3	106.6
8210113	87.9	81.5	88.6	103.8	131.0	99.3	88.1	147.3	89.3	84.9	90.3	82.5	92.2
8210114	74.9	83.1	152.3	85.6	79.6	85.9	78.6	105.2	84.8	87.0	81.9	70.0	90.8
8210115	91.2	111.1	102.1	99.7	100.9	104.2	94.5	94.3	90.8	86.7	96.1	94.3	130.6
8210116	80.5	218.5	88.2	84.8	192.9	103.7	81.7	81.9	81.5	82.6	92.8	94.1	79.1
8210117	18.1	79.1	88.2	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
8210118	88.9	79.5	85.4	100.1	90.5	90.8	85.2	91.7	82.9	83.7	92.8	87.2	88.7
8210119	82.9	77.3	87.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
MEAN	81.5 S-	95.7	96.1	98.8	109.4 St	104.9	95.7	102.6 St	95.8	96.3	90.1 St	87.5	103.7
S.D.	18.2	15.9	27.2	15.7	38.1	22.7	31.9	25.2	35.8	24.2	10.9	20.5	34.1
N	20	20	20	17	17	17	17	16	16	16	16	16	11

S- = Statistically significantly lower than control at $p \leq 0.05$.
St = Statistically significantly higher than control at $p \leq 0.05$.
----- = No value due to death of the animal.
[a] Values in grams.

000062

APPENDIX 4 (Continued)

INDIVIDUAL CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG %	BAND %	LYM'H %	ATY.LYMPH %	MONO %	EOS %	BASO %	META %	MYEL %	PROERAN %	BLAST %	NRBC/ 100 WBC
1	8210000	9	0	81	0	2	1	0	0	0	0	0	0
0	8210001	12	0	84	0	1	1	0	0	0	0	0	0
mg/kg/day	8210002	12	0	84	0	2	1	0	0	0	0	0	0
	8210003	18	0	80	0	2	0	0	0	0	0	0	0
	8210004	10	0	90	0	0	0	0	0	0	0	0	0
	8210005	14	0	83	0	0	1	0	0	0	0	0	1
	8210006	13	0	87	0	0	0	0	0	0	0	0	0
	8210007	17	0	82	0	0	1	0	0	0	0	0	0
	8210008	16	0	82	0	1	1	0	0	0	0	0	0
	8210009	15	0	83	0	2	0	0	0	0	0	0	0
2	8210040	17	0	82	0	0	1	0	0	0	0	0	0
100	8210041	14	0	84	0	0	1	0	0	0	0	0	0
mg/kg/day	8210042	26	0	74	0	0	0	0	0	0	0	0	0
	8210043	7	0	91	0	1	1	0	0	0	0	0	0
	8210044	9	0	88	0	2	1	0	0	0	0	0	0
	8210045	13	0	86	0	0	1	0	0	0	0	0	1
	8210046	13	0	84	0	1	0	0	0	0	0	0	0
	8210047	13	0	83	0	4	0	0	0	0	0	0	0
	8210048	26	0	73	0	1	0	0	0	0	0	0	0
	8210049	20	0	76	0	2	2	0	0	0	0	0	2
3	8210082	18	0	81	0	1	0	0	0	0	0	0	
300	8210084	85	0	14	0	1	0	0	0	0	0	0	1
mg/kg/day	8210086	7	0	92	0	1	0	0	0	0	0	0	2
	8210087	10	0	88	0	1	1	0	0	0	0	0	0
	8210088	19	0	81	0	0	0	0	0	0	0	0	0
	8210089	8	0	87	0	1	2	0	0	0	0	0	0
	8210090	12	0	86	0	1	1	0	0	0	0	0	0
	8210092	9	0	91	0	0	0	0	0	0	0	0	0
	8210093	26	0	72	0	2	0	0	0	0	0	0	0
	8210094	52	0	48	0	0	0	0	0	0	0	0	0
4	8210120	27	0	69	1	1	2	0	0	0	0	0	0
900	8210122	17	0	82	0	1	0	0	0	0	0	0	0
mg/kg/day	8210123	18	0	81	0	1	0	0	0	0	0	0	0
	8210124	10	0	90	0	0	0	0	0	0	0	0	0
	8210125	33	0	66	0	0	1	0	0	0	0	0	1
	8210126	39	0	60	0	0	1	0	0	0	0	0	0
	8210127	34	0	64	0	0	1	0	0	0	0	0	1
	8210128	29	0	71	0	0	0	0	0	0	0	0	0
	8210129	27	0	72	0	1	0	0	0	0	0	0	0
	8210130	19	0	77	0	2	2	0	0	0	0	0	0

000065

APPENDIX 4 (Continued)

INDIVIDUAL RBC MORPHOLOGY
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL	ANIMAL NO.	RBC MORPHOLOGY
1	8210000	SLIGHT POLY.
0	8210001	SLIGHT POLY.
	8210002	SLIGHT POLY.
mg/kg/day	8210003	SLIGHT POLY.
	8210004	SLIGHT POLY.
	8210005	SLIGHT POLY.
	8210006	SLIGHT POLY.
	8210007	SLIGHT POLY.
	8210008	SLIGHT POLY.
	8210009	SLIGHT POLY.
2	8210040	SLIGHT POLY.
100	8210041	SLIGHT POLY.
	8210042	SLIGHT POLY.
mg/kg/day	8210043	SLIGHT POLY.
	8210044	SLIGHT POLY.
	8210045	SLIGHT POLY.
	8210046	SLIGHT POLY.
	8210047	SLIGHT POLY.
	8210048	SLIGHT POLY.
	8210049	SLIGHT POLY.
3	8210082	SLIGHT POLY.
300	8210084	SLIGHT POLY., 2 HYPERSEG. NEUTROPHILES
	8210086	SLIGHT POLY.
mg/kg/day	8210087	SLIGHT POLY.
	8210088	SLIGHT POLY.
	8210089	SLIGHT POLY.
	8210090	SLIGHT POLY.
	8210092	SLIGHT POLY.
	8210093	SLIGHT POLY.
	8210094	SLIGHT POLY.
4	8210120	SLIGHT POLY.
900	8210122	SLIGHT POLY.
	8210123	SLIGHT POLY.
mg/kg/day	8210124	SLIGHT POLY.
	8210125	SLIGHT POLY.
	8210126	SLIGHT POLY.
	8210127	SLIGHT POLY.
	8210128	SLIGHT POLY.
	8210129	SLIGHT POLY.
	8210130	SLIGHT POLY.

000096

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700611 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	RBC 10^{6}/cmm	WBC 10^{3}/cmm	HGB G/DL	HCT %	PLATELET 10^{3}/cmm
1	8210000	8.51	10.9	18.0	50.0	345
0	8210001	8.82	8.3	14.8	47.0	340
mg/kg/day	8210002	8.38	6.3	16.8	49.0	340
	8210003	8.57	9.6	14.9	46.0	335
	8210004	9.03	9.8	17.2	49.0	330
	8210005	7.99	8.8	17.5	47.5	330
	8210006	8.20	8.4	17.1	47.5	330
	8210007	8.26	7.2	17.0	48.5	330
	8210008	8.34	8.3	17.2	49.0	340
	8210009	8.47	6.9	17.6	49.0	295
	MEAN	8.45	8.5	17.2	48.3	325
	S.D.	0.26	1.4	0.4	1.2	20
	N	10	10	10	10	10
2	8210040	7.92	9.0	17.4	47.0	325
100	8210041	9.00	8.4	17.1	47.0	325
mg/kg/day	8210042	9.36	9.7	18.2	47.0	310
	8210043	8.85	9.9	17.5	50.5	345
	8210044	9.40	9.7	17.8	45.0	330
	8210045	7.68	9.1	17.8	47.0	320
	8210046[a]	7.79	9.2	16.4	46.0	325
	8210047	7.92	8.0	17.4	48.5	320
	8210048	8.18	12.0	17.4	48.5	280
	8210049	8.79	9.2	18.4	52.0	260
	MEAN	8.49	9.4	17.3	47.5	290
	S.D.	0.66	1.1	1.1	3.3	41
	N	10	10	10	10	10
3	8210086	8.56	8.9	16.8	48.0	330
300	8210087	8.10	7.7	15.7	46.5	335
mg/kg/day	8210088	8.18	8.4	16.4	48.0	340
	8210089	9.02	6.4	18.2	50.0	345
	8210090	8.70	9.6	17.9	49.5	335
	8210092	8.35	9.4	16.5	48.0	330
	8210093	8.32	7.5	16.5	48.0	345
	8210095	8.38	9.0	16.3	48.5	-----
	8210096	9.66	9.0	17.8	48.0	405
	8210097	9.15	7.2	17.2	49.5	280
	MEAN	8.71	8.3	16.9	48.1	262 S-
	S.D.	0.62	1.1	0.8	1.5	74
	N	10	10	10	10	9
4	8210120	8.21	7.1	18.7	54.0	320
900	8210122	8.58	6.2	17.3	48.5	375
mg/kg/day	8210124	8.87	10.3	19.8	55.0	330
	8210125	9.58	8.8	17.8	51.0	335
	8210126	7.88	7.7	15.8	45.0	350
	8210127	9.31	6.5	17.7	52.0	345
	8210128	8.40	9.1	15.9	47.0	350
	8210129	8.49	8.0	16.1	47.5	350
	8210131	8.46	8.7	17.3	49.5	350
	8210132	8.47	8.4	16.5	46.5	325
	MEAN	8.70	8.1	17.2	49.4	284 S-
	S.D.	0.47	1.3	1.4	3.3	52
	N	10	10	10	10	10

----- = Quantity of blood not sufficient for analysis.

S- = Statistically significantly lower than control at $p \leq 0.05$.

[a] Blood clotted; sample was redrawn.

000067

APPENDIX 4 (Continued)
INDIVIDUAL CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION OF PET 7003B11 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG %	BAND %	LYMPH %	ATY.LYMPH %	MONO %	EOS %	BASO %	META %	MYEL %	PROGRAN %	BLAST %	NRBC/ 100 WBC
1	8210000	7	0	90	0	2	1	0	0	0	0	0	0
0	8210001	18	0	75	0	7	0	0	0	0	0	0	0
mg/kg/day	8210002	24	0	74	0	2	0	0	0	0	0	0	0
	8210003	16	0	82	0	1	1	0	0	0	0	0	1
	8210004	15	0	83	0	2	0	0	0	0	0	0	1
	8210005	8	0	86	0	5	1	0	0	0	0	0	0
	8210006	23	0	71	0	4	2	0	0	0	0	0	0
	8210007	16	1	78	0	4	1	0	0	0	0	0	0
	8210008	13	0	84	0	1	0	0	0	0	0	0	0
	8210009	19	0	77	0	4	0	0	0	0	0	0	0
2	8210040	19	0	78	0	3	0	0	0	0	0	0	1
100	8210041	14	0	84	0	2	0	0	0	0	0	0	0
mg/kg/day	8210042	13	0	82	0	5	0	0	0	0	0	0	0
	8210043	20	0	78	0	2	0	0	0	0	0	0	1
	8210044	20	0	76	0	3	1	0	0	0	0	0	0
	8210045	18	0	78	0	4	0	0	0	0	0	0	0
	8210046[a]	56	0	40	0	4	0	0	0	0	0	0	0
	8210047	24	0	75	0	1	0	0	0	0	0	0	0
	8210048	21	0	74	0	2	2	0	0	0	0	0	0
	8210049	16	0	81	0	2	1	0	0	0	0	0	0
3	8210086	21	0	75	0	4	0	0	0	0	0	0	0
300	8210087	17	0	74	0	4	1	0	0	0	0	0	0
mg/kg/day	8210088	21	0	79	0	0	0	0	0	0	0	0	0
	8210089	24	0	70	0	5	1	0	0	0	0	0	0
	8210090	24	0	70	0	5	1	0	0	0	0	0	0
	8210092	25	0	73	0	1	1	0	0	0	0	0	0
	8210093	20	1	76	0	0	3	0	0	0	0	0	0
	8210095	15	0	83	0	2	0	0	0	0	0	0	0
	8210096	29	0	65	0	4	2	0	0	0	0	0	1
	8210097	33	0	63	0	2	2	0	0	0	0	0	1
4	8210120	28	0	67	0	5	0	0	0	0	0	0	0
900	8210122	39	0	55	0	6	0	0	0	0	0	0	0
mg/kg/day	8210124	41	0	56	0	3	0	0	0	0	0	0	0
	8210125	34	0	60	0	6	0	0	0	0	0	0	0
	8210126	27	0	72	0	1	0	0	0	0	0	0	0
	8210127	31	0	63	0	5	1	0	0	0	0	0	0
	8210128	31	0	66	0	3	0	0	0	0	0	0	0
	8210129	42	0	51	0	6	1	0	0	0	0	0	0
	8210131	38	0	58	0	4	0	0	0	0	0	0	0
	8210132	24	0	69	0	6	1	0	0	0	0	0	0

[a] Blood clotted; sample was redrawn.

000068

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL PATHOLOGY DATA-ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK DIOXIN ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROMYN	BLAST	NRBC/ 100 WBC
1	0210000	763	0	9810	0	210	107	0	0	0	0	0	0
0	0210001	1474	0	4220	0	581	0	0	0	0	0	0	0
mg/kg/day	0210002	1512	0	4668	0	126	0	0	0	0	0	0	0
	0210003	1536	0	7078	0	96	96	0	0	0	0	0	1
	0210004	1470	0	8130	0	126	0	0	0	0	0	0	0
	0210005	704	0	7530	0	440	88	0	0	0	0	0	1
	0210006	1978	0	4180	0	344	172	0	0	0	0	0	0
	0210007	1152	72	5472	0	432	72	0	0	0	0	0	0
	0210008	1079	0	7130	0	88	0	0	0	0	0	0	0
	0210009	1311	0	5311	0	276	0	0	0	0	0	0	0
	MEAN	1300	7	6830	0	279	54	0	0	0	0	0	0
	S.D.	384	23	1568	0	167	62	0	0	0	0	0	0
	N	10	10	10	10	10	10	10	10	10	10	10	10
2	0210040	1710	0	7020	0	270	0	0	0	0	0	0	0
100	0210041	1176	0	7050	0	140	0	0	0	0	0	0	1
mg/kg/day	0210042	1261	0	7950	0	462	0	0	0	0	0	0	0
	0210043	1900	198	7524	0	198	0	0	0	0	0	0	0
	0210044	1940	0	7372	0	291	97	0	0	0	0	0	0
	0210045	1638	0	7098	0	364	0	0	0	0	0	0	0
	0210046	2352	0	3480	0	348	0	0	0	0	0	0	0
	0210047	1920	0	6000	0	60	0	0	0	0	0	0	0
	0210048	2080	0	6080	0	240	0	0	0	0	0	0	0
	0210049	1472	0	7452	0	184	92	0	0	0	0	0	0
	MEAN	2113	20	7004	0	265	19	0	0	0	0	0	0
	S.D.	1170	63	1370	0	116	46	0	0	0	0	0	0
	N	10	10	10	10	10	10	10	10	10	10	10	10
3	0210086	1869	0	6675	0	154	0	0	0	0	0	0	0
300	0210087	1309	0	5852	0	462	77	0	0	0	0	0	0
mg/kg/day	0210088	1804	0	6020	0	774	0	0	0	0	0	0	0
	0210089	1536	0	6480	0	320	64	0	0	0	0	0	0
	0210090	2304	0	6720	0	480	96	0	0	0	0	0	0
	0210092	2350	0	6864	0	94	94	0	0	0	0	0	0
	0210093	1500	75	5700	0	0	225	0	0	0	0	0	0
	0210095	1350	0	7470	0	180	0	0	0	0	0	0	0
	0210096	2610	0	5805	0	348	180	0	0	0	0	0	0
	0210097	2376	0	4536	0	144	144	0	0	0	0	0	1
	MEAN	1901 S+	8	6017	0	317	98	0	0	0	0	0	0
	S.D.	477	24	970	0	226	78	0	0	0	0	0	0
	N	10	10	10	10	10	10	10	10	10	10	10	10
4	0210120	1980	0	4757	0	355	0	0	0	0	0	0	0
900	0210122	2418	0	3410	0	372	0	0	0	0	0	0	0
mg/kg/day	0210124	4223	0	5760	0	309	0	0	0	0	0	0	0
	0210125	2992	0	5280	0	528	0	0	0	0	0	0	0
	0210126	2002	0	5544	0	154	0	0	0	0	0	0	0
	0210127	2015	0	4093	0	325	65	0	0	0	0	0	0
	0210128	2821	0	4004	0	273	0	0	0	0	0	0	0
	0210129	3760	0	4080	0	160	0	0	0	0	0	0	0
	0210131	3306	0	5044	0	348	0	0	0	0	0	0	0
	0210132	2016	0	5796	0	504	84	0	0	0	0	0	0
	MEAN	2754 S+	0	4978 S-	0	333	15	0	0	0	0	0	0
	S.D.	809	0	871	0	121	32	0	0	0	0	0	0
	N	10	10	10	10	10	10	10	10	10	10	10	10

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

690000

20623

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA - ABSOLUTE DIFFERENTIAL LEUKOCYTE COUN*
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 14 MALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
1	8210000	763	0	9810	0	218	109	0	0	0	0	0
0	8210001	1493	0	6224	0	580	0	0	0	0	0	0
	8210002	1511	0	4661	0	125	0	0	0	0	0	0
mg/kg/day	8210003	1535	0	7871	0	95	95	0	0	0	0	0
	8210004	1469	0	8133	0	195	0	0	0	0	0	0
	8210005	707	0	7567	0	439	87	0	0	0	0	0
	8210006	1977	0	6105	0	343	171	0	0	0	0	0
	8210007	1152	72	5472	0	432	72	0	0	0	0	0
	8210008	1078	0	7137	0	82	0	0	0	0	0	0
	8210009	1310	0	5312	0	275	0	0	0	0	0	0
	8210010	990	0	8514	0	396	0	0	0	0	0	0
	8210011	1342	0	6161	0	394	0	0	0	0	0	0
	8210012	1430	0	8910	0	550	110	0	0	0	0	0
	8210013	1055	0	8255	0	287	0	0	0	0	0	0
	8210014	801	0	7832	0	267	0	0	0	0	0	0
	8210015	872	0	9701	0	327	0	0	0	0	0	0
	8210016	1455	0	7279	0	272	90	0	0	0	0	0
	8210017	630	0	8100	0	270	0	0	0	0	0	0
	8210018	594	0	8316	0	792	198	0	0	0	0	0
	8210019	1140	0	7790	0	475	95	0	0	0	0	0
	MEAN	1165	4	7458	0	341	51	0	0	0	0	0
	S.D.	368	16	1414	0	175	64	0	0	0	0	0
	N	20	20	20	20	20	20	20	20	20	20	20
2	8210040	1710	0	7019	0	270	0	0	0	0	0	0
100	8210041	1176	0	7056	0	168	0	0	0	0	0	0
	8210042	1261	0	7954	0	485	0	0	0	0	0	0
mg/kg/day	8210043	1980	198	7524	0	198	0	0	0	0	0	0
	8210044	1940	0	7372	0	291	97	0	0	0	0	0
	8210045	1637	0	7097	0	363	0	0	0	0	0	0
	8210046	5152	0	3680	0	368	0	0	0	0	0	0
	8210047	1920	0	6000	0	80	0	0	0	0	0	0
	8210048	2880	0	8880	0	240	0	0	0	0	0	0
	8210049	1472	0	7452	0	184	92	0	0	0	0	0
	8210050	924	0	7056	0	252	168	0	0	0	0	0
	8210051	959	0	8351	0	287	0	0	0	0	0	0
	8210052	1077	0	8427	0	293	0	0	0	0	0	0
	8210053	575	0	8639	0	383	0	0	0	0	0	0
	8210054	617	0	9166	0	411	102	0	0	0	0	0
	8210055	802	0	5985	0	510	0	0	0	0	0	0
	8210056	1360	0	6630	0	510	0	0	0	0	0	0
	8210057	1070	0	9309	0	321	0	0	0	0	0	0
	8210058	1576	0	6390	0	331	0	0	0	0	0	0
	8210059	1305	0	6960	0	435	0	0	0	0	0	0
	MEAN	1570	10	7347	0	319	23	0	0	0	0	0
	S.D.	1004	44	1314	0	117	49	0	0	0	0	0
	N	20	20	20	20	20	20	20	20	20	20	20

000070

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA - ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 14 MALES

GROUP NO. / DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
3	8210086	1869	0	6675	0	356	0	0	0	0	0	0
300	8210087	1309	0	5852	0	462	77	0	0	0	0	0
mg/kg/day	8210088	1805	0	6019	0	773	0	0	0	0	0	0
	8210089	1535	0	4479	0	319	63	0	0	0	0	0
	8210090	2303	0	6719	0	479	95	0	0	0	0	0
	8210092	2350	0	6862	0	94	94	0	0	0	0	0
	8210093	1500	75	5700	0	0	225	0	0	0	0	0
	8210095	1350	0	7470	0	180	0	0	0	0	0	0
	8210096	2610	0	5850	0	360	180	0	0	0	0	0
	8210097	2376	0	4536	0	144	144	0	0	0	0	0
	8210098	770	0	6314	0	616	0	0	0	0	0	0
	8210099	2079	0	5236	0	231	154	0	0	0	0	0
	MEAN	1821 S+	6	5976 S-	0	335	86	0	0	0	0	0
	S.D.	546	22	912	0	224	78	0	0	0	0	0
	N	12	12	12	12	12	12	12	12	12	12	12
4	8210120	1988	0	4757	0	355	0	0	0	0	0	0
900	8210122	2418	0	3410	0	372	0	0	0	0	0	0
mg/kg/day	8210124	4222	0	5767	0	308	0	0	0	0	0	0
	8210125	2991	0	5279	0	527	0	0	0	0	0	0
	8210126	2001	0	5544	0	154	0	0	0	0	0	0
	8210127	2015	0	4095	0	325	65	0	0	0	0	0
	8210128	2820	0	6005	0	272	0	0	0	0	0	0
	8210129	3760	0	4080	0	160	0	0	0	0	0	0
	8210131	3306	0	5046	0	348	0	0	0	0	0	0
	8210132	2016	0	5796	0	504	84	0	0	0	0	0
	8210133	3131	0	8119	0	231	115	0	0	0	0	0
	8210134	1955	0	6290	0	255	0	0	0	0	0	0
	8210137	2538	0	6204	0	658	0	0	0	0	0	0
	8210138	2080	0	5760	0	160	0	0	0	0	0	0
	MEAN	2660 S+	0	5439 S-	0	331	19	0	0	0	0	0
	S.D.	736	0	1163	0	149	39	0	0	0	0	0
	N	14	14	14	14	14	14	14	14	14	14	14

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000071

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	RBC 10^6/cmm	WBC 10^3/cmm	HGB G/DL	HCT %	PLATELET 10^3/cmm
1 0 mg/kg/day	8210020	7.76	6.4	15.8	45.0	410
	8210021	8.41	6.8	17.8	50.0	350
	8210022	7.61	6.0	16.0	45.0	395
	8210023	8.25	6.0	17.7	48.0	390
	8210024	8.42	6.6	18.2	48.0	325
	8210025	7.67	6.3	15.7	48.0	420
	8210026	8.01	5.6	17.0	47.0	370
	8210027	8.06	6.5	17.0	49.0	375
	8210028	7.92	8.5	17.7	45.0	360
	8210029	8.28	6.9	18.1	46.5	110
	MEAN	8.04	6.6	17.1	47.2	351
	S.D.	0.30	0.8	1.0	1.8	89
	N	10	10	10	10	10
2 100 mg/kg/day	8210060	8.39	6.5	17.4	48.0	320
	8210061	7.98	7.0	16.5	47.0	355
	8210062	7.90	6.6	16.4	47.0	375
	8210063	7.95	7.6	17.0	47.0	395
	8210064	8.23	7.7	17.5	49.0	355
	8210065	8.28	7.9	17.1	47.0	385
	8210066	8.09	6.3	16.9	47.0	340
	8210067	9.08	8.3	19.1	51.0	-----
	8210068	7.87	5.7	18.0	47.0	310
	8210069	8.67	7.2	17.0	49.0	350
	MEAN	8.24	7.1	17.3	47.9	354
	S.D.	0.39	0.8	0.8	1.4	28
	N	10	10	10	10	9
3 300 mg/kg/day	8210100	8.10	6.8	16.7	47.0	280
	8210101	7.86	6.5	15.8	45.0	330
	8210102	7.93	7.0	16.6	48.0	335
	8210103	8.27	6.9	17.3	48.0	345
	8210104	7.18	6.8	16.8	46.0	325
	8210105	8.50	8.2	18.2	49.0	365
	8210106	9.05	7.7	20.0	51.0	325
	8210107	8.89	7.4	18.9	50.0	315
	8210108	9.23	7.8	19.4	54.0	285
	8210109	9.30	9.7	17.0	49.0	240
	MEAN	8.43	7.5 S+	17.7	48.7	318
	S.D.	0.69	0.9	1.4	2.6	38
	N	10	10	10	10	10
4 900 mg/kg/day	8210145	9.05	10.5	17.5	49.0	270
	8210150	9.11	7.3	18.1	51.0	285
	8210151	7.87	7.8	18.3	49.0	305
	8210152	7.39	7.5	17.5	50.0	350
	8210153	8.48	14.4	18.6	51.0	370
	8210154	8.75	7.9	18.4	49.0	330
	8210155	8.41	9.0	16.9	49.0	230
	8210157	8.06	8.7	17.5	49.5	300
	8210159	[illegible]	7.9	17.0	48.0	330
	MEAN	8.32	9.0 S+	17.8	49.5 S+	308
	S.D.	0.59	2.3	0.6	1.0	43
	N	9	9	9	9	9

----- = Quantity of blood not sufficient for analysis.

S+ = Statistically significantly higher than control at $p \leq 0.05$.

APPENDIX 4 (Continued)

INDIVIDUAL CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG %	BAND %	LYMPH %	ATY.LYMPH %	MONO %	EOS %	BASO %	META %	MYEL %	PROGRAN %	BLAST %	NRBC/ 100 WBC
1	8210020	18	0	80	0	1	1	0	0	0	0	0	0
0	8210021	11	0	84	0	2	1	0	0	0	0	0	0
mg/kg/day	8210022	13	0	84	0	2	1	0	0	0	0	0	0
	8210023	14	0	84	0	0	1	0	0	0	0	0	0
	8210024	9	0	87	0	1	3	0	0	0	0	0	0
	8210025	12	0	84	0	2	2	0	0	0	0	0	0
	8210026	7	0	92	0	0	1	0	0	0	0	0	0
	8210027	12	0	87	0	0	1	0	0	0	0	0	0
	8210028	15	0	82	0	2	1	0	0	0	0	0	0
	8210029	13	0	85	0	1	1	0	0	0	0	0	1
2	8210040	13	0	85	0	1	1	0	0	0	0	0	0
100	8210041	17	0	79	0	1	1	0	0	0	0	0	0
mg/kg/day	8210042	11	0	88	0	0	1	0	0	0	0	0	0
	8210043	8	0	88	0	2	2	0	0	0	0	0	0
	8210044	5	0	92	0	1	2	0	0	0	0	0	0
	8210045	7	0	91	0	0	2	0	0	0	0	0	0
	8210046	4	0	93	0	1	2	0	0	0	0	0	0
	8210047	8	0	91	0	0	1	0	0	0	0	0	0
	8210048	12	0	88	0	0	0	0	0	0	0	0	0
	8210049	14	0	84	0	0	0	0	0	0	0	0	0
3	8210100	19	0	78	0	2	1	0	0	0	0	0	0
300	8210101	20	0	78	0	0	2	0	0	0	0	0	0
mg/kg/day	8210102	19	0	79	0	1	1	0	0	0	0	0	0
	8210103	15	0	82	0	1	2	0	0	0	0	0	0
	8210104	17	0	82	0	1	0	0	0	0	0	0	0
	8210105	15	0	84	0	1	0	0	0	0	0	0	1
	8210106	7	0	88	0	1	2	0	0	0	0	0	0
	8210107	4	0	93	0	1	2	0	0	0	0	0	0
	8210108	12	0	88	0	0	0	0	0	0	0	0	0
	8210109	7	0	91	0	0	2	0	0	0	0	0	0
4	8210145	30	0	70	0	0	0	0	0	0	0	0	0
900	8210150	28	0	72	0	0	0	0	0	0	0	0	0
mg/kg/day	8210151	28	0	68	0	1	3	0	0	0	0	0	0
	8210152	28	0	70	0	0	2	0	0	0	0	0	0
	8210153	14	0	80	0	1	5	0	0	0	0	0	0
	8210154	12	0	84	0	0	4	0	0	0	0	0	0
	8210155	15	0	83	0	0	2	0	0	0	0	0	0
	8210157	12	0	87	0	0	1	0	0	0	0	0	0
	8210158	14	0	84	1	1	0	0	0	0	0	0	0

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APPENDIX 4 (Continued)

INDIVIDUAL RBC MORPHOLOGY
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NO.	RBC MORPHOLOGY
1	8210020	SLIGHT POLY.
0	8210021	SLIGHT POLY.
	8210022	SLIGHT POLY.
mg/kg/day	8210023	SLIGHT POLY.
	8210024	SLIGHT POLY.
	8210025	SLIGHT POLY.
	8210026	SLIGHT POLY.
	8210027	SLIGHT POLY.
	8210028	SLIGHT POLY.
	8210029	SLIGHT POLY.
2	8210060	SLIGHT POLY.
100	8210061	SLIGHT POLY.
	8210062	SLIGHT POLY.
mg/kg/day	8210063	SLIGHT POLY.
	8210064	SLIGHT POLY.
	8210065	SLIGHT POLY.
	8210066	SLIGHT POLY.
	8210067	SLIGHT POLY.
	8210068	SLIGHT POLY.
	8210069	SLIGHT POLY.
3	8210100	SLIGHT POLY.
300	8210101	SLIGHT POLY.
	8210102	SLIGHT POLY.
mg/kg/day	8210103	SLIGHT POLY.
	8210104	SLIGHT POLY.
	8210105	SLIGHT POLY.
	8210106	SLIGHT POLY.
	8210107	SLIGHT POLY.
	8210108	SLIGHT POLY.
	8210109	FEW MACRO., SLIGHT POLY.
4	8210145	SLIGHT POLY.
900	8210150	SLIGHT POLY.
	8210151	SLIGHT POLY.
mg/kg/day	8210152	SLIGHT POLY.
	8210153	SLIGHT POLY.
	8210154	SLIGHT POLY.
	8210155	SLIGHT POLY.
	8210157	SLIGHT POLY.
	8210158	SLIGHT POLY.

000074

APPENDIX 4 (Continued)
INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	RBC 10^{-6}/cmm	WBC 10^{-3}/cmm	HGB G/DL	HCT %	PLATELET 10^{-3}/cmm
1 0 mg/kg/day	8210020	7.50	9.5	17.1	46.0	355
	8210021	7.95	6.7	17.5	48.0	310
	8210022	8.10	4.6	16.9	46.0	305
	8210023	7.20	5.7	16.7	44.0	-----
	8210024	8.32	5.8	17.3	46.0	330
	8210025	6.14	7.8	17.8	49.0	390
	8210026	7.74	8.0	17.6	48.5	355
	8210027	7.43	7.6	16.4	45.5	350
	8210028	7.12	7.7	16.3	46.0	265
	8210029	7.33	5.6	16.4	47.0	340
	MEAN	7.55	6.9	17.0	46.6	333
	S.D.	0.43	1.5	0.5	1.5	36
	N	10	10	10	10	9
2 100 mg/kg/day	8210061	7.12	7.7	16.4	48.0	350
	8210062	7.59	8.2	16.6	48.0	285
	8210063	7.[illegible]	7.8	16.4	48.0	295
	8210064	7.43	9.0	16.6	47.0	260
	8210065	6.07	7.1	16.7	47.0	270
	8210066	6.41	6.9	15.9	47.0	330
	8210067	6.73	5.9	16.7	47.0	280
	8210068	7.00	7.2	16.4	46.5	285
	8210069	7.35	7.2	15.8	45.0	295
	8210070	7.03	8.0	15.7	49.0	290
	MEAN	7.02 S-	7.5	16.3 S-	47.3	294 S-
	S.D.	0.50	0.8	0.4	1.1	27
	N	10	10	10	10	10
3 300 mg/kg/day	8210101	7.54	6.7	16.1	47.5	220
	8210102	8.30	7.3	17.4	48.0	195
	8210103	8.38	6.7	18.0	48.5	195
	8210104	7.78	5.0	17.1	47.5	220
	8210105	6.71	8.0	16.8	47.0	240
	8210106	7.88	8.8	17.7	50.0	230
	8210107	7.17	7.0	16.9	47.0	270
	8210108	7.42	7.7	16.1	46.0	225
	8210109	7.30	9.5	16.7	48.0	290
	8210110	7.04	7.0	15.8	45.0	275
	MEAN	7.53	7.4	16.9	47.5	236 S-
	S.D.	0.55	1.2	0.7	1.4	33
	N	10	10	10	10	10
4 900 mg/kg/day	8210152	7.01	10.7	16.4	46.0	325
	8210153	8.54	7.5	17.3	48.5	280
	MEAN	7.78	9.1	16.9	47.3	303
	S.D.	1.08	2.3	0.6	1.8	32
	N	2	2	2	2	2

----- = Quantity of blood not sufficient for analysis.

S- = Statistically significantly lower than control at $p \leq 0.05$.

APPENDIX 4 (Continued)
INDIVIDUAL CLINICAL HEMATOLOGY DATA
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG %	BAND %	LYMPH %	ATY.LYMPH %	MONO %	EOS %	BASO %	PETA %	MYEL %	PROMYAM %	BLAST %	NRBC/ 100 WBC
1	8210020	18	0	79	0	3	0	0	0	0	0	0	0
0	8210021	10	0	88	0	1	1	0	0	0	0	0	0
mg/kg/day	8210022	13	0	84	0	3	0	0	0	0	0	0	0
	8210023	13	0	85	0	2	1	0	0	0	0	0	0
	8210024	14	0	84	0	2	0	0	0	0	0	0	0
	8210025	20	0	77	0	3	0	0	0	0	0	0	0
	8210026	20	0	75	0	4	1	0	0	0	0	0	0
	8210027	13	0	80	0	7	0	0	0	0	0	0	0
	8210028	10	0	84	0	4	2	0	0	0	0	0	0
	8210029	14	0	79	0	6	1	0	0	0	0	0	0
2	8210061	9	0	89	0	2	0	0	0	0	0	0	0
100	8210062	14	0	83	0	3	1	0	0	0	0	0	0
mg/kg/day	8210063	8	0	89	0	3	0	0	0	0	0	0	0
	8210064	15	0	79	0	5	1	0	0	0	0	0	0
	8210065	10	0	82	0	5	3	0	0	0	0	0	0
	8210066	15	0	81	0	2	0	0	0	0	0	0	0
	8210067	21	0	74	0	3	0	0	0	0	0	0	0
	8210068	17	0	79	0	4	0	0	0	0	0	0	0
	8210069	13	0	80	0	7	0	0	0	0	0	0	0
	8210070	20	1	74	0	3	0	0	0	0	0	0	0
3	8210101	15	0	80	0	4	1	0	0	0	0	0	0
300	8210102	14	0	81	0	3	2	0	0	0	0	0	0
mg/kg/day	8210103	26	0	65	0	6	2	0	0	0	0	0	0
	8210104	17	0	79	0	3	1	0	0	0	0	0	0
	8210105	23	0	73	0	3	1	0	0	0	0	0	0
	8210106	17	0	81	0	1	1	0	0	0	0	0	0
	8210107	12	0	85	0	2	1	0	0	0	0	0	0
	8210108	15	0	83	0	2	0	0	0	0	0	0	0
	8210109	8	0	91	0	1	0	0	0	0	0	0	0
	8210110	22	0	77	0	1	0	0	0	0	0	0	0
4	8210152	23	2	74	0	1	0	0	0	0	0	0	0
900	8210153	27	0	70	0	2	1	0	0	0	0	0	0
mg/kg/day													

000076

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA-ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 760811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROMAN	BLAST	NRBC/ 100 WBC
1	8210020	1710	0	7505	0	285	0	0	0	0	0	0	0
0	8210021	470	0	5076	0	47	47	0	0	0	0	0	1
mg/kg/day	8210022	598	0	3044	0	138	0	0	0	0	0	0	2
	8210023	741	0	4845	0	57	57	0	0	0	0	0	0
	8210024	912	0	4872	0	114	0	0	0	0	0	0	2
	8210025	1540	0	4004	0	0	234	0	0	0	0	0	0
	8210026	1400	0	4000	0	320	80	0	0	0	0	0	2
	8210027	988	0	6080	0	532	0	0	0	0	0	0	0
	8210028	770	0	4158	0	308	154	0	0	0	0	0	0
	8210029	784	0	3424	0	336	56	0	0	0	0	0	0
	MEAN	1023	0	5576	0	214	45	0	0	0	0	0	1
	S.D.	428	0	1981	0	144	77	0	0	0	0	0	1
	N	10	10	10	10	10	10	10	10	10	10	10	10
2	8210041	493	0	4053	0	154	0	0	0	0	0	0	0
100	8210042	1148	0	6724	0	246	82	0	0	0	0	0	1
mg/kg/day	8210043	624	0	4474	0	390	312	0	0	0	0	0	0
	8210044	1350	0	7110	0	450	90	0	0	0	0	0	1
	8210045	710	0	5022	0	355	213	0	0	0	0	0	1
	8210046	1035	0	5727	0	138	0	0	0	0	0	0	2
	8210047	1239	0	4484	0	177	0	0	0	0	0	0	2
	8210048	1224	0	5508	0	306	0	0	0	0	0	0	0
	8210069	936	0	5740	0	561	0	0	0	0	0	0	0
	8210070	1400	00	6000	0	240	0	0	0	0	0	0	0
	MEAN	1056	0	5607	0	294	70	0	0	0	0	0	1
	S.D.	317	25	742	0	127	110	0	0	0	0	0	1
	N	10	10	10	10	10	10	10	10	10	10	10	10
3	8210101	1005	0	5360	0	240	47	0	0	0	0	0	2
300	8210102	1022	0	5913	0	219	146	0	0	0	0	0	0
mg/kg/day	8210103	1742	0	4355	0	402	201	0	0	0	0	0	2
	8210104	850	0	3950	0	100	100	0	0	0	0	0	0
	8210105	1040	0	5040	0	240	80	0	0	0	0	0	1
	8210106	1496	0	7120	0	88	88	0	0	0	0	0	0
	8210107	840	0	5950	0	210	0	0	0	0	0	0	0
	8210108	1232	0	4217	0	231	0	0	0	0	0	0	0
	8210109	855	0	7980	0	570	95	0	0	0	0	0	0
	8210110	1540	0	5390	0	70	0	0	0	0	0	0	0
	MEAN	1242	0	5810	0	240	78	0	0	0	0	0	1
	S.D.	385	0	1184	0	152	66	0	0	0	0	0	1
	N	10	10	10	10	10	10	10	10	10	10	10	10
4	8210152	2461	214	7918	0	107	0	0	0	0	0	0	0
900	8210153	2025	0	5250	0	150	75	0	0	0	0	0	0
mg/kg/day	MEAN	2243	St 107	6584	0	129	38	0	0	0	0	0	0
	S.D.	308	151	1887	0	30	53	0	0	0	0	0	0
	N	2	2	2	2	2	2	2	2	2	2	2	2

St = Statistically significantly higher than control at $p \leq 0.05$.

000077

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA - ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 14 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
1	8210020	1710	0	7505	0	285	0	0	0	0	0	0
0	8210021	670	0	5896	0	67	67	0	0	0	0	0
mg/kg/day	8210022	598	0	3864	0	138	0	0	0	0	0	0
	8210023	741	0	4845	0	57	57	0	0	0	0	0
	8210024	811	0	4871	0	115	0	0	0	0	0	0
	8210025	1559	0	6005	0	0	233	0	0	0	0	0
	8210026	1600	0	6000	0	320	80	0	0	0	0	0
	8210027	987	0	6080	0	532	0	0	0	0	0	0
	8210028	770	0	6468	0	308	154	0	0	0	0	0
	8210029	784	0	4424	0	336	56	0	0	0	0	0
	8210030	1691	0	6941	0	267	0	0	0	0	0	0
	8210031	1410	0	6639	0	165	82	0	0	0	0	0
	8210032	648	0	5073	0	117	58	0	0	0	0	0
	8210033	951	0	5643	0	135	67	0	0	0	0	0
	8210034	1034	0	7708	0	658	0	0	0	0	0	0
	8210035	536	0	6030	0	134	0	0	0	0	0	0
	8210036	660	0	4730	0	55	55	0	0	0	0	0
	8210037	1105	0	6970	0	425	0	0	0	0	0	0
	8210038	870	0	7221	0	609	0	0	0	0	0	0
	8210039	497	0	6461	0	142	0	0	0	0	0	0
	MEAN	982	0	5969	0	243	45	0	0	0	0	0
	S.D.	399	0	1066	0	190	61	0	0	0	0	0
	N	20	20	20	20	20	20	20	20	20	20	20
2	8210061	693	0	6853	0	154	0	0	0	0	0	0
100	8210062	1148	0	6724	0	246	82	0	0	0	0	0
mg/kg/day	8210063	623	0	6473	0	389	311	0	0	0	0	0
	8210064	1350	0	7110	0	450	90	0	0	0	0	0
	8210065	710	0	5822	0	355	213	0	0	0	0	0
	8210066	1035	0	5726	0	137	0	0	0	0	0	0
	8210067	1238	0	4483	0	176	0	0	0	0	0	0
	8210068	1224	0	5688	0	288	0	0	0	0	0	0
	8210069	935	0	5760	0	504	0	0	0	0	0	0
	8210070	1600	80	6080	0	240	0	0	0	0	0	0
	8210071	1143	0	7391	0	263	0	0	0	0	0	0
	8210072	1167	0	5693	0	364	72	0	0	0	0	0
	8210073	1035	0	6363	0	0	0	0	0	0	0	0
	8210074	1305	0	7134	0	174	87	0	0	0	0	0
	8210075	935	0	7225	0	340	0	0	0	0	0	0
	8210076	959	0	4991	0	447	0	0	0	0	0	0
	8210077	859	0	7395	0	343	0	0	0	0	0	0
	8210078	423	0	9539	0	529	105	0	0	0	0	0
	8210079	1002	0	4660	0	235	0	0	0	0	0	0
	MEAN	1020	4	6374	0	297	51	0	0	0	0	0
	S.D.	282	18	1175	0	137	86	0	0	0	0	0
	N	19	19	19	19	19	19	19	19	19	19	19

000078

APPENDIX 4 (Continued)

INDIVIDUAL AND MEAN CLINICAL HEMATOLOGY DATA - ABSOLUTE DIFFERENTIAL LEUKOCYTE COUNT
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 14 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	SEG	BAND	LYMPH	ATY.LYMPH	MONO	EOS	BASO	META	MYEL	PROGRAN	BLAST
3	8210101	1005	0	5360	0	268	67	0	0	0	0	0
300	8210102	1021	0	5912	0	218	145	0	0	0	0	0
mg/kg/day	8210103	1741	0	4355	0	402	201	0	0	0	0	0
	8210104	850	0	3950	0	100	100	0	0	0	0	0
	8210105	1840	0	5840	0	240	80	0	0	0	0	0
	8210106	1495	0	7127	0	87	87	0	0	0	0	0
	8210107	840	0	5950	0	210	0	0	0	0	0	0
	8210108	1232	0	6237	0	231	0	0	0	0	0	0
	8210109	855	0	7979	0	570	95	0	0	0	0	0
	8210110	1540	0	5390	0	70	0	0	0	0	0	0
	8210112	1295	0	3617	0	431	53	0	0	0	0	0
	8210113	1394	0	6150	0	492	164	0	0	0	0	0
	8210114	840	0	7224	0	336	0	0	0	0	0	0
	8210115	1050	0	6150	0	300	0	0	0	0	0	0
	8210116	1215	0	6236	0	647	0	0	0	0	0	0
	8210118	375	0	6825	0	300	0	0	0	0	0	0
	MEAN	1162	0	5894	0	306	62	0	0	0	0	0
	S.D.	383	0	1176	0	168	67	0	0	0	0	0
	N	16	16	16	16	16	16	16	16	16	16	16
4	8210152	2461	214	7918	0	107	0	0	0	0	0	0
900	8210153	2025	0	5250	0	150	75	0	0	0	0	0
mg/kg/day	MEAN	2243 S+	107	6584	0	129	38	0	0	0	0	0
	S.D.	308	151	1887	0	30	53	0	0	0	0	0
	N	2	2	2	2	2	2	2	2	2	2	2

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000079

APPENDIX 5

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL	ANIMAL	GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO	T.CHOL. MG/DL	CALCIUM MG/DL
1	8210000	104	18	32	143	7.1	4.7	1.96	52	11.3
0	8210001	104	17	27	150	6.9	4.4	1.74	47	10.4
mg/kg/day	8210002	104	17	30	124	6.9	4.5	1.74	46	10.2
	8210003	98	17	29	125	6.9	4.5	1.88	48	10.8
	8210004	101	20	37	121	6.9	4.5	1.88	45	10.8
	8210005	104	17	27	154	6.9	4.5	1.88	48	10.8
	8210006	104	15	29	137	6.3	4.2	2.00	46	10.1
	8210007	114	17	34	138	6.7	4.6	2.19	52	10.5
	8210008	97	19	34	129	7.1	4.6	1.84	55	11.4
	8210009	119	17	34	130	6.5	4.4	2.10	54	12.0
	MEAN	105	17	31	140	6.8	4.5	1.92	52	11.4
	S.D.	7	1	3	16	0.3	0.1	0.14	4	0.4
	N	10	10	10	10	10	10	10	10	10
2	8210040	121	19	27	156	7.3	4.8	1.92	51	11.7
100	8210041	107	17	27	152	6.3	4.2	2.00	39	10.4
mg/kg/day	8210042	93	22	41	185	7.9	5.2	1.93	52	9.4
	8210043	104	17	28	155	6.8	4.5	1.94	45	11.4
	8210044	98	18	28	155	7.0	4.5	1.80	45	11.4
	8210045	115	14	24	140	6.5	4.4	2.10	48	11.0
	8210046	104	17	31	147	6.4	4.4	2.00	48	11.0
	8210047	90	15	30	124	7.0	4.9	2.33	55	11.0
	8210048	98	19	29	148	6.9	4.6	2.00	44	11.0
	8210049	110	21	33	150	6.9	4.6	2.00	49	11.0
	MEAN	104	18	30	151	6.9	4.6	2.00	52	11.3
	S.D.	10	2	5	15	0.4	0.2	0.14	14	0.8
	N	10	10	10	10	10	10	10	10	10
3	8210082	110	32	52	317	7.6	5.1	2.04	37	11.6
300	8210084	102	79	46	407	8.7	5.5	1.72	62	10.9
mg/kg/day	8210086	93	16	33	165	6.6	4.5	2.14	35	11.4
	8210087	104	15	36	146	6.7	4.8	2.53	34	11.9
	8210088	100	16	32	145	6.4	4.2	1.91	43	12.3
	8210089	115	17	48	150	7.1	4.6	1.84	39	12.0
	8210090	98	18	29	148	7.0	4.7	2.04	34	10.9
	8210092	97	17	28	155	7.2	4.7	1.88	43	12.0
	8210093	133	28	48	217	7.7	5.1	1.76	43	11.8
	8210094	61	54	38	270	9.0	5.8	1.81	43	11.3
	MEAN	101	29	41 S+	224 S+	7.4	4.9 S+	1.99	40 S-	11.6
	S.D.	18	21	10	109	0.9	0.5	0.23	10	0.5
	N	10	10	10	10	10	10	10	10	10
4	8210120	96	19	41	209	7.9	[illegible]	2.16	41	11.3
900	8210122	108	18	32	189	7.4	4.9	1.81	39	[illegible]
mg/kg/day	8210123	87	23	43	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	8210124	94	19	49	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	8210125	101	17	44	237	7.8	[illegible]	[illegible]	47	[illegible]
	8210126	117	18	48	255	7.2	[illegible]	[illegible]	[illegible]	[illegible]
	8210127	81	17	43	178	7.7	[illegible]	[illegible]	47	[illegible]
	8210128	82	17	39	148	7.1	[illegible]	[illegible]	38	[illegible]
	8210129	104	17	42	194	7.6	[illegible]	[illegible]	30	[illegible]
	8210130	70	24	32	200	7.3	4.9	2.04	29	11.6
	MEAN	94 S-	19	40 S+	201 S+	7.7 S+	5.1 S+	1.98	37 S-	12.1 S+
	S.D.	14	3	5	28	0.4	0.2	0.18	7	0.3
	N	10	10	10	10	10	10	10	10	10

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

080000

APPENDIX 5 (Continued)
INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 MALES

GROUP NO. DOSE LEVEL	ANIMAL	Na MMOL/L	K MMOL/L	Cl MMOL/L
1	8210000	160	6.1	-----
0	8210001	151	6.2	-----
mg/kg/day	8210002	153	5.7	-----
	8210003	158	6.3	-----
	8210004	152	5.8	-----
	8210005	145	5.8	-----
	8210006	145	5.1	-----
	8210007	145	5.3	-----
	8210008	144	5.4	-----
	8210009	143	6.2	-----
	MEAN	150	5.8	0
	S.D.	6	0.4	0
	N	10	10	0
2	8210040	160	8.0	-----
100	8210041	156	5.7	-----
mg/kg/day	8210042	160	7.6	-----
	8210043	144	5.4	-----
	8210044	154	6.2	-----
	8210045	145	5.3	-----
	8210046	144	6.8	-----
	8210047	151	7.3	-----
	8210048	145	6.1	-----
	8210049	145	6.2	-----
	MEAN	150	6.5 S+	
	S.D.	7	0.9	0
	N	10	10	0
3	8210082	-----	-----	-----
300	8210084	-----	-----	-----
mg/kg/day	8210086	148	7.4	-----
	8210087	149	7.4	-----
	8210088	145	5.2	-----
	8210089	147	7.0	-----
	8210090	160	6.7	-----
	8210092	148	6.2	-----
	8210093	145	5.2	-----
	8210094	143	6.5	-----
	MEAN	148	6.5	0
	S.D.	5	0.9	0
	N	8	8	0
4	8210120	152	5.8	-----
900	8210122	160	6.7	-----
mg/kg/day	8210123	-----	-----	-----
	8210124	160	7.0	-----
	8210125	143	6.4	-----
	8210126	145	5.8	-----
	8210127	143	6.8	-----
	8210128	142	6.1	-----
	8210129	149	7.0	-----
	8210130	151	5.3	-----
	MEAN	150	6.3	0
	S.D.	7	0.6	0
	N	9	9	0

----- = Quantity of blood not sufficient for analysis.
S+ = Statistically significantly higher than control at p≤0.05.

000081

APPENDIX 5 (Continued)

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
DP PET 790411 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A/G RATIO	T.CHOL. MG/DL	CALCIUM MG/DL
1	8210000	82	16	43	107	8.0	4.0	1.50	72	12.8
0	8210001	103	18	39	110	7.4	4.0	1.71	81	9.2
mg/kg/day	8210002	82	17	37	99	7.2	4.4	1.48	82	11.3
	8210003	97	17	45	94	7.0	4.0	1.43	77	10.1
	8210004	82	17	44	92	7.0	4.2	1.50	55	10.9
	8210005	81	16	44	100	7.0	4.2	1.50	74	11.2a
	8210006	89	15	37	112	7.0	4.2	1.50	92	9.8
	8210007	88	15	37	98	7.0	4.5	1.55	86	12.7
	8210008	82	16	46	115a	7.0	4.4	1.69	68	11.0
	8210009	83	17	49	114a	7.7	4.4	1.40	103a	11.5a
	MEAN	84	16	42	107	7.3	4.4	1.61	79	11.1
	S.D.	8	1	8	21	0.3	0.2	0.11	14	1.2
	N	10	10	10	10	10	10	10	10	10
2	8210040	78	15	38	102	7.3	4.3	1.50	67	12.5
100	8210041	74	15	41	98	7.7	4.7	1.57	78	12.8
mg/kg/day	8210042	72	21	50	126	8.0	4.9	1.58	63	4.3
	8210043	94	17	35	91	7.3	4.8	1.85	61	11.4
	8210044	88	17	37	98	7.2	4.8	1.71	79	11.8
	8210045	98	16	45	120	7.2	4.8	1.66	82	12.3
	8210046	90	17	51	92	8.4	5.2	1.63	80	10.4a
	8210047	81	17	50	110	8.1	5.0	1.61	77	9.9
	8210048	83	15	44	107	7.1	4.7	1.97	74	7.8a
	8210049	89	17	50	107	7.1	4.7	1.74	100	11.3a
	MEAN	85	17	44	110	7.7	4.8 S+	1.63	77	10.5
	S.D.	8	2	7	13	0.4	0.2	0.11	14	2.4
	N	10	10	10	10	10	10	10	10	10
3	8210086	71	16	47	125	8.0	4.9	1.58	78	9.2
300	8210087	80	15	36	132	7.3	4.4	1.78	64	7.8
mg/kg/day	8210088	59	18	44	108	6.9	4.4	1.74	49	9.8
	8210089	74	18	49	119	6.8	4.4	1.83	49	11.2
	8210090	65	18	34	121	7.2	4.6	1.77	49	12.5
	8210092	74	18	40	111	8.0	4.9	1.58	61	8.2
	8210093	69	15	56	112	7.4	4.7	1.62	55	12.3
	8210095	72	16	37	110	7.4	4.8	1.71	65	12.3
	8210096	80	14	50	94	7.8	5.0	1.79	60	12.8
	8210097	88	15	39	132	7.9	4.9	1.63	78	9.1
	MEAN	73 S-	15	42	117	7.5	4.7	1.70	59 S-	10.3
	S.D.	8	2	8	11	0.4	0.2	0.07	12	2.0
	N	10	10	10	10	10	10	10	10	10
4	8210120	49	22	73	215	8.7	5.3	1.56	47	13.9
900	8210122	65	23	43	126	8.2	5.1	1.65	40	13.9
mg/kg/day	8210124	91	17	63	128	9.1	5.5	1.53	39	13.9
	8210125	68	22	70	204	9.3	5.6	1.51	56	13.7
	8210126	59	13	55	161	8.1	5.0	1.61	48	7.4
	8210127	63	12	41	146	8.0	5.1	1.76	41	11.9
	8210128	62	12	48	120	8.0	4.9	1.70	36	4.7a
	8210129	62	34	58	163	7.9	4.9	1.63	52	10.5a
	8210131	63	17	19	141	8.0	5.3	1.51	40	10.3
	8210132	72	17	38	116	8.3	5.3	1.77	41	8.2
	MEAN	65 S-	19	55 S+	153 S+	8.4 S+	5.2 S+	1.63	48 S-	10.9
	S.D.	11	6	12	34	0.6	0.3	0.11	9	2.8
	N	10	10	10	10	10	10	10	10	10

S+ = Statistically significantly higher than control at p≤0.05.
S- = Statistically significantly lower than control at p≤0.05.
a = Value from repeat draw.

000082

APPENDIX 5 (Continued)

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL	Na MMOL/L	K MMOL/L	Cl MMOL/L
1	8210000	149	5.6	104
0	8210001	149	5.1	104
mg/kg/day	8210002	148	5.1	105
	8210003	152	5.3	-----
	8210004	148	5.2	104
	8210005	145	5.3	101
	8210006	146	5.1	101
	8210007	148	5.2	103
	8210008	149	5.0	103
	8210009	147	5.3	102
	MEAN	148	5.3	103
	S.D.	2	0.4	1
	N	10	10	9
2	8210040	148	5.3	-----
100	8210041	148	5.7	103
mg/kg/day	8210042	149	5.6	103
	8210043	146	5.1	103
	8210044	148	5.1	104
	8210045	146	5.4	102
	8210046	151	6.2	107
	8210047	149	5.1	104
	8210048	147	5.1	103
	8210049	153	6.5	107
	MEAN	149	5.6	104
	S.D.	2	0.5	2
	N	10	10	9
3	8210086	147	5.4	102
300	8210087	147	5.4	104
mg/kg/day	8210088	146	5.4	102
	8210089	151	5.5	107
	8210090	147	5.1	104
	8210092	147	5.5	104
	8210093	148	5.1	103
	8210095	148	5.2	103
	8210096	-----	-----	-----
	8210097	147	5.5	103
	MEAN	148	5.5	104
	S.D.	1	0.4	2
	N	9	9	9
4	8210120	148	5.9	-----
900	8210122	146	5.8	105
mg/kg/day	8210124	-----	-----	-----
	8210125	147	5.9	103
	8210126	147	5.1	104
	8210127	151	-----	-----
	8210128	148	5.6	103
	8210129	146	5.2	98
	8210131	149	6.2	104
	8210132	151	5.5	104
	MEAN	148	5.7	103
	S.D.	2	0.4	3
	N	9	8	7

----- = Quantity of blood not sufficient for analysis.

000083

APPENDIX 5 (Continued)

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 5 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO %	T.CHOL. MG/DL	CALCIUM MG/DL
1	8210020	107	13	31	114	6.6	4.2	1.75	96	10.8
0	8210021	100	23	30	131	7.2	4.7	1.88	89	11.6
mg/kg/day	8210022	94	15	26	128	6.1	4.0	1.90	88	10.8
	8210023	104	17	27	121	7.1	4.5	1.73	102	11.7
	8210024	93	18	24	117	6.9	4.3	1.65	94	11.4
	8210025	101	12	24	113	6.8	4.4	1.83	94	11.0
	8210026	103	15	29	105	6.7	4.3	1.79	87	11.2
	8210027	95	16	25	110	6.6	4.4	2.00	91	11.4
	8210028	99	18	27	108	6.5	4.1	1.71	91	11.1
	8210029	94	20	26	104	6.6	4.3	1.87	91	11.3
	MEAN	99	17	27	115	6.7	4.3	1.81	92	11.3
	S.D.	5	3	2	9	0.3	0.2	0.10	4	0.3
	N	10	10	10	10	10	10	10	10	10
2	8210060	100	13	33	136	6.7	4.4	1.91	96	11.1
100	8210061	109	18	27	106	6.8	4.3	1.72	88	11.1
mg/kg/day	8210062	97	14	24	120	6.3	4.2	2.00	99	10.8
	8210063	101	16	24	102	6.9	4.3	1.65	104	11.4
	8210064	92	14	23	132	6.6	4.3	1.87	91	11.4
	8210065	109	17	27	115	6.8	4.4	1.83	99	11.2
	8210066	95	14	27	117	6.5	4.4	2.10	85	11.1
	8210067	76	14	33	124	6.9	4.7	2.14	100	12.0
	8210068	101	17	23	112	6.6	4.2	1.75	88	10.7
	8210069	96	16	31	109	6.6	4.3	1.87	90	11.6
	MEAN	98	15	27	117	6.7	4.4	1.88	94	11.3
	S.D.	9	2	4	11	0.2	0.1	0.16	6	0.4
	N	10	10	10	10	10	10	10	10	10
3	8210100	101	19	41	148	7.1	4.7	1.96	107	11.9
300	8210101	109	12	30	127	6.4	4.3	2.05	78	11.2
mg/kg/day	8210102	99	14	35	122	6.4	4.2	1.91	82	11.4
	8210103	103	17	27	136	6.5	4.2	1.83	94	11.4
	8210104	112	16	28	151	7.0	4.5	1.80	79	11.5
	8210105	119	18	32	154	6.9	4.6	2.00	83	11.3
	8210106	90	18	28	123	6.6	4.4	2.00	87	11.1
	8210107	96	18	34	143	7.1	4.6	1.84	111	11.5
	8210108	97	18	31	158	6.7	4.7	2.35	81	10.9
	8210109	111	21	41	125	6.7	4.3	1.79	82	8.0
	MEAN	104	17	33 S+	139 S+	6.7	4.5 S+	1.95	86	11.0
	S.D.	9	3	5	14	0.3	0.2	0.17	14	1.1
	N	10	10	10	10	10	10	10	10	10
4	8210150	106	27	38	244	7.4	4.5	1.55	78	10.9
900	8210151	81	18	38	183	7.1	4.7	1.96	68	11.8
mg/kg/day	8210152	103	21	35	153	7.9	5.0	1.72	84	12.3
	8210153	105	15	41	180	7.5	4.9	1.88	74	12.3
	8210154	110	15	50	200	7.4	4.9	1.96	73	12.3
	8210155	89	11	37	152	7.1	4.6	1.84	82	11.5
	8210157	78	15	41	175	6.9	4.4	1.74	96	12.0
	8210158	91	13	31	137	6.7	4.5	2.05	70	12.0
	8210145	89	13	36	152	6.7	4.5	2.05	73	11.4
	MEAN	95	16	39 S+	168 S+	7.2 S+	4.7 S+	1.86	78 S-	11.8 S+
	S.D.	12	5	5	39	0.4	0.2	0.16	9	0.5
	N	9	9	9	9	9	9	9	9	9

S+ = Statistically significantly higher than control at $p \leq 0.05$.

S- = Statistically significantly lower than control at $p \leq 0.05$.

000084

APPENDIX 5 (Continued)

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 760811 TO RATS
WEEK 3 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	Na MMOL/L	K MMOL/L	Cl MMOL/L
1	8210020	148	5.4	-----
0	8210021	154	6.8	-----
mg/kg/day	8210022	156	5.7	-----
	8210023	157	6.4	-----
	8210024	154	6.4	-----
	8210025	156	6.3	-----
	8210026	145	6.2	-----
	8210027	144	6.8	-----
	8210028	147	5.7	-----
	8210029	145	5.3	-----
		143	5.7	-----
	MEAN	150	6.0	
	S.D.	6	0.5	0
	N	10	10	0
				0
2	8210060	155	6.8	-----
100	8210061	155	6.4	-----
mg/kg/day	8210062	148	7.3	-----
	8210063	147	5.2	-----
	8210064	153	5.9	-----
	8210065	145	5.7	-----
	8210066	146	5.7	-----
	8210067	147	5.5	-----
	8210068	147	7.0	-----
	8210069	146	5.7	-----
			6.0	-----
	MEAN	150	6.2	
	S.D.	5	0.7	0
	N	10	10	0
				0
3	8210100	156	7.4	-----
300	8210101	155	6.7	-----
mg/kg/day	8210102	159	6.1	-----
	8210103	149	5.7	-----
	8210104	160	6.1	-----
	8210105	143	5.5	-----
	8210106	148	7.3	-----
	8210107	145	5.7	-----
	8210108	140	5.5	-----
	8210109	149	5.4	-----
	MEAN	150	6.1	
	S.D.	7	0.8	0
	N	10	10	0
				0
4	8210150	158	6.2	-----
900	8210151	158	7.1	-----
mg/kg/day	8210152	157	6.7	-----
	8210153	-----	-----	-----
	8210154	143	6.6	-----
	8210155	149	6.6	-----
	8210157	144	6.0	-----
	8210158	143	7.0	-----
	8210145	145	5.9	-----
	MEAN	150	6.5	
	S.D.	7	0.4	0
	N	8	8	0
				0

----- = Quantity of blood not sufficient for analysis.

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APPENDIX 5 (Continued)
INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS
WEEK 13 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL	GLUCOSE MG/DL	BUN MG/DL	SGPT U/L	ALP U/L	T.PROT G/DL	ALBUMIN G/DL	A:G RATIO	T.CHOL. MG/DL	CALCIUM MG/DL
1	8210020	75	16	42	80	7.2	4.5	1.67	110	10.2
0	8210021	71	18	40	92	7.8	4.9	1.69	109	12.3
mg/kg/day	8210022	83	19	38	100	7.7	4.8	1.66	111	11.3
	8210023	80	18	28	78	7.7	4.7	1.57	113	11.5
	8210024	75	19	40	73	7.6	4.5	1.45	109	11.2
	8210025	81	17	38	78	7.7	4.8	1.66	132	9.6
	8210026	94	18	46	104	8.2	4.9	1.48	130	11.2a
	8210027	80	19	55	86	7.3	4.5	1.61	131	11.5
	8210028	72	18	35	82	6.4	4.0	1.67	90	11.5a
	8210029	71	18	43	80	6.7	4.1	1.58	113	10.7a
	MEAN	78	17	40	85	7.4	4.6	1.60	115	11.2
	S.D.	7	2	7	10	0.5	0.3	0.08	14	1.0
	N	10	10	10	10	10	10	10	10	10
2	8210061	57	18	41	80	7.7	4.8	1.66	111	9.9
100	8210062	81	18	35	63	7.5	4.6	1.39	126	12.7
mg/kg/day	8210063	74	15	35	56	7.7	4.8	1.66	115	8.9
	8210064	67	17	30	90	7.4	4.5	1.44	111	11.5
	8210065	84	16	45	85	8.0	4.9	1.55	136	11.8
	8210066	80	14	33	94	b	4.5	1.58	117	9.9
	8210067	73	15	36	74	7.1	4.4	1.63	118	12.4
	8210068	80	17	34	88	7.1	4.3	1.54	114	9.3
	8210069	89	15	37	94	6.9	4.0	1.82	89	12.7
	8210070	85	15	41	79	6.9	4.3	1.65	124	9.3
	MEAN	75	16	37	81	7.3	4.5	1.63	116	10.1
	S.D.	10	1	4	13	0.5	0.3	0.08	12	2.8
	N	10	10	10	10	9	10	9	10	10
3	8210101	79	14	53	113	7.2	4.6	1.77	116	12.4
300	8210102	71	19	49	134	7.5	4.7	1.68	98	12.2
mg/kg/day	8210103	66	16	43	119	7.4	4.6	1.64	106	12.4
	8210104	83	14	39	93	7.8	4.8	1.60	115	12.2
	8210105	98	16	37	113	8.0	4.9	1.76	105	11.2a
	8210106	75	15	35	117	7.6	4.4	1.62	100	11.8a
	8210107	79	16	32	91	7.8	4.7	1.50	98	-----
	8210108	66	12	42	114	6.4	4.3	2.05	103	10.2
	8210109	74	23	48	104	6.4	4.3	1.87	89	9.3a
	8210110	73	14	31	68	7.3	4.6	1.70	119	11.5
	MEAN	76	16	45	107 S+	7.2	4.5	1.72 S+	105	11.5
	S.D.	9	3	9	19	0.4	0.2	0.15	10	1.1
	N	10	10	10	10	10	10	10	10	9
4	8210152	67	16	42	109	8.2	5.0	1.56	105	12.3
900	8210153	89	22	44	175	8.4	5.1	1.77	84	10.7a
mg/kg/day	MEAN	78	19	43	142 S+	8.3	5.1	1.66	95	11.5
	S.D.	16	4	1	47	0.1	0.2	0.14	15	1.1
	N	2	2	2	2	2	2	2	2	2

a = Value from repeat draw.
b = Total protein value (4.4) believed to be in error; therefore, value was excluded from the mean. Blood sample was insufficient for repeat analysis.
----- = Quantity of blood not sufficient for analysis.
S+ = Statistically significantly higher than control at p≤0.05.

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APPENDIX 5 (Continued)

INDIVIDUAL AND MEAN CLINICAL CHEMISTRY VALUES
THIRTEEN WEEK DIETARY ADMINISTRATION
OF FCF FOOD# 10 RATS
WEEK 13 FEMALES

GROUP NO. / DOSE LEVEL	ANIMAL	Na mMOL/L	K mMOL/L	Cl mMOL/L
1	0210020	148	5.4	106
0	0210021	-----	-----	-----
mg/kg/day	0210022	144	5.8	103
	0210023	-----	-----	-----
	0210024	153	[illegible]	-----
	0210025	147	[illegible]	[illegible]
	0210026	149	[illegible]	[illegible]
	0210027	145	[illegible]	[illegible]
	0210028	148	[illegible]	[illegible]
	0210029	142	[illegible]	[illegible]
	MEAN	148	5.6	105
	S.D.	3	0.4	1
	N	8	8	7
2	0210061	147	[illegible]	104
100	0210062	146	[illegible]	107
mg/kg/day	0210063	147	[illegible]	105
	0210064	144	[illegible]	[illegible]
	0210065	146	[illegible]	[illegible]
	0210066	148	[illegible]	[illegible]
	0210067	148	[illegible]	[illegible]
	0210068	145	[illegible]	[illegible]
	0210069	147	[illegible]	[illegible]
	0210070	146	[illegible]	[illegible]
	MEAN	147	5.4	105
	S.D.	1	0.4	2
	N	10	10	10
3	0210101	148	[illegible]	107
300	0210102	143	[illegible]	[illegible]
mg/kg/day	0210103	[illegible]	[illegible]	[illegible]
	0210104	[illegible]	[illegible]	[illegible]
	0210105	147	[illegible]	[illegible]
	0210106	-----	-----	-----
	0210107	-----	-----	-----
	0210108	[illegible]	[illegible]	-----
	0210109	146	[illegible]	103
	0210110	147	[illegible]	102
				105
	MEAN	144 S-	5.5	104
	S.D.	1	0.4	2
	N	8	9	8
4	0210152	152	5.9	110
900	0210153	142	4.3	101
mg/kg/day	MEAN	147	5.1	106
	S.D.	7	1.1	6
	N	2	2	2

----- = Quantity of blood not sufficient for analysis.

S- = Statistically significantly lower than control at $p \leq 0.05$.

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KEY TO APPENDIX 6

INDIVIDUAL URINALYSIS VALUES

APPEARANCE

Color	TURBID
LY = Light yellow	C = Clear
Y = Yellow	CL = Cloudy
DY = Dark yellow	H = Hazy

PROTEIN

0 = Negative
T = Trace
1+ = 30 MG/DL
2+ = 100 MG/DL
3+ = 300 MG/DL
4+ = >2000 MG/DL

GLUCOSE

0 = Negative
T = .1 G/DL
1+ = .25 G/DL
2+ = .5 G/DL
3+ = 1 G/DL
4+ = ≥ 2 G/DL

KETONES

0 = Negative
S = -20. MG/DL
M = 30-40 MG/DL
L = 80-100 MG/DL

BILIRUBIN

0 = Negative
+ = > .2-.4 MG/DL

UROBILINOGEN

N = Normal

OCCULT BLOOD

0 = Negative
T = Trace
T-H = Trace Hemolyzed Blood
T-NH = Trace Nonhemolyzed Blood
1+ = Small Amount
2+ = Moderate Amount
3+ = Large Amount

WBC, RBC, EPITH, CAST, CRYSTAL, SPERMATOZOA, AND TRICHOMONAS

RARE
#-# = Approximate Amount/Field, i.e., 1-2 or 4-5, etc.
TNTC = Too Numerous To Count
- = None Observed
T. PHOS = (Crystal Type)-Triple Phosphate
R. GRAN = Rare Granular

BACTERIA, YEAST, MUCUS THREADS, AND AMORPHOUS

RARE = 1 or 2/Field
FEW = 3 to 10/Field
1+ = 10-100/Field
2+ = 100-200/Field
3+ = >200/Field
4+ = Too Numerous To Count
- = None Observed

APPENDIX 6

INDIVIDUAL URINALYSIS DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

WEEK 5 MALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	APPEAR	SP. GR.	pH	PROT	GLUC	KET	BILI	UROBIL	OCCULT BLOOD	MICROSCOPIC FINDINGS							
											WBC	RBC	EPITH	BACT	AMORPH	CASTS	CRYSTALS	SPERM
1	8210000	C-Y	1.046	7.5	1+	0	0	0	N	T-N	0-1	2-3	0-1	-	Few	-	2-3 T. Phos	0-1
0	8210001	N-DY	1.021	8.5	1+	0	0	0	N	3+	0-1	3-4	0-1	1+	Few	-	2-3 T. Phos	2-3
mg/kg/day	8210002	N-Y	1.035	6.5	T	0	0	0	N	1+	0-1	0-1	0-1	Few	1+	-	2-3 T. Phos	0-1
	8210003	CL-Y	1.017	8.5	1+	0	0	0	N	T-NH	1-2	5-6	0-1	Few	1+	-	-	2-3
	8210004	C-Y	1.021	7.0	0	0	0	0	N	1+	0-1	0-1	0-1	Few	-	-	2-3 T. Phos	-
	8210005	C-Y	1.021	8.5	T	0	0	0	N	T-N	2-3	0-1	0-1	Few	1+	-	2-3 T. Phos	1-2
	8210006	CL-DY	1.024	8.5	2+	0	0	0	N	3+	Rare	Rare	Rare	Few	1+	-	4-5 T. Phos	0-1
	8210007	N-LY	1.026	7.5	0	0	0	0	N	T-NH	1-2	0-1	0-1	Few	1+	-	2-3 T. Phos	2-3
	8210008	C-LY	1.044	8.5	2+	0	0	0	N	T-NH	0-1	Rare	0-1	Few	-	-	2-4 T. Phos	-
	8210009	CL-Y	1.064	8.0	1+	0	0	0	N	1+	1-2	0-1	0-1	Few	2+	-	8-10 T. Phos	0-1
2	8210040	C-Y	1.016	8.0	1+	0	0	0	N	1+	2-3	0-1	0-1	Few	-	-	-	1-2
100	8210041	CL-Y	1.016	8.0	0	0	0	0	N	1+	1-2	0-1	Rare	1+	2+	-	-	2-3
mg/kg/day	8210042	N-Y	1.040	7.0	0	0	0	0	N	0	0-1	1-2	2-3	Few	1+	-	3-5 T. Phos	-
	8210043	N-Y	1.016	8.0	1+	0	0	0	N	T-NH	2-3	2-3	0-1	Few	-	-	-	4-5
	8210044	C-LY	1.014	8.0	T	0	0	0	N	0	2-3	4-5	2-3	Few	1+	-	-	2-3
	8210045	CL-DY	1.034	8.5	1+	0	0	0	N	2+	0-1	0-1	0-1	2+	3+	-	8-10 T. Phos	-
	8210046	N-DY	1.021	6.5	2+	0	0	0	N	3+	0-1	2-3	0-1	Few	-	-	-	0-1
	8210047	N-Y	1.017	8.0	0	0	0	0	N	T-N	Rare	2-3	0-1	Few	1+	-	-	2-3
	8210048	C-LY	1.028	8.5	T	0	0	0	N	3+	1-2	4-5	2-3	2+	1+	-	0-1 T. Phos	1-2
	8210049	CL-Y	1.020	8.0	T	0	0	0	N	T-N	2-3	2-3	2-3	Few	Few	-	8-10 T. Phos	2-3
3	8210082	N-Y	1.046	7.5	0	0	0	0	N	1+	0-1	0-1	1-2	Few	-	-	0-1 T. Phos	-
300	8210083	C-LY	1.022	7.0	0	0	0	0	N	0	0-1	0-1	1-2	Few	1+	-	-	-
mg/kg/day	8210084	N-LY	1.012	8.0	0	0	0	0	N	2+	0-1	0-1	2-3	Few	1+	-	-	0-1
	8210086	N-Y	1.026	8.5	0	0	0	0	N	1+	1-2	2-3	0-1	Few	1+	-	4-5 T. Phos	0-1
	8210087	N-Y	1.023	8.5	0	0	0	0	N	3+	0-1	-	0-1	Few	1+	-	1-2 T. Phos	-
	8210088	N-Y	1.024	8.5	1+	0	0	0	N	0	0-1	Rare	2-3	Few	-	-	8-10 T. Phos	2-3
	8210089	CL-Y	1.030	7.5	T	0	0	0	N	3+	1-2	0-1	1-2	3+	1+	-	TNTC T. Phos	0-1
	8210090	CL-Y	1.054	7.5	1+	0	0	0	N	T-NH	0-1	0-1	0-1	Few	Few	-	3-4 T. Phos	-
	8210091	CL-DY	1.016	8.5	2+	0	0	0	N	3+	0-1	Rare	Rare	Few	1+	-	8-10 T. Phos	2-3
	8210092	C-Y	1.016	8.5	T	0	0	0	N	1+	1-2	0-1	0-1	1+	1+	-	8-10 T. Phos	1-2
4	8210120	C-LY	1.018	7.0	0	0	0	0	N	0	0-1	0-1	1-2	Few	1+	-	-	-
900	8210122	N-Y	1.020	7.0	1+	0	0	0	N	T	0-1	-	0-1	-	-	-	2-3 T. Phos	-
mg/kg/day	8210123	N-DY	1.033	7.0	1+	0	0	0	N	2+	1-2	0-1	0-1	Few	1+	-	2-3 T. Phos	-
	8210124	CL-Y	1.026	6.5	1+	0	0	0	N	T	1-2	0-1	1-2	Few	1+	-	-	1-2
	8210125	N-Y	1.024	6.0	T	0	0	0	N	T-NH	0-1	0-1	2-3	1+	-	-	-	0-1
	8210126	C-LY	1.012	7.0	0	0	0	0	N	T-N	2-3	0-1	1-2	Few	Few	-	-	-
	8210127	C-Y	1.012	7.0	0	0	0	0	N	T-N	1-2	2-3	1-2	Few	-	-	-	2-3
	8210128	CL-Y	1.042	6.0	1+	0	0	0	N	0	0-1	2-3	1-3	Few	1+	R. Gran	-	-
	8210129	C-LY	1.011	6.5	0	0	0	0	N	0	0-1	-	0-1	-	-	-	-	-
	8210130	C-Y	1.042	6.0	T	0	0	0	N	T	1-2	2-4	0-1	-	Few	-	-	-

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APPENDIX 6 (Continued)

INDIVIDUAL URINALYSIS DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

WEEK 13 MALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	APPEAR	SP. GR.	pH	PROT	GLUC	KET	BILI	OCCULT BLOOD	MICROSCOPIC FINDINGS WBC	RBC	EPITH	BACT	AMORPH	CASTS	CRYSTALS	SPERM
1	8210000	LY-H	1.022	7.0	2+	0	0	0	T	-	-	0-1	-	Few	-	-	-
0	8210001	LY-H	1.027	7.5	3+	0	0	0	T	Rare	-	0-1	-	Few	-	-	-
mg/kg/day	8210002	LY-H	1.074	6.5	4+	0	0	0	0	0-1	-	Rare	-	Few	-	-	-
	8210003	LY-H	1.074	7.0	4+	0	0	0	T	-	-	0-1	Rare	Few	-	0-1 T. Phos	-
	8210004	LY-H	1.074	7.0	4+	0	0	0	T	-	-	0-1	-	Few	-	-	1-3
	8210005	LY-H	1.010	7.5	T	0	0	0	T	Rare	-	Rare	2+	Few	-	-	0-2
	8210006	LY-H	1.032	8.0	4+	0	0	0	T	Rare	-	-	Few	Few	-	-	1-3
	8210007	LY-H	1.019	8.0	1+	0	0	0	T	Rare	-	Rare	Few	Few	-	-	6-10
	8210008	LY-H	1.021	8.0	3+	0	0	0	0	-	-	Rare	Few	Few	-	-	-
	8210009	LY-H	1.021	8.0	2+	0	0	0	T	0-1	-	0-1	1+	Few	-	1-2 T. Phos	10-15
2	8210040	LY-H	1.027	7.5	3+	0	0	0	0	-	-	0-1	-	Few	-	0-2 T. Phos	0-3
100	8210041	LY-H	1.033	7.5	4+	0	0	0	T	0-1	0-1	0-1	Few	Few	-	0-2 T. Phos	0-4
mg/kg/day	8210042	LY-H	1.028	7.2	3+	0	0	0	T	0-4	0-1	0-3	1+	Few	-	0-3 T. Phos	0-2
	8210043	LY-H	1.060	7.0	4+	0	0	0	T	0-1	-	1-2	1+	Few	-	1-3 T. Phos	0-1
	8210044	LY-H	1.066	7.0	3+	0	0	0	T	0-4	Rare	0-3	Few	Few	-	-	2-4
	8210045	LY-H	1.013	7.5	3+	0	0	0	T	0-2	-	0-1	3+	Few	-	-	0-2
	8210046	LY-H	1.016	7.5	1+	0	0	0	0	Rare	-	Rare	Few	Few	-	-	-
	8210047	LY-H	1.014	7.0	1+	0	0	0	0	0-1	0-1	Rare	3+	Few	-	-	-
	8210048	LY-C	1.008	8.0	T	0	0	0	0	-	0-4	0-1	4+	Few	-	-	-
	8210049	LY-H	1.007	7.5	1+	0	0	0	0	1-2	0-1	0-2	4+	Few	-	0-1 T. Phos	5-10
3	8210086	LY-C	1.014	6.0	1+	0	0	0	0	0-1	-	0-4	Few	-	-	-	-
300	8210087	LY-H	1.020	6.0	4+	0	0	0	T	0-2	0-1	0-2	Few	Few	-	-	2-4
mg/kg/day	8210088	LY-C	1.010	6.0	1+	0	0	0	T	0-3	-	0-1	1+	Few	-	-	0-5
	8210089	LY-H	1.017	6.5	1+	0	0	0	T	0-2	0-1	2-4	Few	Few	-	-	4-6
	8210090	LY-H	1.023	7.0	2+	0	0	0	T	0-1	-	0-2	Few	Few	-	-	2-6
	8210092	LY-H	1.027	8.0	2+	0	0	0	T	1-4	0-1	0-3	1+	4+	-	1-5 T. Phos	0-4
	8210093	LY-H	1.014	7.5	1+	0	0	0	T	-	-	Rare	-	-	-	-	0-2
	8210095	LY-H	1.018	7.5	1+	0	0	0	0	Rare	Rare	0-1	Rare	-	-	-	-
	8210096	LY-H	1.011	7.0	T	0	0	0	T	0-1	-	Rare	2+	-	-	-	-
	8210097	LY-H	1.026	6.5	3+	0	0	0	0	0-1	-	0-1	Few	Few	-	-	0-3
4	8210120	LY-H	1.029	7.0	4+	0	0	0	T	0-1	0-2	0-1	Few	Few	-	-	-
900	8210122	LY-H	1.025	6.5	4+	0	0	0	T	Rare	0-1	0-1	Few	Few	-	-	-
mg/kg/day	8210124	LY-H	1.027	6.5	3+	0	0	0	T	2-4	0-1	1-3	1+	Few	-	-	0-3
	8210125	LY-H	1.008	6.5	1+	0	0	0	0	0-1	-	0-1	Few	Few	-	-	-
	8210126	LY-H	1.022	6.0	3+	0	0	0	0	0-1	0-1	Rare	Few	Few	-	-	-
	8210127	LY-H	1.007	8.0	1+	0	0	0	0	Rare	Rare	-	1+	Few	-	-	-
	8210128	LY-H	1.028	6.0	2+	0	0	0	0	0-4	0-1	0-1	1+	Few	-	-	-
	8210129	LY-H	1.009	6.0	2+	0	0	0	0	2-4[a]	0-1	0-1	Few	-	-	-	-
	8210131	LY-H	1.018	7.5	3+	0	0	0	T	0-2	0-1	0-2	1+	Few	-	-	-
	8210132	LY-H	1.018	6.5	3+	0	0	0	0	2-6	0-2	1-2	1+	Few	-	-	0-2

[a]Rare WBC clumping.

060000

APPENDIX 6 (Continued)

INDIVIDUAL URINALYSIS DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

WEEK 5 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	APPEAR	SP. GR.	pH	PROT	GLUC	KET	BILI	UROBIL	OCCULT BLOOD	MICROSCOPIC FINDINGS						
											WBC	RBC	EPITH	BACT	AMORPH	CASTS	CRYSTALS
1	8210020	CL-Y	1.040	8.5	T	0	0	0	N	3+	0-1	0-1	0-1	1+	2+	-	4-5 T. Phos
0	8210021	CL-Y	1.034	7.0	0	0	0	0	N	T-N	2-3	2-3	0-1	-	1+	-	2-3 T. Phos
mg/kg/day	8210022	N-Y	1.070	7.0	T	0	0	0	N	T-N	0-1	0-1	0-1	-	-	-	-
	8210023	C-Y	1.023	6.5	0	0	0	0	N	0	Rare	-	0-1	-	-	-	-
	8210024	CL-Y	1.029	8.0	T	0	0	0	N	0	1-2	0-1	0-1	-	3+	-	2-3 T. Phos
	8210025	C-Y	1.015	8.0	0	0	0	0	N	1+	0-1	1-2	1-2	Few	Few	-	-
	8210026	C-Y	1.027	7.5	0	0	0	0	N	0	0-1	-	0-1	-	Few	-	1-2 T. Phos
	8210027	N-Y	1.024	7.5	1+	0	0	0	N	1+	0-1	2-3	0-1	Few	-	-	0-1 T. Phos
	8210028	C-Y	1.015	8.0	0	0	0	0	N	0	2-3	0-1	2-3	Few	-	-	-
	8210029	C-Y	1.022	8.0	0	0	0	0	N	2+	0-1	2-3	0-1	Few	Few	-	-
2	8210060	C-Y	1.031	7.5	T	0	0	0	N	3+	0-1	1-2	0-1	Few	Few	-	-
100	8210061	N-LY	1.036	6.5	1+	0	0	0	N	0	1-2	4-5	0-1	Few	-	-	-
mg/kg/day	8210062	C-LY	1.019	8.0	0	0	0	0	N	T-N	0-1	0-1	0-1	Few	-	-	-
	8210063	C-LY	1.016	8.0	0	0	0	0	N	0	0-1	Rare	0-1	-	1+	-	-
	8210064	N-LY	1.013	6.5	0	0	0	0	N	1+	1-2	2-3	0-1	Few	1+	-	-
	8210065	N-Y	1.028	7.5	T	0	0	0	N	3+	0-1	1-2	0-1	Few	2+	-	0-1 T. Phos
	8210066	CL-Y	1.011	8.0	0	0	0	0	N	T-N	1-2	0-1	2-3	3+	1+	-	-
	8210067	N-Y	1.031	6.5	0	0	0	0	N	T-N	Rare	Rare	1-2	Few	-	-	-
	8210068	C-Y	1.017	7.5	0	0	0	0	N	T-N	1-2	4-5	0-1	Few	-	-	-
	8210069	C-LY	1.012	7.0	0	0	0	0	N	1+	0-1	1-2	0-1	1+	1+	-	-
3	8210100	C-Y	1.034	6.0	T	0	0	0	N	0	1-2	Rare	Rare	-	-	-	-
300	8210101	C-DY	1.038	6.5	T	0	0	0	N	2+	0-1	1-2	0-1	Few	Few	-	Rare T. Phos
mg/kg/day	8210102	C-LY	1.011	8.0	0	0	0	0	N	1+	0-1	0-1	0-1	Few	-	-	-
	8210103	C-Y	1.013	6.5	0	0	0	0	N	2+	0-1	0-1	0-1	Few	1+	-	-
	8210104	C-Y	1.035	7.0	0	0	0	0	N	T	1-2	1-2	0-1	-	1+	-	-
	8210105	C-LY	1.007	8.0	0	0	0	0	N	T-N	0-1	1-2	1-2	Few	-	-	-
	8210106	C-Y	1.020	6.5	0	0	0	0	N	0	1-2	Rare	Rare	Few	-	-	-
	8210107	N-Y	1.060	7.0	T	0	0	0	N	1+	0-1	0-1	0-1	-	1+	-	0-1 T. Phos
	8210108	C-Y	1.008	7.5	0	0	0	0	N	0	1-2	0-1	2-3	Few	-	-	-
	8210109	C-Y	1.017	7.5	0	0	0	0	N	T-N	0-1	Rare	1-2	Few	1+	-	1-2 T. Phos
4[a]	8210145	C-Y	1.021	6.5	0	0	0	0	N	T-NN	0-1	1-2	0-1	Rare	-	-	-
900	8210150	N-Y	1.026	6.0	0	0	0	0	N	3+	2-3	2-4	0-1	Few	1+	-	-
mg/kg/day	8210151	N-Y	1.036	6.5	T	0	0	0	N	1+	0-1	0-1	0-1	Few	-	-	-
	8210152	C-Y	1.033	6.5	T	0	0	0	N	0	2-3	0-1	2-3	Few	1+	-	-
	8210153	C-Y	1.030	6.0	0	0	0	0	N	0	3-4	0-2	0-1	Few	-	-	-
	8210154	N-Y	1.031	7.0	0	0	0	0	N	1+	2-3	0-1	0-1	Few	1+	-	2-3 T. Phos
	8210155	C-Y	1.021	8.5	0	0	0	0	N	T-N	0-1	1-2	0-1	Few	-	-	-
	8210157	C-Y	1.028	6.0	0	0	0	0	N	1+	1-2	Rare	Rare	Few	Few	-	-
	8210158	C-LY	1.033	6.0	0	0	0	0	N	0	0-1	1-2	0-1	Few	-	-	-

[a]Analysis of Group 4 animals possible for nine animals only due to death of all other animals.

160091

APPENDIX 6 (Continued)

INDIVIDUAL URINALYSIS DATA

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

WEEK 13 FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	APPEAR	SP. GR.	pH	PROT	GLUC	KET	BILI	OCCULT BLOOD	MICROSCOPIC FINDINGS WBC	RBC	EPITH	BACT	AMORPH	CASTS	CRYSTALS	YEAST
1	8210020	LY-H	1.072	6.5	0	0	0	0	T	Rare	-	Rare	-	Few	-	-	-
0	8210021	LY-H	1.091	7.0	0	0	0	0	T	0-1	-	0-1	Few	Few	-	-	2-8
mg/kg/day	8210022	LY-H	1.029	7.5	0	0	0	0	0	-	-	Rare	-	Few	-	-	-
	8210023	LY-C	1.022	7.5	0	0	0	0	0	0-1	-	Rare	-	Few	-	-	-
	8210024	LY-C	1.032	6.5	T	0	0	0	0	Rare	-	Rare	-	Few	-	0-1 T. Phos	-
	8210025	LY-H	1.013	8.0	0	0	0	0	T	Rare	-	-	4+	Few	-	-	-
	8210026	LY-C	1.008	7.5	0	0	0	0	0	Rare	-	Rare	2+	Few	-	-	-
	8210027	LY-C	1.010	8.0	0	0	0	0	0	Rare	10-15	Rare	2+	Few	-	-	-
	8210028	LY-C	1.010	7.5	0	0	0	0	0	Rare	Rare	Rare	1+	Few	-	-	Few
	8210029	LY-H	1.009	8.0	0	0	0	0	0	0-1	-	-	Few	3+	-	-	-
2	8210061	LY-C	1.013	7.0	0	0	0	0	0	Rare	-	Rare	Few	Few	-	-	-
100	8210062	LY-H	1.029	6.0	0	0	0	0	T	0-1	Rare	0-1	-	Few	-	-	-
mg/kg/day	8210063	LY-CL	1.015	7.0	0	0	0	0	T	0-1	-	0-1	2+	Few	-	-	-
	8210064	LY-C	1.022	7.0	0	0	0	0	0	-	-	Rare	-	Few	-	-	-
	8210065	LY-H	1.022	7.0	0	0	0	0	0	Rare	-	-	Few	Few	-	-	-
	8210066	LY-C	1.010	7.0	0	0	0	0	0	Rare	-	-	1+	Few	-	-	0-3
	8210067	LY-C	1.024	6.5	0	0	0	0	T	Rare	0-3	Rare	Few	Few	-	-	-
	8210068	LY-H	1.020	6.5	0	0	0	0	T	Rare	0-2	Rare	Few	Few	-	-	-
	8210069	LY-H	1.025	7.0	0	0	0	0	0	Rare	-	-	Few	Few	-	-	-
	8210070	LY-H	1.028	8.0	0	0	0	0	0	-	-	Rare	-	Few	-	-	-
3	8210101	LY-H	1.007	6.5	0	0	0	0	0	-	-	-	-	Few	-	-	-
300	8210102	LY-H	1.018	8.0	0	0	0	0	0	-	-	Rare	-	Few	-	0-4 T. Phos	-
mg/kg/day	8210103	LY-H	1.028	6.5	1+	0	0	0	T	0-1	0-2	Rare	-	Few	-	-	-
	8210104	LY-H	1.021	8.0	0	0	0	0	0	-	-	-	-	Few	-	-	-
	8210105	LY-H	1.010	6.5	0	0	0	0	0	0-1	-	0-1	1+	Few	-	-	-
	8210106	LY-H	1.020	7.0	0	0	0	0	0	0-2	0-2	Rare	Few	Few	-	-	-
	8210107	LY-H	1.015	6.5	0	0	0	0	0	-	-	Rare	-	Few	-	-	-
	8210108	LY-H	1.016	7.0	0	0	0	0	0	Rare	Rare	Rare	Few	Few	-	-	-
	8210109	LY-C	1.011	7.5	0	0	0	0	0	0-1	-	Rare	Few	Few	-	-	-
	8210110	LY-CL	1.016	8.0	0	0	0	0	T	2-6	0-1	1-4	Few	Few	-	-	-
4	8210152	LY-H	1.020	6.0	0	0	0	0	0	0-1	-	0-1	Few	Few	-	-	-
900	8210153	LY-C	1.014	6.5	0	0	0	0	0	Rare	-	-	Few	Few	-	-	-
mg/kg/day																	

260092

APPENDIX 7

INDIVIDUAL GROSS NECROPSY FINDINGS - DEATHS AND MORIBUND SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION OF PET 700811 IN RATS MALES[a]

	GROUP 3								GROUP 4							
ANIMAL NUMBER	8 2 1 0 0 8 0	8 2 1 0 0 8 1	8 2 1 0 0 8 2	8 2 1 0 0 8 3	8 2 1 0 0 8 4	8 2 1 0 0 8 5	8 2 1 0 0 9 1	8 2 1 0 0 9 4	8 2 1 0 1 2 1	8 2 1 0 1 2 3	8 2 1 0 1 2 4	8 2 1 0 1 2 5	8 2 1 0 1 2 7	8 2 1 0 1 3 0	8 2 1 0 1 3 5	8 2 1 0 1 3 6
NO GROSS LESIONS				X	X		X							X		
TISSUE AND OBSERVATION																
BRAIN																
Swollen, outer surface dull pinkish congested															X	
Swollen and red																X
EYE																
Opaque						X										
Right eye damaged (during necropsy)													X			
LIVER																
Mottled			X								X	X	X			
LUNG																
Bright red		X														
Mottled									X						X	
Pale										X						

[a]No deaths or moribund sacrifices occurred in Groups 1 and 2.

000093

APPENDIX 7 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - DEATHS AND MORIBUND SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
MALES

	GROUP 3								GROUP 4							
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
ANIMAL	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
NUMBER	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
IMPAIRED	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MORIBUND	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
AGE	8	8	8	8	8	8	9	9	2	2	2	2	2	3	3	3
LOG	0	1	2	3	4	5	1	4	1	3	4	5	7	0	5	6
TISSUE AND OBSERVATION																
MANDIBULAR LYMPH NODE																
Reddened												X				
STOMACH																
A few 0.1 to 0.2 cm black foci on glandular mucosa		X														
Interior wall multiple dark foci																X
TESTIS																
Soft											X					
THYMUS																
Reddened			X													
THYROID																
Reddened											X					
URINARY BLADDER																
Distended with red tinged fluid; a few irregular scattered reddened areas on mucosa (0.2 - 0.4 cm); appeared hemorrhagic	X															
Contained red tinged fluid; serosa reddened; two pinpoint red foci on mucosa; contained cystic calculi					X											
Filled with red tinged fluid														X		

000094

APPENDIX 7 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - DEATHS AND MORIBUND SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

		GROUP																											
		1	2		3					4																			
		8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
A	N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
N	U	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M	B	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
A	E	2	6	0	0	0	0	1	1	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5
L	R	1	0	1	0	1	3	7	1	7	9	0	1	2	3	4	5	6	7	8	9	0	1	4	5	6	7	8	9
NO GROSS LESIONS					X	X						X	X											X	X				X
TISSUE AND OBSERVATION																													
ADRENAL																													
Both 2x normal size												X																	
Red and enlarged																					X								
BRAIN																													
Meninges reddened								X									X				X								
Streaks of red throughout											X																		
Swollen, congested, and dull pink															X														
Slightly swollen																	X	X	X		X				X				
Red																			X										
Slightly congested																										X			
EYE																													
Right opaque				X																									
INTESTINE																													
Filled or distended with gas												X			X					X									

000095

APPENDIX 7 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - DEATHS AND MORIBUND SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

	GROUP																													
	1	2		3							4																			
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
ANUMBER	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
NUTRITION	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IMPACTION	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MBAE	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ALER	2	6	6	0	0	0	0	1	1	1	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5	5
LR	1	0	1	0	1	3	7	1	7	9	0	1	2	3	4	5	6	7	8	9	0	1	4	5	6	7	8	9		
TISSUE AND OBSERVATION																														
KIDNEY																														
Left, brown spots																				X										
LIVER																														
White pinpoint focus on right median lobe	X																													
Raised nodules on right and left median lobe												X																		
Several white foci on right and left median lobe																		X												
Mottled with brown spots 0.2 x 0.1 cm																				X										
Mottled																											X			
LUNG																														
Spongy																											X			
Pale			X																		X									
Failed to collapse, spongy and mottled							X																							
Mottled								X	X																					
Left, reduced and firm														X																
Mottled, dark red, and pink												X																		
Left, dark red																		X												
Anterior portion purplish and slightly firm																			X											
Right apical lobe congested and firm; left lung pale, reduced, and firm																									X					

960000

APPENDIX 7 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - DEATHS AND MORIBUND SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

		GROUP																														
		1	2		3							4																				
		8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
A	N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
N	U	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M	B	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
A	E	2	6	6	0	0	0	0	1	1	1	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5	5
L	R	1	0	1	0	1	3	7	1	7	9	0	1	2	3	4	5	6	7	8	9	0	1	4	5	6	7	8	9			
TISSUE AND OBSERVATION																																
OVARY																																
Cyst on left ovary																							X									
Clear cyst on left ovary, 0.1 cm																													X			
SPLEEN																																
Dark black spots on end																						X										
STOMACH																																
A 1.0 x 1.0 cm dark red focus on the glandular mucosa												X																				
Two linear red foci (0.6-1.0 cm) on glandular mucosa																	X															
THYMUS																																
Reddened			X	X			X																X									
TRACHEA																																
Contained froth									X																							
URINARY BLADDER																																
Distended with blood tinged urine; suffusive hemorrhages in wall																				X												

000097

APPENDIX 8

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
MALES

GROUP 1 - 0 mg/kg/day

		8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
A	N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
N	U	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
I	M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M	B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A	E	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
L	R	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
NO GROSS LESIONS		X	X	X	X	X	X	X	X	X	X										
TISSUE AND OBSERVATION																					
LIVER																					
Large multilocular herniation of dorsal median lobe														X							
LUNG																					
Red patchy areas; white spots on both diaphragmatic lobes											X										
MANDIBULAR LYMPH NODE																					
Reddened													X			X					
THYMUS																					
Reddened and mottled											X			X							
Reddened													X		X	X	X	X	X	X	X

860000

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
MALES

	GROUP 2 - 100 mg/kg/day																		
ANIMAL	8 2 1 0 0 4 0	8 2 1 0 0 4 1	8 2 1 0 0 4 2	8 2 1 0 0 4 3	8 2 1 0 0 4 4	8 2 1 0 0 4 5	8 2 1 0 0 4 6	8 2 1 0 0 4 7	8 2 1 0 0 4 8	8 2 1 0 0 4 9	8 2 1 0 0 5 0	8 2 1 0 0 5 1	8 2 1 0 0 5 2	8 2 1 0 0 5 3	8 2 1 0 0 5 4	8 2 1 0 0 5 5	8 2 1 0 0 5 6	8 2 1 0 0 5 7	8 2 1 0 0 5 8	8 2 1 0 0 5 9
NO GROSS LESIONS	X	X		X		X		X		X									X
TISSUE AND OBSERVATION																			
MANDIBULAR LYMPH NODES																			
Red or reddened								X							X	X	X		
MEDIASTINAL LYMPH NODE																			
Slightly enlarged		X								X			X						X
LIVER																			
Linear white streak approximately 2 cm long on left lateral lobe							X												
LUNG																			
A few <1 mm white foci on both diaphragmatic lobes		X																	
Anterior dorsal surface of left lung slightly firm and pale				X															
Moderate multifocal mottling of of all lobes					X														
Few pinpoint white spots all lobes										X									X
THYMUS																			
Reddened												X	X	X	X	X	X	Y	

660000

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
MALES

	GROUP 3 - 300 mg/kg/day											
	8	8	8	8	8	8	8	8	8	8	8	8
A N	2	2	2	2	2	2	2	2	2	2	2	2
N U	1	1	1	1	1	1	1	1	1	1	1	1
I M	0	0	0	0	0	0	0	0	0	0	0	0
M B	0	0	0	0	0	0	0	0	0	0	0	0
A E	8	8	8	8	9	9	9	9	9	9	9	9
L R	6	7	8	9	0	2	3	5	6	7	8	9
NO GROSS LESIONS			X			X	X	X	X			
TISSUE AND OBSERVATION												
BRONCHIAL LYMPH NODE												
Slightly enlarged				X								
EYE												
Right smaller than normal	X											
Hardarian gland right eye, enlarged and dark		X										
KIDNEY												
Slightly enlarged, dark, and mottled				X								
LUNG												
A few <1 mm white foci on both diaphragmatic lobes		X		X								
All lobes mottled					X							
Pinpoint white spots, all lobes; distal portion of right diaphragmatic lobe slightly mottled										X		
Pinpoint white spots on all lobes											X	
MANDIBULAR LYMPH NODE												
Slightly reddened												X
MEDIASTINAL LYMPH NODE												
Slightly enlarged					X					X		
THYMUS												
Reddened												X

000100

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
MALES

	GROUP 4 - 900 mg/kg/day										
	8	8	8	8	8	8	8	8	8	8	8
ANIMAL	2	2	2	2	2	2	2	2	2	2	2
NUMBER	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	0
	1	1	1	1	1	1	1	1	1	1	1
	2	2	2	2	2	3	3	3	3	3	3
	0	2	6	8	9	1	2	3	4	7	8	9
NO GROSS LESIONS		X	X	X	X		X			X	X
TISSUE AND OBSERVATION											
EPIDIDYMIS											
3.0 mm white spot on right side						X					
Left, small nodule								X			
LIVER											
Enlarged							X				
LUNG											
Left anterior lobe reddened and firm	X										
THYMUS											
Reddened							X		X		

001001

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

	GROUP 1 - 0 mg/kg/day																	
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
A N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
N U	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
I M	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A E	2	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3
L R	0	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
NO GROSS LESIONS	X	X			X	X						X						
TISSUE AND OBSERVATION																		
EYE																		
Right, enlarged, protruding, firm and filled with organized blood clot							X											
Conjunctival exudate, right eye									X									
LUNG																		
Few pinpoint white spots on both diaphragmatic lobes										X								
MANDIBULAR LYMPH NODE																		
Slightly red or reddened			X							X					X			
OVARY																		
Cystic, left				X										X				
SPLEEN																		
Enlarged, engorged with blood								X										
THYMUS																		
Reddened										X	X		X		X		X	X	X
UTERUS																		
Thin walled and distended with clear fluid							X		X									

000102

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

	GROUP 2 - 100 mg/kg/day																
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
ANIMAL	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7
	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
NO GROSS LESIONS		X	X	X	X	X		X			X	X		X				
TISSUE AND OBSERVATION																		
LIVER																		
Diffusely pale, slight	X																	
Herniated									X									
LUNG																		
Pinpoint white foci on all lobes															X			
MANDIBULAR LYMPH NODE																		
Slightly reddened or reddened										X					X		X	
MEDIASTINAL LYMPH NODE																		
Slightly enlarged									X									
OVARY																		
Left, 0.5 cm cyst													X					
PANCREAS																		
A 1.5 mm nodule anterior; red with pale center							X											
THYMUS																		
Reddened										X					X	X	X	X

000103

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

	GROUP 3 - 300 mg/kg/d										GROUP 4[a]	
	8	8	8	8	8	8	8	8	8	8	8	8
ANIMAL	2	2	2	2	2	2	2	2	2	2	2	2
NUMBER	1	1	1	1	1	1	1	1	1	1	1	1
IMMB	0	0	0	0	0	0	0	0	0	0	0	0
MBAE	1	1	1	1	1	1	1	1	1	1	1	1
AELR	0	0	0	0	0	0	1	1	1	1	1	1
	2	4	5	6	8	9	0	2	3	4	5	6	8	2	3
NO GROSS LESIONS		X			X		X				X	X			
TISSUE AND OBSERVATION															
MANDIBULAR LYMPH NODE															
Enlarged											X				
Reddened						X									
MEDIASTINAL LYMPH NODE															
Enlarged or slightly enlarged			X							X					
LIVER															
Diffusely pale, moderate	X														
Herniation on medial lobe, 3.4 in diameter										X					
Herniation of liver through diaphragm															X
LUNG															
Left diaphragmatic lobe mottled	X														
Multiple white spots 1 mm on all lobes			X												
Mottled, bronchioles distended				X											
Anterior dorsal surface of left lung inflated														X	
Pinpoint white spots on azygous lobe															X

aDose level, 900 mg/kg/day.

0001104

APPENDIX 8 (Continued)

INDIVIDUAL GROSS NECROPSY FINDINGS - TERMINAL SACRIFICES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 IN RATS
FEMALES

	GROUP 3 - 300 mg/kg/day												GROUP 4[a]	
	9	8	8	8	8	8	8	8	8	8	8	8	8	8
ANIMAL	2	2	2	2	2	2	2	2	2	2	2	2	2	2
NUMBER	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	1	1	1	1	1	1	5	5
	2	4	5	6	8	9	0	2	3	4	5	6	2	3
TISSUE AND OBSERVATION														
OVARY														
Left, 0.5 cm cyst								X						
Left, 1.5 cm cyst									X					
PANCREATIC LYMPH NODE														
Reddened				X										
THYMUS														
Reddened										X	X			
UTERUS														
Enlarged, thin walled and filled with clear fluid			X											

[a]Dose level, 900 mg/kg/day.

000105

APPENDIX 9

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	LUNG ABS (g)	LUNG REL (%)	KIDNEY[a] ABS (g)	KIDNEY[a] REL (%)	ADRENAL[a] ABS (g)	ADRENAL[a] REL (%)	LIVER ABS (g)	LIVER REL (%)	HEART ABS (g)	HEART REL (%)
1	8210000	268	1.500	0.560	2.060	0.769	0.058	0.022	8.360	3.119	1.080	0.403
0	8210001	278	1.260	0.453	2.245	0.808	0.060	0.022	8.372	3.012	1.119	0.403
mg/kg/day	8210002	254	1.334	0.526	2.039	0.803	0.080	0.031	7.394	2.911	0.984	0.387
	8210003	240	1.328	0.511	2.069	0.796	0.107	0.041	7.413	2.928	0.975	0.375
	8210004	242	1.281	0.519	1.911	0.774	0.067	0.027	6.530	2.644	0.845	0.342
	8210005	252	1.347	0.535	2.085	0.827	0.104	0.041	7.017	2.785	0.914	0.363
	8210006	240	1.197	0.499	1.858	0.774	0.391	0.163	7.251	3.021	0.962	0.401
	8210007	267	1.246	0.467	2.362	0.885	0.071	0.027	8.157	3.055	0.902	0.338
	8210008	249	1.068	0.429	2.057	0.826	0.106	0.043	7.334	2.946	0.927	0.372
	8210009	282	1.262	0.448	2.038	0.723	0.073	0.026	7.927	2.811	1.029	0.365
	8210010	263	1.426	0.542	2.188	0.832	0.123	0.047	7.838	2.980	0.950	0.361
	8210011	275	1.195	0.435	2.124	0.772	0.074	0.027	7.777	2.828	0.564	0.205
	8210012	338	1.356	0.401	2.444	0.729	0.377	0.112	9.963	2.948	1.135	0.336
	8210013	269	1.352	0.503	2.330	0.906	0.100	0.037	8.127	3.021	1.067	0.397
	8210014	272	1.533	0.564	2.333	0.858	0.057	0.021	7.757	2.852	1.076	0.396
	8210015	309	1.488	0.482	2.465	0.798	0.179	0.058	9.460	3.061	1.044	0.339
	8210016	304	1.540	0.507	2.518	0.828	0.170	0.056	9.538	3.138	1.064	0.350
	8210017	250	1.357	0.543	2.257	0.903	0.062	0.025	8.179	3.272	0.876	0.350
	8210018	280	1.232	0.440	2.204	0.787	0.062	0.022	8.578	3.064	0.943	0.337
	8210019	292	1.232	0.422	2.543	0.871	0.062	0.021	8.495	2.909	1.000	0.342
	MEAN	272	1.327	0.489	2.213	0.813	0.119	0.043	8.083	2.965	0.973	0.358
	S.D.	24	0.124	0.049	0.204	0.052	0.097	0.035	0.854	0.142	0.126	0.043
	N	20	20	20	20	20	20	20	20	20	20	20
2	8210040	275	1.226	0.446	2.324	0.845	0.044	0.016	8.784	3.194	0.944	0.343
100	8210041	280	1.380	0.493	2.270	0.811	0.208	0.074	8.547	3.053	1.074	0.384
mg/kg/day	8210042	222	1.132	0.510	1.651	0.744	0.087	0.039	6.537	2.945	0.793	0.357
	8210043	295	1.352	0.458	2.360	0.800	0.103	0.035	8.907	3.019	0.993	0.337
	8210044	273	1.684	0.617	2.094	0.768	0.092	0.034	8.287	3.036	1.033	0.378
	8210045	266	1.369	0.515	2.196	0.824	0.100	0.038	7.998	3.007	1.015	0.382
	8210046	260	1.204	0.463	1.951	0.750	0.131	0.050	7.587	2.918	0.932	0.358
	8210047	243	1.339	0.551	2.178	0.896	0.090	0.037	7.008	2.884	0.961	0.395
	8210048	278	1.499	0.539	2.323	0.836	0.068	0.024	8.560	3.079	1.129	0.406
	8210049	274	1.381	0.504	2.342	0.855	0.125	0.046	8.083	2.950	1.002	0.366
	8210050	271	1.333	0.492	2.497	0.921	0.156	0.058	8.829	3.258	0.917	0.338
	8210051	283	1.389	0.491	2.377	0.840	0.240	0.085	8.363	2.955	0.995	0.352
	8210052	284	1.459	0.510	2.591	0.904	0.138	0.048	8.977	3.139	1.002	0.350
	8210053	276	1.383	0.501	2.321	0.841	0.068	0.025	8.474	3.070	1.046	0.379
	8210054	265	1.214	0.458	1.888	0.712	0.054	0.020	8.277	3.123	0.881	0.332
	8210055	282	1.364	0.484	2.339	0.829	0.127	0.045	8.909	3.159	1.120	0.397
	8210056	285	1.311	0.460	2.063	0.724	0.074	0.026	8.732	3.064	0.954	0.335
	8210057	265	1.318	0.497	2.343	0.884	0.098	0.037	8.401	3.170	1.021	0.385
	8210058	230	1.163	0.506	2.104	0.915	0.114	0.050	8.345	3.628	0.823	0.358
	8210059	270	1.143	0.423	2.178	0.807	0.064	0.024	8.027	2.973	1.020	0.378
	MEAN	269	1.332	0.496	2.220	0.825	0.109	0.041	8.282	3.081 S+	0.983	0.366
	S.D.	18	0.131	0.042	0.218	0.062	0.049	0.017	0.631	0.163	0.086	0.023
	N	20	20	20	20	20	20	20	20	20	20	20

NOTE: All tissues weighed fresh except where noted.
[a] = Total weight of paired organs.
S+ = Statistically significantly higher than control at p≤0.05.

000106

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES

GROUP NO. / DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	LUNG ABS (g)	LUNG REL (%)	KIDNEY[a] ABS (g)	KIDNEY[a] REL (%)	ADRENAL[a] ABS (g)	ADRENAL[a] REL (%)	LIVER ABS (g)	LIVER REL (%)	HEART ABS (g)	HEART REL (%)
3 300 mg/kg/day	8210086	250	1.220	0.491	1.987	0.795	0.121	0.048	8.575	3.430	0.950	0.380
	8210087	252	1.348	0.535	2.142	0.850	0.140	0.056	7.778	3.087	0.884	0.351
	8210088	231	1.072	0.464	1.954	0.846	0.053	0.023	7.277	3.150	0.972	0.429
	8210089	230	1.440	0.626	1.770	0.770	0.133	0.058	7.384	3.212	1.334	0.580
	8210090	229	1.492	0.652	2.026	0.885	0.124	0.054	8.074	3.525	0.883	0.386
	8210092	255	1.364	0.535	1.897	0.744	0.075	0.029	9.288	3.642	1.071	0.420
	8210093	247	1.301	0.527	2.133	0.864	0.066	0.027	8.444	3.508	0.965	0.391
	8210095	251	1.385	0.552	2.264	0.902	0.135	0.054	10.113	4.029	0.957	0.381
	8210096	229	1.181	0.516	2.096	0.915	0.101	0.044	9.325	4.072	0.844	0.369
	8210097	219	1.339	0.611	1.991	0.909	0.103	0.047	7.718	3.524	0.846	0.375
	8210098	217	1.294	0.596	1.898	0.875	0.121	0.056	8.174	3.767	0.858	0.395
	8210099	248	1.107	0.446	2.009	0.810	0.069	0.028	9.718	3.919	0.852	0.344
	MEAN	238 S-	1.298	0.547 S+	2.016 S-	0.848	0.103	0.044	8.524	3.580 S+	0.972	0.409 S+
	S.D.	14	0.130	0.065	0.129	0.055	0.030	0.013	0.912	0.322	0.171	0.085
	N	12	12	12	12	12	12	12	12	12	12	12
4 900 mg/kg/day	8210120	201	0.961	0.478	1.805	0.898	0.077	0.038	9.102	4.528	0.802	0.399
	8210122	214	1.208	0.564	1.995	0.932	0.097	0.045	8.974	4.194	0.818	0.382
	8210126	180	1.201	0.667	1.554	0.863	0.065	0.036	7.709	4.283	0.788	0.438
	8210128	184	1.136	0.617	1.949	1.059	0.098	0.053	9.344	5.078	0.810	0.440
	8210129	180	1.179	0.655	1.943	1.079	0.122	0.068	8.296	4.609	0.844	0.469
	8210131	205	1.152	0.562	2.064	1.008	0.130	0.063	10.310	5.033	0.904	0.441
	8210132	195	1.135	0.582	2.058	1.055	0.077	0.039	9.349	4.805	0.982	0.504
	8210133	180	1.154	0.641	2.104	1.169	0.033	0.018	10.403	5.824	0.834	0.463
	8210134	201	1.639	0.815	2.435	1.210	0.061	0.030	10.217	5.083	1.774	0.883
	8210137	226	1.187	0.525	2.137	0.946	0.167	0.074	10.799	4.778	0.871	0.385
	8210138	180	1.002	0.557	2.057	1.143	0.047	0.026	9.082	5.044	0.772	0.429
	8210139	231	1.083	0.469	1.921	0.832	0.066	0.029	12.461	5.394	0.794	0.344
	MEAN	198 S-	1.170 S-	0.594 S+	2.002 S-	1.016 S+	0.087	0.043	9.480 S+	4.888 S+	0.916	0.465 S+
	S.D.	18	0.167	0.094	0.208	0.124	0.038	0.018	1.262	0.460	0.276	0.139
	N	12	12	12	12	12	12	12	12	12	12	12

NOTE: All tissues weighed fresh except where noted.

[a] = Total weight of paired organs.

S- = Statistically significantly lower than control at $p \leq 0.05$.

S+ = Statistically significantly higher than control at $p \leq 0.05$.

0001107

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	BRAIN ABS (g)	BRAIN REL (%)	THYROID/PARA [a,b] ABS (g)	THYROID/PARA [a,b] REL (%)	SPLEEN ABS (g)	SPLEEN REL (%)	THYMUS ABS (g)	THYMUS REL (%)	TESTIS/EPID [a] ABS (g)	TESTIS/EPID [a] REL (%)
1	8210000	268	1.730	0.646	0.014	0.005	0.750	0.280	0.200	0.075	4.040	1.507
0	8210001	278	1.934	0.696	0.015	0.005	0.674	0.242	0.169	0.061	3.961	1.425
mg/kg/day	8210002	254	1.751	0.689	0.016	0.006	0.624	0.246	0.196	0.077	3.970	1.563
	8210003	260	1.963	0.755	0.005	0.002	0.624	0.240	1.990	0.765	3.944	1.525
	8210004	247	1.691	0.685	0.018	0.007	0.612	0.248	0.224	0.091	4.135	1.674
	8210005	252	1.744	0.692	0.016	0.006	0.726	0.288	0.206	0.082	4.020	1.595
	8210006	240	1.790	0.746	0.016	0.007	0.667	0.278	0.211	0.088	4.220	1.758
	8210007	267	1.777	0.666	0.016	0.006	0.599	0.224	0.152	0.057	3.956	1.482
	8210008	249	1.825	0.733	0.022	0.009	0.597	0.240	0.217	0.087	3.337	1.340
	8210009	282	2.030	0.720	0.027	0.010	0.782	0.277	0.152	0.054	4.204	1.491
	8210010	263	1.847	0.702	0.020	0.008	0.653	0.248	0.238	0.090	4.041	1.537
	8210011	275	1.736	0.631	0.021	0.008	0.603	0.219	0.329	0.120	4.224	1.536
	8210012	338	1.795	0.531	0.027	0.008	0.670	0.198	0.337	0.100	4.450	1.317
	8210013	269	1.824	0.678	0.023	0.009	0.536	0.199	0.345	0.128	4.542	1.688
	8210014	272	1.878	0.690	0.020	0.007	0.544	0.200	0.263	0.097	4.366	1.605
	8210015	309	2.015	0.652	0.023	0.007	0.640	0.207	0.212	0.069	4.099	1.327
	8210016	304	1.981	0.652	0.026	0.009	0.689	0.227	0.234	0.078	4.200	1.382
	8210017	250	1.806	0.722	0.023	0.009	0.537	0.215	0.222	0.089	4.017	1.607
	8210018	280	1.864	0.666	0.024	0.009	0.607	0.217	0.192	0.069	4.184	1.494
	8210019	292	1.858	0.636	0.018	0.006	0.533	0.183	0.228	0.078	3.967	1.359
	MEAN	272	1.842	0.679	0.020	0.007	0.633	0.234	0.316	0.118	4.095	1.511
	S.D.	24	0.099	0.050	0.005	0.002	0.070	0.030	0.398	0.154	0.245	0.125
	N	20	20	20	20	20	20	20	20	20	20	20
2	8210040	275	1.832	0.666	0.017	0.006	0.660	0.240	0.147	0.053	4.367	1.588
100	8210041	280	1.812	0.647	0.022	0.008	0.529	0.189	0.286	0.102	4.308	1.539
mg/kg/day	8210042	222	1.724	0.777	0.028	0.013	0.733	0.330	0.188	0.085	3.767	1.697
	8210043	295	1.986	0.673	0.021	0.007	0.693	0.235	0.267	0.091	4.365	1.480
	8210044	273	1.793	0.657	0.051	0.008	0.677	0.248	0.241	0.088	4.157	1.523
	8210045	266	1.810	0.680	0.021	0.008	0.627	0.236	0.204	0.077	4.204	1.580
	8210046	260	1.814	0.698	0.020	0.008	0.733	0.282	0.212	0.082	4.141	1.593
	8210047	243	1.779	0.732	0.020	0.008	0.675	0.278	0.173	0.071	3.891	1.601
	8210048	278	1.747	0.628	0.023	0.008	0.701	0.252	0.197	0.071	4.267	1.535
	8210049	274	1.820	0.664	0.019	0.007	0.754	0.275	0.253	0.092	4.355	1.589
	8210050	271	1.948	0.719	0.024	0.009	0.616	0.227	2.700	0.996	4.290	1.583
	8210051	283	1.818	0.642	0.023	0.008	0.608	0.215	0.230	0.081	4.256	1.504
	8210052	286	1.928	0.674	0.029	0.010	0.670	0.234	0.266	0.093	4.232	1.480
	8210053	276	1.865	0.676	0.019	0.007	0.564	0.204	0.333	0.121	4.364	1.581
	8210054	265	1.776	0.670	0.022	0.008	0.616	0.232	0.229	0.086	4.028	1.520
	8210055	282	1.956	0.694	0.022	0.008	0.637	0.226	0.229	0.081	4.012	1.423
	8210056	285	1.903	0.668	0.021	0.007	0.683	0.240	0.196	0.069	4.184	1.468
	8210057	265	1.935	0.730	0.019	0.007	0.651	0.246	0.225	0.085	4.318	1.629
	8210058	230	1.767	0.768	0.023	0.010	0.455	0.198	0.175	0.076	3.837	1.668
	8210059	270	1.880	0.696	0.023	0.009	0.564	0.209	0.249	0.092	4.509	1.670
	MEAN	269	1.845	0.688	0.022	0.008 S+	0.642	0.240	0.350	0.130	4.193	1.563
	S.D.	18	0.076	0.040	0.003	0.001	0.074	0.033	0.555	0.204	0.196	0.073
	N	20	20	20	20	20	20	20	20	20	20	20

NOTE: All tissues weighed fresh except where noted.
[a] = Total weight of paired organs.
[b] = Fixed weight.
S+ = Statistically significantly higher than control at p≤0.05.

000108

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

MALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	BRAIN ABS (g)	BRAIN REL (%)	THYROID/PARA[a,b] ABS (g)	THYROID/PARA[a,b] REL (%)	SPLEEN ABS (g)	SPLEEN REL (%)	THYMUS ABS (g)	THYMUS REL (%)	TESTIS/EPID[a] ABS (g)	TESTIS/EPID[a] REL (%)
3	8210086	250	1.953	0.781	0.018	0.007	0.666	0.266	0.198	0.079	3.988	1.595
300	8210087	252	1.932	0.767	0.021	0.008	0.649	0.258	0.221	0.088	3.938	1.563
mg/kg/day	8210088	231	1.699	0.735	0.016	0.007	0.573	0.248	0.120	0.052	3.753	1.625
	8210089	230	1.740	0.843	0.020	0.009	0.642	0.279	0.159	0.069	3.949	1.726
	8210090	229	1.739	0.759	0.017	0.008	0.626	0.273	0.181	0.079	3.968	1.733
	8210092	255	1.712	0.671	0.018	0.007	0.667	0.262	0.239	0.094	3.898	1.529
	8210093	247	1.894	0.767	0.019	0.008	0.754	0.305	0.222	0.090	3.357	1.359
	8210095	251	1.758	0.700	0.020	0.008	0.618	0.246	0.224	0.089	4.090	1.629
	8210096	229	1.811	0.791	0.017	0.007	0.587	0.256	0.190	0.083	3.873	1.691
	8210097	219	1.925	0.879	0.018	0.008	0.668	0.305	0.201	0.092	3.756	1.715
	8210098	217	1.745	0.804	0.015	0.007	0.475	0.219	0.212	0.098	3.509	1.617
	8210099	248	1.778	0.717	0.019	0.008	0.438	0.177	0.355	0.143	3.534	1.425
	MEAN	238 S-	1.824	0.768 S+	0.018	0.008	0.614	0.258 S+	0.210	0.088	3.803 S-	1.601
	S.D.	14	0.098	0.059	0.002	0.001	0.087	0.035	0.056	0.021	0.227	0.118
	N	12	12	12	12	12	12	12	12	12	12	12
4	8210121	201	1.750	0.871	0.021	0.010	0.518	0.258	0.183	0.091	1.470	0.731
900	8210122	214	1.766	0.825	0.020	0.009	0.645	0.301	0.118	0.055	2.113	0.987
mg/kg/day	8210126	180	1.587	0.882	0.025	0.014	0.469	0.261	0.095	0.053	1.407	0.782
	8210128	184	1.622	0.882	0.025	0.014	0.453	0.246	0.151	0.082	1.674	0.971
	8210129	180	1.429	0.794	0.023	0.013	0.704	0.391	0.144	0.081	1.786	0.992
	8210131	205	1.642	0.801	0.020	0.010	0.608	0.297	0.164	0.080	1.955	0.954
	8210132	195	1.652	0.847	0.022	0.011	0.651	0.334	0.216	0.111	1.871	0.959
	8210133	180	1.644	0.913	0.022	0.012	0.472	0.262	0.111	0.062	1.888	1.049
	8210134	201	1.580	0.786	0.020	0.010	0.544	0.271	0.123	0.061	2.027	1.008
	8210137	226	1.772	0.784	0.027	0.012	0.549	0.243	0.192	0.085	2.077	0.919
	8210138	180	1.441	0.801	0.020	0.011	0.422	0.234	0.120	0.067	1.588	0.882
	8210139	231	1.671	0.723	0.014	0.006	0.316	0.137	0.159	0.069	2.274	0.984
	MEAN	198 S-	1.630 S-	0.826 S+	0.022	0.011 S+	0.529 S-	0.270 S+	0.148	0.075	1.846 S-	0.931 S-
	S.D.	18	0.111	0.054	0.003	0.002	0.111	0.061	0.037	0.017	0.267	0.093
	N	12	12	12	12	12	12	12	12	12	12	12

NOTE: All tissues weighed fresh except where noted.

[a] = Total weight of paired organs.

[b] = Fixed weight.

S- = Statistically significantly lower than control at $p \leq 0.05$.

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000109

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	LUNG ABS (g)	LUNG REL (%)	KIDNEY [a] ABS (g)	KIDNEY [a] REL (%)	ADRENAL [a] ABS (g)	ADRENAL [a] REL (%)	LIVER ABS (g)	LIVER REL (%)	HEART ABS (g)	HEART REL (%)
3	8210102	150	1.109	0.739	1.194	0.796	0.090	0.060	4.648	3.099	0.664	0.443
300	8210104	164	1.065	0.649	1.401	0.854	0.079	0.048	5.259	3.207	0.441	0.403
mg/kg/day	8210105	149	1.066	0.715	1.433	0.962	0.092	0.062	4.591	3.081	0.624	0.419
	8210106	149	1.311	0.880	1.314	0.882	0.071	0.048	4.815	3.232	0.633	0.425
	8210108	147	1.093	0.744	1.212	0.824	0.137	0.093	4.889	3.326	0.658	0.448
	8210109	140	0.839	0.599	1.160	0.829	0.065	0.046	4.637	3.312	0.671	0.479
	8210110	168	1.030	0.620	1.582	0.965	0.135	0.082	5.585	3.405	0.776	0.473
	8210112	147	0.956	0.650	1.476	1.004	0.089	0.061	5.721	3.892	0.646	0.439
	8210113	151	1.064	0.705	1.406	0.931	0.091	0.060	5.770	3.821	0.709	0.470
	8210114	141	1.051	0.745	1.320	0.936	0.102	0.072	4.598	3.261	0.568	0.403
	8210115	162	0.920	0.568	1.524	0.941	0.093	0.057	5.819	3.592	0.730	0.451
	8210114	150	1.009	0.673	1.420	0.947	0.120	0.080	5.170	3.447	0.691	0.461
	8210118	153	0.945	0.618	1.356	0.886	0.114	0.076	5.162	3.374	0.653	0.427
	MEAN	151 S-	1.035	0.686 S+	1.369	0.904 S+	0.098 S+	0.065 S+	5.129 S+	3.389 S+	0.668	0.441
	S.D.	8	0.114	0.082	0.127	0.064	0.023	0.015	0.471	0.250	0.051	0.025
	N	13	13	13	13	13	13	13	13	13	13	13
4	8210152	140	0.925	0.661	1.264	0.903	0.083	0.059	6.583	4.702	0.577	0.412
900	8210153	146	0.970	0.664	1.432	0.981	0.122	0.084	7.314	5.010	0.655	0.449
mg/kg/day	MEAN	143 S-	0.948	0.663	1.348	0.942 S+	0.103	0.071	6.949 S+	4.856 S+	0.616 S-	0.430
	S.D.	4	0.032	0.003	0.119	0.055	0.028	0.017	0.517	0.217	0.055	0.026
	N	2	2	2	2	2	2	2	2	2	2	2

NOTE: All tissues weighed fresh except where noted.

[a] = Total weight of paired organs.

S- = Statistically significantly lower than control at $p \leq 0.05$.

S+ = Statistically significantly higher than control at $p \leq 0.05$.

000110

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	LUNG ABS (g)	LUNG REL (%)	KIDNEY[a] ABS (g)	KIDNEY[a] REL (%)	ADRENAL[a] ABS (g)	ADRENAL[a] REL (%)	LIVER ABS (g)	LIVER REL (%)	HEART ABS (g)	HEART REL (%)
1 0 mg/kg/day	8210020	168	1.447	0.861	1.395	0.830	0.061	0.036	4.800	2.857	0.715	0.426
	8210022	166	1.101	0.663	1.183	0.713	0.125	0.075	4.649	2.801	0.669	0.403
	8210023	152	0.863	0.568	1.224	0.807	0.057	0.038	4.240	2.803	0.685	0.451
	8210024	155	1.104	0.714	1.493	0.965	0.061	0.039	4.342	2.802	0.773	0.499
	8210025	166	1.070	0.645	1.291	0.791	0.087	0.052	4.308	2.595	0.633	0.381
	8210026	155	1.053	0.679	1.344	0.867	0.069[b]	0.045	4.253	2.743	0.707	0.456
	8210027	153	0.918	0.600	1.313	0.858	0.141	0.092	4.733	3.093	0.671	0.439
	8210028	158	0.974	0.616	1.454	0.920	0.080	0.051	4.954	3.135	0.717	0.454
	8210029	154	0.965	0.619	1.338	0.868	0.073	0.047	4.397	2.819	0.650	0.417
	8210030	143	1.036	0.448	1.357	0.949	0.065	0.045	5.054	3.102	0.751	0.441
	8210031	161	0.823	0.511	1.369	0.850	0.082	0.051	4.618	2.868	0.619	0.384
	8210032	157	0.881	0.561	1.440	0.735	0.064	0.041	4.671	2.975	0.663	0.422
	8210033	155	0.845	0.545	1.374	0.886	0.090	0.058	4.564	2.945	0.606	0.391
	8210034	151	0.975	0.644	1.326	0.944	0.076	0.050	4.813	3.187	0.693	0.459
	8210035	167	0.945	0.566	1.301	0.779	0.045	0.027	4.718	2.825	0.710	0.425
	8210036	157	0.973	0.620	1.295	0.825	0.058	0.037	4.579	2.917	0.655	0.417
	8210037	170	1.029	0.605	1.410	0.829	0.074	0.044	4.895	2.879	0.673	0.396
	8210038	154	1.041	0.676	1.259	0.818	0.060	0.039	4.672	3.034	0.676	0.439
	8210039	145	0.762	0.462	1.440	0.873	0.067	0.041	4.559	2.743	0.683	0.414
	MEAN	159	0.991	0.621	1.345	0.845	0.079	0.050	4.660	2.926	0.682	0.428
	S.D.	6	0.147	0.085	0.081	0.060	0.023	0.015	0.224	0.162	0.042	0.031
	N	19	19	19	19	19	19	19	19	19	19	19
2 100 mg/kg/day	8210062	161	0.869	0.540	1.316	0.817	0.054	0.034	4.603	2.859	0.621	0.386
	8210063	158	1.040	0.658	1.362	0.862	0.060	0.038	4.750	3.006	0.674	0.426
	8210064	158	1.006	0.637	1.195	0.756	0.064	0.042	4.392	2.780	0.575	0.364
	8210065	154	0.826	0.536	1.337	0.863	0.071	0.050	4.278	2.778	0.735	0.477
	8210066	160	1.040	0.650	1.302	0.814	0.054	0.035	4.355	2.722	0.591	0.369
	8210067	162	0.985	0.608	1.405	0.867	0.063[b]	0.039	5.055	3.120	0.777	0.480
	8210068	170	1.147	0.675	1.414	0.833	0.093	0.055	5.114	3.008	0.723	0.425
	8210069	159	0.887	0.558	1.470	0.925	0.089	0.056	4.872	3.064	0.687	0.432
	8210070	152	1.071	0.491	1.410	0.920	0.126	0.083	4.981	3.277	0.724	0.474
	8210071	157	0.989	0.630	1.321	0.841	0.096	0.061	4.672	2.976	0.748	0.489
	8210072	160	0.862	0.539	1.333	0.833	0.080	0.050	4.815	3.009	0.705	0.441
	8210073	145	1.013	0.699	1.172	0.808	0.075	0.052	4.848	3.343	0.582	0.401
	8210074	149	0.918	0.616	1.367	0.917	0.128	0.086	4.888	3.281	0.628	0.421
	8210075	160	1.043	0.652	1.265	0.791	0.068	0.043	5.027	3.142	0.633	0.396
	8210076	165	0.814	0.493	1.302	0.838	0.081	0.049	5.110	3.097	0.625	0.379
	8210077	160	1.007	0.629	1.469	0.918	0.065	0.041	5.043	3.527	0.713	0.446
	8210078	142	0.873	0.615	1.310	0.923	0.047	0.033	4.763	3.354	0.709	0.499
	8210079	154	0.862	0.560	1.305	0.847	0.132	0.086	5.485	3.492	0.711	0.462
	MEAN	157	0.957	0.610	1.341	0.855	0.082	0.052	4.881 S+	3.113 S+	0.677	0.432
	S.D.	7	0.095	0.060	0.081	0.051	0.026	0.017	0.378	0.262	0.063	0.043
	N	18	18	18	18	18	18	18	18	18	18	18

NOTE: All tissues weighed fresh except where noted.
[a] - Total weight of paired organs.
[b] = Fixed weight; Fresh weight appeared to be in error.
S+ = Statistically significantly higher than control at $p \leq 0.05$.

0001111

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	BRAIN ABS (g)	BRAIN REL (%)	THYROID/PARA [a,b] ABS (g)	THYROID/PARA [a,b] REL (%)	SPLEEN ABS (g)	SPLEEN REL (%)	THYMUS ABS (g)	THYMUS REL (%)	OVARY [a] ABS (g)	OVARY [a] REL (%)
1	8210020	168	1.812	1.079	0.017	0.010	0.568	0.338	0.369	0.220	0.075	0.045
0	8210022	166	1.870	1.127	0.018	0.011	0.641	0.386	0.200	0.120	0.103	0.062
mg/kg/day	8210023	152	1.590	1.046	0.015	0.010	0.540	0.355	0.153	0.101	0.092	0.061
	8210024	155	1.759	1.135	0.017	0.011	0.532	0.343	0.165	0.106	0.127	0.082
	8210025	166	1.599	0.963	0.025	0.015	0.582	0.351	0.154	0.093	0.113	0.068
	8210026	155	1.772	1.143	0.019	0.012	0.544	0.345	0.216	0.139	0.097	0.063
	8210027	153	1.780	1.163	0.013	0.008	0.734	0.480	0.203	0.133	0.109	0.071
	8210028	158	1.480	0.937	0.016	0.010	0.878	0.556	0.168	0.106	0.099	0.063
	8210029	154	1.656	1.062	0.016	0.010	0.760	0.487	0.175	0.112	0.094	0.062
	8210030	163	1.746	1.071	0.018	0.011	0.468	0.287	0.273	0.167	0.182	0.112
	8210031	161	1.650	1.025	0.016	0.010	0.396	0.246	0.227	0.141	0.113	0.070
	8210032	157	1.633	1.040	0.014	0.009	0.416	0.265	0.274	0.175	0.116	0.074
	8210033	155	1.713	1.105	0.021	0.014	0.353	0.228	0.211	0.136	0.071	0.046
	8210034	151	1.779	1.178	0.014	0.009	0.439	0.291	0.232	0.154	0.169	0.112
	8210035	167	1.732	1.037	0.020	0.012	0.538	0.322	0.181	0.108	0.103	0.062
	8210036	157	1.781	1.134	0.016	0.010	0.403	0.257	0.167	0.106	0.108	0.069
	8210037	170	1.843	1.084	0.019	0.011	0.488	0.287	0.288	0.169	0.080	0.047
	8210038	154	1.624	1.055	0.026	0.017	0.398	0.258	0.173	0.112	0.094	0.061
	8210039	165	1.561	0.946	0.021	0.013	0.370	0.224	0.140	0.085	0.092	0.056
	MEAN	159	1.704	1.070	0.018	0.011	0.531	0.333	0.209	0.131	0.107	0.068
	S.D.	6	0.105	0.070	0.004	0.002	0.143	0.092	0.058	0.034	0.028	0.018
	N	19	19	19	19	19	19	19	19	19	19	19
2	8210062	161	1.532	0.952	0.015	0.009	0.553	0.343	0.189	0.117	0.086	0.053
100	8210063	158	1.779	1.126	0.018	0.011	0.558	0.353	0.163	0.103	0.114	0.072
mg/kg/day	8210064	158	1.614	1.022	0.017	0.011	0.618	0.391	0.185	0.117	0.095	0.060
	8210065	154	1.743	1.132	0.020	0.013	0.593	0.385	0.175	0.114	0.102	0.066
	8210066	160	1.771	1.107	0.013	0.008	0.605	0.378	0.185	0.116	0.128	0.080
	8210067	162	1.698	1.047	0.019	0.012	0.626	0.386	0.211	0.130	0.113	0.070
	8210068	170	1.835	1.079	0.014	0.008	0.617	0.363	0.193	0.114	0.090	0.053
	8210069	159	1.730	1.088	0.017	0.011	0.602	0.379	0.219	0.138	0.130	0.082
	8210070	152	1.735	1.141	0.014	0.009	0.597	0.393	0.205	0.135	0.072	0.047
	8210071	157	1.585	1.010	0.014	0.009	0.476	0.303	0.246	0.157	0.106	0.068
	8210072	160	1.632	1.020	0.014	0.009	0.424	0.265	0.247	0.154	0.132	0.083
	8210073	145	1.669	1.151	0.016	0.011	0.399	0.275	0.172	0.119	0.065	0.045
	8210074	149	1.686	1.132	0.014	0.009	0.409	0.274	0.252	0.169	0.155	0.104
	8210075	160	1.749	1.093	0.015	0.009	0.495	0.309	0.271	0.169	0.102	0.064
	8210076	165	1.667	1.010	0.012	0.007	0.393	0.238	0.165	0.100	0.080	0.048
	8210077	160	1.757	1.098	0.080	0.050	0.434	0.271	0.217	0.136	0.103	0.064
	8210078	142	1.643	1.157	0.012	0.008	0.336	0.237	0.174	0.123	0.107	0.075
	8210079	154	1.833	1.190	0.015	0.010	0.306	0.199	0.228	0.148	0.088	0.057
	MEAN	157	1.703	1.086	0.019	0.012	0.502	0.319	0.205	0.131	0.104	0.066
	S.D.	7	0.082	0.064	0.015	0.010	0.107	0.063	0.033	0.021	0.023	0.015
	N	18	18	18	18	18	18	18	18	18	18	18

NOTE: All tissues weighed fresh except where noted.
[a] = Total weight of paired organs.
[b] = Fixed weights.

APPENDIX 9 (Continued)

INDIVIDUAL AND MEAN ABSOLUTE AND RELATIVE ORGAN/BODY WEIGHTS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

FEMALES

GROUP NO. DOSE LEVEL	ANIMAL NUMBER	BODY WT. (g)	BRAIN ABS (g)	BRAIN REL (%)	THYROID/PARA [a,b] ABS (g)	THYROID/PARA [a,b] REL (%)	SPLEEN ABS (g)	SPLEEN REL (%)	THYMUS ABS (g)	THYMUS REL (%)	OVARY [a] ABS (g)	OVARY [a] REL (%)
3	8210102	150	1.689	1.126	0.002	0.001	0.542	0.361	0.160	0.107	0.133	0.089
300	8210104	164	1.618	0.987	0.019	0.012	0.565	0.345	0.168	0.102	0.081	0.049
mg/kg/day	8210105	149	1.811	1.215	0.017	0.011	0.617	0.415	0.196	0.132	0.069	0.046
	8210106	149	1.588	1.066	0.018	0.012	0.600	0.403	0.232	0.156	0.117	0.079
	8210108	147	1.566	1.065	0.017	0.012	0.538	0.365	0.185	0.126	0.077	0.052
	8210109	140	1.595	1.139	0.019	0.014	0.705	0.504	0.176	0.126	0.077	0.055
	8210110	164	1.724	1.051	0.022	0.013	0.579	0.353	0.210	0.150	0.099	0.060
	8210112	147	1.684	1.146	0.021	0.014	0.389	0.265	0.252	0.154	0.133	0.090
	8210113	151	1.654	1.095	0.020	0.013	0.384	0.254	0.185	0.126	0.131	0.087
	8210114	141	1.764	1.251	0.017	0.012	0.405	0.287	0.093	0.042	0.107	0.076
	8210115	162	1.344	0.842	0.021	0.013	0.440	0.272	0.204	0.145	0.124	0.077
	8210116	150	1.744	1.163	0.016	0.011	0.387	0.258	0.270	0.167	0.047	0.045
	8210118	153	1.721	1.125	0.016	0.010	0.409	0.267	0.240	0.160	0.098	0.064
	MEAN	151 S-	1.656	1.098	0.017	0.011	0.505	0.334	0.202	0.132	0.101	0.067
	S.D.	8	0.114	0.104	0.005	0.003	0.108	0.074	0.044	0.029	0.025	0.017
	N	13	13	13	13	13	13	13	13	13	13	13
4	8210152	140	1.606	1.147	0.018	0.013	0.544	0.390	0.203	0.145	0.112	0.080
900	8210153	146	1.580	1.082	0.018	0.012	0.496	0.340	0.091	0.062	0.079	0.054
mg/kg/day	MEAN	143 S-	1.593	1.115	0.018	0.013	0.521	0.365	0.147	0.104	0.096	0.067
	S.D.	4	0.018	0.046	0.000	0.000	0.035	0.034	0.079	0.058	0.023	0.018
	N	2	2	2	2	2	2	2	2	2	2	2

NOTE: All tissues weighed fresh except where noted.

a = Total weight of paired organs.

b = Fixed weight.

S- = Statistically significantly lower than control at $p \leq 0.05$.

APPENDIX 10

ANALYSIS OF DOSING SOLUTIONS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

SAMPLE GROUP	THEORETICAL VALUE (g/ml)	ACTUAL VALUE (g/ml)				DATE PREPARED AND ANALYZED
1	0.0	0.0				10-15-82
2	0.1505		0.1432			10-15-82
2	0.1505		0.1485			10-15-82
2	0.1505		0.1489			10-15-82
3	0.3339			0.3257		10-15-82
3	0.3339			0.3430		10-15-82
3	0.3339			0.3527		10-15-82
4	0.5629				0.5409	10-15-82
4	0.5629				0.5648	10-15-82
4	0.5629				0.5551	10-15-82
2	0.1505		0.1543			11-12-82
3	0.3339			0.3153		11-12-82
1	0.0	0.0				11-12-82
2	0.1505		0.1542			11-12-82
2	0.1505		0.1473			11-12-82
2	0.1505		0.1483			11-12-82
3	0.3339			0.3219		11-12-82
3	0.3339			0.3214		11-12-82
3	0.3339			0.3146		11-12-82
4	0.5629				0.5235	11-12-82
4	0.5629				0.5219	11-12-82
4	0.5629				0.5247	11-12-82
1	0.0	0.0				12-9-82
2	0.1505		0.1416			12-9-82
2	0.1505		0.1356			12-9-82
2	0.1505		0.1356			12-9-82
3	0.3339			0.3145		12-9-82
3	0.3339			0.3031		12-9-82
3	0.3339			0.3060		12-9-82
4	0.5629				0.5474	12-9-82
4	0.5629				0.5502	12-9-82
4	0.5629				0.5530	12-9-82
	MEAN:	0.0	0.1453	0.3218	0.5424	
% Variation from Theoretical:		0	-3.5	-3.6	-3.6	

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APPENDIX 11

FEED ANALYSIS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

Ralston Purina Company
Analytical Services
Checkerboard Square
St. Louis, Missouri 63188

TO RICHMOND, IN

CC RICHMOND, IND.
D.C.SHELTON, 3RS
J.R.SNYDER, 22S

LAB NO 173392 ENTERED 09/15/82 REPORTED 09/24/82 RHI 5002

CERTIFIED RODENT CHOW MEAL
LOT NUMBER SEP 10 82 2H

ASSAY	ANALYSIS	UNITS	LOW-LIMIT	HIGH-LIMIT
PROTEIN (N X 6.25)	21.5	%	20.0	
FAT (ACID HYDRO.)	5.65	%	4.50	
FIBER (CRUDE)	4.99	%		5.50
ARSENIC	0.406	PPM		1.00
CADMIUM	0.106	PPM		0.500
CALCIUM	1.01	%		
LEAD	0.221	PPM		1.50
MERCURY	LESS THAN 0.05 PPM			
PHOSPHORUS	0.795	%		
SELENIUM	0.137	PPM		

AFLATOXIN

TOTAL:LESS THAN 10 PPB

ORGANOPHOSPHATE PEST

	(PPM)		(PPM)
THIMET.....	LESS THAN 0.02	DIAZINON.....	LESS THAN 0.02
DISULFOTON.....	LESS THAN 0.02	METHYL PARATHION...	LESS THAN 0.02
MALATHION.....	0.06	PARATHION.....	LESS THAN 0.02
THIODAN.....	LESS THAN 0.02	ETHION.....	LESS THAN 0.02
TRITHION.....	LESS THAN 0.02		

PESTICIDE & PCB

	(PPM)		(PPM)
ALDRIN.....	LESS THAN 0.02	DIELDRIN.....	LESS THAN 0.02
ENDRIN.....	LESS THAN 0.02	HEPTACHLOR.....	LESS THAN 0.02
HEPTACHLOR EPOXIDE.	LESS THAN 0.02	LINDANE.....	LESS THAN 0.02

The term "Less Than" or the use of the symbol < is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" or < does not imply that traces of analyte were present. Samples submitted to Analytical Services for routine analysis will be retained for a minimum of thirty (30) days after the report of analysis is issued. Extended storage requirements must be brought to the attention of Analytical Services prior to or at the time of sample submission.

R1171K-8107

000116

Ralston Purina Company
Analytical Services
Checkerboard Square
St. Louis, Missouri 63188

RT LAB NUMBER 173392

CERTIFIED RODENT CHOW MEAL
LOT NUMBER SEP 10 82 2H

PESTICIDE & PCB (CONTINUED)

DDT.....	LESS THAN 0.02	DDE.....	LESS THAN 0.02
CHLORDANE.....	LESS THAN 0.02	PCB.....	LESS THAN 0.15

FOR ADDITIONAL INFORMATION, PLEASE CONTACT:
(1) FOR ASSAY METHODOLOGY - CHARLIE SCHROEDER 314-982-2383
(2) FOR NUTRITIONAL INTERPRETATION-DR.D.C.SHELTON 314-982-3513
(3) ALL OTHER QUESTIONS-RICHMOND, IN., MANUFACTURING PLANT 317-962-9561

SIGNED C. H. Schroeder DATE 09/24/82
BY AND FOR ANALYTICAL SERVICES

The term "Less Than" or the use of the symbol (<) is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" or (<) does not imply that traces of analyte were present. Samples submitted to Analytical Services for routine analysis will be retained for a minimum of thirty (30) days after the report of analysis is issued. Extended storage requirements must be brought to the attention of Analytical Services prior to or at the time of sample submission.

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APPENDIX 12

WATER ANALYSIS

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

analytics
P.O. Box 25249
Richmond, VA 23260

ANALYSIS REPORT

ANALYTICS NO. S0074877
GROUP NO.
ACCOUNT NO. 62901
DATE February 8, 1983

Mr. Paul Swidersky
Borriston Laboratories, Inc.
5050 Beech Place
Temple Hills, MD 20748

SAMPLE TYPE: Water

DATE RECEIVED: 11-23-82

REMARKS: P.O. 1992 - mg/L = milligrams per liter, mcg/L = micrograms per liter

Test	Result	
Fluoride	0.81	mg/L
Nitrate (as N)	0.44	mg/L
Cyanide	< 0.005	mg/L
PCB's (as AROCLOR 1242)	< 1.0	mcg/L
Chloroform	1,210	mcg/L
Bromodichloromethane	< 10	mcg/L
Chlorodibromomethane	< 10	mcg/L
Bromoform	< 10	mcg/L
Arsenic	< 0.0025	mg/L
Barium	< 0.125	mg/L
Cadmium	< 0.00025	mg/L
Chromium	< 0.00125	mg/L
Lead	< 0.000625	mg/L
Mercury	< 0.0005	mg/L
Selenium	< 0.0025	mg/L
Silver	< 0.00025	mg/L
Endrin	< 1.0	mcg/L
Lindane	< 1.0	mcg/L
Methoxychlor	< 1.0	mcg/L
Toxaphene	< 5.0	mcg/L
2,4-D	< 1.0	mcg/L
2,4,5-TP Silvex	< 1.0	mcg/L
Chlordane	< 5.0	mcg/L
Heptachlor	< 1.0	mcg/L
Heptachlor Epoxide	< 1.0	mcg/L
Malathion	< 1.0	mcg/L
Dieldrin	< 1.0	mcg/L
Total Coliforms	< 2.2	MPN/100 ml

James A. Calpin, CIH

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analytics
P.O. Box 25249
Richmond, VA 23260

ANALYSIS REPORT

ANALYTICS NO. S0079629
GROUP NO.
ACCOUNT NO. 62901
DATE March 15, 1983

Mr. Paul Swidersky
Borriston Laboratories, Inc.
9050 Beech Place
Temple Hills, MD 20748

SAMPLE TYPE: Water

DATE RECEIVED: 3-1-83

REMARKS: Repeat analysis.
mcg/L = micrograms per liter

Sample #	Chloroform Content, mcg/L
(Lab Blank)	< 5.0
2 Borriston Lab 2-23-83	39

Previous high result may have resulted in cross contamination en route or in laboratory.

James A. Calpin, CIH

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MAXIMUM ALLOWABLE LEVELS OF ORGANIC AND INORGANIC CHEMICALS[a]

INORGANIC CHEMICALS

Arsenic.....0.05 mg/l
Barium.....1 mg/l
Cadmium.....0.010 mg/l
Chromium.....0.05 mg/l
Lead.....0.05 mg/l
Mercury.....0.002 mg/l
Nitrate (as N)...10 mg/l
Selenium.....0.01 mg/l
Silver.....0.05 mg/l
Fluoride.....1.4-2.4 mg/l

ORGANIC CHEMICALS

Endrin.....0.0002 mg/l
Lindane.....0.004 mg/l
Methoxychlor.....0.1 mg/l
Toxaphene.....0.005 mg/l
2,4-D.....0.1 mg/l
2,4,5-TP Silvex.....0.01 mg/l
Heptachlor.....20 ppb
Malathion.....2.5 ppm
Dieldrin.....20 ppb
PCB's.....50 ppb
Aflatoxins..... 5 ppb
Nitrosamines.....10 ppb
Diethylstibestrol..... 1 ppb
(Estrogenic Activity)

BACTERIA

Coliforms < 1/100 ml

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[a]Current contaminants set by Primary Drinking Water Regulations, Title 40 part 141, Safe Drinking Water Act.

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APPENDIX 13

PROTOCOL ACCOUNTABILITY

THIRTEEN-WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

A. Environment:

- Protocol Section, 16.2.2: Animals will be housed in air-conditioned rooms set to maintain 21±2°C.

- Study Procedure: Temperatures ranged from 19-27°C. Exceptions to the protocol, including extent and duration, are on file as part of the raw data.

B. Environment:

- Protocol Section, 16.2.2: Animals will be housed in air-conditioned rooms set to maintain 40-60% relative humidity.

- Study Procedure: Relative humidity is not controlled at Barriston Laboratories but is recorded on a hygrothermograph. Humidity was between 20-80%. The extent and duration of departure from relative humidity requirements are on file as part of the raw data.

C. Cleaning:

- Protocol Section, 16.2.3: Drop sheets are to be changed at least 3 times/week.

- Study Procedure: The following exceptions occurred: Weeks -2 and -1, bedding was changed only once during each week; Study Weeks 5, 6, 10, and 12, bedding was changed only twice during each of these weeks.

D. Cleaning:

- Protocol Section, 16.2.3: Racks and cages to be washed at least once every 2 weeks.

- Study procedure: Racks and cages were changed only once during the study, during Week 9.

E. Contaminants

- Protocol Section, 16.4: The testing facility will assure that the diet used in this study does not contain any listed contaminants at levels greater than: aflatoxin, 5 ppb; estrogenic activity (DES eq.), 1 ppb; PCB's, 50 ppb; and nitrosamines, 10 ppb.

- Study Procedure: Estrogenic activity and nitrosamine level were not included as part of the Guaranteed Analysis provided by Analytic Services of the Ralston Purina Company. The lowest level of quantitation by Ralston Purina was aflatoxin, <10 ppb and PCB's, <150 ppb.

APPENDIX 13 (Continued)

PROTOCOL ACCOUNTABILITY

THIRTEEN-WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

F. Mortality Observations

- Protocol Section, 16.6.2: Mortality observations will be made twice daily, at least 7 hours apart weekdays, at least 4 hours on weekends and holidays.

- Study Procedure: Mortality observations were occasionally made without 7 hours expiring between observations on weekdays and without 4 hours passing on the weekends. Exact times of the observations were recorded and are part of the raw data.

APPENDIX 14

CLINICAL PATHOLOGY REFERENCES

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

HEMATOLOGY

Erythrocyte and Leukocyte Counts

Hemoglobin and Hematocrit Measurements

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   Instruction Manual for the Counter Model ZF
2. Coulter Hemoglobinometer Instruction Manual
3. Coulter RBC/MCV/HCT Computer Operator's Manual
4. Coulter Diluter II Operator's Guide
5. Damon/IEC Division, Needham Heights, Mass. IEC Micro Hematocrit MB Centrifuge - Operating and Maintenance Manual
6. Clinical Diagnosis by Laboratory Methods. Todd-Sanford, Davidsohn and Henry. 15th Edition (1974)

Thrombocyte Count (Automated Platelet Count)

1. Mansber, H.P., Optical Techniques of Platelet Counting - Advance in automated Analysis. Technicon International Congress (1969) Vol. 1; White Plains, New York. Mediad Incorporated (1970), pp 213-219

Trombocyte Count (Manual Platelet Count)

1. Miescher, P.A., and Gerarde, H.W.
   A one-step method for counting Leukocytes and Platelets; Tech. Bull. Reg. Med. Tech. 36:10, 246-251 (Oct. 1966)
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CHEMISTRY

Alkaline Phosphatase (Modified Bessey-Lowry-Brock)

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Blood Urea Nitrogen-BUN (Modified Urease Method)

1. Karmen, A.J., Clin. Invest. 34, 131 (1955)

Cholesterol Total (Enzymatic)

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CHEMISTRY (Continued)

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Total Protein (Biuret Technique)

1. Henry, R.J.; Sobel, C. and Berkman, S.; Anal. Chem. 2, 1491 (1957)

Alanine Aminotransferase (SGPT)

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2. Bergmeryewr, H.U., Scheibe, P., and Wahlefeld, A.W.; Clin. Chem., 24, 58 (1978)

Calcium (Atomic Absorption Spectrophotometry)

1. F.J. Fernandez and H.L. Kahn, Clin. Chem. Newsletter 3, 24(1971)
2. D.L. Trudeau and E.F. Freier, Clin. Chem. 13, 101 (1967)
3. J.B. Willis, Anal. Chem. 33, 556 (1961)

Sodium, Potassium, and Chloride, Nova 4+4 Ion Specific Analyzer.

Albumin and A:G Ratio, Computer-Generated Calculations

URINALYSIS

1. Modern Urinalysis; Ames Co., Division of Miles Laboratories, Inc. (1973)
2. Diagnosis by Laboratory Methods. 15th Edition, Todd-Sanford, Davidsohn and Henry, (1974)

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APPENDIX 15

CLINICAL PATHOLOGY - NORMAL RANGES FOR FISCHER RATS[a]

THIRTEEN WEEK GAVAGE ADMINISTRATION
OF PET 700811 TO RATS

HEMATOLOGY[b]

PARAMETER	NORMAL RANGE	
	MALE	FEMALE
RBC (10^6/cmm)	7.93 - 8.97	6.69 - 8.41
WBC (10^3/cmm)	5.7 - 11.3	3.9 - 9.9
HGB (g/dl)	16.8 - 18.0	16.0 - 18.0
HCT (%)	45.9 - 51.1	43.6 - 49.6
Platelets (10^3/cmm)	285 - 365	261 - 405

CLINICAL CHEMISTRY[b]

PARAMETER	NORMAL RANGE	
	MALE	FEMALE
Glucose (mg/dl)	70 - 102	64 - 92
BUN (mg/dl)	14 - 18	14 - 20
SGPT (u/l)	25 - 59	25 - 55
ALP (u/l)	85 - 121	65 - 105
T. PROT (g/dl)	6.8 - 8.2	6.3 - 8.5
Albumin (g/dl)	4.2 - 5.0	4.0 - 5.2
A:G Ratio	1.39 - 1.83	1.44 - 1.76
T. CHOL (mg/dl)	51 - 107	87 - 143
Ca (mg/dl)	8.8 - 13.2	9.2 - 13.2
Na (mmol/l)[c]	139 - 151	139 - 151
K (mmol/l)[c]	4.4 - 9.7	4.4 - 9.7
Cl (mmol/l)[c]	84 - 112	84 - 112

[a]Ages 18 to 19 weeks.

[b]Based on values taken from 10 untreated animals at Borriston.

[c]Ranges were obtained from Met Path; no differentiation was made between the sexes.

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APPENDIX 15 (Continued)

Normal Hematology Values (Continued)
Fisher Rats - Coulter Counter ZF-5
Age: 18-19 Weeks

Differential White Blood Cell Counts

Parameters	(%) Males	(%) Females	(No of Cells/cumm) Males	(No of Cells/cumm) Females
Neutrophiles	3-23	5-21	192-2668	220-2100
Lymphocytes	71-93	75-91	4544-10788	3300-9100
Monocytes	0-8	0-7	0-928	0-700
Eosinophiles	0-2	0-2	0-232	0-200

2 Standard Deviations
Number: 10 animals/sex
Fasting State
Bleed Site: Orbital Sinus

Generated: January 1983
Borriston Laboratories, Inc.

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ADDENDUM I

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.,

PATHOLOGY REPORT

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

BORRISTON PROJECT NUMBER 3401

THIRTEEN-WEEK GAVAGE ADMINISTRATION OF PET TO RATS

PATHOLOGY REPORT

Submitted to:

Borriston Laboratories, Inc.
Temple Hills, Maryland 20748

April 18, 1983

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

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PATHOLOGY SUMMARY

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

BORRISTON PROJECT NUMBER 3401

THIRTEEN-WEEK GAVAGE ADMINISTRATION
OF PET TO RATS

PATHOLOGY SUMMARY

Sections of tissue from 160 male and female Fischer 344 rats were examined microscopically for histologic lesions. The rats had been used on a thirteen-week study to evaluate the toxic effects of PET when given daily by gavage to the animals at varying dosage levels. Another objective of the study was to determine, if possible, which organs would have histopathologic changes as a result of having been given the test material.

The rats were divided into four groups with each group having an equal number of males and females. One group received the compound vehicle, virgin olive oil, and served as controls. The other groups received, in addition, the test material, PET, as outlined in the following study design:

Group	Treatment	Dosage Level	Number of Animals	
			Males	Females
1	Control	0 mg/kg/day	20	20
2	PET	100 mg/kg/day	20	20
3	PET	300 mg/kg/day	20	20
4	PET	900 mg/kg/day	20	20

The rats were sacrificed and necropsied at the termination of the study or earlier if they died or were in a moribund condition. Tissues were preserved in 10% neutral buffered formalin, then processed

and stained with hematoxylin and eosin for microscopic evaluation. In accordance with the study protocol, the following tissues were examined from Groups 1 (control) and 4 (high dose): brain, pituitary, spinal cord (cervical, thoracic, lumbar), eyes with harderian glands, salivary glands (mandibular), thyroids, parathyroids, trachea, thymus, esophagus, heart, aorta, spleen, adrenals, pancreas, skin with mammary gland, tongue, head (cross through ear canals and midsnout), duodenum, jejunum, ileum, colon, cecum, rectum, mesenteric lymph node, mandibular lymph node, urinary bladder, testes with epididymides, prostate, seminal vesicles, ovaries, uterus (cervix/corpus uteri), fallopian tubes, vagina, skeletal muscle with sciatic nerve, bone with marrow (sternum or femur), lungs, liver (median and left lateral), kidneys, stomach (cardiac, fundic, pyloric), and all gross lesions. Only the liver and kidney and any abnormal appearing tissues were processed from the rats in Groups 2 and 3.

RESULTS

Microscopic findings for each tissue examined from each animal are given in the Histopathology Incidence Tables and summarized by group and sex in the Summary Incidence Tables. Abnormal gross observations noted at the time of necropsy, together with the corresponding microscopic findings, if appropriate, are listed in the Correlation of Gross and Microscopic Findings Tables.

Fourteen of the twenty Group 4 male rats had testicular atrophy and decreased spermatogenesis. Sperm were also decreased or absent from

the epididymides in these animals. A single Group 1 rat had testicular atrophy and the accompanying aspermatogenesis and aspermia. Eight of the Group 4 rats that had atrophic testicles also had sperm granulomas in the epididymides; four also had atrophy of the seminal vesicles. The atrophic genital organs may have been associated with malnutrition and weight loss; the relationship of sperm granulomas to any of these changes is unknown. Microscopic findings for the testicles from Groups 2 and 3 males will be submitted as an addendum to this report.

There were no microscopic changes in the ovaries or other organs of the female reproductive system that were comparable to those in the males. The incidence of congestion was greater in a number of tissues from the Group 4 males and females than in the controls. This change is probably associated with the increased number of deaths and moribund animals in Group 4.

Few other inflammatory, degenerative, or developmental changes were present in the remaining tissues. Inflammatory changes of the eye and its adnexa, lung, and kidney were present in both males and females in the control and high dose animals with about equal frequency. A few examples of centrilobular hepatocytomegaly were seen in the livers of both test and control rats. There were rare ovarian cysts and distended uteri in the females. The only findings in the gastrointestinal tract were nematodiasis in the colon and single examples of bile staining in the stomach and submucosal hemorrhages in the jejunum.

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CONCLUSIONS

Administration of PET by gavage to Fischer 344 rats for thirteen weeks was associated with testicular atrophy and hypospermatogenesis of the testes and hypospermia or aspermia of the epididymides in the males that received 900 mg/kg/day. A number of these animals also had sperm granulomas in the epididymides. There were no histopathologic changes in the other tissues from the males or any tissues from the females that appeared to be related to administration of the test material.

C. E. Gilmore

CHARLEY E. GILMORE, D.V.M.
Veterinary Pathologist

April 18, 1983

CEG/dmk

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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

QUALITY ASSURANCE
REPORT CERTIFICATION

Client Name Borriston Laboratories, Inc. Client Study No. 3401

Study Director Dr. William O. Iverson Pathologist Dr. Charley E. Gilmore

Study Title Thirteen-Week Gavage Administration of PET to Rats

Test Article PET 700811 Species Rats

The final report for this study was reviewed by Experimental Pathology Laboratories Quality Assurance Unit on April 18, 1983. All findings were reported to the Study Director and Management on April 18, 1983.

Janet Milazzo

4/18/83

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SUMMARY INCIDENCE TABLES

SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
BRAIN (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Congestion												
CERVICAL SPINAL CORD (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
LUMBAR SPINAL CORD (NO. EXAMINED)	(20)		(20)							(11)	(7)	(18)
THORACIC SPINAL CORD (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
PITUITARY (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
Cyst	1		1							1		1
ADRENAL (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Cortical Hypertrophy												
Congestion												

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
THYROID (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Atrophy											1	1
Congestion											1	1
PARATHYROID (NO. EXAMINED)	(19)		(19)							(11)	(7)	(18)
EYE (NO. EXAMINED)	(20)		(20)				(1)	(1)	(2)	(12)	(8)	(20)
Panophthalmitis												
Phthisis Bulbi							1		1		1	1
Anterior Uveitis												
Ruptured											1	1
Retinal Detachment							1		1			
Orbital Cellulitis	1		1								1	1
Posterior Uveitis	1		1									
HARDERIAN GLAND (NO. EXAMINED)	(20)		(20)				(1)		(1)	(12)	(8)	(20)
Subacute Adenitis	5		5								2	2
Pigment							1		1			

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
HEART (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Congestion	1		1									
AORTA (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
SPLEEN (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Pigment	3		3								1	1
SALIVARY GLAND (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
MANDIBULAR LYMPH NODE (NO. EXAMINED)	(17)		(17)	(4)		(4)	(1)		(1)	(12)	(7)	(19)
Lymphocytic Hyperplasia	1		1							1	1	2
Congestion	2		2	4		4	1		1		4	4
THYMUS (NO. EXAMINED)	(20)		(20)	(7)		(7)	(1)	(1)	(2)	(12)	(7)	(19)
Congestion	10		10	6		6	1	1	2	1	4	5

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
TRACHEA (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
ESOPHAGUS (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
TONGUE (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
LUNG (NO. EXAMINED)	(20)		(20)	(5)		(5)	(5)	(1)	(6)	(12)	(8)	(20)
Peribronchial Lymphocytic Hyperplasia	1		1	1		1						
Focal Subacute Alveolitis	2		2	3		3	5		5	3	1	4
Focal Hemorrhage	1		1									
Congestion	1		1					1	1	1	5	6
Focal Pneumonocyte Hyperplasia	1		1	2		2	1		1	1		1
Focal Atelectasis												
LIVER (NO. EXAMINED)	(20)		(20)	(20)		(20)	(12)	(8)	(20)	(12)	(8)	(20)
Focal Capsulitis	1		1	1		1						
Centrilobular Hepatocytomegaly				2		2	1	1	2		2	2
Congestion								1	1		2	2

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Experimental Pathology Laboratories, Inc.

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
LIVER (CONTINUED)												
Focal Hyperplasia												
Focal Hepatocytomegaly								1	1			
KIDNEY (NO. EXAMINED)	(20)		(20)	(20)		(20)	(12)	(8)	(20)	(12)	(8)	(20)
Regenerative Tubules										1		1
Chronic Nephropathy							1		1			
Congestion											3	3
STOMACH (NO. EXAMINED)	(20)		(20)					(1)	(1)	(12)	(8)	(20)
Bile Pigment								1	1			
DUODENUM (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
PANCREAS (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
JEJUNUM (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Submucosal Hemorrhage												
ILEUM (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
COLON (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Nematodiasis	2		2								2	2
CECUM (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
RECTUM (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
TESTIS (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Atrophy	1		1							12	2	14
Aspermatogenesis	1		1							4		4
Hypospermatogenesis										8	2	10

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Experimental Pathology Laboratories, Inc.
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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
EPIDIDYMIS (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
Aspermia	1		1							5		5
Hypospermia										7	3	10
Sperm Granuloma										6	2	8
Atrophy											1	1
PROSTATE (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
Subacute Prostatitis											1	1
SEMINAL VESICLE (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Inspissated Secretion										1		1
Atrophy											4	4
URINARY BLADDER (NO. EXAMINED)	(20)		(20)					(2)	(2)	(12)	(8)	(20)
Distended	1		1					1	1		4	4
Protein Cast	3		3									
Submucosal Hemorrhage								1	1			

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
MESENTERIC LYMPH NODE (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
Congestion	1		1							1		1
SKELETAL MUSCLE (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
SCIATIC NERVE (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
SKIN (NO. EXAMINED)	(20)		(20)							(12)	(7)	(19)
MAMMARY GLAND (NO. EXAMINED)	(14)		(14)							(4)	(3)	(7)
BONE (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
BONE MARROW (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Hypocellular										1		1

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
HEAD (NO. EXAMINED)	(20)		(20)							(12)	(8)	(20)
Acute Rhinitis												
Otitis Interna												
MEDIASTINAL LYMPH NODE (NO. EXAMINED)				(4)		(4)	(2)		(2)			
Lymphocytic Hyperplasia				2		2	1		1			
BRONCHIAL LYMPH NODE (NO. EXAMINED)							(1)		(1)			

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Experimental Pathology Laboratories, Inc.

SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
BRAIN (NO. EXAMINED)	(19)	(1)	(20)					(1)	(1)	(2)	(18)	(20)
Congestion											4	4
CERVICAL SPINAL CORD (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
LUMBAR SPINAL CORD (NO. EXAMINED)	(19)	(1)	(20)							(2)	(15)	(17)
THORACIC SPINAL CORD (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
PITUITARY (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
Cyst											1	1
ADRENAL (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Cortical Hypertrophy											1	1
Congestion											2	2

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
THYROID (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Atrophy												
Congestion												
PARATHYROID (NO. EXAMINED)	(18)	(1)	(19)							(2)	(18)	(20)
EYE (NO. EXAMINED)	(19)	(1)	(20)		(1)	(1)		(1)	(1)	(2)	(18)	(20)
Panophthalmitis	2		2								1	1
Phthisis Bulbi	1		1									
Anterior Uveitis	1		1									
Ruptured												
Retinal Detachment												
Orbital Cellulitis												
Posterior Uveitis												
HARDERIAN GLAND (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Subacute Adenitis	8	1	9								5	5
Pigment												

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
HEART (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Congestion												
AORTA (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
SPLEEN (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
Pigment												
SALIVARY GLAND (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
MANDIBULAR LYMPH NODE (NO. EXAMINED)	(19)	(1)	(20)	(3)		(3)	(2)		(2)	(1)	(16)	(17)
Lymphocytic Hyperplasia	1		1									
Congestion	1		1	3		3	2		2		4	4
THYMUS (NO. EXAMINED)	(19)	(1)	(20)	(5)	(2)	(7)	(2)	(1)	(3)	(2)	(15)	(17)
Congestion	4	1	5	4	2	6	2	1	3		5	5

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Experimental Pathology Laboratories, Inc.

SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
TRACHEA (NO. EXAMINED)	(19)	(1)	(20)					(1)	(1)	(2)	(18)	(20)
ESOPHAGUS (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
TONGUE (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
LUNG (NO. EXAMINED)	(19)	(1)	(20)	(1)		(1)	(3)	(4)	(7)	(2)	(18)	(20)
Peribronchial Lymphocytic Hyperplasia	1		1									
Focal Subacute Alveolitis	6		6	1		1	2		2			
Focal Hemorrhage												
Congestion	1		1				1	1	2		10	10
Focal Pneumonocyte Hyperplasia							1		1			
Focal Atelectasis								1	1	1	3	4
LIVER (NO. EXAMINED)	(19)	(1)	(20)	(18)	(2)	(20)	(13)	(7)	(20)	(2)	(18)	(20)
Focal Capsulitis												
Centrilobular Hepatocytomegaly	2		2		1	1		1	1			
Congestion								2	2		9	9

EPL
Experimental Pathology Laboratories, Inc.
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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
LIVER (CONTINUED)												
Focal Hyperplasia											1	1
Focal Hepatocytomegaly							1		1			
KIDNEY (NO. EXAMINED)	(19)	(1)	(20)	(18)	(2)	(20)	(13)	(7)	(20)	(2)	(18)	(20)
Regenerative Tubules	2		2								1	1
Chronic Nephropathy	1		1							1		1
Congestion								2	2		7	7
STOMACH (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Bile Pigment												
DUODENUM (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
PANCREAS (NO. EXAMINED)	(19)	(1)	(20)	(1)		(1)				(2)	(18)	(20)

EPL
Experimental Pathology Laboratories, Inc.
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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
JEJUNUM (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Submucosal Hemorrhage											1	1
ILEUM (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
COLON (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Nematodiasis											1	1
CECUM (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
RECTUM (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
OVARY (NO. EXAMINED)	(19)	(1)	(20)	(1)		(1)	(2)		(2)	(2)	(18)	(20)
Parovarian Cyst	1		1								1	1
Cyst, NOS							1		1			

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
CERVIX (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
UTERUS (NO. EXAMINED)	(19)	(1)	(20)				(1)		(1)	(2)	(18)	(20)
Distended	1		1				1		1			
FALLOPIAN TUBE (NO. EXAMINED)	(18)	(1)	(19)							(2)	(18)	(20)
VAGINA (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
URINARY BLADDER (NO. EXAMINED)	(17)	(1)	(18)							(2)	(17)	(19)
Distended											3	3
Protein Cast												
Submucosal Hemorrhage												
MESENTERIC LYMPH NODE (NO. EXAMINED)	(19)	(1)	(20)							(2)	(16)	(18)
Congestion												

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
SKELETAL MUSCLE (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
SCIATIC NERVE (NO. EXAMINED)	(19)	(1)	(20)							(2)	(16)	(18)
SKIN (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
MAMMARY GLAND (NO. EXAMINED)	(8)	(1)	(9)							(2)	(14)	(16)
BONE (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
BONE MARROW (NO. EXAMINED)	(19)	(1)	(20)							(2)	(17)	(19)
Hypocellular												
HEAD (NO. EXAMINED)	(19)	(1)	(20)							(2)	(18)	(20)
Acute Rhinitis											2	2
Otitis Interna											1	1

0001155

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SUMMARY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats

	Group 1			Group 2			Group 3			Group 4		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
MEDIASTINAL LYMPH NODE (NO. EXAMINED)				(1)		(1)	(2)		(2)			
Lymphocytic Hyperplasia				1		1	2		2			
PANCREATIC LYMPH NODE (NO. EXAMINED)												

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HISTOPATHOLOGY INCIDENCE TABLES

GROUP	DOSE/ CONCENTRATION	COMPOUND
1	0 mg/kg/da	PET 700811
2	100 mg/kg/da	PET 700811
3	300 mg/kg/da	PET 700811
4	900 mg/kg/da	PET 700811

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	82100000	82100001	82100002	82100003	82100004	82100005	82100006	82100007	82100008	82100009	82100010	82100011	82100012	82100013	82100014	82100015	82100016	82100017	82100018	82100019
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion																				
CERVICAL SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LUMBAR SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
THORACIC SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PITUITARY	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X
Cyst											P									
ADRENAL	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cortical Hypertrophy																				
Congestion																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Atrophy																				
Congestion																				
PARATHYROID	X	X	X	N	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EYE	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Panophthalmitis																				
Phthisis Bulbi																				
Anterior Uveitis																				
Ruptured																				

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	82100001	82100012	82100023	82100034	82100045	82100056	82100067	82100078	82100089	82100090	82100101	82100112	82100123	82100134	82100145	82100156	82100167	82100178	82100189	82100190
EYE (CONTINUED)																				
Retinal Detachment																				
Orbital Cellulitis						4														
Posterior Uveitis						4														
HARDERIAN GLAND	X	X		X	X	X		X	X	X	X	X	X	X	X			X		X
Subacute Adenitis			1				1									2	3		1	
Pigment																				
HEART	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X
Congestion											1									
AORTA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SPLEEN	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X			X	X
Pigment															2		1	1		
SALIVARY GLAND	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MANDIBULAR LYMPH NODE	N	X	X	X	X	X	X	X	X		N		N	X		X	X	X	X	X
Lymphocytic Hyperplasia										1										
Congestion												2			2					
THYMUS	X	X	X	X	X	X	X	X	X	X										
Congestion											3	1	1	2	1	1	1	1	2	1

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210000001	8210000002	8210000003	8210000004	8210000005	8210000006	8210000007	8210000008	8210000009	8210000010	8210000011	8210000012	8210000013	8210000014	8210000015	8210000016	8210000017	8210000018	8210000019
TRACHEA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TONGUE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LUNG	X	X		X	X	X		X	X	X		X	X	X		X	X	X	X
Peribronchial Lymphocytic Hyperplasia			1																
Focal Subacute Alveolitis			1											3					
Focal Hemorrhage						1													
Congestion										2									
Focal Pneumonocyte Hyperplasia										3									
Focal Atelectasis																			
LIVER	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Focal Capsulitis												2							
Centrilobular Hepatocytomegaly																			
Congestion																			
Focal Hyperplasia																			
Focal Hepatocytomegaly																			
KIDNEY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Regenerative Tubules																			
Chronic Nephropathy																			
Congestion																			

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	82100001	82100002	82100003	82100004	82100005	82100006	82100007	82100008	82100009	82100010	82100011	82100012	82100013	82100014	82100015	82100016	82100017	82100018	82100019
STOMACH	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Bile Pigment																			
DUODENUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PANCREAS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
JEJUNUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Submucosal Hemorrhage																			
ILEUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
COLON		X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
Nematodiasis	P							P											
CECUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
RECTUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TESTIS	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X
Atrophy								5											
Aspermatogenesis								P											
Hypospermatogenesis																			

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210000	8210001	8210002	8210003	8210004	8210005	8210006	8210007	8210008	8210009	8210010	8210011	8210012	8210013	8210014	8210015	8210016	8210017	8210018	8210019
EPIDIDYMIS	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
Aspermia									P											
Hypospermia																				
Sperm Granuloma																				
Atrophy																				
PROSTATE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Subacute Prostatitis																				
SEMINAL VESICLE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Inspissated Secretion																				
Atrophy																				
URINARY BLADDER	X	X	X	X	X	X	X	X	X	X	X		X	X		X	X			X
Distended												P								
Protein Cast															P			P	P	
Submucosal Hemorrhage																				
MESENTERIC LYMPH NODE	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Congestion														1						
SKELETAL MUSCLE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SCIATIC NERVE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	82100000	82100001	82100002	82100003	82100004	82100005	82100006	82100007	82100008	82100009	82100010	82100011	82100012	82100013	82100014	82100015	82100016	82100017	82100018	82100019
SKIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MAMMARY GLAND	X	N	N	X	X	X	X	X	X	N	N	N	X	N	X	X	X	X	X	X
BONE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BONE MARROW	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hypocellular																				
HEAD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Acute Rhinitis																				
Otitis Interna																				

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe, High

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 2

ANIMAL NUMBER	8210040	8210041	8210042	8210043	8210044	8210045	8210046	8210047	8210048	8210049	8210050	8210051	8210052	8210053	8210054	8210055	8210056	8210057	8210058	8210059
MANDIBULAR LYMPH NODE																				
Lymphocytic Hyperplasia																				
Congestion								1							2	2	1			
THYMUS														X						
Congestion												1	1		1	2	2	2		
LUNG				X																
Peribronchial Lymphocytic																				
Hyperplasia																			1	
Focal Subacute Alveolitis		3			3					2										
Focal Hemorrhage																				
Congestion																				
Focal Pneumonocyte Hyperplasia		2			1															
Focal Atelectasis																				
LIVER	X		X	X		X		X	X	X	X	X	X	X	X	X	X	X	X	X
Focal Capsulitis							2													
Centrilobular Hepatocytomegaly		1			1															
Congestion																				
Focal Hyperplasia																				
Focal Hepatocytomegaly																				
KIDNEY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Regenerative Tubules																				
Chronic Nephropathy																				
Congestion																				

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Key: P = Present; 1 = Minimal; 2 = Slight; 3 = Moderate; 4 = Moderately Severe/High; 5 = Severe/High; N = No Section; I = Incomplete Section; A = Autolysis; X = Not Remarkable

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 2

ANIMAL NUMBER	821004 0	821004 1	821004 2	821004 3	821004 4	821004 5	821004 6	821004 7	821004 8	821004 9	821005 0	821005 1	821005 2	821005 3	821005 4	821005 5	821005 6	821005 7	821005 8	821005 9
MEDIASTINAL LYMPH NODE		X																	X	
Lymphocytic Hyperplasia										1			2							

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	821008 6	821008 7	821008 8	821008 9	821009 0	821009 2	821009 3	821009 5	821009 6	821009 7	821009 8	821009 9
EYE												
Panophthalmitis												
Phthisis Bulbi	3											
Anterior Uveitis												
Ruptured												
Retinal Detachment	5											
Orbital Cellulitis												
Posterior Uveitis												
HARDERIAN GLAND												
Subacute Adenitis												
Pigment		3										
MANDIBULAR LYMPH NODE												
Lymphocytic Hyperplasia												
Congestion											2	
THYMUS												
Congestion											1	
LUNG												
Peribronchial Lymphocytic												
Hyperplasia												
Focal Subacute Alveolitis		3		2	2				1	1		
Focal Hemorrhage												
Congestion												
Focal Pneumonocyte Hyperplasia					1							

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	821000886	821000887	821000888	821000889	821000890	821000892	821000893	821000895	821000896	821000897	821000898	821000899
LUNG (CONTINUED)												
Focal Atelectasis												
LIVER	X	X	X	X	X	X		X	X	X	X	X
Focal Capsulitis												
Centrilobular Hepatocytomegaly							1					
Congestion												
Focal Hyperplasia												
Focal Hepatocytomegaly												
KIDNEY	X	X	X		X	X	X	X	X	X	X	X
Regenerative Tubules												
Chronic Nephropathy				1								
Congestion												
STOMACH												
Bile Pigment												
URINARY BLADDER												
Distended												
Protein Cast												
Submucosal Hemorrhage												
MEDIASTINAL LYMPH NODE											X	
Lymphocytic Hyperplasia					1							

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Key P = Present, 1 = Minimal, 5 = Severe/High; N = No Section, 2 = Slight, I = Incomplete Section; A = Autolysis, 3 = Moderate; X = Not Remarkable, 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	821086	821087	821088	821089	821090	821092	821093	821095	821096	821097	821098	821099
BRONCHIAL LYMPH NODE				X								

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	821000	821001	821002	821003	821004	821005	821091	821094
EYE						X		
Panophthalmitis								
Phthisis Bulbi								
Anterior Uveitis								
Ruptured								
Retinal Detachment								
Orbital Cellulitis								
Posterior Uveitis								
HARDERIAN GLAND								
Subacute Adenitis								
Pigment								
MANDIBULAR LYMPH NODE								
Lymphocytic Hyperplasia								
Congestion								
THYMUS								
Congestion			3					
LUNG								
Peribronchial Lymphocytic								
Hyperplasia								
Focal Subacute Alveolitis								
Focal Hemorrhage								
Congestion		1						
Focal Pneumonocyte Hyperplasia								

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Key P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	821000 80	821000 81	821000 82	821000 83	821000 84	821000 85	821000 91	821000 94
LUNG (CONTINUED)								
Focal Atelectasis								
LIVER	X	X		X	X		X	
Focal Capsulitis								
Centrilobular Hepatocytomegaly			2					
Congestion						2		
Focal Hyperplasia								
Focal Hepatocytomegaly							1	
KIDNEY	X	X	X	X	X	X	X	X
Regenerative Tubules								
Chronic Nephropathy								
Congestion								
STOMACH								
Bile Pigment		1						
URINARY BLADDER						X		
Distended	P							
Protein Cast								
Submucosal Hemorrhage	2							
MEDIASTINAL LYMPH NODE								
Lymphocytic Hyperplasia								

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	82100080	82110081	82110082	82110083	82110084	82110085	82110091	82110094
BRONCHIAL LYMPH NODE								

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	821012	821022	821026	821028	821029	821031	821032	821033	821034	821037	821038	821039
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X
Congestion												
CERVICAL SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X
LUMBAR SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	N
THORACIC SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X
PITUITARY	X	X		X	X	X	X	X	X	X	X	X
Cyst			P									
ADRENAL	X	X	X	X	X	X	X	X	X	X	X	X
Cortical Hypertrophy												
Congestion												
THYROID	X	X	X	X	X	X	X	X	X	X	X	X
Atrophy												
Congestion												
PARATHYROID	X	X	N	X	X	X	X	X	X	X	X	X
EYE	X	X	X	X	X	X	X	X	X	X	X	X
Panophthalmitis												
Phthisis Bulbi												
Anterior Uveitis												
Ruptured												

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	82101202	82101022	82101226	82101028	82101229	82101031	82101323	82101333	82101034	82101337	82101038	82101339
EYE (CONTINUED)												
Retinal Detachment												
Orbital Cellulitis												
Posterior Uveitis												
HARDERIAN GLAND	X	X	X	X	X	X	X	X	X	X	X	X
Subacute Adenitis												
Pigment												
HEART	X	X	X	X	X	X	X	X	X	X	X	X
Congestion												
AORTA	X	X	X	X	X	X	X	X	X	X	X	X
SPLEEN	X	X	X	X	X	X	X	X	X	X	X	X
Pigment												
SALIVARY GLAND	X	X	X	X	X	X	X	X	X	X	X	X
MANDIBULAR LYMPH NODE	X	X	X	X	X	X	X	X	X		X	X
Lymphocytic Hyperplasia										2		
Congestion												
THYMUS	X	X	X	X	X	X	X	X	X		X	X
Congestion										2		

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8210120	8210122	8210126	8210128	8210129	8210131	8210132	8210133	8210134	8210137	8210138	8210139
TRACHEA	X	X	X	X	X	X	X	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X	X	X	X	X	X	X	X
TONGUE	X	X	X	X	X	X	X	X	X	X	X	X
LUNG	X	X		X		X	X	X		X		X
Peribronchial Lymphocytic Hyperplasia												
Focal Subacute Alveolitis			2		3				1			
Focal Hemorrhage												
Congestion			1									
Focal Pneumonocyte Hyperplasia										1		
Focal Atelectasis												
LIVER	X	X	X	X	X	X	X	X	X	X	X	X
Focal Capsulitis												
Centrilobular Hepatocytomegaly												
Congestion												
Focal Hyperplasia												
Focal Hepatocytomegaly												
KIDNEY	X	X	X	X	X	X	X	X	X		X	X
Regenerative Tubules										1		
Chronic Nephropathy												
Congestion												

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8210120	8210122	8210126	8210128	8210129	8210131	8210132	8210133	8210134	8210137	8210138	8210139
STOMACH	X	X	X	X	X	X	X	X	X	X	X	X
Bile Pigment												
DUODENUM	X	X	X	X	X	X	X	X	X	X	X	X
PANCREAS	X	X	X	X	X	X	X	X	X	X	X	X
JEJUNUM	X	X	X	X	X	X	X	X	X	X	X	X
Submucosal Hemorrhage												
ILEUM	X	X	X	X	X	X	X	X	X	X	X	X
COLON	X	X	X	X	X	X	X	X	X	X	X	X
Nematodiasis												
CECUM	X	X	X	X	X	X	X	X	X	X	X	X
RECTUM	X	X	X	X	X	X	X	X	X	X	X	X
TESTIS												
Atrophy	4	3	3	3	4	4	4	4	3	3	3	2
Aspermatogenesis	P				P	P	P					
Hypospermatogenesis		4	4	3				4	3	3	3	1

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	82101012 20	82101012 26	82101012 28	82101012 29	82101013 01	82101013 02	82101013 03	82101013 04	82101013 37	82101013 38	82101013 39
EPIDIDYMIS											
Aspermia	P		P		P	P	P				
Hypospermia		4		4				4	4	3	3 1
Sperm Granuloma				P		P	P		P	P	P
Atrophy											
PROSTATE	X	X	X	X	X	X	X	X	X	X	X X
Subacute Prostatitis											
SEMINAL VESICLE	X	X	X	X	X		X	X	X	X	X X
Inspissated Secretion					P						
Atrophy											
URINARY BLADDER	X	X	X	X	X	X	X	X	X	X	X X
Distended											
Protein Cast											
Submucosal Hemorrhage											
MESENTERIC LYMPH NODE	X	X	X	X	X	X	X	X	X	X	X
Congestion											2
SKELETAL MUSCLE	X	X	X	X	X	X	X	X	X	X	X X
SCIATIC NERVE	X	X	X	X	X	X	X	X	X	X	X X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8210120	8210122	8210126	8210128	8210129	8210131	8210132	8210133	8210134	8210137	8210138	8210139
SKIN	X	X	X	X	X	X	X	X	X	X	X	X
MAMMARY GLAND	N	N	X	X	N	X	N	N	N	X	N	N
BONE	X	X	X	X	X	X	X	X	X	X	X	X
BONE MARROW	X	X	X	X	X	X	X		X	X	X	X
Hypocellular								1				
HEAD	X	X	X	X	X	X	X	X	X	X	X	X
Acute Rhinitis												
Otitis Interna												

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Key P = Present, 1 = Minimal, 5 = Severe/High, N = No Section, 2 = Slight, I = Incomplete Section, A = Autolysis, 3 = Moderate, X = Not Remarkable, 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

Study
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821012	821023	821124	821025	821027	821130	821035	821036
BRAIN	X	X	X	X	X	X	X	X
Congestion								
CERVICAL SPINAL CORD	X	X	X	X	X	X	X	X
LUMBAR SPINAL CORD	N	X	X	X	X	X	X	X
THORACIC SPINAL CORD	X	X	X	X	X	X	X	X
PITUITARY	X	X	X	X	X	N	X	X
Cyst								
ADRENAL	X	X	X	X	X	X	X	X
Cortical Hypertrophy								
Congestion								
THYROID		X	X	X	X	X	X	X
Atrophy	3							
Congestion	1							
PARATHYROID	N	X	X	X	X	X	X	X
EYE		X	X	X		X	X	
Panophthalmitis								
Phthisis Bulbi					5			
Anterior Uveitis								
Ruptured							P	

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	8210121	8210123	8210124	8210125	8210127	8210130	8210135	8210136
EYE (CONTINUED)								
Retinal Detachment								
Orbital Cellulitis	3							
Posterior Uveitis								
HARDERIAN GLAND		X	X		X	X	X	X
Subacute Adenitis	4			1				
Pigment								
HEART	X	X	X	X	X	X	X	X
Congestion								
AORTA	X	X	X	X	X	X	X	X
SPLEEN	X	X	X	X	X	X	X	
Pigment								1
SALIVARY GLAND	X	X	X	X	X	X	X	X
MANDIBULAR LYMPH NODE		X			N			X
Lymphocytic Hyperplasia	3							
Congestion			2	1		1	2	
THYMUS	X	X	N		X			
Congestion				1		2	2	1

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Key: P — Present; 1 — Minimal; 5 — Severe/High; N — No Section; 2 — Slight; I — Incomplete Section; A — Autolysis; 3 — Moderate; X — Not Remarkable; 4 — Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	8210121	8210123	8210124	8210125	8210127	8210130	8210135	8210136
TRACHEA	X	X	X	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X	X	X	X
TONGUE	X	X	X	X	X	X	X	X
LUNG			X		X			
Peribronchial Lymphocytic								
Hyperplasia								
Focal Subacute Alveolitis				1				
Focal Hemorrhage								
Congestion	3	1				1	1	1
Focal Pneumonocyte Hyperplasia								
Focal Atelectasis								
LIVER		X		X		X		X
Focal Capsulitis								
Centrilobular Hepatocytomegaly			1				1	
Congestion	2				1			
Focal Hyperplasia								
Focal Hepatocytomegaly								
KIDNEY		X		X		X	X	X
Regenerative Tubules								
Chronic Nephropathy								
Congestion	3		2		1			

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	8210121	8210123	8210124	8210125	8210127	8210130	8210135	8210136
STOMACH	X	X	X	X	X	X	X	X
Bile Pigment								
DUODENUM	X	X	X	X	X	X	X	X
PANCREAS	X	X	X	X	X	X	N	X
JEJUNUM	X	X	X	X	X	X	X	X
Submucosal Hemorrhage								
ILEUM	X	X	X	X	X	X	X	X
COLON	X	X	X	X	X			X
Nematodiasis						P	P	
CECUM	X	X	X	X	X	X	X	X
RECTUM	X	X	X	X	X	X	X	X
TESTIS	X	X		X		X	X	X
Atrophy			2		3			
Aspermatogenesis								
Hypospermatogenesis			2		3			

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Key: P – Present; 1 – Minimal; 5 – Severe/High; N – No Section; 2 – Slight; I – Incomplete Section; A – Autolysis; 3 – Moderate; X – Not Remarkable; 4 – Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821023	821004	821011	821025	821027	821030	821035	821036
EPIDIDYMIS	N	X		X		X		X
Aspermia								
Hypospermia			3		3		2	
Sperm Granuloma			P		P			
Atrophy							2	
PROSTATE		X	X	X	X	X	N	X
Subacute Prostatitis	1							
SEMINAL VESICLE		X		X	X			X
Inspissated Secretion								
Atrophy	2		1			3	3	
URINARY BLADDER	X		X		X	X		
Distended		P		P			P	P
~~Protein Cast~~								
Submucosal Hemorrhage								
MESENTERIC LYMPH NODE	X	X	X	X	X	X	X	N
Congestion								
SKELETAL MUSCLE	X	X	X	X	X	X	X	X
SCIATIC NERVE	X	X	N	X	X	X	X	X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821012	821003	821014	821025	821017	821030	821035	821036
SKIN	X	X	X	N	X	X	X	X
MAMMARY GLAND	N	X	N	N	X	N	N	X
BONE	X	X	X	X	X	X	X	X
BONE MARROW	X	X	X	X	X	X	X	X
Hypocellular								
HEAD	X	X	X	X	X	X	X	X
Acute Rhinitis								
Otitis Interna								

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Key P = Present, 1 = Minimal, 5 = Severe/High; N = No Section, 2 = Slight, I = Incomplete Section; A = Autolysis, 3 = Moderate; X = Not Remarkable, 4 = Moderately Severe, High

GROUP	DOSE/ CONCENTRATION	COMPOUND
1	0 mg/kg/day	PET 700811
2	100 mg/kg/da	PET 700811
3	300 mg/kg/da	PET 700811
4	900 mg/kg/da	PET 700811

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210020	8210022	8210023	8210024	8210025	8210026	8210027	8210028	8210029	8210030	8210031	8210032	8210033	8210034	8210035	8210036	8210037	8210038	8210039
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion																			
CERVICAL SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LUMBAR SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
THORACIC SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PITUITARY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cyst																			
ADRENAL	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Cortical Hypertrophy																			
Congestion																			
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Atrophy																			
Congestion																			
PARATHYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	N
EYE	X	X	X	X	X	X				X	X	X	X	X	X	X	X	X	X
Panophthalmitis							5	5											
Phthisis Bulbi								5											
Anterior Uveitis									3										
Ruptured																			

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	821002	821002	821002	821002	821002	821002	821002	821002	821002	821003	821003	821003	821003	821003	821003	821003	821003	821003	821003
EYE (CONTINUED)																			
Retinal Detachment																			
Orbital Cellulitis																			
Posterior Uveitis																			
HARDERIAN GLAND			X		X	X		X	X	X	X		X		X	X		X	
Subacute Adenitis	2	2		2			4					1		1			1		2
Pigment																			
HEART	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion																			
AORTA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SPLEEN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pigment																			
SALIVARY GLAND	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MANDIBULAR LYMPH NODE	X	X		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X
Lymphocytic Hyperplasia														1					
Congestion			2																
THYMUS	X	X	X	X	X	X	X	X	X	X		X		X		X	X	X	
Congestion											1		1		1				1

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Experimental Pathology Laboratories, Inc.

Key: P = Present, 1 = Minimal, 5 = Severe/High; N = No Section, 2 = Slight, I = Incomplete Section; A = Autolysis, 3 = Moderate; X = Not Remarkable, 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210020	8210022	8210023	8210024	8210025	8210026	8210027	8210028	8210029	8210030	8210031	8210032	8210033	8210034	8210035	8210036	8210037	8210038	8210039
TRACHEA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TONGUE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LUNG	X	X	X				X		X		X	X	X	X	X	X	X		X
Peribronchial Lymphocytic																			
Hyperplasia										1									
Focal Subacute Alveolitis				3	1	3		1		2								3	
Focal Hemorrhage																			
Congestion						1													
Focal Pneumonocyte Hyperplasia																			
Focal Atelectasis																			
LIVER	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X
Focal Capsulitis																			
Centrilobular Hepatocytomegaly			1												1				
Congestion																			
Focal Hyperplasia																			
Focal Hepatocytomegaly																			
KIDNEY	X		X		X	X	X		X	X	X	X	X	X	X	X	X	X	X
Regenerative Tubules		2		1															
Chronic Nephropathy								1											
Congestion																			

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	820020	820102	820123	820124	820125	820126	820127	820128	820129	820130	820131	820132	820133	820134	820135	820136	820137	820138	820139
STOMACH	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Bile Pigment																			
DUODENUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PANCREAS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
JEJUNUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Submucosal Hemorrhage																			
ILEUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
COLON	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Nematodiasis																			
CECUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
RECTUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
OVARY	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X
Parovarian Cyst														P					
Cyst, NOS																			
CERVIX	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; i = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe, High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210020	8210022	8211023	8210024	8210025	8210026	8210027	8210028	8210029	8210030	8210031	8210032	8210033	8210034	8211035	8210036	8210037	8210038	8210039
UTERUS	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X
Distended									P										
FALLOPIAN TUBE	N	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
VAGINA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
URINARY BLADDER	X	X	X	X	X	X	X	X	N	X	X	X	N	X	X	X	X	X	X
Distended																			
Protein Cast																			
Submucosal Hemorrhage																			
MESENTERIC LYMPH NODE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion																			
SKELETAL MUSCLE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SCIATIC NERVE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SKIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MAMMARY GLAND	N	X	N	N	X	N	N	X	X	N	N	X	N	N	X	N	X	X	N
BONE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	8210020	8210022	8210023	8210024	8210025	8210026	8210027	8210028	8210029	8210030	8210031	8210032	8210033	8210034	8210035	8210036	8210037	8210038	8210039
BONE MARROW	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hypocellular																			
HEAD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Acute Rhinitis																			
Otitis Interna																			

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

ANIMAL NUMBER	8 2 1 0 0 2 1
BRAIN	X
Congestion	
CERVICAL SPINAL CORD	X
LUMBAR SPINAL CORD	X
THORACIC SPINAL CORD	X
PITUITARY	X
Cyst	
ADRENAL	X
Cortical Hypertrophy	
Congestion	
THYROID	X
Atrophy	
Congestion	
PARATHYROID	X
EYE	X
Panophthalmitis	
Phthisis Bulbi	
Anterior Uveitis	
Ruptured	

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

ANIMAL NUMBER	8 2 1 0 0 2 1
EYE (CONTINUED)	
Retinal Detachment	
Orbital Cellulitis	
Posterior Uveitis	
HARDERIAN GLAND	
Subacute Adenitis	1
Pigment	
HEART	X
Congestion	
AORTA	X
SPLEEN	X
Pigment	
SALIVARY GLAND	X
MANDIBULAR LYMPH NODE	X
Lymphocytic Hyperplasia	
Congestion	
THYMUS	
Congestion	2

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

ANIMAL NUMBER	8 2 1 0 0 2 1
TRACHEA	X
ESOPHAGUS	X
TONGUE	X
LUNG	X
Peribronchial Lymphocytic	
Hyperplasia	
Focal Subacute Alveolitis	
Focal Hemorrhage	
Congestion	
Focal Pneumonocyte Hyperplasia	
Focal Atelectasis	
LIVER	X
Focal Capsulitis	
Centrilobular Hepatocytomegaly	
Congestion	
Focal Hyperplasia	
Focal Hepatocytomegaly	
KIDNEY	X
Regenerative Tubules	
Chronic Nephropathy	
Congestion	

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

ANIMAL NUMBER	8 2 1 0 0 2 1
STOMACH	X
Bile Pigment	
DUODENUM	X
PANCREAS	X
JEJUNUM	X
Submucosal Hemorrhage	
ILEUM	X
COLON	X
Nematodiasis	
CECUM	X
RECTUM	X
OVARY	X
Parovarian Cyst	
Cyst, NOS	
CERVIX	X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

ANIMAL NUMBER	8210021
UTERUS	X
Distended	
FALLOPIAN TUBE	X
VAGINA	X
URINARY BLADDER	X
Distended	
Protein Cast	
Submucosal Hemorrhage	
MESENTERIC LYMPH NODE	X
Congestion	
SKELETAL MUSCLE	X
SCIATIC NERVE	X
SKIN	X
MAMMARY GLAND	X
BONE	X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 1

	ANIMAL NUMBER 82100211
BONE MARROW	X
Hypocellular	
HEAD	X
Acute Rhinitis	
Otitis Interna	

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000197

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 2

ANIMAL NUMBER	821006	821006	821006	821006	821006	821006	821006	821006	821007	821007	821007	821007	821007	821007	821007	821007	821007	821007
	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79
EYE																		
Panophthalmitis																		
Phthisis Bulbi																		
Anterior Uveitis																		
Ruptured																		
Retinal Detachment																		
Orbital Cellulitis																		
Posterior Uveitis																		
MANDIBULAR LYMPH NODE																		
Lymphocytic Hyperplasia																		
Congestion										1						2		2
THYMUS										X								
Congestion															1	1	1	2
LUNG																		
Peribronchial Lymphocytic																		
Hyperplasia																		
Focal Subacute Alveolitis																2		
Focal Hemorrhage																		
Congestion																		
Focal Pneumonocyte Hyperplasia																		
Focal Atelectasis																		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 2

ANIMAL NUMBER	821062	821063	821064	821065	821066	821067	821068	821069	821070	821071	821072	821073	821074	821075	821076	821077	821078	821079
LIVER	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Focal Capsulitis																		
Centrilobular Hepatocytomegaly																		
Congestion																		
Focal Hyperplasia																		
Focal Hepatocytomegaly																		
KIDNEY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Regenerative Tubules																		
Chronic Nephropathy																		
Congestion																		
PANCREAS							X											
OVARY													X					
Parovarian Cyst																		
Cyst, NOS																		
MEDIASTINAL LYMPH NODE																		
Lymphocytic Hyperplasia									1									

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 2

ANIMAL NUMBER	8 2 1 0 0 6 0	8 2 1 0 0 6 1
EYE		X
Panophthalmitis		
Phthisis Bulbi		
Anterior Uveitis		
Ruptured		
Retinal Detachment		
Orbital Cellulitis		
Posterior Uveitis		
MANDIBULAR LYMPH NODE		
Lymphocytic Hyperplasia		
Congestion		
THYMUS		
Congestion	1	3
LUNG		
Peribronchial Lymphocytic		
Hyperplasia		
Focal Subacute Alveolitis		
Focal Hemorrhage		
Congestion		
Focal Pneumonocyte Hyperplasia		
Focal Atelectasis		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 2

ANIMAL NUMBER	82100060	82100061
LIVER		X
Focal Capsulitis		
Centrilobular Hepatocytomegaly	1	
Congestion		
Focal Hyperplasia		
Focal Hepatocytomegaly		
KIDNEY	X	X
Regenerative Tubules		
Chronic Nephropathy		
Congestion		
PANCREAS		
OVARY		
Parovarian Cyst		
Cyst, NOS		
MEDIASTINAL LYMPH NODE		
Lymphocytic Hyperplasia		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	821024	821004	821005	821006	821008	821009	821010	821012	821013	821014	821015	821016	821018
BRAIN													
Congestion													
EYE													
Panophthalmitis													
Phthisis Bulbi													
Anterior Uveitis													
Ruptured													
Retinal Detachment													
Orbital Cellulitis													
Posterior Uveitis													
MANDIBULAR LYMPH NODE													
Lymphocytic Hyperplasia													
Congestion						1				1			
THYMUS													
Congestion										1	2		
TRACHEA													
LUNG													
Peribronchial Lymphocytic													
Hyperplasia													
Focal Subacute Alveolitis	3		1										
Focal Hemorrhage													
Congestion	1												

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	821024	821045	821056	821068	821089	821090	821102	821123	821134	821156	821168	821181
LUNG (CONTINUED)												
Focal Pneumonocyte Hyperplasia			2									
Focal Atelectasis												
LIVER	X	X	X	X	X	X	X		X	X	X	X	X
Focal Capsulitis												
Centrilobular Hepatocytomegaly												
Congestion												
Focal Hyperplasia												
Focal Hepatocytomegaly								1				
KIDNEY	X	X	X	X	X	X	X	X	X	X	X	X	X
Regenerative Tubules												
Chronic Nephropathy												
Congestion												
OVARY									X			
Parovarian Cyst												
Cyst, NOS								P				
UTERUS												
Distended			P									
MEDIASTINAL LYMPH NODE												
Lymphocytic Hyperplasia			1							2		

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000203

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	8210102	8210104	8210105	8210106	8210108	8210109	8210110	8210112	8210113	8210114	8210115	8210116	8210118
PANCREATIC LYMPH NODE				N									

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Key: P – Present, 1 – Minimal, 5 – Severe/High, N – No Section, 2 – Slight, I – Incomplete Section, A – Autolysis, 3 – Moderate, X – Not Remarkable, 4 – Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	82100100	82101001	82101003	82101007	82101011	82101017	82101019
BRAIN					X		
Congestion							
EYE	X						
Panophthalmitis							
Phthisis Bulbi							
Anterior Uveitis							
Ruptured							
Retinal Detachment							
Orbital Cellulitis							
Posterior Uveitis							
MANDIBULAR LYMPH NODE							
Lymphocytic Hyperplasia							
Congestion							
THYMUS							
Congestion				3			
TRACHEA						X	
LUNG	X				X		
Peribronchial Lymphocytic							
Hyperplasia							
Focal Subacute Alveolitis							
Focal Hemorrhage							
Congestion						2	

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	82101001	82201101	82201103	82201007	82201101	82201171	82101009
LUNG (CONTINUED)							
Focal Pneumonocyte Hyperplasia							
Focal Atelectasis							2
LIVER	X	X	X	X			
Focal Capsulitis							
Centrilobular Hepatocytomegaly					1		
Congestion						1	1
Focal Hyperplasia							
Focal Hepatocytomegaly							
KIDNEY	X	X	X	X			X
Regenerative Tubules							
Chronic Nephropathy							
Congestion					1	1	
OVARY							
Parovarian Cyst							
Cyst, NOS							
UTERUS							
Distended							
MEDIASTINAL LYMPH NODE							
Lymphocytic Hyperplasia							

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000206

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	821010	821010	821010	821010	821011	821011	821011
	010003	010011	010037	010107	011011	011177	011199
PANCREATIC LYMPH NODE							

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000207

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8 2 1 0 1 5 2	8 2 1 0 1 5 3
BRAIN	X	X
Congestion		
CERVICAL SPINAL CORD	X	X
LUMBAR SPINAL CORD	X	X
THORACIC SPINAL CORD	X	X
PITUITARY	X	X
Cyst		
ADRENAL	X	X
Cortical Hypertrophy		
Congestion		
THYROID	X	X
Atrophy		
Congestion		
PARATHYROID	X	X
EYE	X	X
Panophthalmitis		
Phthisis Bulbi		
Anterior Uveitis		
Ruptured		

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000208

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8 2 1 0 1 5 2	8 2 1 0 1 5 3
EYE (CONTINUED)		
Retinal Detachment		
Orbital Cellulitis		
Posterior Uveitis		
HARDERIAN GLAND	X	X
Subacute Adenitis		
Pigment		
HEART	X	X
Congestion		
AORTA	X	X
SPLEEN	X	X
Pigment		
SALIVARY GLAND	X	X
MANDIBULAR LYMPH NODE	X	N
Lymphocytic Hyperplasia		
Congestion		
THYMUS	X	X
Congestion		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	88221100115523
TRACHEA	X X
ESOPHAGUS	X X
TONGUE	X X
LUNG	X
Peribronchial Lymphocytic	
Hyperplasia	
Focal Subacute Alveolitis	
Focal Hemorrhage	
Congestion	
Focal Pneumonocyte Hyperplasia	
Focal Atelectasis	1
LIVER	X X
Focal Capsulitis	
Centrilobular Hepatocytomegaly	
Congestion	
Focal Hyperplasia	
Focal Hepatocytomegaly	
KIDNEY	X
Regenerative Tubules	
Chronic Nephropathy	1
Congestion	

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	88210155	82101523
STOMACH	X	X
Bile Pigment		
DUODENUM	X	X
PANCREAS	X	X
JEJUNUM	X	X
Submucosal Hemorrhage		
ILEUM	X	X
COLON	X	X
Nematodiasis		
CECUM	X	X
RECTUM	X	X
OVARY	X	X
Parovarian Cyst		
Cyst, NOS		
CERVIX	X	X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	88 22 11 00 11 55 22 33
UTERUS	X X
Distended	
FALLOPIAN TUBE	X X
VAGINA	X X
URINARY BLADDER	X X
Distended	
Protein Cast	
Submucosal Hemorrhage	
MESENTERIC LYMPH NODE	X X
Congestion	
SKELETAL MUSCLE	X X
SCIATIC NERVE	X X
SKIN	X X
MAMMARY GLAND	X X
BONE	X X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Scheduled Sacrifices

Group 4

ANIMAL NUMBER	8 2 1 0 1 5 2	8 2 1 0 1 5 3
BONE MARROW	X	X
Hypocellular		
HEAD	X	X
Acute Rhinitis		
Otitis Interna		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821040	821041	821042	821043	821044	821045	821046	821047	821048	821049	821050	821051	821054	821055	821056	821057	821058	821059
BRAIN	X		X	X		X	X	X	X			X	X	X	X	X	X	X
Congestion		2			1					1	1							
CERVICAL SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
LUMBAR SPINAL CORD	X	N	X	X	X	X	X	X	X	X	N	X	X	X		A	X	N
THORACIC SPINAL CORD	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PITUITARY	X	X	X		X	X	N	X	X	X	X	X	X	X	X	X	X	X
Cyst				P														
ADRENAL		X	X	X	X	X	X	X	X	X		X	X	X	X	X		X
Cortical Hypertrophy	2																	
Congestion											2						1	
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Atrophy																		
Congestion																		
PARATHYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EYE	X	X	X	X	A	X	X	X	X	X	A	X	X		X	X	X	X
Panophthalmitis														2				
Phthisis Bulbi																		
Anterior Uveitis																		
Ruptured																		

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821040	821041	821042	821043	821044	821045	821046	821047	821048	821049	821050	821051	821054	821055	821056	821057	821058	821059
EYE (CONTINUED)																		
Retinal Detachment																		
Orbital Cellulitis																		
Posterior Uveitis																		
HARDERIAN GLAND		X	X	X	X	X	X	X	X	X		X	X	X		X		
Subacute Adenitis	4										2				3		1	1
Pigment																		
HEART	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion																		
AORTA	X	X	X	X	X	X	X	N	X	X	X	X	X	X	X	X	X	X
SPLEEN	X	X	X	X	X	N	X	X	X	X	A	X	X	X	X	X	X	X
Pigment																		
SALIVARY GLAND	X	X	X	X	X	X	X	X	X	X	X	X	X	Y	X	X	X	X
MANDIBULAR LYMPH NODE	X		N	X	X	N	X		X			X	X	X	X	X	X	X
Lymphocytic Hyperplasia																		
Congestion		1						2		1	2							
THYMUS	N	X	X			X	X		X	N			X	X	X	X	X	N
Congestion				1	2			2			4	1						

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	82101401	82101441	82101442	82101443	82101444	82101445	82101446	82101447	82101448	82101449	82101450	82101551	82101554	82101555	82101556	82101557	82101558	82101559
TRACHEA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ESOPHAGUS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TONGUE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	N
LUNG				X		X	X					X	X					
Peribronchial Lymphocytic																		
Hyperplasia																		
Focal Subacute Alveolitis																		
Focal Hemorrhage																		
Congestion		2	1		1			2	1	2	3			1		1	1	
Focal Pneumonocyte Hyperplasia																		
Focal Atelectasis	2														2			1
LIVER			X		X	X	X		X			X	X	X				X
Focal Capsulitis																		
Centrilobular Hepatocytomegaly																		
Congestion	1	1		1				1		1	1				1	1	1	
Focal Hyperplasia		1																
Focal Hepatocytomegaly																		
KIDNEY			X		X	X	X		X			X	X	X	X	X		X
Regenerative Tubules				1														
Chronic Nephropathy																		
Congestion	1	3		1				1		1	1						1	

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Key P = Present, 1 = Minimal, 5 = Severe/High, N = No Section, 2 = Slight, I = Incomplete Section, A = Autolysis, 3 = Moderate, X = Not Remarkable, 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

001
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	821040	821041	821042	821043	821044	821045	821046	821047	821048	821049	821050	821051	821054	821055	821056	821057	821058	821059
STOMACH	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Bile Pigment																		
DUODENUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PANCREAS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
JEJUNUM		X	X	X	X	X	X	X	X	X	A	X	X	X	X	X	X	X
Submucosal Hemorrhage	2																	
ILEUM	X	X	X	X	X	X	X	X	X	X	A	X	X	X	X	X	X	X
COLON	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Nematodiasis		P																
CECUM	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
RECTUM	X	X	X	X	X	X	X	X	X	X	A	X	X	X	X	X	X	X
OVARY	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X
Parovarian Cyst																P		
Cyst, NOS																		
CERVIX	X	X	X	X	X	X	X	X	X	A	X	X	X	X	X	X	X	X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	82140	82141	82142	82143	82144	82145	82146	82147	82148	82149	82150	82151	82154	82155	82156	82157	82158	82159
UTERUS	X	X	X	X	X	X	X	X	X	A	X	X	X	X	X	X	X	X
Distended																		
FALLOPIAN TUBE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
VAGINA	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
URINARY BLADDER	X	X	X			X	X	N		A	X	X	X	X	X	X	X	X
Distended				P	P				P									
Protein Cast																		
Submucosal Hemorrhage																		
MESENTERIC LYMPH NODE	X	X	N	X	X	X	X	X	X	X	N	X	X	X	X	X	X	X
Congestion																		
SKELETAL MUSCLE	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
SCIATIC NERVE	X	X	X	X	X	X	X	X	N	X	X	X	X	X	X	N	X	X
SKIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	N
MAMMARY GLAND	X	N	X	X	X	X	X	X	X	N	X	X	X	X	X	X	N	N
BONE	X	X	X	X	X	X	X	N	X	X	X	X	X	X	X	X	X	X

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HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Female Rats
Moribund Sacrifice & Deaths

Group 4

ANIMAL NUMBER	82140	82141	82142	82143	82144	82145	82146	82147	82148	82149	82150	82151	82154	82155	82156	82157	82158	82159
BONE MARROW	X	X	X	X	X	X	X	N	X	X	X	X	X	X	X	X	X	X
Hypocellular																		
HEAD	X	X	X	X	X	X	X	X	X		X	X	X	X		X	X	
Acute Rhinitis										3								1
Otitis Interna															1			

EPL
Experimental Pathology Laboratories, Inc.

Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe High

000219

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS TABLES

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 1 - Sacrificed Dosage Level: 0 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210010	Thymus	Reddened, mottled	Congestion
	Lungs	Red patchy areas	Congestion
	Lungs - both diaphragmatic lobes	White spots	Focal pneumonocyte hyperplasia
8210011	Mandibular lymph nodes	Reddened	Congestion
	Thymus	Reddened	Congestion
8210012	Thymus	Reddened, mottled	Congestion
	Liver	Large multilocular herniation of dorsal median lobe	Focal capsulitis
8210013	Thymus	Reddened	Congestion
8210014	Mandibular lymph node	Reddened	Congestion
	Thymus	Reddened	Congestion
8210015	Thymus	Slight reddening	Congestion
8210016	Thymus	Reddened	Congestion
8210017	Thymus	Reddened	Congestion
8210018	Thymus	Reddened	Congestion
8210019	Thymus	Reddened	Congestion

000221

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 2 - Sacrificed Dosage Level: 100 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210041	Lung - both diaphragmatic lobes	Few < 1 mm white foci	Focal subacute alveolitis; focal pneumonocyte hyperplasia
	Mediastinal lymph nodes	Slightly enlarged	No corresponding lesion
8210043	Lung - left anterior dorsal surface	Slightly firm and pale	No corresponding lesion
8210044	Lungs - all lobes	Multifocal mottling, moderate	Focal subacute alveolitis; focal pneumonocyte hyperplasia
8210046	Liver - left lateral lobe	Linear white streak approximately 2 cm in length	Focal capsulitis
8210047	Mandibular lymph node	Red in color	Congestion
8210049	Mediastinal lymph nodes	Slightly enlarged	Lymphocytic hyperplasia
	Lungs - all lobes	Few pinpoint white spots	Focal subacute alveolitis
8210051	Thymus	Slightly red	Congestion
8210052	Thymus	Slightly red	Congestion
	Mediastinal lymph node	Slightly enlarged	Lymphocytic hyperplasia
8210053	Thymus	Reddened	No corresponding lesion
8210054	Mandibular lymph nodes	Reddened	Congestion
	Thymus	Reddened	Congestion
8210055	Mandibular lymph nodes	Reddened	Congestion
	Thymus	Reddened	Congestion
8210056	Mandibular lymph nodes	Reddened	Congestion

000222

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 2 - Sacrificed Dosage Level: 100 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210056 (Cont'd)	Thymus	Reddened	Congestion
8210057	Thymus	Reddened	Congestion
8210058	Mediastinal lymph node	Slightly enlarged	No corresponding lesion
	Lung - all lobes	Pinpoint white spots	Peribronchial lymphocytic hyperplasia

000223

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 3 - Sacrificed Dosage Level: 300 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210086	Eye - right	Smaller than normal	Phthisis bulbi; retinal detachment
8210087	Lung - both diaphragmatic lobes	Few < 1 mm white foci	Focal subacute alveolitis
	Harderian gland - right eye	Enlarged, darkened	Pigment
8210089	Kidneys - bilateral	Slightly enlarged, darkened, mottled	Chronic nephropathy
	Lungs - both diaphragmatic lobes	White spots < 1 mm	Focal subacute alveolitis
	Bronchial lymph node	Slightly enlarged	No corresponding lesion
8210090	Lungs - all lobes	Mottled	Focal subacute alveolitis; Focal pneumonocyte hyperplasia
	Mediastinal lymph node	Slightly enlarged	Lymphocytic hyperplasia
8210097	Lung - all lobes	Pinpoint white spots	Focal subacute alveolitis
	Lungs - right diaphragmatic lobe, distal portion	Slightly mottled	No corresponding lesion
8210098	Lungs - all lobes	Pinpoint white spots	Focal subacute alveolitis
	Mediastinal lymph node	Slightly enlarged	No corresponding lesion
8210099	Mandibular lymph node	Slightly reddened	Congestion
	Thymus	Reddened	Congestion

000224

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 3 - Moribund/Deaths Dosage Level: 300 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210080	Urinary bladder	Distended with red-tinged fluid, a few irregular scattered reddened areas 0.2-0.4 cm on mucosa, appears hemorrhagic	Distended; submucosal hemorrhage
8210081	Lungs	Bright red	Congestion
	Stomach - glandular mucosa	A few 0.1 cm to 0.2 cm black foci	Bile pigment
8210082	Thymus	Reddened	Congestion
	Liver	Mottled	Centrilobular hepatocytomegaly
8210085	Eyes	Opaque	No corresponding lesion
	Urinary bladder	Contains red-tinged fluid, serosa reddened, (2) pinpoint red foci on mucosa, also cystic calculi contained within bladder	No corresponding lesion

000225

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 4 - Sacrificed Dosage Level: 900 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210120	Lungs - left anterior lobe	Reddened and firm	No corresponding lesion
8210131	Epididymis - right	3.0 mm white spot	Sperm granuloma
8210133	Thymus	Reddened	No corresponding lesion
	Liver	Large	No corresponding lesion
8210134	Epididymis - left	Small nodule	Sperm granuloma
8210137	Thymus	Reddened	Congestion

000226

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Males Group Number: 4 - Moribund/Deaths Dosage Level: 900 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210121	Testes	Soft	No corresponding lesion
	Lungs	Mottled	Congestion
	Thyroids	Reddened	Congestion
8210123	Lungs	Pale	No corresponding lesion
8210124	Liver	Mottled	Centrilobular hepatocytomegaly
8210125	Mandibular lymph nodes	Reddened	Congestion
	Liver	Mottled	No corresponding lesion
8210127	Liver	Mottled	Congestion
	Eye - right	Damaged	Phthisis bulbi
8210135	Brain	Swollen, outer surface dull pinkish color, appears congested	No corresponding lesion
	Lungs	Mottled	Congestion
	Urinary bladder	Filled with red-tinged fluid	Distended
8210136	Stomach - interior wall	Multiple dark foci	No corresponding lesion
	Brain	Swollen and red	No corresponding lesion

000227

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 1 - Sacrificed Dosage Level: 0 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210023	Mandibular lymph node	Slightly red	Congestion
8210024	Ovary - left	Cystic	No corresponding lesion
8210027	Eye - right	Enlarged, protruding, firm, filled with organized blood clot	Panophthalmitis
	Uterus	Thin walled, distended with clear fluid, moderate	No corresponding lesion
8210028	Spleen	Enlarged, engorged with blood	No corresponding lesion
8210029	Eye - right	Slight conjunctival exudate	Anterior uveitis
	Uterus	Thin walled, moderately filled with clear fluid	Distended
8210030	Mandibular lymph nodes	Reddened	No corresponding lesion
	Thymus	Reddened	No corresponding lesion
	Lungs - both diaphragmatic lobes	Few pinpoint white spots	Focal subacute alveolitis; peribronchial lymphocytic hyperplasia
8210031	Thymus	Reddened	Congestion
8210033	Thymus	Reddened	Congestion
8210034	Ovary - left	Cyst	Parovarian cyst
8210035	Thymus	Reddened	Congestion
8210036	Mandibular lymph nodes	Reddened	No corresponding lesion
8210037	Thymus	Reddened	No corresponding lesion

000228

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 1 - Sacrificed Dosage Level: 0 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210038	Thymus	Slightly reddened	No corresponding lesion
8210039	Thymus	Slightly reddened	Congestion

000229

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 1 - Moribund/Deaths Dosage Level: 0 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210021	Liver - right median lobe	White pinpoint focus	No corresponding lesion

000230

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 2 - Sacrificed Dosage Level: 100 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210062	Liver	Diffusely pale, slightly	No corresponding lesion
8210068	Pancreas	1.5 mm nodule on head on pancreas, nodule reddened with pale center	No corresponding lesion
8210070	Mediastinal lymph node	Slightly enlarged	Lymphocytic hyperplasia
	Liver	Herniated, medium, probably agonal	No corresponding lesion
8210071	Mandibular lymph node	Slightly reddened	Congestion
	Thymus	Red	No corresponding lesion
8210074	Ovary - left	0.5 cm cyst	No corresponding lesion
8210076	Thymus	Reddened	Congestion
8210077	Mandibular - right	Reddened	Congestion
	Thymus	Reddened	Congestion
	Lungs - all lobes	Pinpoint white foci	Focal subacute alveolitis
8210078	Thymus	Reddened	Congestion
8210079	Mandibular lymph node	Slightly reddened	Congestion
	Thymus	Reddened	Congestion

000231

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 2 - Moribund/Deaths Dosage Level: 100 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210060	Thymus	Reddened	Congestion
8210061	Thymus	Reddened	Congestion

000232

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 3 - Sacrificed Dosage Level: 300 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210102	Liver	Diffusely pale, moderately	No corresponding lesion
	Lung - all lobes	Mottled, slightly	Congestion; focal subacute alveolitis
8210105	Mediastinal lymph node	Enlarged	Lymphocytic hyperplasia
	Lungs - all lobes	Multiple white spots 1 mm in size and less	Focal subacute alveolitis
	Uterus	Enlarged, thin walled, filled with clear fluid	Distended
8210106	Lungs	Mottled, bronchioles distended	Focal pneumonocyte hyperplasia
	Pancreatic lymph node	Reddened	No section
8210109	Mandibular lymph node	Reddened	Congestion
8210112	Ovary - left	0.5 cm cyst	Cyst, NOS
8210113	Ovary - left	1.5 cm cyst	No corresponding lesion
8210114	Thymus	Reddened	Congestion
	Liver - medial lobe	Herniation 3.4 in diameter	No corresponding lesion
	Mediastinal lymph node	Slightly enlarged	Lymphocytic hyperplasia
8210115	Mandibular lymph nodes	Slightly large	No corresponding lesion
	Thymus	Reddened	Congestion

000233

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 3 - Moribund/Deaths Dosage Level: 300 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210100	Lungs	Pale	No corresponding lesion
	Eye - right	Opaque	No corresponding lesion
8210107	Thymus	Reddened	Congestion
8210111	Brain	Meninges reddened	No corresponding lesion
	Lungs	Failed to collapse when the thorax was opened, spongy and mottled	No corresponding lesion
8210117	Trachea	Froth in trachea	No corresponding lesion
	Lungs	Mottled	Congestion
8210119	lungs	Mottled	Focal atelectasis

000234

3401
13 Week Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rats Sex: Females Group Number: 4 - Moribund/Deaths Dosage Level: 900 mg/kg/day

Animal Number	Client's Tissue Identification	Client's Gross Observations	Microscopic Observations
8210148 (Cont'd)	Urinary bladder	Distended with blood-tinged urine, suffusive hemorrhages in wall	Distended
8210149	Intestinal tract	Filled with air	No corresponding lesion
8210150	Liver	Mottled with brown spots 0.2 x 0.1 cm	Congestion
	Spleen	Dark black spots on the end	Autolysis
	Adrenals	Red and enlarged	Congestion
	Kidney - left	Brown spots	Congestion
	Brain	All over brain meninges reddened and slightly swollen	Congestion
8210151	Lungs	Pale	No corresponding lesion
	Thymus	Reddened	Congestion
	Ovary - left	Cyst	No corresponding lesion
8210156	Brain	Swollen, slightly congested	No corresponding lesion
	Lung - right apical lobe	Congested, slightly firm	Focal atelectasis
	Lung - left	Pale, appears reduced, firm (slightly)	Focal atelectasis
8210157	Ovary - left	Clear cyst, 0.1 cm	Parovarian cyst
8210158	Lungs	Spongy	No corresponding lesion
	Liver	Mottled	Congestion

000237

ADDENDUM II

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.,

ADDENDUM PATHOLOGY REPORT

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

BORRISTON PROJECT NUMBER 3401

THIRTEEN-WEEK GAVAGE ADMINISTRATION OF PET TO RATS

ADDENDUM PATHOLOGY REPORT

Submitted to:

Borriston Laboratories, Inc.
Temple Hills, Maryland 20748

May 23, 1983

ADDENDUM PATHOLOGY SUMMARY

EPL

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

BORRISTON PROJECT NUMBER 3401

THIRTEEN-WEEK GAVAGE ADMINISTRATION
OF PET TO RATS

ADDENDUM PATHOLOGY SUMMARY

This is an addendum to the original pathology report for this study submitted on April 18, 1983. In the original study, fourteen of the twenty Group 4 (900 mg/kg/day) male rats had atrophy and decreased or absent spermatogenesis of the testicles; a single control rat had a similar change. This addendum reports the microscopic findings in the testicles from male rats in Groups 2 (100 mg/kg/day) and 3 (300 mg/kg/day). The findings for the testicles from each rat in these two groups are shown in the Histopathology Incidence Tables.

RESULTS

Sections of testicles from all of the male rats in Group 2 appeared normal. There was no microscopic indication of atrophy in the sections of testicles from Group 3 rats; however, two of the animals had minimal hypospermatogenesis. This change was characterized by occasional tubules having a decrease in spermatids in the tubule lining cells and no mature sperm in the lumens. The change was of such a slight degree there was no apparent decrease in the bulk of the testicle.

CONCLUSIONS

While there was an associated atrophy and decreased spermatogenesis of the testes in more than one-half of the male rats that received 900 mg/kg/day of the test compound, PET, for thirteen weeks, changes in those that received 300 mg/kg/day were minimal with an incidence similar to that of the controls. There was no microscopic testicular effect in the rats that received the lower dose of 100 mg/kg/day.

C. E. Gilmore

CHARLEY E. GILMORE, D.V.M.
Veterinary Pathologist

May 23, 1983

CEG/dmk

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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

QUALITY ASSURANCE REPORT CERTIFICATION

Client Name Borriston Laboratories, Inc. Client Study No. 3401

Study Director Dr. William O. Iverson Pathologist Dr. Charley E. Gilmore

Study Title Thirteen-Week Gavage Administration of PET to Rats (Addendum Report)

Test Article PET 700811 Species Rats

All parts of the pathology phase of this study, including the final report, were reviewed by Experimental Pathology Laboratories Quality Assurance Unit on May 17 - May 23, 1983. All findings were reported to the Study Director and Management.

Janet Milazzo

5/23/83

HISTOPATHOLOGY INCIDENCE TABLES

Group	Dose/ Concentration	Compound
2	100 mg/kg/day	PET 700811
3	300 mg/kg/day	PET 700811

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 2

ANIMAL NUMBER	82100040	82100041	82100042	82100043	82100044	82100045	82100046	82100047	82100048	82100049	82100050	82100051	82100052	82100053	82100054	82100055	82100056	82100057	82100058	82100059
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Atrophy																				
Aspermatogenesis																				
Hypospermatogenesis																				

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Scheduled Sacrifices

Group 3

ANIMAL NUMBER	8210086	8210087	8210088	8210089	8210090	8210092	8210093	8210095	8210096	8210097	8210098	8210099
TESTIS	X	X	X	X	X	X	X		X	X	X	X
Atrophy												
Aspermatogenesis												
Hypospermatogenesis								1				

000247

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

3401
13 Week Sacrifice
Male Rats
Moribund Sacrifice & Deaths

Group 3

ANIMAL NUMBER	82100080	82100081	82100082	82100083	82100084	82100085	82100091	82100094
TESTIS	X	X	X		X	X	X	X
Atrophy								
Aspermatogenesis								
Hypospermatogenesis				1				

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Key: P = Present, 1 = Minimal, 5 = Severe/High, N = No Section, 2 = Slight, I = Incomplete Section, A = Autolysis, 3 = Moderate, X = Not Remarkable, 4 = Moderately Severe/High

3401
13 Week Sacrifice

Species: Rats Sex: Fem

Animal Number	Client's Tissue Identification
8210152	Lung - left lobe
8210153	Liver - left lobe
	Lung - azygous lobe

000235

CERTIFICATE OF AUTHENTICITY

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END

3401
13 Week Sacrifice

Species: Rats Sex: Fe

Animal Number	Client's Tissue Identi
8210140	Adrenals - both
	Intestines
	Lung - left
	Small intestines
8210141	Lungs
	Liver - right media
	Liver - left median
	Brain
8210144	Brain
	Intestinal tract
8210145	Brain
8210146	Brain
	Stomach - glandular
8210147	Lung - left lobe
	Liver - right and l median lobe
	Brain
8210148	Lungs - anterior po

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