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13. ABSTRACT *(Maximum 200 words)* Subchronic toxic effects of 1,3,5-Trinitrobenzene (TNB) in male and female Fischer 344 rats were evaluated by feeding powdered certified laboratory chow diet supplemented with varied concentrations of TNB (0, 66.67, 400 and 800 mg/kg diet) so as to achieve a final target dose of 0, 5, 30 and 60 mg/kg b.w. for ninety days. Food intake in the 400 and 800 mg TNB dose groups of both sexes was reduced throughout the study and resulted in a significant decrease in absolute body weights. The calculated average TNB dosage was 4, 25 and 49 mg/kg/day for females and 4, 21 and 44 mg/kg/day for males. A decrease in testicular weight in males and increase in relative spleen weight of both sexes in the 400 and 800 mg TNB dose groups were noted. Also, the relative brain weight was increased in the male 400 and 800 mg TNB dose groups while the relative liver weight was increased in 800 mg TNB dose group of both sexes. Histopathological examinations suggested that the susceptible organs for TNB toxicity were kidney (hyaline droplets), spleen (extramedullary hematopoiesis) and testes (seminiferous tubular degeneration). Hematology and clinical chemistry studies indicated a decrease in red blood cell count and hematocrit, a decrease in alkaline phosphatase, an increase in reticulocytes and increased methemoglobin concentration as compared to controls in both sexes.

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Compliance Statement

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 21 of the U.S. Code of Federal Regulations Part 792 issued August 17, 1989. All deviations from the protocol and/or GLPs are listed in Appendix K. There were no deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

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QUALITY ASSURANCE STATEMENT

The portions of this toxicology project performed and reported by Pathology Associates, Inc. has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Environmental Protection Agency. The following table is a record of the inspections/audits performed and reported by the QAU.

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07-29-94	Final	07-29-94
07-27-94	Final	07-27-94
02-02-93	Trimming	02-03-93
02-02-93	Embedding	02-03-93
01-26-93	Necropsy	01-27-93
12-18-92	Food/Water Consumption	12-21-92
12-14-92	Blood Collection	12-15-92
11-09-92	Food/Water Consumption	11-11-92

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7-29-94
Date

Study Number: 92-003

QUALITY ASSURANCE STATEMENT

This clinical pathology data has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Environmental Protection Agency. Results of these activities indicate that the portions of the study performed by PAI conformed with GLP standards and applicable Standard Operating Procedures. The following table is a record of the inspections/audits performed and reported by the QAU.

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Director
Feb 12, 1993	Hematology: Summary of Tests (45-Day)	Feb 18, 1993
Feb 12, 1993	Hematology: Individual Animal Report (45-Day)	Feb 18, 1993
Feb 12, 1993	Hematology: Individual Animal by Group (45-Day)	Feb 18, 1993
Feb 12, 1993	Chemistry: Summary of Tests (45-Day)	Feb 18, 1993
Feb 12, 1993	Chemistry: Individual Animal Report (45-Day)	Feb 18, 1993
Feb 12, 1993	Chemistry: Individual Animal by Group (45-Day)	Feb 18, 1993
Feb 12, 1993	Hematology: Summary of Tests (90-Day)	Feb 18, 1993
Feb 12, 1993	Hematology: Individual Animal Report (90-Day)	Feb 18, 1993
Feb 12, 1993	Hematology: Individual Animal by Group (90-Day)	Feb 18, 1993

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Study # 92-002
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Study Timetable:

Study Initiation: October 13, 1992

Initiation of Dosing: October 29 and 30, 1992

Completion of Necropsy: January 26 and 27, 1993

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INTRODUCTION

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, it has been suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct (Burlinson, 1980). It is also found in aquatic systems and surface soils as a by-product of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of these compounds (Walsh and Jenkins, 1992).

Toxicity data on these compounds are limited. The oral LD_{50} of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD_{50} of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits were noted. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs (Fitzgerald et. al., 1992 a,b,c). Some of the toxicological effects of DNB are: formation of methemoglobin, testicular degeneration and reproductive failure, weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin (Von Burg, 1989). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Dermatitis, liver atrophy, spleen effects, headaches, weight loss and respiratory irritation were reported following tetryl exposure (U.S. EPA, 1990). Atmospheric concentration of 1.5 mg/m^3 or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in the Salmonella mutagenesis assay (McGregor et. al., 1989). TNB has also been shown to form adducts of blood proteins and tissue DNA in rats (Reddy et. al., 1991).

Objective of the Study

This study was conducted in order to evaluate the toxicity of TNB when administered in the diet for 90 days and to provide data to select doses for a 2 year chronic study.

MATERIALS AND METHODS

Test Material Preparation

1,3,5-Trinitrobenzene powder (CAS #99-35-4) was prepared by Dr. W. Koppes at the Naval Surface Warfare Center and determined to be 99.83% pure which was confirmed by the U.S. Army Biomedical Research and Development Laboratory and the U.S. EPA. Analysis by HPLC revealed no detectable impurities. Certified powdered Purina Laboratory Chow 5002 was purchased (Ralston-Purina Co., St. Louis, MO) and stored at 4°C until used. TNB diets were prepared weekly. First, 1.2 g of TNB was added to 50 g of powdered diet in a mortar and thoroughly ground with a pestle. Afterwards 200 g of the diet was added and mixed for 15 minutes followed by 550 g and mixed for an additional 15 minutes. Finally, the remaining diet (700 g) was added and mixed for 30 minutes in a mechanical mixer (Kitchen Aid, St. Joseph, MI)) for uniform distribution of TNB in the diet. This was verified by determining the TNB concentration in the diet, taken from each of the 1 kg mixtures, by quantitative analysis done by HPLC. The premixed diet (0.8 g/kg) was further diluted with fresh powdered diet to obtain the desired TNB concentration in the lower dose groups. The diet feeders were refilled twice a week and changed weekly.

Analyses of the TNB-feed mixtures were carried out on acetone extracts of the mixtures, utilizing a Waters 600E chromatography system (Waters, Milford, MA), equipped with a 490E programmable multiwavelength detector, operating at 254 nm. The entire chromatography system was interfaced with a Berthold HPLC computer program, Version 1.65 (Berthold, Nashua, NH). The TNB was eluted from a Zorbax C-8 column (9.4 mm x 25 cm) (MAC-DOD Analytical, Chadds Ford, PA) with a water-methanol gradient, at a flow rate of 3 ml/min. The gradient had an initial condition of 20% methanol which was increased in a linear fashion from 20% to 50% in 15 minutes and then to 65% in 25 minutes, and finally to 100% in 10 minutes. The column was washed for an additional 5 minutes and brought back to 20% methanol by reverse gradient and equilibrated for an additional 10 minutes at initial conditions before the next sample was injected. Working standards were prepared in Burdick and Jackson HPLC grade high purity methanol (Baxter, Obetz, OH). Analytical data of these mixtures is presented in Appendix I.

Animals and Maintenance

Male and female Fischer 344 rats, confirmed free of viral antibodies, bacteria and parasites, were obtained from Charles River Laboratories, Kingston, New York. The animals, 7-8 weeks old and weighing approximately 120-130 g when delivered, were held for 1 week in quarantine prior to initiation of treatment. The animals were housed in a temperature (20-22°C) and humidity (40-60%) controlled room on a 12:12 hour light:dark cycle. For the study, they were housed individually in polycarbonate cages and water was administered ad libitum. Animal identification was done using electronic implants (Bio Medic, Maywood, NJ) with the rats assigned to control and treatment groups according to a computer-generated set of random numbers. The weight variation of the animals of each sex used did not exceed ± 2 s.d. of the mean weight at the time of delivery. The cages were

identified with a color-coded identification card indicating the animal and treatment group. All aspects of the study were conducted in compliance with the guidelines of the American Association for Accreditation of Laboratory Animal Care.

All rats were observed twice daily for physiological and behavioral responses as well as for mortality or morbidity. Food and water consumption were recorded twice weekly. Body weights were taken prior to the start of the study, once weekly during the study and at the final sacrifice.

Experiment Design

Group	No. of Animals	Sex	Diet Concentration mg TNB/kg	Target Dose mg/kg b. w./day
1	10	F	0	0
2	10	F	800	60
3	10	F	400	30
4	10	F	66.67	5
5	10	M	0	0
6	10	M	800	60
7	10	M	400	30
8	10	M	66.67	5

Hematology and Clinical Chemistry

Hematology and clinical chemistry analyses were done on days 45 and 90. Hematology parameters were assessed using a Serono-Baker Hematology Analyzer, Model 9000, coupled to a computer running Labcat® software (Innovation Programming, Inc., Princeton, NJ). Total red and white blood cell counts, platelet count, differential leukocyte count, hemoglobin, and packed cell volume were measured and computed. Methemoglobin samples were analyzed on a IL 482 Co-Oximeter. Heinz bodies were determined using the crystal violet procedure (Lee et. al., 1993) with microscopic examination for positive cells (>5 Heinz bodies).

Clinical chemistry was performed using a Cobas Fara II centrifugal analyzer with a non-selective electrode (ISE) module. This system was also interfaced with a personal computer and the Labcat software system. Clinical chemistry analytes included sodium, potassium, total protein, albumin, calcium, total bilirubin, blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, glucose and alkaline phosphatase.

Statistical Evaluation

Males and females were considered separately in all statistical analyses. A one-factor (dose) analysis of variance (ANOVA) was used to analyze normally-distributed measures: body weights, organ weights, organ weight ratios, food and water consumption, hematology and clinical chemistry. When a treatment effect was noted ($p \leq 0.05$, F-test) the difference between the control and the treatment groups was probed using a multiple comparison procedure (Dunnett's t-test).

Necropsy and Histopathology

Prior to necropsy, the animals were anesthetized with pentobarbital (60 mg/kg bw, i. p.) and blood samples were collected via cardiac puncture after the body weight was recorded. Following euthanasia via exsanguination, all external surfaces, orifices, external surface of the brain, cervical tissues, all organs, and the thoracic, abdominal and pelvic cavities were examined for gross lesions.

During necropsy the following tissues were weighed: brain, liver, spleen, kidneys, adrenals, lungs, thymus, testes w/epididymides, ovaries, and heart.

The following tissues were harvested from each animal and preserved in 10% neutral buffered formalin:

skin
mandibular and
mesenteric lymph nodes
mammary glands
thigh muscle
sciatic nerve
sternum
femur with marrow
thymus
trachea
lungs with bronchi
heart and aorta
thyroid
parathyroids
esophagus
stomach
duodenum
jejunum
tongue
salivary gland
ileum
colon
cecum
rectum
liver
pancreas
spleen
kidneys
adrenals
urinary bladder
seminal vesicles
prostate
testes, including epididymides
ovaries
uterus
nasal cavity with turbinates
brain
pituitary
preputial or clitoral glands
Zymbal's gland
thoracic spinal cord

Subsequently, these tissues were trimmed, processed and embedded in paraffin. Blocks were sectioned at 5µ and slides were prepared and stained with hematoxylin and eosin. All tissues were examined in the high dose and control groups of both sexes. The spleen, testes and kidneys (males only) were identified as target organs and examined in the appropriate groups.

The inflammatory and degenerative lesions were graded according to severity using a scale of one to four (minimal, mild, moderate or marked). Data were tabulated according to individual animal and summarized by group. In addition, the gross observations and microscopic diagnoses were correlated for each animal. Labcat histopathology software was used for data management.

Specimen, Raw data, and Final Report Storage

All tissue specimens, blocks and slides, raw data and final report will be placed in the U.S. EPA storage facility.

RESULTS

Food and Water Consumption

Overall food and water consumption data are listed in Table 1, while weekly data is given in Appendix A. The food consumption data shows a significant decrease ($p \leq .05$) in the 800 and 400 mg TNB dose groups of both sexes and the 66.67 mg female dose group. Water consumption revealed no significant changes in males while females receiving 400 and 800 mg TNB were increased.

Using the food consumption data, the average daily dose levels of TNB received by group is presented in Table 2.

Body Weights, Organ Weights and Weight Ratios

The mean group values for the weekly body weights are listed in Tables 3 (females) and 4 (males) while organ weights (heart, brain, spleen, adrenals, thymus, ovaries/testes, kidneys, lungs and liver) are given in Tables 5 (females) and 6 (males). Mean group values for organ to body weight ratios are present in Tables 7 (females) and 8 (males). Individual body weights are found in Appendix B with individual organ weights present in Appendix C.

Significant decreases ($p \leq 0.05$) from control terminal body weights were noted in both sexes in the 800 and 400 mg TNB dose groups. The remaining groups did not display these decreased values.

Organ weights as a percent of the total body weight were significantly ($p \leq 0.05$) different from controls for the following organs:

Brain - The 800 and 400 mg TNB dose groups (males) had increased values.
Spleen - The 800 and 400 mg TNB dose groups of both sexes had increased values.
Testes - The 800 and 400 mg TNB dose groups (males) had decreased values.
Liver - The 800 mg TNB dose group of both sexes had increased values along with the 400 mg TNB dose group (males).
Lungs - Increased values were present in the 800 mg TNB dose group (males).

Hematology

Hematology analyses performed were total white blood cell count (WBC), platelet count, red blood count (RBC), methemoglobin (MetHb), hemoglobin (HGB), hematocrit (HCT), reticulocytes, Heinz bodies and differential leukocyte count at 45 and 90 days. Group data are summarized in Tables 9-12. Individual data are listed in Appendix D.

1. WBC and Differential:

At 45 days, only females in the 800 and 66.67 mg TNB dose groups had a significant increase ($p \leq 0.05$) in total while blood cell count while at 90 days the only significant change amongst the groups in either sex was a minimal increase noted in low dose males. A relative shift to an increased segmented neutrophil percentage with a decreased lymphocyte count was evident in this same group and in low dose females. However, at 45 days the shift was to a higher lymphocyte count in the two female groups which had an elevated WBC.

2. RBC:

At 45 days, both sexes in the 800 and 400 mg TNB dose groups had significantly decreased ($p \leq 0.05$) values while at 90 days a significant decrease ($p \leq 0.05$) in total red cell count was present in the same female groups and in all treated male groups.

3. Hemoglobin:

At 45 days, all female groups and males receiving 800 and 400 mg TNB had significantly decreased ($p \leq 0.05$) hemoglobin levels while at 90 days a significant decrease ($p \leq 0.05$) was featured in all treated male groups and in females receiving 800 and 400 mg TNB.

4. Hematocrit:

At 45 days, all female groups and males receiving 800 mg TNB had significantly decreased ($p \leq 0.05$) hematocrit values while at 90 days a significant decrease ($p \leq 0.05$) was noted in females receiving 800 mg TNB while females in the 66.67 mg TNB dose group displayed an increased value. There were no significant changes in the males.

5. Platelets:

At 45 days, females in the 800 and 400 mg TNB dose groups had significantly increased ($p \leq 0.05$) platelet values while at 90 days there were no significant changes in any group.

6. Reticulocytes:

At 45 days, males in the 800 and 400 mg TNB dose groups had significantly increased ($p \leq 0.05$) reticulocyte values along with the 800 mg female group while at 90 days, a significant increase ($p \leq 0.05$) in reticulocytes was noted in all female groups and in the male 800 mg TNB dose group.

7. Methemoglobin: (Jewish Hospital, Cincinnati, Ohio, performed these analyses)

At both 45 and 90 days, a significant increase ($p \leq 0.05$) was present in both sexes in the 800 and 400 mg TNB dose groups.

8. Heinz Bodies:

At both 45 and 90 days, there were no significant changes in any group.

Clinical Chemistry

The mean group values for each analyte are compiled in Tables 13-16. Individual data are present in Appendix E.

1. Total Protein:

At 45 days, females receiving 400 mgTNB had a significant increase ($p \leq 0.05$) in total protein while at 90 days there were no signficant differences amongst the groups except for a minimal increase in the male 400 mg TNB dose group.

2. Albumin:

At 45 days, there were no significant changes in albumin levels while at 90 days males in the 800 and 400 mg TNB dose groups and females in the 800 and 66.67 mg TNB dose groups were significantly ($p \leq 0.05$) increased.

3. Calcium:

At 45 days, the only significant change was a decreased calcium level in the male 66.67 mg TNB dose group while at 90 days there were no significant differences amongst the groups.

4. Total Bilirubin:

At 45 days, total bilirubin was marginally decreased in females receiving 66.67 mg TNB while at 90 days females in the 800 mg TNB dose group was the only group to show a significant change ($p \leq 0.05$).

5. Blood Urea Nitrogen (BUN):

At 45 days, there were no significant changes in blood urea nitrogen levels while at 90 days, males in the 800 and 400 mg TNB dose groups were significantly ($p \leq 0.05$) increased.

6. Creatinine:

At 45 days, there were no significant changes in creatinine levels while at 90 days the low dose (66.67 mg TNB) males were the only group which showed significant change ($p \leq 0.05$).

7. Aspartate Aminotransferase (AST):

At 45 and 90 days, there were no significant changes in aspartate aminotransferase levels.

8. Alanine Aminotransferase (ALT):

At 45 days, males receiving 800 and 66.67 mg TNB diet had significantly decreased ($p \leq 0.05$) alanine aminotransferase levels while at 90 days there were no significant differences amongst the groups.

9. Alkaline Phosphatase (ALK Phos):

At 45 days, males receiving 400 and 66.67 mg TNB diet had significantly decreased ($p \leq 0.05$) alkaline phosphatase values while at 90 days there were no significant differences amongst the groups.

10. Sodium:

At 45 and 90 days, there were no significant changes in sodium levels.

11. Potassium:

At 45 and 90 days, there were no significant changes in potassium levels.

12. Glucose:

At 45 and 90 days, there were no significant changes in glucose values.

Clinical Observations

Clinical observations are listed in Appendix F. There were no clinical observations that were meaningful.

Ophthalmology Findings (Appendix G)

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study which is a common finding in Fischer 344 rats of both sexes. In the time since performing the initial ophthalmic examination the corneal dystrophy lesions progressed in severity in almost all animals. This is an expected finding. The remaining abnormalities were sporadic and did not appear to be a dose-related effect. Conjunctivitis and keratitis are found routinely in Fischer 344 rats, becoming more

frequent with increased age, and most likely are related to the corneal dystrophy lesions. A single, anterior capsular cataract was also noted.

Mortality

There were no early deaths in any of the groups.

Gross Pathology

Gross lesions noted at the terminal sacrifice were mainly confined to males in the 800 and 400 mg TNB dose groups and involved a mild to moderate reduction in testicular size.

Histopathology (Appendix H)

All tissues were histopathologically examined in control and high dose animals of both sexes. The spleen was examined in all groups of both sexes while the kidneys and testes in all male rats only. Significant changes were noted in the testes, spleen, bone marrow and kidneys.

The testes were characterized in the 800 and 400 mg TNB dose groups by moderate to severe seminiferous tubular degeneration. The affected tubules were lined by fewer spermatogenic cells and contained a reduced number of mature spermatides. Cell debris and some multinucleated cells were also present in the tubules as well as in the ducts of the epididymis. The diameter of the affected tubules was decreased with the interstitium being more condensed and prominent.

The kidneys of male rats in all groups exhibited an increased incidence of cortical tubular hyaline droplet deposition. Many of these droplets were large and irregular resulting in prominent tubular degeneration with a compensatory increase in tubular regeneration.

The spleen and bone marrow both featured minimal to moderate erythroid cell hyperplasia. This was evident in both sexes in the 800 and 400 mg TNB dose groups. Only the spleen was examined in all the animals since this same compensatory change can be noted in multiple organs. Regenerative anemia, as noted by the hematology results, was the probable initiating factor for this response.

The remaining diagnoses as listed in the tables should be considered spontaneous since their incidence levels were low except for the inflammatory changes noted in the clitoral/preputial glands. Considering the lesion severity level in these glands, the remaining animals were not examined.

SUMMARY

Fischer 344 rats were fed diets containingTNB with a calculated average intake of 4.3, 24.7 and 49.3 mg TNB/kg b.w./day (females) and 3.9, 22.7 and 44.2 mg/kg b.w./day (males) for ninety days and the following significant toxicological effects of TNB were observed:

1. A significant decrease in average daily food consumption followed by a significant decrease in body weight in male and female rats receiving 400 and 800 mg TNB diet.

2. In male rats receiving 400 and 800 mg TNB diet, a significant increase in relative brain and liver weights, and a significant decrease in relative testes weights were noted. The relative spleen weights in both sexes were significantly increased.

3. A significant decrease in total red cell count was apparent in both sexes receiving 400 and 800 mg TNB diet. In contrast. a significant increase in the percent of reticulocytes in male rats receiving 400 and 800 mg TNB diet and in all female groups was noted as compared to control groups. This suggests the occurrence of toxicity induced regenerative anemia.

4. A decrease in hemoglobin content in all dose groups in males and a significant increase in methemoglobin were observed in both sexes receiving 400 and 800 mg TNB diet. There were no biologically meaningful differences in total white cell count or in the distribution of cell type between the groups.

5. Microscopic examination revealed significant changes in the testes (moderate to severe seminiferous tubular degeneration) in high dose groups (400 and 800 mg TNB diet), and cortical tubular hyaline droplet deposition in the kidney of all male rats receiving TNB.

6. The spleen and bone marrow featured mild to moderate erythroid cell hyperplasia in male and female rats receiving 400 and 800 mg TNB diet.

Table 1: Food and Water Consumption

Dose (mg TNB/kg diet)	Food (g/kg b.w./day)	Water (g/kg b.w./day)
	Females	
0	67.81±0.77	91.17±1.06
800	60.31±1.08 *	104.21±1.81 *
400	61.53±0.74 *	98.19±1.28 *
66.67	64.33±0.95 *	94.34±1.08
	Males	
0	59.45±0.82	75.18±3.35
800	53.78±0.93 *	76.70±1.01
400	56.82±0.84 *	74.98±0.91
66.67	59.34±0.84	72.69±1.01

Mean ± Standard Error.

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 2: Calculated Daily TNB Consumption

Group	Sex	Dose Groups (mg TNB/kg diet)	Expected Target Dose (mg TNB/kg b.w.)	Calculated Dose
1	F	0	0	
2	F	800	60	49.28±0.88
3	F	400	30	24.70±0.33
4	F	66.67	5	4.29±0.05
5	M	0	0	
6	M	800	60	44.16±0.85
7	M	400	30	22.73±0.35
8	M	66.67	5	3.91±0.05

Mean ± Standard Error

Table 3: Body Weights (grams)/Females

	Dose Groups (mg TNB/kg diet)			
Week	0	800	400	66.67
1	160.73±1.19	162.31±0.78	159.88±1.74	161.02±1.57
2	163.86±1.06	160.98±1.41	161.56±1.81	166.76±1.47
3	169.38±0.90	167.06±0.97	168.11±1.47	172.17±1.86
4	175.47±1.25	170.98±0.85	172.16±1.50	177.47±1.59
5	179.23±1.42	174.68±1.57	176.85±1.63	183.70±1.76
6	180.62±1.62	174.71±1.42 *	177.32±1.14	184.53±2.22
7	183.27±1.68	175.02±1.45 *	176.90±1.57 *	187.33±2.31
8	184.14±2.15	176.90±1.73 *	179.73±1.37	189.35±2.45
9	184.98±1.94	178.05±1.37 *	181.17±1.52	191.36±2.08 *
10	188.64±1.98	181.32±2.03 *	186.01±1.24	194.80±2.05
11	189.00±1.88	183.25±1.88	186.62±1.25	196.46±2.35 *
12	192.55±2.15	188.12±1.53	190.06±1.61	199.41±2.20 *
13	192.55±2.15	188.12±1.53	190.06±1.61	199.41±2.20 *

Mean ± Standard Error

* Significantly different from the control group ($p \leq .05$) by Dunnett's test.

Table 4: Body Weights (grams)/Males

	Dose Groups (mg TNB/kg diet)			
Week	0	800	400	66.67
1	213.51±2.49	210.25±1.97	205.99±2.33	209.07±2.40
2	229.26±3.08	213.58±1.87 *	215.26±2.64 *	224.28±2.95
3	248.18±3.39	224.74±1.91 *	230.81±3.27 *	241.86±3.55
4	264.31±3.47	234.65±2.06 *	241.96±4.22 *	256.40±4.19
5	278.62±3.79	243.82±2.25 *	260.14±3.54 *	269.34±4.81
6	286.29±4.06	251.15±2.12 *	258.20±4.88 *	274.75±5.12
7	296.91±4.91	255.91±1.89 *	265.59±4.74 *	286.03±5.38
8	296.42±5.63	258.25±2.03 *	266.73±4.12 *	286.87±5.23
9	302.01±6.18	263.32±1.75 *	272.83±4.28 *	292.37±5.66
10	318.66±6.68	274.67±1.69 *	286.25±4.91 *	306.07±6.30
11	326.07±6.93	280.13±1.35 *	293.88±4.63 *	314.53±6.19
12	329.45±7.14	283.41±1.57 *	297.11±4.42 *	318.45±6.10
13	329.45±7.14	283.41±1.57 *	297.11±4.42 *	318.45±6.10

Mean ± Standard Error

* Significantly different from the control group ($p \leq .05$) by Dunnett's test.

Table 5: Organ Weights (grams)/Females

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Liver	5.03±0.11	5.24±0.07	5.09±0.08	5.23±0.05
Kidneys	1.34±0.02	1.28±0.02	1.30±0.02	1.31±0.01
Heart	0.66±0.01	0.63±0.00	0.66±0.01	0.68±0.01
Ovaries	0.14±0.01	0.12±0.01	0.12±0.01	0.16±0.01
Brain	1.79±0.02	1.75±0.02	1.77±0.03	1.79±0.02
Spleen	0.44±0.01	0.62±0.01 *	0.54±0.02 *	0.46±0.01
Adrenals	0.09±0.00	0.07±0.00	0.07±0.00	0.08±0.00
Lungs	0.98±0.03	0.95±0.02	0.93±0.03	1.00±0.02
Thymus	0.24±0.02	0.19±0.01 *	0.21±0.01	0.22±0.01

Mean ± Standard Error.

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 6: Organ Weights (grams)/Males

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Liver	6.26±1.29	8.63±0.19	8.21±0.74	8.06±0.88
Kidneys	2.23±0.08	1.91±0.03 *	2.01±0.04 *	2.15±0.07
Heart	0.97±0.02	0.84±0.02 *	0.89±0.01 *	0.97±0.02
Testes	4.58±0.12	2.49±0.05 *	2.83±0.20 *	4.43±0.11
Brain	1.89±0.02	1.82±0.02	1.84±0.02	1.87±0.03
Spleen	0.63±0.02	0.85±0.03 *	0.71±0.01 *	0.61±0.02
Adrenals	0.07±0.00	0.07±0.00	0.06±0.01	0.07±0.00
Lungs	1.30±0.05	1.21±0.02	1.18±0.02	1.33±0.06
Thymus	0.30±0.03	0.22±0.02 *	0.24±0.02	0.25±0.01

Mean ± Standard Error.

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 7: Organ-to-Body Weight Ratios and Terminal Body Weights/Females

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Body Weight(g)	181.04±1.50	170.69±1.47 *	174.53±1.49 *	186.67±2.15
Liver (%)	2.78±0.07	3.07±0.04 *	2.92±0.04	2.80±0.03
Kidneys (%)	0.74±0.01	0.75±0.01	0.75±0.01	0.70±0.01
Heart (%)	0.37±0.01	0.37±0.00	0.38±0.01	0.37±0.01
Ovaries (%)	0.08±0.01	0.06±0.01	0.07±0.00	0.08±0.01
Brain (%)	0.99±0.01	1.03±0.02	1.02±0.02	0.96±0.02
Spleen (%)	0.24±0.00	0.36±0.01 *	0.31±0.01 *	0.24±0.00
Adrenals (%)	0.04±0.00	0.04±0.00	0.04±0.00	0.04±0.00
Lungs (%)	0.54±0.02	0.55±0.01	0.53±0.02	0.54±0.02
Thymus (%)	0.13±0.01	0.11±0.00	0.12±0.01	0.12±0.00

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 8: Organ-to- Body Weight Ratios and Terminal Body Weights/Males

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Body Weight(g)	318.40±6.65	264.89±1.66 *	280.61±4.03 *	305.93±5.55
Liver (%)	2.90±0.05	3.26±0.06 *	3.28±0.07 *	2.96±0.04
Kidneys (%)	0.70±0.01	0.72±0.01	0.71±0.01	0.70±0.01
Heart (%)	0.31±0.01	0.32±0.01	0.32±0.01	0.32±0.01
Testes (%)	1.44±0.04	0.94±0.02 *	1.00±0.06 *	1.45±0.02
Brain (%)	0.60±0.01	0.69±0.01 *	0.66±0.01 *	0.61±0.01
Spleen (%)	0.20±0.00	0.32±0.01 *	0.25±0.01 *	0.20±0.01
Adrenals (%)	0.02±0.00	0.03±0.00	0.02±0.00	0.02±0.00
Lungs (%)	0.41±0.01	0.46±0.01 *	0.42±0.01	0.43±0.01
Thymus (%)	0.09±0.01	0.08±0.01	0.09±0.01	0.08±0.00

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 9: Hematology Values in Females
45 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
RBC ($x10^6/\mu l$)	7.60 ±0.163	6.68* ±0.295	6.88* ±0.182	7.27 ±0.225
Hemoglobin (g/DL)	15.2 ±0.50	14.1* ±0.36	14.1* ±0.30	14.8 ±0.25
Hematocrit (%)	43.3 ±0.72	39.9* ±1.62	40.1* ±0.97	41.0* ±1.47
WBC ($x10^3/\mu L$)	3.9 ±0.68	5.2* ±0.91	4.8 ±0.44	5.2* ±0.77
Platelets (%)	811 ±33.5	961* ±75.5	898* ±46.6	876 ±20.1
Segmented Leukocytes ($x10^3/\mu L$)	0.9 ±0.29	1.0 ±0.13	1.1 ±0.24	1.2 ±0.22
Lymphocytes ($x10^3/\mu L$)	2.9 ±0.44	4.0* ±0.80	3.6 ±0.31	3.9* ±0.78
Heinz Bodies (%)	0 ±0.0	0 ±0.0	0 ±0.0	0 ±0.0
Monocytes ($x10^3/\mu L$)	0.1 ±0.04	0.1 ±0.04	0.1 ±0.08	0.1 ±0.05
Eosinophils ($x10^3/\mu L$)	0.0 ±0.00	0.1 ±0.09	0.0 ±0.00	0.0 ±0.00
Reticulocytes (%)	1.9 ±0.38	4.8* ±0.96	2.3 ±1.36	1.7 ±0.34
MetHb (%)	1.06 ±0.52	6.20* ±1.62	4.88* ±0.98	1.04 ±0.34

Mean ± SD
* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 1[illegible] Hematology Values in Males
45 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
RBC ($x10^6/\mu l$)	8.44 ±0.289	7.24* ±0.299	7.76* ±0.334	8.25 ±0.221
Hemoglobin (g/DL)	15.9 ±0.44	14.2* ±0.54	14.6* ±0.61	15.1 ±0.17
Hematocrit (%)	44.2 ±1.51	40.0* ±1.87	41.9 ±1.68	43.1 ±1.51
WBC ($x10^3/\mu L$)	7.0 ±1.71	6.6 ±0.97	6.9 ±0.83	6.1 ±0.83
Platelets (%)	849 ±76.6	949 ±68.0	343 ±42.5	891 ±62.0
Segmented Leukocytes ($x10^3/\mu L$)	1.6 ±0.18	1.5 ±0.24	1.6 ±0.33	1.7 ±0.13
Lymphocytes ($x10^3/\mu L$)	5.1 ±1.40	5.0 ±0.80	5.2 ±0.71	4.3 ±0.75
Heinz Bodies (%)	0 ±0.0	0 ±0.0	0 ±0.0	0 ±0.0
Monocytes ($x10^3/\mu L$)	0.2 ±0.12	0.1 ±0.07	0.1 ±0.07	0.2 ±0.06
Eosinophils ($x10^3/\mu L$)	0.0 ±0.09	0.0 ±0.04	0.0 ±0.00	0.0 ±0.00
Reticulocytes (%)	1.8 ±0.47	4.8* ±1.03	3.6* ±0.82	2.0 ±0.38
MetHb (%)	0.82 ±0.29	6.36* ±0.70	4.60* ±0.67	1.40 ±0.58

Mean ± SD
* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 11: Hematology Values in Females
90 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
RBC ($x10^6/\mu l$)	7.45 ±0.38	6.39* ±0.33	6.94* ±0.24	7.39 ±0.13
Hemoglobin (g/dL)	15.7 ±0.52	14.1* ±0.43	14.1* ±0.35	15.6 ±0.39
Hematocrit (%)	41.1 ±2.52	36.1* ±1.80	39.0 ±1.17	46.1* ±6.68
WBC ($x10^3/\mu L$)	8.4 ±1.47	9.0 ±1.07	9.1 ±1.34	9.7 ±1.01
Platelets ($x10^3/\mu L$)	883 ±51.1	958 ±107.4	858 ±110.2	840 ±59.1
Segmented Leukocytes (%)	20 ±2.7	19 ±1.5	19 ±3.3	24* ±3.4
Lymphocytes (%)	80 ±2.7	80 ±1.6	80 ±3.3	75* ±3.9
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
Monocytes (%)	0 ±0.3	0 ±0.3	0 ±0.0	1 ±1.2
Eosinophils (%)	0 ±0.3	0 ±0.4	1 ±1.0	0 ±0.6
Reticulocytes (%)	1.5 ±0.24	2.8* ±0.68	3.2* ±0.83	2.8* ±0.90
MetHb (%)	0.63 ±0.60	3.26* ±0.65	2.84* ±0.54	1.22 ±0.35

Mean ± SD
* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 12: Hematology Values in Males
90 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
RBC ($x10^6/\mu l$)	8.09 ±0.82	7.09* ±0.39	7.26* ±0.45	6.80* ±1.47
Hemoglobin (g/dL)	19.9 ±4.70	13.9* ±0.45	14.8* ±2.76	12.0* ±2.76
Hematocrit (%)	46.2 ±10.80	45.1 ±5.93	42.2 ±8.02	35.6 ±13.36
WBC ($x10^3/\mu L$)	9.4 ±1.51	10.8 ±1.89	10.7 ±1.40	12.8* ±1.06
Platelets ($x10^3/\mu L$)	1184 ±570.5	951 ±127.2	987 ±348.9	1371 ±1042.3
Segmented Leukocytes (%)	19 ±2.4	17 ±2.9	20 ±2.9	27* ±6.4
Lymphocytes (%)	81 ±2.4	82 ±2.8	80 ±2.5	72* ±7.1
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
Monocytes (%)	0 ±0.7	0 ±0.0	0 ±0.6	1 ±0.7
Eosinophils (%)	0 ±0.3	0 ±0.7	0 ±0.4	1 ±1.4
Reticulocytes (%)	2.0 ±0.34	4.3* ±0.91	2.9 ±0.60	2.0 ±0.14
MetHb (%)	0.95 ±0.38	5.46* ±0.82	4.43* ±0.95	1.64 ±0.28

Mean ± SD
* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 13: Clinical Chemistry Values for Females
45 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Glucose (mg/dl)	154 ±11.8	168 ±19.8	148 ±8.3	157 ±14.5
BUN (mg/dl)	31 ±2.5	33 ±2.6	34 ±2.4	33 ±4.6
Creatinine (mg/dl)	0.5 ±0.15	0.5 ±0.22	0.4 ±0.25	0.6 ±0.10
ALK Phos. (U/L)	165 ±12.3	166 ±16.2	146 ±48.5	143 ±27.7
AST (U/L)	162 ±59.8	137 ±70.2	126 ±26.3	106 32.0
ALT (U/L)	68 ±48.5	56 ±44.5	49 ±12.5	45 ±3.8
Potassium (mmol/L)	5.6 ±0.41	6.0 ±1.23	6.7 ±1.59	5.3 ±0.14
Albumin (g/dl)	4.0 ±0.04	4.3 ±0.24	3.9 ±0.24	4.1 ±0.08
Calcium (mg/dl)	11.6 ±0.62	10.9 ±0.28	10.8 ±0.35	11.1 ±0.24
Sodium (mmol/L)	135 ±8.4	140 ±20.3	147 ±28.0	145 ±12.2
Total Bilirubin (mg/dl)	0.2 ±0.05	0.2 ±0.00	0.2 ±0.05	0.1* ±0.05
Total Protein (g/dl)	7.0 ±0.26	7.2 ±0.36	7.9* ±0.52	7.6 ±0.65

Mean ± SD
* Significantly different from the control group (P≤ 0.05) by the Dunnett's test.

Table 14: Clinical Chemistry Values for Males
45 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Glucose (mg/dl)	195 ±11.4	197 ±12.1	170 27.2	196 ±7.7
BUN (mg/dl)	31 ±1.2	33 ±3.6	29 ±1.5	30 ±3.2
Creatinine (mg/dl)	0.7 ±0.17	0.7 ±0.05	0.6 ±0.08	0.6 ±0.05
ALK Phos. (U/L)	221 ±32.0	162 ±77.7	118* ±17.5	114* ±10.5
AST (U/L)	153 ±24.6	160 ±14.3	116 ±38.1	125 38.8
ALT (U/L)	87 ±23.8	53* ±6.1	66 ±4.9	63* ±12.1
Potassium (mmol/L)	5.4 ±0.23	6.0 ±0.56	5.4 ±0.06	5.6 ±0.63
Albumin (g/dl)	4.2 ±0.42	4.2 ±0.34	4.1 ±0.10	3.9 ±0.27
Calcium (mg/dl)	11.5 ±1.00	9.9 ±1.89	10.9 ±0.51	6.8* ±0.96
Sodium (mmol/L)	133 ±8.1	142 ±13.1	148 ±4.5	144 ±3.6
Total Bilirubin (mg/dl)	0.1 ±0.00	0.1 ±0 04	0.1 ±0.06	0.1 ±0.00
Total Protein (g/dl)	7.8 ±0.35	7.9 ±0.52	7.7 ±0.26	8.0 ±0.29

Mean ± SD
* Significantly different from the control group (P≤ 0.05) by the Dunnett's test.

Table 15: Clinical Chemistry Values for Females
90 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Glucose (mg/dl)	143.8 ± 20.18	141.9 ± 19.2	157.4 ± 22.38	153.2 ± 20.12
BUN (mg/dl)	15.8 ± 5.69	19.2 ± 1.62	18.5 ± 2.01	18.0 ± 1.76
Creatinine (mg/dl)	0.51 ± 0.03	0.53 ± 0.05	0.53 ± 0.05	0.55 ± 0.05
Alk phos (IU/L)	85.5 ± 14.82	90.3 ± 10.79	80.8 ± 8.34	80.4 ± 8.88
AST (IU/L)	102.9 ± 42.35	127.8 ± 57.03	119.6 ± 46.32	110.3 ± 31.63
ALT (IU/L)	65.9 ± 29.27	69.5 ± 19.16	75.6 ± 24.35	69.9 ± 20.85
Potassium (mEq/L)	5.79 ± 2.24	5.76 ± 1.25	5.71 ± 0.74	5.17 ± 0.54
Albumin (g/dl)	4.16 ± 0.14	4.34 ± 0.13*	4.30 ± 0.14	4.36 ± 0.12*
Calcium (mg/dl)	10.48 ± 0.26	10.50± 0.24	10.49 ± 0.19	10.53 ± 0.37
Sodium (mEq/L)	140.6 ± 2.01	142.3 ± 2.11	141.1 ± 2.13	141.2 ± 1.55
Total Bilirubin (mg/dl)	0.10 ±0.00	0.14 ± 0.05*	0.12 ± 0.04	0.10 ± 0.00
Total Protein (g/dl)	6.18 ± 0.25	6.29 ± 0.30	6.29 + 0.28	6.41 ± 0.23

Mean ± SD
* Significantly different from controls; $p \leq 0.05$ by Dunnett's test.

Table 16: Clinical Chemistry Values for Males
90 Days

	Dose Groups (mg TNB/kg diet)			
	0	800	400	66.67
Glucose (mg/dl)	212.4 ± 43.87	192.9 ± 16.51	198.3 ± 25.94	193.1 ± 13.99
BUN (mg/dl)	18.3 ± 1.77	21.1 ± 1.52*	20.8 ± 3.22*	19.5 ± 2.17
Creatinine (mg/dl)	0.60 ± 0.05	0.60 ± 0.00	0.60 ± 0.00	0.56 ± 0.05*
Alk phos (IU/L)	106.8 ± 11.67	105.0 ± 12.41	107.5 ± 28.72	107.1 ± 11.24
AST (IU/L)	119.6 ± 38.57	131.0 ± 35.17	176.6 ± 108.13	125.3 ± 44.19
ALT (IU/L)	88.0 ± 22.39	79.5 ± 19.13	113.4 ± 59.69	82.5 ± 18.73
Potassium (mEq/L)	6.03 ± 1.16	5.33 ± 0.40	5.62 ± 0.63	5.39 ± 0.68
Albumin (g/dl)	4.46 ± 0.23	4.76 ± 0.16*	4.72 ± 0.17*	4.48 ± 0.27
Calcium (mg/dl)	10.96 ± 0.28	10.83 ± 0.35	10.97 ± 0.37	10.86 ± 0.36
Sodium (mEq/L)	141.6 ± 0.97	142.3 ± 0.95	142.3 ± 0.95	141.8 ± 1.14
Total Bilirubin (mg/dl)	0.10 ± 0.00	0.12 ± 0.04	0.14 ± 0.05	0.11 ± 0.03
Total Protein (g/dl)	6.56 ± 0.29	6.84 ± 0.25	6.99 ± 0.32*	6.64 ± 0.23

Mean ± SD
* Significantly different from controls; $p \leq 0.05$ by Dunnett's test.

APPENDIX A

FOOD AND WATER CONSUMPTION

Weekly Food and Water Consumption
Group Means

Group	Sex	Diet Concentration (mg TNB/kg)	Food (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5
1	F	0	84.01 ± 2.22	87.00 ± 1.97	102.82 ± 1.47	90.55 ± 1.52	87.22 ± 1.49
2	F	800	83.25 ± 4.45	82.30 ± 4.26	102.42 ± 3.87	86.36 ± 5.03	75.64 ± 1.79
3	F	400	75.76 ± 4.18	78.68 ± 1.17	92.33 ± 1.69	82.07 ± 1.69	77.30 ± 0.85
4	F	66.67	90.33 ± 1.26	84.08 ± 2.43	98.42 ± 2.14	86.43 ± 2.17	85.74 ± 1.50
5	M	0	103.66 ± 2.09	114.85 ± 2.18	137.14 ± 2.36	118.11 ± 1.55	120.40 ± 1.77
6	M	800	80.96 ± 3.99	99.24 ± 4.01	130.00 ± 9.35	104.82 ± 4.78	98.90 ± 2.16
7	M	400	97.59 ± 4.27	100.26 ± 2.89	118.93 ± 3.02	103.92 ± 1.64	101.68 ± 1.92
8	M	66.67	105.36 ± 3.18	110.27 ± 2.45	131.62 ± 2.60	119.38 ± 3.75	112.95 ± 2.39

Group	Sex	Diet Concentration (mg TNB/kg)	Water (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5
1	F	0	118.87 ± 1.93	116.45 ± 2.05	134.90 ± 2.27	113.40 ± 1.51	109.85 ± 2.85
2	F	800	117.76 ± 3.02	126.16 ± 3.57	146.32 ± 4.13	126.90 ± 3.15	123.39 ± 4.80
3	F	400	123.18 ± 4.06	123.50 ± 3.35	138.12 ± 4.95	120.50 ± 3.20	117.70 ± 4.19
4	F	66.67	121.98 ± 3.22	120.15 ± 3.28	138.23 ± 3.04	119.31 ± 3.73	120.73 ± 4.05
5	M	0	121.86 ± 5.55	144.14 ± 3.14	229.41 ± 59.68	145.30 ± 3.88	146.14 ± 4.33
6	M	800	110.29 ± 3.15	127.61 ± 3.48	153.85 ± 2.90	142.23 ± 4.35	144.07 ± 2.73
7	M	400	115.34 ± 2.06	136.29 ± 3.76	155.79 ± 5.20	141.58 ± 3.21	137.77 ± 3.98
8	M	66.67	125.51 ± 2.45	136.90 ± 3.22	161.48 ± 3.78	139.68 ± 4.24	137.95 ± 4.67

* Mean ± Standard Error

Weekly Food and Water Consumption
Group Means

Group	Sex	Diet Concentration (mg TNB/kg)	Food (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10
1	F	0	84.12 ± 1.62	84.60 ± 2.15	71.25 ± 1.11	81.18 ± 0.80	79.28 ± 1.36
2	F	800	68.64 ± 1.07	72.95 ± 1.65	60.56 ± 1.00	69.99 ± 1.88	67.42 ± 1.86
3	F	400	74.27 ± 1.51	77.38 ± 1.45	64.79 ± 2.02	72.57 ± 1.10	70.43 ± 1.24
4	F	66.67	82.42 ± 1.43	83.01 ± 2.28	69.47 ± 0.92	78.83 ± 1.35	78.36 ± 2.05
5	M	0	121.55 ± 2.98	117.50 ± 3.46	99.51 ± 2.36	113.28 ± 3.56	113.99 ± 3.37
6	M	800	102.12 ± 3.54	99.72 ± 4.16	83.81 ± 1.98	98.86 ± 1.82	91.81 ± 1.85
7	M	400	102.70 ± 2.33	107.68 ± 2.13	86.92 ± 2.32	101.20 ± 2.52	97.06 ± 2.41
8	M	66.67	115.33 ± 2.11	115.58 ± 3.02	97.33 ± 2.15	109.05 ± 2.93	106.66 ± 2.50

Group	Sex	Diet Concentration (mg TNB/kg)	Water (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10
1	F	0	108.99 ± 2.86	111.77 ± 2.04	92.77 ± 1.14	109.37 ± 2.67	112.01 ± 3.13
2	F	800	127.10 ± 6.62	125.17 ± 7.12	105.98 ± 4.82	121.02 ± 8.22	123.32 ± 6.89
3	F	400	117.64 ± 4.16	118.65 ± 4.35	98.58 ± 4.63	118.64 ± 5.05	117.81 ± 4.58
4	F	66.67	122.77 ± 3.48	121.59 ± 4.01	99.80 ± 2.83	116.66 ± 3.34	118.42 ± 3.58
5	M	0	148.27 ± 5.31	140.63 ± 3.80	121.41 ± 3.84	135.72 ± 5.22	139.80 ± 4.57
6	M	800	141.02 ± 4.00	139.84 ± 4.19	121.62 ± 2.46	139.07 ± 3.79	136.22 ± 3.69
7	M	400	139.75 ± 4.65	138.88 ± 3.96	114.54 ± 3.37	135.39 ± 4.56	135.38 ± 4.19
8	M	66.67	142.71 ± 4.73	138.37 ± 4.91	118.02 ± 3.75	135.75 ± 4.26	135.73 ± 4.20

* Mean ± Standard Error

Weekly Food and Water Consumption
Group Means

Group	Sex	Diet Concentration (mg TNB/kg)	Food (g/wk) Week 11	Week 12	Week 13
1	F	0	81.38 ± 1.20	85.20 ± 0.88	50.45 ± 0.84
2	F	800	68.61 ± 2.47	76.13 ± 1.11	41.30 ± 1.00
3	F	400	71.04 ± 1.51	80.70 ± 1.65	43.00 ± 0.89
4	F	66.67	80.33 ± 1.35	82.72 ± 1.17	47.85 ± 0.85
5	M	0	116.70 ± 3.44	122.58 ± 2.83	87.96 ± 2.24
6	M	800	93.99 ± 1.17	101.54 ± 2.08	67.39 ± 0.47
7	M	400	103.27 ± 2.26	108.79 ± 2.63	72.07 ± 1.35
8	M	66.67	111.33 ± 2.41	118.90 ± 2.33	82.51 ± 1.93

Group	Sex	Diet Concentration (mg TNB/kg)	Water (g/wk) Week 11	Week 12	Week 13
1	F	0	116.16 ± 2.92	118.45 ± 2.94	72.16 ± 2.74
2	F	800	129.94 ± 7.48	136.93 ± 5.98	92.08 ± 9.68
3	F	400	121.75 ± 4.58	129.55 ± 4.35	76.57 ± 2.80
4	F	66.67	123.95 ± 3.61	123.59 ± 3.22	76.57 ± 1.74
5	M	0	143.68 ± 5.37	143.31 ± 4.55	107.89 ± 3.49
6	M	800	142.24 ± 5.12	142.13 ± 4.47	104.64 ± 3.09
7	M	400	144.83 ± 4.17	145.73 ± 3.83	105.24 ± 3.19
8	M	66.67	139.90 ± 4.23	143.44 ± 4.00	105.13 ± 2.95

* Mean ± Standard Error

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5	Water (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5
1	1	88.3	80.8	100.6	87.1	82.7	124.0	107.3	130.1	111.0	99.4
	2	87.9	91.1	111.8	89.6	85.5	114.3	111.5	132.4	103.8	100.8
	3	88.8	99.9	103.4	101.8	88.0	126.0	126.0	136.2	114.5	115.5
	4	68.7	87.3	105.7	91.6	91.8	113.9	116.4	135.8	112.2	112.2
	5	76.9	88.6	97.6	89.1	86.6	118.7	116.3	126.2	108.4	93.7
	6	85.5	80.9	94.5	83.4	85.2	111.6	110.9	124.8	114.6	113.7
	7	80.7	81.3	102.8	89.9	78.5	112.8	113.1	141.9	115.0	111.7
	8	90.5	92.8	104.4	92.7	95.3	123.7	123.5	139.9	116.0	116.6
	9	90.5	83.8	103.4	92.2	90.2	115.5	114.0	133.5	118.7	111.8
	10	82.3	83.5	104.0	88.1	88.4	128.2	125.5	148.2	119.8	123.1
2	11	80.5	98.6	116.9	*	86.2	137.3	147.9	172.1	*	150.3
	12	73.7	68.7	85.4	76.9	73.0	107.1	110.9	139.4	119.3	113.3
	13	67.9	75.1	101.1	104.6	80.6	112.6	129.8	151.8	128.7	125.5
	14	81.2	92.6	105.4	*	76.0	109.6	118.9	139.2	128.4	118.4
	15	78.3	73.4	101.3	97.1	82.1	118.1	131.0	145.6	141.3	128.3
	16	87.6	89.6	102.2	71.0	72.5	117.6	118.8	127.6	119.8	101.6
	17	81.9	91.7	102.3	84.3	68.1	110.6	120.7	137.0	117.8	108.4
	18	86.8	*	120.4	97.2	74.4	128.5	139.9	159.3	141.1	145.5
	19	119.6	*	*	*	70.3	123.8	126.3	153.8	129.0	121.1
	20	75.0	68.7	86.8	73.4	73.2	112.4	117.4	137.4	116.7	121.5

* Excessive Spillage

Replacement Numbers: 3 = R-01; 4 = R-02; 6 = R-03; 7 = R-04

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 1	Week 2	Week 3	Week 4	Week 5
3	21	84.6	77.2	90.3	77.5	78.5	138.5	142.1	161.5	127.4	132.7
	22	80.0	75.4	98.1	89.2	80.2	123.3	122.0	138.7	124.1	116.5
	23	84.5	78.5	91.9	81.0	77.4	117.0	122.8	138.3	121.9	114.8
	24	83.2	82.2	97.7	85.0	81.9	133.9	123.8	139.1	122.3	115.8
	25	82.0	82.5	94.4	89.4	77.4	119.3	129.9	140.2	123.9	133.8
	26	71.9	72.4	81.7	73.4	74.6	114.8	117.8	129.8	120.0	117.4
	27	76.4	*	*	83.8	78.2	102.8	107.5	113.5	100.0	91.5
	28	39.9	77.4	88.2	80.2	77.0	146.3	111.6	122.2	111.4	115.9
	29	77.7	82.8	93.4	84.9	72.6	115.9	120.5	133.3	115.7	105.4
	30	77.4	79.7	94.8	76.3	75.2	120.0	137.0	164.6	138.3	133.2
4	31	88.6	87.3	105.2	86.7	83.5	131.2	129.4	149.7	119.8	128.8
	32	90.6	72.9	94.1	82.1	83.7	114.4	107.2	123.0	106.5	105.3
	33	90.2	85.1	96.7	90.3	87.1	136.2	132.7	150.5	143.5	146.9
	34	89.4	*	100.9	*	82.6	116.1	127.0	142.1	133.2	132.7
	35	93.8	90.2	104.4	85.9	86.0	121.0	129.9	137.4	111.8	104.3
	36	86.3	80.7	96.0	81.7	85.1	134.3	116.4	145.1	108.7	119.9
	37	99.3	97.3	108.6	99.9	95.3	127.3	129.0	143.5	125.9	120.1
	38	85.0	80.2	91.1	81.9	80.2	105.7	112.6	132.8	117.0	116.7
	39	90.8	77.2	86.8	78.6	81.7	121.9	107.6	132.9	116.4	119.4
	40	89.3	85.8	100.4	90.8	92.2	111.7	109.7	125.3	110.3	113.2

* Excessive Spillage

Replacement Numbers: 39 = R-05

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10	Water (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10
1	1	81.7	79.1	68.3	80.6	80.0	103.6	107.4	90.8	103.9	108.9
	2	83.0	*	76.7	82.1	75.8	96.6	*	91.9	95.7	101.3
	3	85.3	90.0	73.3	84.0	76.3	112.8	116.9	96.1	110.1	111.4
	4	87.9	83.2	72.3	80.0	81.8	108.7	112.6	95.9	116.3	125.1
	5	77.1	74.3	69.8	82.9	74.9	92.5	101.6	88.6	100.3	93.7
	6	81.3	80.3	71.1	80.8	77.8	108.5	104.9	93.4	114.2	113.7
	7	76.6	83.2	64.2	80.0	76.3	113.8	111.0	91.0	113.3	112.8
	8	88.2	89.8	73.7	84.4	89.6	115.6	118.1	96.1	122.5	125.8
	9	92.7	95.4	69.3	75.5	79.5	117.6	119.4	86.6	102.3	108.7
	10	87.4	86.1	73.8	81.5	80.8	120.2	114.0	97.3	115.1	118.7
2	11	76.0	84.3	62.8	77.7	74.7	145.5	148.7	113.9	142.6	136.2
	12	68.3	75.1	66.2	70.6	65.0	173.5	171.6	133.1	169.0	169.5
	13	69.0	76.8	61.3	70.4	59.7	118.3	119.7	100.3	106.3	110.0
	14	66.8	69.2	59.7	67.5	63.0	107.8	109.1	*	101.1	98.2
	15	71.8	70.2	59.6	73.4	68.8	131.2	124.4	104.3	120.9	126.6
	16	63.5	66.2	59.0	56.6	60.7	102.9	95.7	90.1	79.0	102.3
	17	66.2	67.5	57.3	65.8	62.6	114.8	108.7	90.1	109.2	105.1
	18	67.5	74.0	55.1	73.9	72.8	138.3	140.1	122.1	148.1	141.8
	19	68.0	73.3	61.1	75.1	74.6	120.7	122.2	99.9	120.8	126.0
	20	69.3	72.9	63.5	68.9	72.3	118.0	111.5	100.0	113.2	117.5

* Excessive Spillage

Replacement Numbers: 3 = R-01; 4 = R-02; 6 = R-03; 7 = R-04

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10	Water (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10
3	21	73.8	82.2	75.4	78.8	67.3	130.1	140.0	123.5	140.9	133.3
	22	69.1	76.9	65.6	72.5	66.7	120.0	121.9	103.2	121.2	119.6
	23	74.5	67.9	66.8	69.2	71.3	111.9	114.4	101.4	111.5	109.5
	24	83.3	75.9	70.3	76.2	79.8	117.6	103.2	90.9	111.5	113.4
	25	79.1	83.9	72.2	75.1	72.8	123.3	126.1	106.1	119.8	121.5
	26	71.2	73.4	58.6	72.4	71.1	126.3	126.9	106.9	138.5	135.0
	27	71.5	76.5	59.5	69.0	70.6	91.2	97.5	75.2	91.4	101.9
	28	67.6	80.2	63.8	73.4	67.4	112.0	119.0	98.7	113.5	104.5
	29	77.6	77.1	57.0	67.6	67.0	106.4	104.5	75.9	102.8	99.6
	30	75.0	79.8	58.7	71.5	70.3	137.6	133.0	104.0	135.3	139.8
4	31	83.8	79.3	66.5	80.1	77.1	126.2	121.5	102.7	124.8	125.7
	32	80.8	70.6	63.5	76.9	70.0	141.7	107.4	89.9	110.8	106.2
	33	81.2	86.3	71.5	80.6	82.1	139.3	148.5	116.9	136.5	139.9
	34	83.2	77.4	72.6	82.7	83.2	120.3	132.2	112.2	129.3	129.9
	35	79.3	76.0	70.4	81.8	76.9	104.1	104.1	88.2	107.0	104.4
	36	80.5	86.7	70.7	76.4	76.7	119.2	118.9	97.0	110.1	109.2
	37	92.2	95.4	71.6	85.6	89.9	120.7	122.6	96.6	118.8	120.3
	38	77.2	83.5	68.7	73.5	73.5	117.6	119.1	98.9	116.4	121.8
	39	78.5	87.5	67.4	71.6	69.9	122.7	127.5	99.4	107.5	116.0
	40	87.5	87.4	71.8	79.1	84.3	115.9	114.1	96.2	105.4	110.8

* Excessive Spillage

Replacement Numbers: 39 = R-05

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 11	Food (g/wk) Week 12	Food (g/wk) Week 13	Water (g/wk) Week 11	Water (g/wk) Week 12	Water (g/wk) Week 13
1	1	80.5	80.1	50.5	117.4	112.9	82.1
	2	81.0	89.1	52.4	100.9	106.2	65.5
	3	81.4	86.6	50.2	120.6	120.5	75.6
	4	88.5	86.4	53.8	126.8	125.9	72.3
	5	81.0	86.2	45.9	99.4	101.7	55.0
	6	82.2	81.3	46.4	116.0	119.3	64.9
	7	73.6	83.4	49.9	120.4	118.3	79.9
	8	84.4	87.4	53.7	124.9	125.2	82.7
	9	78.7	85.6	50.4	114.3	122.0	71.7
	10	82.5	85.9	51.3	120.9	132.5	71.9
2	11	77.5	75.0	47.7	149.3	146.8	94.3
	12	62.2	78.2	37.3	162.6	175.7	123.2
	13	71.6	82.2	40.7	123.8	123.9	74.4
	14	66.5	72.4	41.7	115.4	115.7	69.1
	15	76.0	79.2	40.6	127.1	137.4	75.7
	16	53.2	73.6	36.8	94.8	120.9	165.3
	17	68.2	70.8	40.3	111.2	123.4	69.8
	18	72.2	78.1	42.8	169.7	158.3	96.0
	19	62.0	77.7	40.8	128.3	140.0	76.4
	20	76.7	74.1	44.3	117.2	127.2	76.6

* Excessive Spillage

Replacement Numbers: 3 = R-01; 4 = R-02; 6 = R-03; 7 = R-04

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 11	Week 12	Week 13	Water (g/wk) Week 11	Week 12	Week 13
3	21	66.3	80.2	46.3	138.6	147.6	89.5
	22	69.1	80.4	44.8	125.9	138.7	81.3
	23	70.7	83.8	39.8	112.5	124.2	67.6
	24	82.0	84.7	46.4	115.7	120.5	70.7
	25	72.2	91.6	45.2	125.5	138.3	79.6
	26	75.0	73.7	44.6	139.7	139.0	86.7
	27	67.1	76.0	41.4	102.4	104.6	62.0
	28	67.9	81.5	38.5	111.5	124.5	69.9
	29	67.4	75.6	41.6	104.9	115.5	76.0
	30	72.7	79.5	41.4	140.8	142.6	82.4
4	31	80.0	85.8	44.8	130.2	127.3	74.6
	32	75.7	78.4	49.6	115.0	117.1	75.0
	33	80.9	87.0	48.1	143.0	139.6	83.4
	34	82.1	77.3	48.4	141.1	133.6	85.8
	35	81.7	78.6	46.0	114.1	108.5	74.6
	36	77.2	84.8	43.7	113.2	115.6	67.0
	37	88.0	87.6	49.5	126.0	126.8	74.2
	38	76.8	81.7	48.4	124.2	131.6	80.8
	39	75.1	83.0	46.9	122.1	124.7	77.6
	40	85.8	83.0	53.1	110.6	111.1	72.7

* Excessive Spillage

Replacement Numbers: 39 = R-05

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5	Water (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5
5	41	112.3	120.0	141.4	118.0	121.3	100.2	143.7	161.4	143.9	142.9
	42	95.1	106.5	129.3	116.7	115.2	85.6	145.4	159.2	141.4	138.9
	43	102.6	116.1	131.9	114.3	115.7	126.3	147.9	169.3	149.8	149.8
	44	111.9	126.4	153.0	127.4	130.4	142.8	162.8	193.5	170.1	172.3
	45	100.1	111.7	136.3	110.6	117.7	127.2	138.3	162.5	134.4	136.7
	46	100.6	117.8	135.8	119.9	123.0	135.8	154.2	175.5	153.1	155.7
	47	109.0	115.1	140.3	118.8	118.2	129.6	136.5	167.1	139.8	137.8
	48	106.5	109.2	135.8	121.7	126.2	133.2	146.4	177.4	155.8	161.1
	49	93.0	104.5	126.5	112.5	112.3	111.9	126.7	*	127.6	125.5
	50	105.5	121.2	141.1	121.2	124.0	126.0	139.5	162.5	137.1	140.7
6	51	98.9	*	*	*	98.2	117.3	134.8	165.0	149.0	145.9
	52	73.8	88.7	128.0	119.4	102.2	102.3	121.9	152.2	146.0	140.2
	53	*	107.9	*	95.3	*	110.3	124.0	147.1	122.9	133.2
	54	82.1	94.8	113.1	*	*	102.5	111.0	147.3	123.9	133.1
	55	*	*	*	*	105.7	123.6	143.8	*	158.9	150.7
	56	89.8	103.0	160.0	*	*	112.6	123.8	152.5	140.2	149.7
	57	67.4	91.5	108.3	96.0	89.9	92.6	122.6	148.4	132.4	135.8
	58	75.7	91.3	114.0	100.8	99.5	103.6	125.2	150.0	133.5	141.5
	59	*	*	*	*	*	122.5	*	*	158.0	152.5
	60	79.0	117.5	156.6	112.6	97.9	115.6	141.4	168.3	157.5	158.0

* Excessive Spillage

Replacement Numbers: 43 = R-06; 50 = R-07; 54 = R-08; 57 = R-09

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5	Water (g/wk) Week 1	Week 2	Week 3	Week 4	Week 5
7	61	110.3	*	*	*	*	*	151.6	*	149.1	152.9
	62	90.6	115.8	132.2	*	98.1	108.9	129.0	139.1	125.9	124.8
	63	118.9	*	*	*	107.6	127.5	*	179.9	155.6	159.9
	64	89.6	97.7	117.2	103.0	102.1	121.0	135.0	152.2	137.8	139.3
	65	95.5	97.9	109.7	107.9	107.6	108.0	121.6	148.1	131.8	129.3
	66	77.9	101.8	118.9	102.1	96.6	117.0	149.1	159.6	143.5	128.3
	67	87.0	*	*	*	102.4	114.7	147.7	161.1	146.6	139.9
	68	109.9	99.8	123.7	105.5	102.4	116.6	133.3	152.7	144.3	141.7
	69	109.4	90.8	109.4	97.3	90.7	110.6	121.9	132.8	128.8	119.4
	70	86.8	98.0	121.4	107.7	107.6	113.8	137.4	176.6	152.4	142.2
8	71	116.2	125.5	146.2	137.6	130.1	137.0	153.2	181.6	161.3	166.7
	72	106.8	117.5	138.8	143.1	112.1	132.7	144.3	173.1	149.8	146.1
	73	99.5	108.5	131.9	112.2	110.9	123.8	134.4	155.6	124.5	127.1
	74	101.5	110.5	133.7	116.0	113.4	120.7	132.8	158.2	143.4	130.9
	75	101.4	114.5	133.0	121.1	119.9	125.3	142.0	170.9	151.8	145.6
	76	92.2	97.9	118.8	106.6	101.0	109.1	119.8	141.4	119.3	116.0
	77	98.6	105.1	119.1	109.0	109.7	130.4	138.5	167.5	144.3	145.8
	78	127.4	106.3	133.6	116.1	109.9	125.4	129.5	152.7	129.6	127.0
	79	102.0	112.6	128.1	117.0	111.5	129.6	147.6	162.0	143.4	146.1
	80	108.0	104.3	133.0	115.1	111.0	121.1	126.9	151.8	129.4	127.2

* Excessive Spillage
Replacement Numbers: 61 = R-10; 79 = R-11

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
5	41	127.6	125.1	105.5	109.9	116.3	147.6	144.0	119.8	127.9	138.3
	42	110.1	107.8	96.5	100.0	96.8	128.8	130.0	111.3	117.0	118.4
	43	120.9	97.9	92.4	129.2	105.8	154.5	133.6	125.3	152.8	133.3
	44	136.7	121.4	109.2	129.7	132.3	175.7	150.2	140.2	156.4	159.0
	45	114.6	115.0	94.8	103.6	107.6	132.0	133.9	109.3	119.1	127.5
	46	124.1	121.9	98.2	118.8	122.1	157.1	151.9	130.4	150.0	152.0
	47	125.7	125.3	100.7	110.5	113.7	149.0	142.5	118.6	127.5	132.7
	48	128.3	131.4	109.0	117.9	120.8	170.0	162.4	139.2	157.4	164.6
	49	104.8	103.9	85.9	96.9	103.3	125.6	121.5	105.3	119.2	133.2
	50	122.7	125.3	102.9	116.3	121.2	142.4	136.3	114.7	129.9	139.0
6	51	109.6	110.8	87.7	103.2	93.3	142.6	158.0	131.1	133.0	135.6
	52	103.1	100.5	85.7	98.1	97.9	140.2	140.9	125.3	142.1	142.7
	53	110.0	118.5	88.2	97.7	95.1	120.2	124.3	115.0	117.9	115.4
	54	97.0	101.3	86.6	102.3	97.3	122.9	127.2	112.4	132.7	124.6
	55	112.0	105.2	89.1	105.4	84.4	153.6	143.1	131.8	147.7	145.8
	56	117.0	97.8	86.6	102.2	97.1	150.6	129.9	112.0	137.0	139.4
	57	91.2	99.1	75.1	97.7	84.8	141.5	148.4	121.7	141.6	137.2
	58	91.5	89.7	82.6	96.2	90.3	131.2	122.7	114.2	127.9	123.5
	59	*	*	*	*	*	152.2	158.2	123.4	152.7	145.4
	60	87.7	74.6	72.7	86.9	86.1	155.2	145.7	129.3	158.1	152.6

* Excessive Spillage

Replacement Numbers: 43 = R-06; 50 = R-07; 54 = R-08; 57 = R-09

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10	Water (g/wk) Week 6	Week 7	Week 8	Week 9	Week 10
7	61	*	*	*	*	*	157.7	*	*	158.3	144.9
	62	100.2	106.5	85.5	107.1	96.2	115.8	123.1	100.2	115.1	118.2
	63	114.7	115.1	101.3	113.0	103.2	159.3	156.6	133.2	156.8	160.3
	64	106.4	100.2	87.4	105.7	98.1	145.1	138.4	121.8	140.8	142.9
	65	104.2	109.4	88.9	94.8	95.7	129.8	134.9	111.6	123.0	118.5
	66	97.3	108.5	84.3	92.0	82.9	130.1	136.2	107.5	125.6	125.2
	67	99.9	106.1	83.9	95.9	100.8	144.8	141.5	114.5	129.8	133.2
	68	101.3	110.5	88.8	104.1	99.4	142.2	146.4	120.1	140.9	138.5
	69	90.9	96.5	74.5	92.3	89.9	122.3	121.1	104.0	124.3	128.6
	70	109.4	116.3	87.7	105.9	107.3	150.4	151.7	118.0	139.3	143.5
8	71	128.4	136.4	110.0	120.2	113.1	167.7	167.5	129.1	144.1	144.9
	72	115.0	113.6	96.1	107.2	105.3	143.7	144.8	128.8	139.8	138.8
	73	114.5	110.9	95.0	106.8	104.8	128.9	128.1	107.2	122.0	121.8
	74	116.4	113.3	98.9	108.2	106.1	139.3	130.7	113.1	129.6	134.2
	75	121.0	120.1	102.4	119.0	107.8	152.0	*	133.7	154.7	140.2
	76	102.0	102.3	83.8	88.4	87.0	118.5	115.8	96.8	106.9	104.9
	77	111.1	114.3	94.3	107.4	106.3	159.0	144.9	124.4	142.6	138.7
	78	114.8	114.9	94.9	116.5	113.5	131.5	131.6	108.7	138.4	141.7
	79	114.4	112.2	96.0	103.2	107.0	151.0	146.9	124.6	144.5	152.1
	80	115.7	117.8	101.9	113.6	115.7	135.5	135.0	113.8	134.9	140.0

* Excessive Spillage
Replacement Numbers: 61 = R-10; 79 = R-11

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 11	Week 12	Week 13	Water (g/wk) Week 11	Week 12	Week 13
5	41	119.3	129.1	86.7	142.5	146.4	106.6
	42	103.1	120.5	84.1	126.5	137.4	102.8
	43	103.0	111.5	81.2	130.0	125.4	98.3
	44	131.2	127.4	99.8	159.9	156.3	122.2
	45	108.2	110.9	81.7	128.1	131.2	97.0
	46	124.8	128.2	88.8	162.5	156.6	117.2
	47	120.4	124.4	92.7	139.3	140.9	109.6
	48	129.3	134.6	94.0	175.7	168.7	126.4
	49	105.2	109.7	77.1	129.4	124.6	93.1
	50	122.5	129.5	93.5	142.9	145.6	105.7
6	51	91.7	105.4	66.2	143.3	141.2	103.7
	52	95.6	102.9	69.7	138.7	138.8	108.4
	53	94.0	112.7	68.1	118.6	126.9	93.5
	54	94.6	98.3	65.2	128.5	127.3	92.3
	55	86.7	102.6	69.2	145.1	149.6	104.1
	56	96.2	105.2	67.0	132.3	134.3	97.7
	57	98.0	94.1	67.1	151.8	140.3	116.3
	58	91.8	100.6	67.0	132.5	134.3	97.9
	59	*	*	*	155.9	155.0	110.3
	60	97.3	92.1	67.0	175.7	173.6	122.2

* Excessive Spillage

Replacement Numbers: 43 = R-06; 50 = R-07; 54 = R-08; 57 = R-09

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 11	Week 12	Week 13	Water (g/wk) Week 11	Week 12	Week 13
7	61	*	*	*	152.9	152.3	116.3
	62	100.9	112.8	71.3	121.3	133.5	94.2
	63	111.8	117.7	77.4	164.3	164.6	119.6
	64	107.5	112.0	70.4	149.9	148.1	111.6
	65	103.7	101.4	69.9	130.1	125.0	88.6
	66	92.7	105.7	65.4	133.1	142.0	98.9
	67	106.1	107.0	72.6	146.5	147.8	103.4
	68	103.8	113.1	73.5	151.8	153.6	111.7
	69	92.9	93.0	69.6	142.3	133.9	98.5
	70	110.0	116.4	78.5	156.1	156.5	109.6
8	71	119.0	123.5	86.8	147.9	152.8	113.1
	72	110.8	113.3	81.1	142.0	145.2	109.3
	73	109.5	112.0	80.4	127.9	136.4	93.7
	74	113.6	120.7	85.6	137.8	140.7	103.2
	75	112.6	123.3	86.9	147.7	153.8	113.0
	76	91.4	102.6	67.5	109.0	112.9	86.0
	77	110.7	120.2	80.4	145.3	149.6	108.3
	78	117.7	123.7	87.4	142.7	143.1	102.2
	79	113.9	123.7	81.4	158.4	158.1	116.0
	80	114.1	126.0	87.6	140.3	141.8	106.5

* Excessive Spillage
Replacement Numbers: 61 = R-10; 79 = R-11

APPENDIX B

BODY WEIGHTS

BODY WEIGHTS

	10/29/92	11/05/92	11/12/92	11/20/92	11/27/92	12/04/92
1-01	162.6	165.3	167.5	172.3	173.9	174.4
1-02	162.2	164.4	170.3	179.0	181.6	183.4
1-R-01	163.0	166.7	171.8	178.3	179.4	183.9
1-R-02	164.7	169.8	173.6	183.3	184.8	189.6
1-05	159.6	163.6	167.9	173.4	179.2	174.2
1-R-03	166.1	165.4	170.7	173.7	178.9	180.8
1-R-04	156.9	161.2	167.4	171.7	174.8	175.1
1-08	159.3	162.6	171.1	177.9	185.4	185.2
1-09	159.4	162.1	169.9	173.9	182.1	181.3
1-10	153.5	157.5	163.6	171.2	172.2	178.3
2-11	167.3		174.7	176.1	183.6	183.1
2-12	162.2	160.1	165.4	171.8	179.8	177.5
2-13	163.6	159.9	165.8	172.6	177.6	178.1
2-14	159.9	157.2	164.4	169.0	172.9	173.7
2-15	162.6	161.1	167.6	174.1	178.7	179.4
2-16	163.3	164.1	168.8	168.4	171.6	170.7
2-17	164.3	159.7	166.2	170.2	168.5	170.5
2-18	159.3	154.7	166.9	168.8	172.3	170.8
2-19	160.7	160.5	167.0	170.9	172.7	171.5
2-20	159.9	161.0	163.8	167.9	169.1	171.8
3-21	170.2	171.4	176.7	178.2	179.8	180.8
3-22	163.4	160.0	165.9	172.3	175.7	178.1
3-23	163.9	163.8	173.6	176.2	180.1	179.6
3-24	162.5	168.7	173.5	176.8	186.9	183.4
3-25	162.2	165.8	167.4	172.6	177.8	175.1
3-26	157.9	154.8	164.0	162.3	168.1	171.8
3-27	154.1	154.3	164.2	168.1	175.6	177.6
3-28	152.7	159.4	164.7	169.1	170.9	172.2
3-29	154.1	158.1	165.4	171.7	178.0	176.6
3-30	157.8	159.3	165.7	174.3	175.6	178.0
4-31	163.9	169.5	177.4	182.9	186.7	191.7
4-32	159.5	168.1	171.8	176.7	182.5	183.2
4-33	166.7	170.5	177.0	179.0	186.7	187.6
4-34	167.7	169.9	176.4	180.0	187.1	189.0
4-35	165.7	164.9	171.3	173.7	178.9	177.8
4-36	160.3	169.6	169.9	179.6	181.6	183.2
4-37	161.5	172.3	181.2	185.7	194.7	195.9
4-38	154.0	158.3	161.6	168.3	174.9	172.9
4-R-05	155.7	164.2	168.4	174.6	179.2	177.7
4-40	155.2	160.3	166.7	174.2	184.7	186.3

WEIGHTS IN GRAMS

BODY WEIGHTS

	10/30/92	11/05/92	11/12/92	11/20/92	11/27/92	12/04/92
5-41	219.5	236.8	257.5	274.7	290.6	296.0
5-42	214.6	225.8	240.1	253.7	266.9	268.3
5-R-06	222.6	239.7	257.6	268.9	280.2	286.8
5-44	219.2	239.5	262.4	279.2	296.9	304.2
5-45	210.1	225.6	246.2	263.4	277.8	284.7
5-46	210.3	225.3	242.5	259.3	274.9	284.5
5-47	209.6	226.4	246.7	262.4	279.2	286.8
5-48	211.8	229.1	248.5	270.3	286.8	298.7
5-49	196.1	207.5	225.6	241.4	254.2	262.4
5-R-07	221.3	236.9	254.7	269.8	278.7	290.5
6-51	220.7	220.7	231.6	240.9	250.9	253.7
6-52	212.7	211.8	222.7	237.3	250.3	251.7
6-53	219.1	222.2	233.6	244.6	248.9	259.5
6-R-08	214.2	217.8	224.8	232.0	240.8	258.3
6-55	209.2	214.2	225.6	235.0	243.5	251.9
6-56	206.1	216.5	230.9	241.4	253.2	257.4
6-R-09	207.3	204.8	218.4	229.2	237.8	243.9
6-58	202.3	205.6	218.3	227.1	236.1	247.4
6-59	206.7	212.8	225.5	234.2	244.8	249.4
6-60	204.2	209.4	216.0	224.8	231.9	238.2
7-R-10	215.7	227.8	244.8	258.9	266.3	272.6
7-62	213.7	219.9	236.9	247.4	258.0	264.7
7-63	212.2	224.2	241.5	257.4	265.4	279.4
7-64	208.7	219.6	233.1	245.0	254.1	264.4
7-65	200.7	211.9	226.7	239.9	251.3	258.2
7-66	207.1	212.1	231.0	240.1	248.7	249.8
7-67	204.6	209.2	224.8	234.3	244.5	249.5
7-68	205.4	217.1	234.8	244.2	256.9	261.5
7-69	190.8	198.6	207.9	210.9	222.6	222.9
7-70	201.0	212.2	226.6	241.5	252.7	259.0
8-71	223.5	241.5	264.2	284.4	299.6	307.5
8-72	212.7	227.9	246.3	260.4	273.2	277.3
8-73	211.1	227.7	243.2	260.3	269.5	278.1
8-74	213.7	229.9	247.9	262.4	274.3	281.4
8-75	213.8	227.9	247.9	262.2	276.4	285.1
8-76	198.8	211.3	224.1	233.8	240.0	244.1
8-77	203.5	218.1	238.1	250.4	262.1	268.9
8-78	205.3	222.3	238.4	253.1	264.5	269.7
8-R-11	209.1	226.1	240.8	251.3	264.4	270.7
8-80	199.2	210.1	227.7	245.7	258.2	264.7

WEIGHTS IN GRAMS

BODY WEIGHTS

	12/11/92	12/18/92	12/24/92	01/04/93	01/11/93	01/18/93
1-01	177.5	178.8	177.8	183.5	186.3	184.6
1-02	182.3	177.9	178.9	184.6	184.4	192.4
1-R-01	185.1	184.4	189.1	190.2	189.6	194.9
1-R-02	190.6	190.4	193.4	195.5	195.4	199.9
1-05	177.6	174.1	180.5	177.9	182.3	181.3
1-R-03	182.9	185.2	185.3	192.4	191.3	194.6
1-R-04	177.1	182.1	178.2	183.6	183.4	186.7
1-08	191.5	195.0	193.2	198.7	201.1	203.6
1-09	187.4	192.8	190.1	190.7	191.2	195.1
1-10	180.7	180.7	183.3	189.3	185.0	192.4
2-11	184.9	187.2	185.7	194.4	194.6	190.6
2-12	175.3	177.1	181.7	181.2	182.0	189.4
2-13	175.8	178.9	179.9	181.2	183.5	192.4
2-14	171.6	170.5	172.4	176.4	179.4	183.5
2-15	180.4	180.4	180.7	187.5	189.9	193.5
2-16	169.6	169.8	174.5	171.8	173.7	177.9
2-17	173.1	170.2	173.2	175.6	178.2	184.7
2-18	172.5	179.8	175.9	184.7	186.4	192.3
2-19	171.7	177.0	175.7	179.9	182.2	188.3
2-20	175.3	178.1	180.8	180.5	182.6	188.6
3-21	177.4	181.7	186.2	186.5	183.2	189.9
3-22	175.3	176.9	180.0	183.0	183.2	190.8
3-23	180.3	180.4	185.2	189.3	189.9	192.2
3-24	189.1	188.7	190.5	195.3	195.7	202.3
3-25	177.1	179.7	180.9	184.8	185.3	187.8
3-26	172.5	172.6	173.8	181.7	183.8	185.8
3-27	173.2	180.3	178.9	186.0	189.2	193.2
3-28	173.2	175.1	177.8	183.2	184.3	185.8
3-29	177.5	181.0	179.0	183.9	185.9	187.0
3-30	173.4	180.9	179.4	186.4	185.7	185.8
4-31	194.9	194.1	194.1	199.3	201.8	205.5
4-32	186.8	184.7	188.6	192.7	191.3	196.2
4-33	188.5	192.3	194.6	197.3	199.6	201.8
4-34	190.2	189.4	192.9	199.2	198.3	199.8
4-35	179.8	180.7	183.4	185.7	189.8	190.8
4-36	186.7	188.9	193.6	196.4	199.3	199.2
4-37	200.0	206.7	204.0	206.4	210.2	213.5
4-38	175.6	179.4	181.3	185.8	185.7	190.0
4-R-05	180.4	186.1	186.7	189.6	188.7	195.5
4-40	190.4	191.2	194.4	195.6	199.9	201.8

WEIGHTS IN GRAMS

BODY WEIGHTS

	12/11/92	12/18/92	12/24/92	01/04/93	01/11/93	01/18/93
5-41	307.8	306.5	313.3	328.6	336.9	338.3
5-42	275.3	270.9	276.6	288.3	297.8	303.1
5-R-06	293.6	275.9	280.1	299.6	306.8	309.4
5-44	317.6	309.4	320.4	340.3	350.0	352.7
5-45	294.3	292.6	294.6	307.9	313.4	313.1
5-46	297.7	303.0	307.4	325.1	332.9	336.8
5-47	299.2	307.0	309.2	323.5	329.5	335.2
5-48	315.1	321.7	330.7	350.4	357.3	363.7
5-49	268.7	271.6	274.5	290.6	294.2	296.5
5-R-07	299.8	305.6	313.3	332.3	341.9	345.7
6-51	260.7	265.0	269.3	277.3	283.5	286.3
6-52	259.9	260.2	262.6	279.8	286.2	289.5
6-53	261.2	264.2	270.5	275.9	282.1	286.8
6-R-08	259.6	258.3	265.5	281.9	285.5	286.0
6-55	254.5	254.4	262.8	272.4	276.8	283.6
6-56	262.5	263.9	266.4	280.7	281.2	286.1
6-R-09	249.4	256.2	256.3	268.2	275.4	272.9
6-58	249.2	248.0	258.2	268.9	277.5	279.3
6-59	256.6	263.9	267.3	274.2	279.3	284.9
6-60	245.5	248.4	254.3	267.4	273.8	278.7
7-R-10	284.3	280.2	290.9	306.1	310.9	317.9
7-62	272.9	272.3	275.0	288.9	297.3	298.3
7-63	282.6	280.7	289.0	309.8	315.0	315.8
7-64	269.3	265.1	270.8	289.9	300.0	301.1
7-65	263.2	263.1	268.3	278.6	288.5	294.4
7-66	254.1	260.3	268.1	278.3	283.3	288.8
7-67	258.2	261.9	265.1	273.6	284.3	288.4
7-68	267.6	272.4	280.0	286.8	295.8	294.4
7-69	232.6	236.1	243.3	256.9	264.3	269.4
7-70	271.1	275.2	277.8	293.6	299.4	302.6
8-71	318.2	320.2	327.3	343.6	350.7	354.3
8-72	288.6	286.3	292.4	301.9	306.5	312.3
8-73	287.9	286.6	290.6	302.1	311.2	316.9
8-74	291.2	286.3	292.3	301.4	309.6	312.4
8-75	299.0	292.6	300.0	316.9	326.4	331.5
8-76	250.5	251.1	252.6	262.2	271.4	276.1
8-77	281.0	285.3	293.4	309.6	319.2	321.7
8-78	279.9	291.0	295.3	310.5	316.6	320.6
8-R-11	284.4	282.7	289.9	301.8	316.1	320.3
8-80	279.6	286.6	294.9	310.7	317.6	318.4

WEIGHTS IN GRAMS

APPENDIX C

ORGAN WEIGHTS

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
1-01	175.18	1.299	0.878	4.668	0.742	0.501	2.665
1-02	181.57	1.511	1.001	4.870	0.832	0.551	2.682
1-R-01	182.45	1.245	0.943	5.001	0.682	0.517	2.741
1-R-02	187.60	1.368	0.896	5.068	0.729	0.478	2.701
1-05	174.01	1.363	1.194	5.893	0.783	0.686	3.387
1-R-03	178.82	1.325	1.000	4.903	0.741	0.559	2.742
1-R-04	178.42	1.263	1.027	4.844	0.708	0.576	2.715
1-08	187.30	1.349	0.946	5.167	0.720	0.505	2.759
1-09	185.42	1.314	0.890	4.700	0.709	0.480	2.535
1-10	179.64	1.317	1.065	5.191	0.733	0.593	2.890
2-11	179.11	1.290	0.929	5.699	0.720	0.519	3.182
2-12	171.17	1.235	0.961	5.096	0.722	0.561	2.977
2-13	173.13	1.273	0.881	4.940	0.735	0.509	2.853
2-14	165.50	1.245	0.917	5.154	0.752	0.554	3.114
2-15	175.43	1.295	1.041	5.338	0.738	0.593	3.043
2-16	163.84	1.195	1.010	5.238	0.729	0.616	3.197
2-17	167.45	1.381	0.961	5.084	0.825	0.574	3.036
2-18	173.03	1.294	0.923	5.086	0.748	0.533	2.939
2-19	168.33	1.254	0.853	5.450	0.745	0.507	3.238
2-20	169.89	1.334	0.985	5.355	0.785	0.580	3.152
3-21	174.91	1.332	0.899	4.805	0.762	0.514	2.747
3-22	170.45	1.190	0.970	4.916	0.698	0.569	2.884
3-23	178.35	1.351	0.865	5.141	0.757	0.485	2.883
3-24	185.54	1.476	1.093	5.526	0.796	0.589	2.978
3-25	172.05	1.314	0.926	5.379	0.764	0.538	3.126
3-26	171.48	1.285	0.812	5.267	0.749	0.474	3.071
3-27	176.90	1.240	1.088	5.128	0.701	0.615	2.899
3-28	171.80	1.273	0.950	4.959	0.741	0.553	2.886
3-29	173.57	1.240	0.819	4.753	0.714	0.472	2.738
3-30	170.20	1.319	0.831	5.008	0.775	0.488	2.942
4-31	191.81	1.293	1.067	5.180	0.674	0.556	2.701
4-32	186.90	1.301	0.940	5.126	0.696	0.503	2.743
4-33	188.45	1.233	0.973	5.190	0.654	0.516	2.754
4-34	189.51	1.304	1.021	5.534	0.688	0.539	2.920
4-35	176.95	1.344	1.126	5.084	0.760	0.636	2.873
4-36	186.58	1.342	0.954	5.184	0.719	0.511	2.778
4-37	196.90	1.338	1.033	5.499	0.680	0.525	2.793
4-38	177.44	1.274	1.012	5.223	0.718	0.570	2.944
4-R-05	179.21	1.342	1.026	5.037	0.749	0.573	2.811
4-40	192.97	1.335	0.876	5.251	0.692	0.454	2.721

Weights in grams.

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
5-41	325.07	2.406	1.232	9.821	0.740	0.379	3.021
5-42	293.65	1.904	1.134	7.979	0.648	0.386	2.717
5-R-06	303.37	2.011	1.179	8.416	0.663	0.389	2.774
5-44	340.44	2.517	1.351	10.834	0.739	0.397	3.182
5-45	305.28	2.051	1.201	8.192	0.672	0.393	2.683
5-46	320.96	2.251	1.426	9.257	0.701	0.444	2.884
5-47	326.14	2.315	1.416	9.793	0.710	0.434	3.003
5-48	350.18	2.534	1.624	10.287	0.724	0.464	2.938
5-49	284.92	1.939	1.172	7.800	0.681	0.411	2.738
5-R-07	333.94	2.401	1.271	10.246	0.719	0.381	3.068
6-51	270.07	1.971	1.353	9.010	0.730	0.501	3.336
6-52	272.11	1.823	1.239	9.089	0.670	0.455	3.340
6-53	268.84	1.989	1.160	9.308	0.740	0.431	3.462
6-R-08	264.17	1.915	1.145	8.600	0.725	0.433	3.255
6-55	265.67	1.820	1.121	8.729	0.685	0.422	3.286
6-56	264.78	2.044	1.238	9.231	0.772	0.468	3.486
6-R-09	254.20	1.761	1.214	7.923	0.693	0.478	3.117
6-58	263.92	1.993	1.192	8.339	0.755	0.452	3.160
6-59	266.15	1.973	1.283	7.464	0.741	0.482	2.804
6-60	259.01	1.776	1.180	8.602	0.686	0.456	3.321
7-R-10	303.87	2.137	1.189	11.649	0.703	0.391	3.834
7-62	277.11	2.093	1.229	9.064	0.755	0.444	3.271
7-63	293.58	2.039	1.151	9.328	0.695	0.392	3.177
7-64	282.79	2.069	1.221	8.885	0.732	0.432	3.142
7-65	274.47	1.896	1.251	8.444	0.691	0.456	3.076
7-66	274.26	1.924	1.109	8.808	0.702	0.404	3.212
7-67	271.27	1.848	1.175	9.187	0.681	0.433	3.387
7-68	281.14	2.112	1.162	9.175	0.751	0.413	3.263
7-69	258.38	1.859	1.089	8.050	0.719	0.421	3.116
7-70	289.23	2.074	1.268	9.513	0.717	0.438	3.289
8-71	339.18	2.545	1.516	10.361	0.750	0.447	3.055
8-72	301.77	2.058	1.199	8.758	0.682	0.397	2.902
8-73	300.76	1.889	1.565	8.664	0.628	0.520	2.881
8-74	304.27	2.137	1.259	8.725	0.702	0.414	2.868
8-75	317.96	2.167	1.587	9.585	0.682	0.499	3.015
8-76	267.72	1.779	1.039	7.306	0.665	0.388	2.729
8-77	305.60	2.191	1.219	9.182	0.717	0.399	3.005
8-78	309.79	2.231	1.425	9.140	0.720	0.460	2.950
8-R-11	305.38	2.123	1.198	9.671	0.695	0.392	3.167
8-80	306.91	2.350	1.280	9.245	0.766	0.417	3.012

GP-ANI NUMBER	BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
1-01	175.18	0.651	1.778	0.381	0.372	1.015	0.217
1-02	181.57	0.689	1.812	0.439	0.379	0.998	0.242
1-R-01	182.45	0.602	1.722	0.421	0.330	0.944	0.231
1-R-02	187.60	0.647	1.901	0.460	0.345	1.013	0.245
1-05	174.01	0.616	1.720	0.449	0.354	0.988	0.258
1-R-03	178.82	0.618	1.697	0.437	0.346	0.949	0.244
1-R-04	178.42	0.692	1.822	0.429	0.388	1.021	0.240
1-08	187.30	0.634	1.723	0.470	0.338	0.920	0.251
1-09	185.42	0.732	1.801	0.431	0.395	0.971	0.232
1-10	179.64	0.731	1.901	0.441	0.407	1.058	0.245
2-11	179.11	0.657	1.704	0.633	0.367	0.951	0.353
2-12	171.17	0.616	1.645	0.610	0.360	0.961	0.356
2-13	173.13	0.616	1.844	0.601	0.356	1.065	0.347
2-14	165.50	0.637	1.884	0.608	0.385	1.138	0.367
2-15	175.43	0.611	1.653	0.653	0.348	0.942	0.372
2-16	163.84	0.586	1.766	0.579	0.358	1.078	0.353
2-17	167.45	0.616	1.776	0.600	0.368	1.061	0.358
2-18	173.03	0.668	1.751	0.699	0.386	1.012	0.404
2-19	168.33	0.663	1.730	0.592	0.394	1.028	0.352
2-20	169.89	0.613	1.733	0.589	0.361	1.020	0.347
3-21	174.91	0.657	1.777	0.383	0.376	1.016	0.219
3-22	170.45	0.655	1.850	0.598	0.384	1.085	0.351
3-23	178.35	0.657	1.793	0.623	0.368	1.005	0.349
3-24	185.54	0.689	1.854	0.654	0.371	0.999	0.352
3-25	172.05	0.665	1.882	0.548	0.387	1.094	0.319
3-26	171.48	0.616	1.678	0.474	0.359	0.979	0.276
3-27	176.90	0.685	1.626	0.550	0.387	0.919	0.311
3-28	171.80	0.617	1.794	0.516	0.359	1.044	0.300
3-29	173.57	0.722	1.740	0.507	0.416	1.002	0.292
3-30	170.20	0.678	1.751	0.568	0.398	1.029	0.334
4-31	191.81	0.687	1.873	0.420	0.358	0.976	0.219
4-32	186.90	0.648	1.705	0.452	0.347	0.912	0.242
4-33	188.45	0.647	1.771	0.464	0.343	0.940	0.246
4-34	189.51	0.681	1.772	0.456	0.359	0.935	0.241
4-35	176.95	0.659	1.753	0.462	0.372	0.991	0.261
4-36	186.58	0.652	1.699	0.433	0.349	0.911	0.232
4-37	196.90	0.739	1.822	0.514	0.375	0.925	0.261
4-38	177.44	0.662	1.819	0.418	0.373	1.025	0.236
4-R-05	179.21	0.679	1.881	0.467	0.379	1.050	0.261
4-40	192.97	0.789	1.798	0.466	0.409	0.932	0.241

GP-ANI NUMBER	BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
5-41	325.07	1.016	1.992	0.631	0.313	0.613	0.194
5-42	293.65	0.934	1.844	0.529	0.318	0.628	0.180
5-R-06	303.37	0.832	1.785	0.602	0.274	0.588	0.198
5-44	340.44	1.065	1.986	0.609	0.313	0.583	0.179
5-45	305.28	0.938	1.863	0.620	0.307	0.610	0.203
5-46	320.96	1.077	1.904	0.653	0.336	0.593	0.203
5-47	326.14	0.970	1.918	0.706	0.297	0.588	0.216
5-48	350.18	0.952	1.857	0.756	0.272	0.530	0.216
5-49	284.92	0.921	1.835	0.596	0.323	0.644	0.209
5-R-07	333.94	1.042	1.953	0.608	0.312	0.585	0.182
6-51	270.07	0.837	1.815	0.798	0.310	0.672	0.295
6-52	272.11	0.901	1.788	0.827	0.331	0.657	0.304
6-53	268.84	0.955	1.968	0.770	0.355	0.732	0.286
6-R-08	264.17	0.743	1.724	0.768	0.281	0.653	0.291
6-55	265.67	0.805	1.888	0.751	0.303	0.711	0.283
6-56	264.78	0.894	1.795	1.029	0.338	0.678	0.389
6-R-09	254.20	0.801	1.796	0.923	0.315	0.707	0.363
6-58	263.92	0.805	1.816	1.024	0.305	0.688	0.388
6-59	266.15	0.812	1.799	0.792	0.305	0.676	0.298
6-60	259.01	0.845	1.826	0.825	0.326	0.705	0.319
7-R-10	303.87	0.884	1.891	0.695	0.291	0.622	0.229
7-62	277.11	0.812	1.801	0.742	0.293	0.650	0.268
7-63	293.58	0.883	1.909	0.706	0.301	0.650	0.240
7-64	282.79	0.912	1.806	0.699	0.323	0.639	0.247
7-65	274.47	0.950	1.812	0.763	0.346	0.660	0.278
7-66	274.26	0.846	1.873	0.649	0.308	0.683	0.237
7-67	271.27	0.895	1.755	0.722	0.330	0.647	0.266
7-68	281.14	0.918	1.824	0.675	0.327	0.649	0.240
7-69	258.38	0.905	1.828	0.681	0.350	0.707	0.264
7-70	289.23	0.913	1.878	0.762	0.316	0.649	0.263
8-71	339.18	1.070	1.998	0.672	0.315	0.589	0.198
8-72	301.77	0.971	1.834	0.621	0.322	0.608	0.206
8-73	300.76	0.988	1.792	0.497	0.329	0.596	0.165
8-74	304.27	0.958	1.928	0.612	0.315	0.634	0.201
8-75	317.96	0.937	1.765	0.571	0.295	0.555	0.180
8-76	267.72	0.884	1.916	0.602	0.330	0.716	0.225
8-77	305.60	1.066	1.873	0.613	0.349	0.613	0.201
8-78	309.79	0.994	1.785	0.624	0.321	0.576	0.201
8-R-11	305.38	0.904	1.798	0.666	0.296	0.589	0.218
8-80	306.91	0.963	1.961	0.654	0.314	0.639	0.213

GP-ANI NUMBER	BODY WEIGHT	ADRENALS WEIGHT	THYMUS WEIGHT	TESTES/ OVARIES WEIGHT	% ADRENALS	% THYMUS	% TESTES/ OVARIES
1-01	175.18	0.082	0.249	0.114	0.047	0.142	0.065
1-02	181.57	0.089	0.275	0.145	0.049	0.151	0.080
1-R-01	182.45	0.101	0.264	0.215	0.055	0.145	0.118
1-R-02	187.60	0.075	0.192	0.170	0.040	0.102	0.091
1-05	174.01	0.100	0.215	0.138	0.057	0.124	0.079
1-R-03	178.82	0.098	0.234	0.170	0.055	0.131	0.095
1-R-04	178.42	0.090	0.198	0.102	0.050	0.111	0.057
1-08	187.30	0.093	0.231	0.153	0.050	0.123	0.082
1-09	185.42	0.059	0.186	0.089	0.032	0.100	0.048
1-10	179.64	0.087	0.347	0.132	0.048	0.193	0.073
2-11	179.11	0.080	0.185	0.134	0.045	0.103	0.075
2-12	171.17	0.090	0.174	0.166	0.053	0.102	0.097
2-13	173.13	0.064	0.177	0.107	0.037	0.102	0.062
2-14	165.50	0.099	0.216	*	0.060	0.131	0.000
2-15	175.43	0.074	0.181	0.121	0.042	0.103	0.069
2-16	163.84	0.056	0.189	0.090	0.034	0.115	0.055
2-17	167.45	0.061	0.216	0.106	0.036	0.129	0.063
2-18	173.03	0.060	0.193	0.091	0.035	0.112	0.053
2-19	168.33	0.072	0.168	0.119	0.043	0.100	0.071
2-20	169.89	0.078	0.239	0.108	0.046	0.141	0.064
3-21	174.91	0.069	0.201	0.123	0.039	0.115	0.070
3-22	170.45	0.086	0.221	0.117	0.050	0.130	0.069
3-23	178.35	0.054	0.189	0.148	0.030	0.106	0.083
3-24	185.54	0.075	0.292	0.124	0.040	0.157	0.067
3-25	172.05	0.083	0.182	0.115	0.048	0.106	0.067
3-26	171.48	0.067	0.214	0.093	0.039	0.125	0.054
3-27	176.90	0.086	0.218	0.151	0.049	0.123	0.085
3-28	171.80	0.085	0.183	0.115	0.049	0.107	0.067
3-29	173.57	0.072	0.208	0.099	0.041	0.120	0.057
3-30	170.20	0.072	0.230	0.101	0.042	0.135	0.059
4-31	191.81	0.076	0.206	0.127	0.040	0.107	0.066
4-32	186.90	0.105	0.251	0.181	0.056	0.134	0.097
4-33	188.45	0.101	0.198	0.173	0.054	0.105	0.092
4-34	189.51	0.089	0.213	0.164	0.047	0.112	0.087
4-35	176.95	0.096	0.196	0.173	0.054	0.111	0.098
4-36	186.58	0.080	0.221	0.210	0.043	0.118	0.113
4-37	196.90	0.061	0.250	0.144	0.031	0.127	0.073
4-38	177.44	0.079	0.221	0.139	0.045	0.125	0.078
4-R-05	179.21	0.083	0.232	0.158	0.046	0.129	0.088
4-40	192.97	0.061	0.255	0.096	0.032	0.132	0.050

* Data is unavailable

GP-ANI NUMBER	BODY WEIGHT	ADRENALS WEIGHT	THYMUS WEIGHT	TESTES/ OVARIES WEIGHT	% ADRENALS	% THYMUS	% TESTES/ OVARIES
5-41	325.07	0.061	0.280	4.852	0.019	0.086	1.493
5-42	293.65	0.083	0.286	4.185	0.028	0.097	1.425
5-R-06	303.37	0.070	0.309	3.840	0.023	0.102	1.266
5-44	340.44	0.065	0.539	4.853	0.019	0.158	1.426
5-45	305.28	0.057	0.311	4.192	0.019	0.102	1.373
5-46	320.96	0.076	0.267	4.683	0.024	0.083	1.459
5-47	326.14	0.080	0.240	4.834	0.025	0.074	1.482
5-48	350.18	0.098	0.301	4.932	0.028	0.086	1.408
5-49	284.92	0.068	0.209	4.913	0.024	0.073	1.724
5-R-07	333.94	0.071	0.229	4.489	0.021	0.069	1.344
6-51	270.07	0.064	0.230	2.587	0.024	0.085	0.958
6-52	272.11	0.061	0.318	2.718	0.022	0.117	0.999
6-53	268.84	0.074	0.232	2.463	0.028	0.086	0.916
6-R-08	264.17	0.055	0.218	2.555	0.021	0.083	0.967
6-55	265.67	0.078	0.206	2.281	0.029	0.078	0.859
6-56	264.78	0.060	0.247	2.544	0.023	0.093	0.961
6-R-09	254.20	0.049	0.128	2.236	0.019	0.050	0.880
6-58	263.92	0.095	0.201	2.627	0.036	0.076	0.995
6-59	266.15	0.072	0.246	2.576	0.027	0.092	0.968
6-60	259.01	0.057	0.200	2.324	0.022	0.077	0.897
7-R-10	303.87	0.084	0.226	4.309	0.028	0.074	1.418
7-62	277.11	0.060	0.234	2.928	0.022	0.084	1.057
7-63	293.58	0.059	0.203	3.597	0.020	0.069	1.225
7-64	282.79	0.089	0.138	2.681	0.031	0.049	0.948
7-65	274.47	0.051	0.270	2.565	0.019	0.098	0.935
7-66	274.26	0.051	0.222	2.420	0.019	0.081	0.882
7-67	271.27	0.054	0.359	2.639	0.020	0.132	0.973
7-68	281.14	0.084	0.284	2.403	0.030	0.101	0.855
7-69	258.38	0.045	0.201	2.311	0.017	0.078	0.894
7-70	289.23	0.068	0.244	2.488	0.024	0.084	0.860
8-71	339.18	0.070	0.253	4.857	0.021	0.075	1.432
8-72	301.77	0.092	0.235	3.916	0.030	0.078	1.298
8-73	300.76	0.071	0.271	4.776	0.024	0.090	1.588
8-74	304.27	0.061	0.236	4.590	0.020	0.078	1.509
8-75	317.96	0.089	0.280	4.635	0.028	0.088	1.458
8-76	267.72	0.060	0.199	3.741	0.022	0.074	1.397
8-77	305.60	0.051	0.274	4.328	0.017	0.090	1.416
8-78	309.79	0.059	0.268	4.342	0.019	0.087	1.402
8-R-11	305.38	0.057	0.219	4.601	0.019	0.072	1.507
8-80	306.91	0.080	0.247	4.511	0.026	0.080	1.470

APPENDIX D

HEMATOLOGY DATA

Hematology Data/Females
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	PLATELETS thsn/ cu mm	WBC COUNT thsn/ cu mm
0	151	7.68	15.5	43.8	769	3.7
	152	7.61	15.4	43.6	800	3.9
	153	7.37	14.6	42.2	859	2.9
	154	7.52	14.8	42.9	825	4.7
	155	7.80	15.8	43.9	801	4.3
800	156	6.43	13.6	38.3	885	4.2
	157	6.48	14.1	39.4	913	4.8
	158	6.50	14.0	38.9	1078	5.7
	159	6.89	14.0	40.6	943	6.5
	160	7.09	14.6	42.4	988	4.7
400	161	7.12	14.5	41.6	930	5.4
	162	7.00	14.1	40.3	840	4.4
	163	6.76	13.7	39.1	856	4.9
	164	6.83	14.1	40.1	940	4.3
	165	6.67	13.9	39.4	926	4.9
66.67	166	7.60	15.1	43.4	846	3.9
	167	7.07	14.4	39.6	893	5.0
	168	7.15	14.8	40.8	872	5.7
	169	7.41	14.9	41.3	873	5.6
	170	7.13	14.8	40.1	896	5.7

Hematology Data/Females
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	METHB %	NEUTRO-PHILS %	LYMPHO-CYTES %	HEINZ BODIES %	RETIC %
0	151	0.9	0.7	2.8	0.0	1.7
	152	0.5	1.0	2.7	0.0	1.5
	153	0.7	0.5	2.3	0.0	2.1
	154	1.7	1.1	3.5	0.0	2.5
	155	1.5	1.2	3.0	0.0	1.9
800	156	8.9	0.9	3.2	0.0	3.6
	157	5.5	0.9	3.7	0.0	4.4
	158	5.1	1.1	4.5	0.0	5.1
	159	5.0	1.2	5.1	0.0	4.7
	160	6.5	1.1	3.4	0.0	6.2
400	161	6.0	1.2	4.1	0.0	3.2
	162	5.2	0.7	3.4	0.0	2.9
	163	5.4	1.2	3.6	0.0	3.3
	164	4.3	1.0	3.3	0.0	2.3
	165	3.5	1.3	3.5	0.0	*
66.67	166	1.6	1.1	2.7	0.0	1.9
	167	0.9	1.5	3.5	0.0	1.4
	168	0.8	1.0	4.4	0.0	2.1
	169	0.8	1.3	4.2	0.0	1.6
	170	1.1	1.0	4.6	0.0	1.3

* = Quantity not sufficient

Hematology Data/Males
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	PLATELETS thsn/ cu mm	WBC COUNT thsn/ cu mm
0	176	8.21	15.3	43.2	805	4.9
	177	8.28	15.6	43.0	982	7.1
	178	8.92	16.4	46.4	824	9.1
	179	8.29	16.1	43.2	793	5.8
	180	8.50	16.1	45.1	839	8.2
800	181	6.89	13.5	37.9	866	5.6
	182	7.61	15.0	42.9	981	7.5
	183	7.22	14.2	39.6	885	6.9
	184	7.46	14.2	40.6	999	7.4
	185	7.02	14.0	39.2	1012	5.5
400	186	8.22	15.5	44.5	883	6.9
	187	7.72	14.0	40.6	959	7.5
	188	7.49	14.2	41.1	975	5.8
	189	7.97	14.9	42.8	983	7.9
	190	7.42	14.3	40.7	916	6.5
66.67	191	8.50	15.2	44.3	853	7.3
	192	8.36	15.2	44.4	871	5.6
	193	*	*	*	*	*
	194	8.07	14.9	42.2	856	6.1
	195	8.05	14.9	41.4	983	5.5

* = Clotted

Hematology Data/Males
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	METHB %	NEUTRO-PHILS %	LYMPHO-CYTES %	HEINZ BODIES %	RETIC %
0	176	0.4	1.4	3.4	0.0	1.8
	177	0.9	1.8	5.1	0.0	2.4
	178	0.9	1.7	6.8	0.0	2.1
	179	0.7	1.5	4.2	0.0	1.5
	180	1.2	1.8	6.2	0.0	1.2
800	181	7.3	1.6	3.9	0.0	4.3
	182	6.1	1.8	5.5	0.0	4.8
	183	6.8	1.3	5.5	0.0	3.4
	184	5.5	1.6	5.6	0.0	5.1
	185	6.1	1.2	4.3	0.0	6.2
400	186	5.5	2.0	4.9	0.0	3.5
	187	4.8	2.0	5.5	0.0	4.1
	188	3.8	1.4	4.3	0.0	4.7
	189	4.8	1.4	6.2	0.0	2.5
	190	4.1	1.4	5.1	0.0	3.4
66.67	191	1.3	1.8	5.4	0.0	1.6
	192	0.6	1.6	3.8	0.0	1.8
	193	1.6	*	*	0.0	2.2
	194	1.3	1.5	4.3	0.0	2.6
	195	2.2	1.7	3.8	0.0	2.0

* = Clotted

Hematology Data/Females
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	PLATELETS thsn/ cu mm	WBC COUNT thsn/ cu mm
0	1	8.01	16.4	45.0	861	7.5
	2	7.55	16.1	41.9	863	10.5
	5	7.95	16.5	44.3	888	8.5
	8	7.51	15.5	41.2	882	9.5
	9	7.19	15.0	39.0	918	9.0
	10	6.68	15.1	36.2	875	7.5
	RO1	7.37	15.6	40.7	792	8.5
	RO2	7.43	15.2	41.4	868	5.5
	RO3	7.59	15.7	41.7	888	7.5
	RO4	7.26	15.5	39.6	996	10.0
800	11	6.48	14.2	36.9	984	8.5
	12	6.55	14.1	36.1	1005	10.5
	13	6.77	15.1	37.6	1035	9.0
	14	5.97	13.9	33.3	905	7.5
	15	6.32	14.3	35.0	1050	9.0
	16	6.12	14.2	35.1	950	8.5
	17	6.49	13.6	36.0	709	9.0
	18	6.00	13.8	34.9	1001	11.0
	19	7.00	14.4	39.9	871	8.0
	20	6.23	13.7	36.6	1059	8.5
400	21	6.84	13.9	38.3	841	9.5
	22	6.77	13.6	38.1	954	12.0
	23	6.89	13.9	38.5	915	8.5
	24	6.70	13.9	37.9	974	9.0
	25	6.88	14.2	39.4	888	7.5
	26	7.06	14.3	39.3	886	9.5
	27	6.65	13.9	37.6	580	8.0
	28	7.28	14.6	41.1	886	9.0
	29	7.38	14.6	40.7	800	10.0
	30	6.93	14.5	38.9	851	7.5
66.67	31	7.33	15.5	40.4	875	10.0
	32	7.36	15.8	40.0	847	9.5
	33	7.52	15.4	41.2	859	8.5
	34	7.53	15.4	41.7	807	9.5
	35	7.24	15.2	39.7	901	11.0
	36	7.41	16.2	48.8	924	10.5
	37	7.25	15.4	45.8	953	8.0
	38	7.61	16.2	57.1	736	10.0
	40	7.24	15.1	49.7	836	11.0
	RO5	7.44	15.8	56.4	757	9.0

Hematology Data/Females
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	METHB %	NEUTRO-PHILS %	LYMPHO-CYTES %	HEINZ BODIES %	RETIC %
0	1	0.5	20	80	0.0	1.6
	2	0.9	18	82	0.0	2.0
	5	0.9	20	80	0.0	1.4
	8	1.6	16	84	0.0	1.5
	9	0.4	23	76	0.0	1.2
	10	0.0	21	79	0.0	1.8
	RO1	0.1	19	81	0.0	1.4
	RO2	0.2	22	78	0.0	1.7
	RO3	0.1	25	75	0.0	1.5
	RO4	1.6	18	81	0.0	1.3
800	11	2.6	19	80	0.0	2.1
	12	3.6	21	79	0.0	2.0
	13	3.3	17	83	0.0	2.5
	14	2.9	18	82	0.0	2.8
	15	3.8	19	80	0.0	2.4
	16	3.2	18	82	0.0	3.5
	17	2.3	22	78	0.0	2.3
	18	2.7	19	81	0.0	3.9
	19	3.8	20	79	0.0	2.7
	20	4.4	20	80	0.0	3.7
400	21	3.2	15	85	0.0	4.5
	22	3.5	16	84	0.0	3.4
	23	1.8	22	78	0.0	2.7
	24	2.4	17	82	0.0	4.7
	25	3.2	23	77	0.0	3.2
	26	3.5	17	83	0.0	2.2
	27	3.0	18	82	0.0	2.4
	28	2.5	19	78	0.0	3.1
	29	2.6	25	75	0.0	2.7
	30	2.7	20	79	0.0	2.9
66.67	31	0.8	19	81	0.0	2.1
	32	0.7	29	69	0.0	2.3
	33	1.4	24	76	0.0	1.9
	34	1.8	20	80	0.0	1.7
	35	1.6	23	77	0.0	2.5
	36	1.3	21	75	0.0	3.1
	37	1.0	22	78	0.0	3.0
	38	1.3	26	74	0.0	4.1
	40	1.0	28	72	0.0	2.9
	RO5	1.3	26	71	0.0	4.4

Hematology Data/Males
90 Days

DOSE GROUPS	ANIMAL	RBC COUNT	HGB	HCT	PLATELETS	WBC COUNT
(mg TNB/kg) diet	#	mill/ cu mm	g/dl	%	thsn/ cu mm	thsn/ cu mm
0	41	7.99	25.6	40.3	1266	10.5
	42	7.25	16.6	36.3	1395	9.8
	44	9.00	16.2	57.2	703	9.5
	45	7.79	17.8	39.6	1017	7.9
	46	9.07	16.3	58.1	723	6.5
	47	8.45	21.9	51.1	1076	9.8
	48	6.80	29.1	33.0	2550	8.5
	49	*	*	*	*	*
	RO6	7.57	19.3	38.2	1191	11.0
	RO7	8.92	16.3	61.6	733	11.0
800	51	6.45	13.3	33.5	1128	11.5
	52	7.19	14.2	50.9	911	14.5
	53	7.53	14.1	47.6	692	9.5
	55	7.32	13.9	51.1	957	13.0
	56	6.98	13.0	48.5	890	10.5
	58	7.27	13.8	45.1	992	10.5
	59	6.42	13.7	35.6	1136	8.0
	60	7.01	13.8	46.7	880	10.5
	RO8	7.47	14.5	46.2	981	10.5
	RO9	7.30	14.2	45.3	944	9.0
400	62	7.60	13.7	50.7	811	12.0
	63	7.87	14.1	47.5	888	9.5
	64	6.93	13.7	32.6	1312	9.0
	65	6.56	12.3	32.5	1092	11.5
	66	7.07	17.3	35.0	1259	8.5
	67	6.63	21.7	33.4	1703	10.0
	68	7.58	13.9	43.7	576	12.5
	69	7.18	14.0	44.6	738	11.5
	70	7.64	13.1	50.8	768	12.0
	R10	7.49	13.8	51.2	718	10.5
66.67	71	*	*	*	*	*
	72	5.76	13.9	26.1	2108	13.5
	73	7.84	10.0	45.0	634	12.0
	74	*	*	*	*	*
	75	*	*	*	*	*
	76	*	*	*	*	*
	77	*	*	*	*	*
	78	*	*	*	*	*
	80	*	*	*	*	*
	R11	*	*	*	*	*

* = Clotted

Hematology Data/Males
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	METHB %	NEUTRO-PHILS %	LYMPHO-CYTES %	HEINZ BODIES %	RETIC %
0	41	1.3	21	79	0.0	1.5
	42	1.1	15	84	0.0	1.7
	44	1.4	18	80	0.0	1.9
	45	0.6	22	78	0.0	2.2
	46	1.0	16	84	0.0	2.1
	47	1.4	17	83	0.0	2.4
	48	0.4	19	81	0.0	**
	49	0.4	*	*	0.0	*
	RO6	0.8	20	80	0.0	2.0
	RO7	1.1	21	78	0.0	2.5
800	51	4.5	20	80	0.0	**
	52	4.4	13	86	0.0	5.5
	53	4.7	16	82	0.0	4.1
	55	5.7	19	81	0.0	3.8
	56	6.2	13	87	0.0	5.9
	58	6.1	20	80	0.0	4.1
	59	6.2	21	79	0.0	3.5
	60	6.0	19	81	0.0	4.2
	RO8	4.5	17	83	0.0	3.1
	RO9	6.3	15	85	0.0	4.7
400	62	4.2	21	79	0.0	2.9
	63	4.8	23	77	0.0	2.4
	64	4.6	15	84	0.0	**
	65	3.6	16	82	0.0	**
	66	5.0	18	82	0.0	**
	67	3.4	21	79	0.0	**
	68	4.0	22	78	0.0	2.1
	69	3.1	24	76	0.0	3.8
	70	6.0	19	80	0.0	2.8
	R10	5.6	19	81	0.0	3.2
66.67	71	1.4	*	*	0.0	*
	72	1.7	22	77	0.0	1.9
	73	1.2	31	67	0.0	2.1
	74	1.9	*	*	0.0	*
	75	1.5	*	*	0.0	*
	76	1.7	*	*	0.0	*
	77	1.6	*	*	0.0	*
	78	1.4	*	*	0.0	*
	80	1.9	*	*	0.0	*
	R11	2.1	*	*	0.0	*

* = Clotted, ** = Quantity not sufficient

APPENDIX E

CLINICAL CHEMISTRY DATA

Clinical Chemistries/Females
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	GLUCOSE mg/dl	CREATININE mg/dl	BUN mg/dl	Na mmol/l	TOTAL PROTEIN g/dl	TOTAL BILIRUBIN mg/dl	AST U/L
0	151	163	0.3	28	132	7.0	0.3	107
	152	149	0.4	31	134	6.8	0.2	186
	153	169	0.5	29	150	6.8	0.2	136
	154	152	0.7	34	130	7.4	0.2	255
	155	139	0.5	33	130	6.8	0.3	125
800	156	169	0.4	32	146	6.9	0.2	125
	157	195	0.7	33	160	6.7	0.2	259
	158	139	0.6	36	120	7.2	0.2	111
	159	169	0.7	36	117	7.5	0.2	109
	160	167	0.2	30	157	7.5	0.2	80
400	161	146	0.3	33	188	8.3	0.2	97
	162	158	0.3	32	135	7.4	0.2	139
	163	*	*	*	*	*	*	*
	164	150	0.1	32	140	7.5	0.2	113
	165	138	0.7	37	125	8.4	0.1	156
66.67	166	172	0.7	35	128	8.5	0.1	138
	167	154	0.5	30	151	7.1	0.1	79
	168	138	0.5	29	146	7.4	0.1	78
	169	*	*	*	*	*	*	*
	170	163	0.6	39	156	7.2	0.0	129

* = Quantity not sufficient

Clinical Chemistries/Females
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN g/dl
0	151	35	166	6.1	11.3	4.0
	152	61	157	5.5	11.6	4.1
	153	46	153	5.9	11.6	4.0
	154	153	165	5.3	12.5	4.0
	155	44	185	5.1	10.8	4.0
800	156	20	161	6.2	10.8	4.1
	157	133	166	7.8	11.1	4.0
	158	48	176	4.7	11.2	4.4
	159	46	186	5.0	10.5	4.2
	160	33	143	6.2	11.0	4.6
400	161	36	125	6.8	11.1	4.1
	162	48	90	5.7	10.9	4.0
	163	*	*	*	*	*
	164	46	167	5.4	10.9	3.7
	165	66	201	8.9	10.3	3.6
66.67	166	49	178	5.1	11.4	4.1
	167	40	125	5.4	10.9	4.0
	168	46	117	5.4	11.0	4.1
	169	*	*	*	*	*
	170	46	152	5.3	10.9	4.2

* = Quantity not sufficient

Clinical Chemistries/Males
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	GLUCOSE mg/dl	CREATININE mg/dl	BUN mg/dl	Na mmol/l	TOTAL PROTEIN g/dl	TOTAL BILIRUBIN mg/dl	AST U/L
0	176	*	*	*	*	*	*	*
	177	198	0.6	30	124	7.8	0.1	125
	178	*	*	*	*	*	*	*
	179	182	0.9	30	140	7.4	0.1	169
	180	204	0.6	32	134	8.1	0.1	166
800	181	210	0.7	39	136	8.8	0.1	170
	182	201	0.6	30	122	7.9	0.2	149
	183	199	0.7	32	155	7.4	0.1	156
	184	196	0.6	31	144	7.9	0.1	145
	185	177	0.7	34	151	7.7	0.1	179
400	186	125	*	*	*	*	*	*
	187	178	0.5	28	148	7.8	0.0	59
	188	179	0.6	28	153	7.3	0.1	132
	189	198	0.7	30	147	7.6	0.0	136
	190	171	0.6	31	142	7.9	0.1	137
66.67	191	199	0.6	33	146	8.1	0.1	138
	192	185	0.7	30	148	7.8	0.1	128
	193	193	0.6	25	140	7.7	0.1	171
	194	196	0.7	32	140	7.8	0.1	125
	195	206	0.6	28	144	8.4	0.1	64

* = Quantity not sufficient

Clinical Chemistries/Males
45 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN g/dl
0	176	*	*	*	*	*
	177	66	189	5.3	11.9	4.5
	178	*	*	*	*	*
	179	113	221	5.7	10.4	3.7
	180	83	253	5.3	12.3	4.3
800	181	58	289	6.8	11.9	4.4
	182	56	186	5.4	11.4	4.5
	183	47	118	6.3	7.1	4.1
	184	45	108	5.6	9.5	3.9
	185	57	111	6.1	9.7	3.8
400	186	*	*	*	*	*
	187	66	103	5.4	10.2	4.0
	188	60	143	5.4	10.7	4.1
	189	67	117	5.3	11.3	4.0
	190	72	110	5.3	11.2	4.2
66.67	191	83	115	5.9	6.8	4.1
	192	60	130	5.6	7.6	3.8
	193	51	105	6.4	6.0	3.7
	194	62	115	4.9	5.8	3.7
	195	57	104	5.0	8.0	4.3

* = Quantity not sufficient

Clinical Chemistries/Females
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	GLUCOSE mg/dl	CREATININE mg/dl	BUN mg/dl	Na mmol/l	TOTAL PROTEIN g/dl	TOTAL BILIRUBIN mg/dl	AST U/L
0	1	139	0.5	0	141	6.4	0.1	98
	2	156	0.5	19	144	5.9	0.1	137
	5	99	0.5	19	138	6.0	0.1	212
	8	157	0.5	15	141	6.2	0.1	84
	9	153	0.5	18	139	6.1	0.1	78
	10	124	0.5	18	140	6.5	0.1	81
	RO1	156	0.6	17	138	5.9	0.1	92
	RO2	136	0.5	18	140	6.2	0.1	94
	RO3	150	0.5	18	143	6.6	0.1	75
	RO4	168	0.5	16	142	6.0	0.1	78
800	11	132	0.5	20	140	6.6	0.2	106
	12	113	0.5	20	142	6.5	0.2	88
	13	123	0.5	18	144	6.6	0.1	121
	14	143	0.5	21	145	6.0	0.1	97
	15	150	0.5	18	143	5.9	0.1	107
	16	163	0.6	18	142	6.6	0.1	157
	17	146	0.5	17	143	6.2	0.2	150
	18	143	0.6	18	143	6.0	0.1	84
	19	178	0.6	20	137	6.6	0.1	274
	20	128	0.5	22	142	6.5	0.2	94
400	21	138	0.5	17	141	6.3	0.2	152
	22	123	0.5	17	146	6.3	0.1	106
	23	138	0.6	23	140	6.9	0.1	77
	24	132	0.5	18	140	6.5	0.1	102
	25	180	0.5	19	143	6.2	0.1	96
	26	164	0.5	21	138	6.2	0.2	139
	27	181	0.5	17	141	6.0	0.1	225
	28	164	0.5	18	140	6.2	0.1	94
	29	176	0.6	18	141	6.4	0.1	139
	30	178	0.6	17	141	5.9	0.1	66
66.67	31	166	0.6	20	141	6.3	0.1	99
	32	182	0.6	19	142	6.4	0.1	144
	33	145	0.5	17	139	6.2	0.1	132
	34	142	0.5	17	141	6.8	0.1	75
	35	145	0.5	19	143	6.3	0.1	94
	36	170	0.6	18	139	6.1	0.1	107
	37	113	0.5	17	140	6.3	0.1	76
	38	170	0.6	17	143	6.5	0.1	139
	40	140	0.5	21	141	6.8	0.1	76
	RO5	159	0.6	15	143	6.4	0.1	161

Clinical Chemistries/Females
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN g/dl
0	1	59	103	5.1	10.3	4.4
	2	92	76	4.4	10.3	4.1
	5	141	91	12.0	10.1	4.0
	8	53	62	5.6	10.7	4.1
	9	55	73	5.9	10.5	4.2
	10	48	111	4.6	10.3	4.1
	RO1	54	93	5.3	10.5	4.0
	RO2	55	82	5.0	10.4	4.2
	RO3	47	75	5.5	11.0	4.4
	RO4	55	89	4.5	10.7	4.1
800	11	56	87	5.9	10.6	4.4
	12	55	108	4.9	10.3	4.4
	13	58	84	5.7	10.7	4.4
	14	72	97	4.8	10.4	4.2
	15	77	88	4.9	10.4	4.2
	16	87	96	5.6	10.1	4.2
	17	73	100	6.1	10.5	4.4
	18	50	69	5.2	10.6	4.2
	19	112	83	9.1	11.0	4.6
	20	55	91	5.4	10.4	4.4
400	21	84	90	6.7	10.3	4.4
	22	62	78	5.2	10.8	4.4
	23	54	97	4.9	10.4	4.5
	24	51	84	6.2	10.5	4.3
	25	82	77	5.6	10.7	4.5
	26	80	85	6.6	10.3	4.2
	27	136	75	6.0	10.4	4.2
	28	77	76	6.1	10.7	4.2
	29	71	78	5.4	10.5	4.2
	30	59	68	4.4	10.3	4.1
66.67	31	70	88	5.1	10.6	4.3
	32	92	80	5.1	10.9	4.4
	33	75	83	5.4	10.2	4.2
	34	55	88	5.8	10.9	4.4
	35	51	70	4.0	10.8	4.4
	36	67	92	5.5	10.3	4.2
	37	44	65	4.6	10.0	4.3
	38	87	83	5.2	10.8	4.4
	40	50	84	5.2	10.8	4.6
	RO5	108	71	5.8	10.8	4.4

Clinical Chemistries/Males
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	GLUCOSE mg/dl	CREATININE mg/dl	BUN mg/dl	Na mmol/l	TOTAL PROTEIN g/dl	TOTAL BILIRUBIN mg/dl	AST U/L
0	41	210	0.6	18	141	6.5	0.1	133
	42	221	0.6	15	142	6.6	0.1	77
	44	245	0.5	16	141	6.8	0.1	98
	45	160	0.6	21	141	6.2	0.1	203
	46	215	0.6	19	142	6.6	0.1	114
	47	158	0.6	20	143	6.4	0.1	127
	48	166	0.6	18	143	6.9	0.1	116
	49	296	0.7	19	140	6.1	0.1	158
	RO6	205	0.6	18	142	6.5	0.1	84
	RO7	248	0.6	19	141	7.0	0.1	86
800	51	199	0.6	22	143	6.7	0.1	158
	52	194	0.6	22	141	6.6	0.1	118
	53	212	0.6	21	141	6.7	0.1	196
	55	206	0.6	23	142	7.1	0.1	95
	56	182	0.6	19	143	6.9	0.2	125
	58	162	0.6	22	143	6.6	0.1	141
	59	198	0.6	20	143	7.1	0.1	171
	60	186	0.6	23	143	7.1	0.2	116
	RO8	214	0.6	19	141	6.5	0.1	104
	RO9	176	0.6	20	143	7.1	0.1	86
400	62	200	0.6	17	142	6.5	0.1	171
	63	240	0.6	19	143	7.1	0.1	126
	64	157	0.6	16	140	6.8	0.2	93
	65	199	0.6	18	142	6.9	0.1	90
	66	185	0.6	21	142	7.3	0.1	97
	67	237	0.6	23	142	7.2	0.1	138
	68	193	0.6	22	143	6.8	0.2	394
	69	185	0.6	24	143	6.6	0.1	120
	70	175	0.6	22	143	7.5	0.2	349
	R10	212	0.6	26	143	7.2	0.2	188
66.67	71	168	0.6	23	144	7.0	0.2	207
	72	185	0.6	16	141	6.5	0.1	90
	73	181	0.5	19	143	6.7	0.1	143
	74	202	0.6	20	141	6.4	0.1	124
	75	217	0.5	18	141	6.9	0.1	75
	76	187	0.5	19	142	6.4	0.1	174
	77	205	0.6	23	143	6.8	0.1	160
	78	190	0.6	20	141	6.8	0.1	103
	80	202	0.5	19	141	6.5	0.1	85
	R11	194	0.6	18	141	6.4	0.1	92

Clinical Chemistries/Males
90 Days

DOSE GROUPS (mg TNB/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN g/dl
0	41	93	110	5.4	10.6	4.4
	42	62	95	6.0	11.1	4.6
	44	73	103	5.7	10.8	4.5
	45	128	134	5.3	10 5	4.1
	46	86	94	5.6	11.0	4.6
	47	124	101	5.0	11.0	4.4
	48	79	106	6.5	11.3	4.7
	49	93	115	9.1	10.9	4.1
	RO6	71	100	5.6	11.0	4.4
	RO7	71	110	6.1	11.4	4.8
800	51	87	109	5.5	10.5	4.7
	52	77	116	5.0	10.5	4.6
	53	102	121	5.5	10.5	4.7
	55	67	107	5.4	11.0	4.9
	56	39	102	5.7	10.5	4.8
	58	89	90	4.7	10.9	4.6
	59	106	116	5.2	11.2	4.9
	60	79	112	5.2	10.7	4.9
	RO8	81	84	5.0	11.0	4.5
	RO9	68	93	6.1	11.5	5.0
400	62	134	87	6.2	10.8	4.5
	63	86	91	6.0	11.0	4.8
	64	63	84	6.8	11.5	4.7
	65	63	87	5.6	11.3	4.6
	66	60	109	5.0	10.5	4.9
	67	116	104	5.5	11.1	4.8
	68	221	102	4.7	10.7	4.5
	69	57	105	5.1	10.4	4.6
	70	202	125	5.4	11.0	5.0
	R10	132	181	5.9	11.4	4.8
66.67	71	69	122	5.0	10.9	4.8
	72	61	93	6.3	10.9	4.4
	73	89	102	5.3	10.9	4.4
	74	95	106	5.3	10.4	4.3
	75	69	113	6.3	11.7	4.9
	76	118	107	4.1	10.9	4.5
	77	105	112	4.8	10.6	4.7
	78	77	124	5.6	10.8	4.5
	80	65	103	5.3	10.5	4.3
	R11	77	89	5.9	11.0	4.0

APPENDIX F

CLINICAL OBSERVATIONS

DATE	GROUP 1 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. Cage #2 had a flooded water bottle. This cut down the food intake for 12/11 to 12/15 time period. All animals look normal.

DATE	GROUP 1 OBSERVATIONS
12/16/92	All animals look normal.
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Holiday. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	Holiday. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats. Final food and water weights were taken. Rats were fasted at 8:00PM.
01/26/93	All rats were necropsied today.

DATE	GROUP 2 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal. Rat 2-19 had food spilled into the cage.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal. Rat 2-19 had spilled food in the cage.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal. 6 of 10 rats have excessive spillage of food in their cages. They are #'s 11,13,14,15,18,and 19. Steps were taken to control this problem. We modified the feeder and plan to reduce the amount of food given on 10-27-92. We will then weigh the high dose groups for food intake every other day, except for weekends.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal. Note: The weighing schedule does not need to change. Half full feeders will last 4 days and that controls the spillage problem.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.

DATE	GROUP 2 OBSERVATIONS
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. All animals look normal.
12/16/92	All animals look normal.
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. Cage #14 had a flooded water bottle. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. Cage #16 had a defective bottle stopper. This was corrected. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats. Final food and water weights were taken. Rats were fasted at 8:00PM.
01/26/93	All rats were necropsied today.

DATE	GROUP 3 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal. Rat 3-22 had food spilled into the cage.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. All animals look normal.
12/16/92	All animals look normal.

DATE	GROUP 3 OBSERVATIONS
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats. Final food and water weights were taken. Rats were fasted at 8:00PM.
01/26/93	All rats were necropsied today.

DATE	GROUP 4 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal. Rat 4-34 had food spilled into the cage.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. All animals look normal.
12/16/92	All animals look normal.

DATE	GROUP 4 OBSERVATIONS
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats. Final food and water weights were taken. Rats were fasted at 8:00PM.
01/26/93	All rats were necropsied today.

DATE	GROUP 5 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. All animals look normal.
12/16/92	All animals look normal.
12/17/92	All animals look normal.

DATE	GROUP 5 OBSERVATIONS
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats.
01/26/93	All rats look normal. Final food and water weights were taken. Rats were fasted at 8:00pm.
01/27/93	All rats were necropsied today.

DATE	GROUP 6 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal. Rat 6-55 had excess food spilled from his cage.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal. Rats 6-55 and 6-59 had excess food spilled in their cages.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal. Rats 6-55 and 6-59 again had excess food spilled in their cages.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal. Five rats have spilled food. They are #'s 51,53,55,56, and 59. This seems to be a dose related problem affecting only the high dose.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal. 6 of 10 rats have excessive spillage of food in their cages. They are #'s 51,52,54,55,56,and 59. Steps were taken to control this problem. We modified the feeder and plan to reduce the amount of food given on 10-27-92. We will then weigh the high dose groups for food intake every other day, except for weekends.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal. Note: The weighing schedule does not need to change. Half full feeders will last 4 days and that controls the spillage problem.

DATE	GROUP 6 OBSERVATIONS
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. Rats 6-53, 6-56, and 6-59 had excess food spilled in the cage. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. No spillage observed when food was weighed. Rat 6-59 food intake for 12/11 to 12/15 is a little high. All animals look normal.
12/16/92	All animals look normal.
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. Rats 6-53 and 6-59 had excess food spilled in the cages. All animals look normal.
12/21/92	Food & Water changed today. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. Rat 6-59 had excess food spilled in the cage. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. Rat 6-59 had excess food spilled in the cage. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.

DATE	GROUP 6 OBSERVATIONS
01/18/93	Food & Water changed today. Rats weighed. All animals look normal. Rat 6-59 had excess food spilled in cage.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats.
01/26/93	All rats look normal. Final food and water weights were taken. Rats were fasted at 8:00pm.
01/27/93	All rats were necropsied today.

DATE	GROUP 7 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal. Rat 7-61 had food spilled in the cage.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal. Rats 7-61 and 7-63 had food spilled in the cage.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal. Rats 7-61, 7-63, and 7-67 all had food spilled from their cages.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal. Rats 7-61, 7-63, and 7-67 all had food spilled into their cages.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/09/92	All animals look normal.

DATE	GROUP 7 OBSERVATIONS
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. No spillage observed when food was weighed. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/16/92	All animals look normal.
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/21/92	Food & Water changed today. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. Rat 7-61 had excess food spilled in the cage. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. No spillage observed when food was weighed. Rat 7-61 food intake for 12/24 to 12/28 is a little high. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats.
01/26/93	All rats look normal. Final food and water weights were taken. Rats were fasted at 8:00pm.
01/27/93	All rats were necropsied today.

DATE	GROUP 8 OBSERVATIONS
10/21/92	Animals were randomized today. Rats weighed.
10/22/92	All animals look normal.
10/23/92	All animals look normal.
10/26/92	All animals look normal.
10/27/92	All animals look normal.
10/28/92	All animals look normal.
10/29/92	Study started today for Females, Groups 1-4. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
10/30/92	Study started today for Males, Groups 5-8. Rats were weighed and new food and water was weighed and placed on cages. All animals look normal.
11/02/92	Food & Water changed today. All animals look normal.
11/03/92	All animals look normal.
11/04/92	All animals look normal.
11/05/92	Food & Water changed today. Rats weighed. All animals look normal.
11/06/92	All animals look normal.
11/09/92	Food & Water changed today. All animals look normal.
11/10/92	All animals look normal.
11/11/92	Holiday. No observations made today.
11/12/92	Food & Water changed today. Rats weighed. All animals look normal.
11/13/92	All animals look normal.
11/16/92	All animals look normal.
11/17/92	Food & Water changed today. All animals look normal.
11/18/92	All animals look normal.
11/19/92	All animals look normal.
11/20/92	Food & Water changed today. Rats weighed. All animals look normal.
11/23/92	All animals look normal.
11/24/92	Food & Water changed today. All animals look normal.
11/25/92	All animals look normal.
11/26/92	Holiday. No observations made today.
11/27/92	Food & Water changed today. Rats weighed. All animals look normal.
11/30/92	All animals look normal.
12/01/92	Food & Water changed today. All animals look normal.
12/02/92	All animals look normal.
12/03/92	All animals look normal.
12/04/92	Food & Water changed today. Rats weighed. All animals look normal.
12/07/92	All animals look normal.
12/08/92	Food & Water changed today. All animals look normal.
12/09/92	All animals look normal.
12/10/92	All animals look normal.
12/11/92	Food & Water changed today. Rats weighed. All animals look normal.
12/14/92	All animals look normal.
12/15/92	Food & Water changed today. Cage #75 had a flooded cage. All animals look normal.
12/16/92	All animals look normal.

DATE	GROUP 8 OBSERVATIONS
12/17/92	All animals look normal.
12/18/92	Food & Water changed today. Rats weighed. All animals look normal.
12/21/92	Food & Water changed today. All animals look normal.
12/22/92	All animals look normal.
12/23/92	All animals look normal.
12/24/92	Food & Water changed today. Rats weighed. All animals look normal.
12/25/92	Christmas Day. No observations made today.
12/28/92	Food & Water changed today. All animals look normal.
12/29/92	All animals look normal.
12/30/92	All animals look normal.
12/31/92	Food & Water changed today. All animals look normal.
01/01/93	New Years Day. No observations made today.
01/04/93	Food & Water changed today. Rats weighed. All animals look normal.
01/05/93	All animals look normal.
01/06/93	All animals look normal.
01/07/93	Food & Water changed today. All animals look normal.
01/08/93	All animals look normal.
01/11/93	Food & Water changed today. Rats weighed. All animals look normal.
01/12/93	All animals look normal.
01/13/93	All animals look normal.
01/14/93	Food & Water changed today. All animals look normal.
01/15/93	All animals look normal.
01/18/93	Food & Water changed today. Rats weighed. All animals look normal.
01/19/93	All animals look normal.
01/20/93	All animals look normal.
01/21/93	Food & Water changed today. All animals look normal.
01/22/93	All animals look normal.
01/25/93	All animals look normal. Eye exams were performed on all rats.
01/26/93	All rats look normal. Final food and water weights were taken. Rats were fasted at 8:00pm.
01/27/93	All rats were necropsied today.

APPENDIX G

OPHTHALMOLOGY FINDINGS

Study No. 92-003 Date 10/26/92

Ophthalmology Report

David A. Wilkie DVM, MS
Diplomate ACVO

Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

Materials and Methods

A preliminary ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).

Results

Initial Examination

The following animals were eliminated from study as a result of ocular abnormalities: 03, 04, 06, 07, 39, 43, 50, 54, 57, 61, and 79. Of the remaining test animals (Numbered 1-100 excluding those animals previously mentioned) the following abnormalities were noted:

Corneal dystrophy (crystals) - All Remaining Animals were affected with mild corneal dystrophy OU

Final Examination

To be performed at 90 days following initiation of testing.

Conclusions

The above findings are compatable with breed and species associated ocular abnormalities. The animals eliminated from testing had either corneal dystrophy of severity greater than mild or cataract. All of the animals remaining on test have mild corneal dystrophy affecting both eyes, a common finding in Fisher 344 rats of both sexes. In a 90 day study such as this the corneal lesions should not progress significantly and do not interfere with examination of the intraocular tissues.

Date: 4/1/93

David A. Wilkie DVM, MS
Diplomate ACVO
Assistant Professor
Department of Veterinary Clinical Sciences
The Ohio State University
1935 Coffey Road
Columbus, Ohio 43210

Study No. 92-003 Date 2/2/93

Ophthalmology Report

David A. Wilkie DVM, MS
Diplomate ACVO

Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

Materials and Methods

A preliminary ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).

Results

Final Examination

Corneal dystrophy (crystals) -	The eyes of all animals examined were affected by corneal dystrophy/crystals. All animals, except 32 and 42 were affected with moderate mild corneal dystrophy OU. Corneal dystrophy was graded as mild in animal 32 and moderate OD, severe OS in animal 42.
Conjunctivitis -	Moderate conjunctivitis was observed in the following animals: R-01 OD; 10 OD; 31 OD
Keratitis -	Severe keratitis was observed in animal R- 06 OS
Cataract -	Mild anterior capsular cataract in animal 36 OD

Conclusions

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study. As stated following the initial examination corneal dystrophy a common finding in Fisher 344 rats of both sexes. In the time since performing the initial ophthalmic examination the corneal dystrophy lesions have progressed in severity in almost all animals. This is an expected finding. The remaining abnormalities are sporadic and do not appear to be a dose-related effected. Conjunctivitis and keratitis are found routinely in Fisher 344 rats, becoming more frequent with increased age, and most likely are related to the corneal dystrophy lesions. A single, anterior capsular cataract was noted.

Date: 4/1/93

David A. Wilkie DVM, MS
Diplomate ACVO
Assistant Professor
Department of Veterinary Clinical Sciences
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Study No. 92-003 Date 2/2/93

Ophthalmology Report

David A. Wilkie DVM, MS
Diplomate ACVO

Initial ophthalmic examination of the Fisher 344 rats in the pre-test period revealed 100% of eyes to be affected with corneal dystrophy. Animals with corneal dystrophy of a severity greater than grade 1 were eliminated from the study. Corneal dystrophy is a common finding in the Fisher 344 rat and 100% affected animals is not unusual. The lesions are known to progress with time, but should not interefere with examination in a 90 day study. In addition, cataract was observed in some animals and they were also eliminated from the study.

On the final ophthalmic examination, corneal dystrophy lesions were found to have progressed in severity in almost all animals. The corneal dystrophy was graded as moderate in all but two animals. Corneal lesions remained mild in one of these two and progressed to severe in one eye of the other rat. This is an expected finding. The progression of the corneal dystrophy was not of a severe enough nature to prevent complete examination of the internal structures of the eye with the exception of the left eye in animal 42. The remaining abnormalities noted were sporadic and do not appear to be a dose-related effected. Conjunctivitis and keratitis are found routinely in Fisher 344 rats, becoming more frequent with increased age, and most likely are related to the corneal dystrophy lesions. A single, anterior capsular cataract was noted.

Date: 2/1/93

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Department of Veterinary Clinical Sciences
The Ohio State University
1935 Coffey Road
Columbus, Ohio 43210

APPENDIX H

GROSS AND HISTOPATHOLOGY DATA

HISTOPATHOLOGY DATA

REPORTS CODE TABLE

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable for evaluation
*	Tissues not examined/not required by protocol
1	Minimal
2	Mild
3	Moderate
4	Marked

Abbreviations

Degen.	Degeneration

(End of Report)

Pathology Associates, Inc.
Study No. 9[illegible]
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 FATES: ALL PAGE 1
DAYS : ALL SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%
BRAIN	# Ex	10		10		0		0		0		0		0	
SCIATIC NERVE	# Ex	10		10		0		0		0		0		0	
SPINAL CORD	# Ex	10		10		0		0		0		0		0	
SALIVARY GLAND	# Ex	10		10		0		0		0		0		0	
PANCREAS	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		0	(0)	1	(10)	0		0		0		0		0	
Degeneration, Acinar		0	(0)	1	(10)	0		0		0		0		0	
MANDIBULAR LYMPH NODE	# Ex	10		10		0		0		0		0		0	
ZYMBAL'S GLAND	# Ex	10		10		0		0		0		0		0	
PITUITARY	# Ex	10		10		0		0		0		0		0	
ADRENALS	# Ex	10		10		0		0		0		0		0	
THYROID	# Ex	10		10		0		0		0		0		0	
Cyst, Squamous		1	(10)	0	(0)	0		0		0		0		0	
PARATHYROID	# Ex	10		9		0		0		0		0		0	
TRACHEA	# Ex	10		10		0		0		0		0		0	
ESOPHAGUS	# Ex	10		10		0		0		0		0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 FATES: ALL PAGE 2
DAYS : ALL SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%
THYMUS	# Ex	9		10		0		0		0		0		0	
Hemorrhage		1	(11)	0	(0)	0		0		0		0		0	
HEART	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		1	(10)	0	(0)	0		0		0		0		0	
COLON	# Ex	10		10		0		0		0		0		0	
JEJUNUM	# Ex	10		10		0		0		0		0		0	
AORTA	# Ex	10		10		0		0		0		0		0	
LIVER	# Ex	10		10		0		1		0		0		0	
Hepatodiapragmatic Nodule		0	(0)	0	(0)	0		1	(100)	0		0		0	
Inflammation, Chronic		1	(10)	1	(10)	0		0	(0)	0		0		0	
Congestion		1	(10)	0	(0)	0		0	(0)	0		0		0	
SPLEEN	# Ex	10		10		10		10		0		0		0	
Pigment, NOS		0	(0)	10	(100)	10	(100)	2	(20)	0		0		0	
Hyperplasia, Erythroid Cell		0	(0)	10	(100)	9	(90)	2	(20)	0		0		0	
Fibrosis		0	(0)	0	(0)	1	(10)	0	(0)	0		0		0	
TONGUE	# Ex	10		10		0		0		0		0		0	
SKELETAL MUSCLE	# Ex	10		10		0		0		0		0		0	
LUNG	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		3	(30)	1	(10)	0		0		0		0		0	
KIDNEYS	# Ex	10		10		0		0		0		0		0	
Mineralization, NOS		6	(60)	4	(40)	0		0		0		0		0	

(Report Continued)

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 FATES: ALL
DAYS : ALL SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%
KIDNEYS	# Ex	10		10		0		0		0		0		0	
Lymphocytic Infiltrates		1	(10)	0	(0)	0		0		0		0		0	
Pigment, NOS		0	(0)	10	(100)	0		0		0		0		0	
URINARY BLADDER	# Ex	10		10		0		0		0		0		0	
STOMACH	# Ex	10		10		0		0		0		0		0	
Foreign Body, Glandular		1	(10)	0	(0)	0		0		0		0		0	
DUODENUM	# Ex	10		10		0		0		0		0		0	
Ectopic Pancreas		1	(10)	0	(0)	0		0		0		0		0	
ILEUM	# Ex	10		10		0		0		0		0		0	
CECUM	# Ex	10		10		0		0		0		0		0	
RECTUM	# Ex	10		10		0		0		0		0		0	
MESENTERIC LYMPH NODE	# Ex	10		10		0		0		0		0		0	
OVARIES	# Ex	10		10		0		0		0		0		0	
UTERUS	# Ex	10		10		0		0		0		0		0	
Dilatation		1	(10)	1	(10)	0		0		0		0		0	
SKIN	# Ex	10		10		0		0		0		0		0	
MAMMARY GLAND	# Ex	9		10		0		0		0		0		0	

(Report Continued)

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 | FATES: ALL | PAGE 4
DAYS : ALL | SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%
CLITORAL GLANDS	# Ex	10		10		0		0		0		0		0	
Lymphocytic Infiltrates		3	(30)	7	(70)	0		0		0		0		0	
Inflammation, Acute		1	(10)	0	(0)	0		0		0		0		0	
Dilatation, Ductal		0	(0)	1	(10)	0		0		0		0		0	
EYES	# Ex	10		10		0		0		0		0		0	
Microgranuloma, Cornea		3	(30)	3	(30)	0		0		0		0		0	
HARDERIAN GLAND	# Ex	10		10		0		0		0		0		0	
Lymphocytic Infiltrates		4	(40)	8	(80)	0		0		0		0		0	
Inflammation, Chronic/Active		0	(0)	2	(20)	0		0		0		0		0	
Inflammation, Chronic		0	(0)	1	(10)	0		0		0		0		0	
FEMUR	# Ex	10		10		0		0		0		0		0	
Pigment, NOS		0	(0)	4	(40)	0		0		0		0		0	
Hyperplasia, Erythroid Cell		0	(0)	9	(90)	0		0		0		0		0	
NASAL CAVITY	# Ex	10		10		0		0		0		0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 | FATES: ALL | PAGE 5
DAYS : ALL | SEX: MALE

GROUP:		1		2		3		4		5		6		7		8	
NUMBER OF ANIMALS:		0		0		0		0		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
BRAIN	# Ex	0		0		0		0		10		10		0		0	
SCIATIC NERVE	# Ex	0		0		0		0		10		10		0		0	
SPINAL CORD	# Ex	0		0		0		0		10		10		0		0	
SALIVARY GLAND	# Ex	0		0		0		0		10		10		0		0	
PANCREAS	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic		0		0		0		0		1	(10)	1	(10)	0		0	
Degeneration, Acinar		0		0		0		0		1	(10)	1	(10)	0		0	
MANDIBULAR LYMPH NODE	# Ex	0		0		0		0		10		10		0		0	
Hyperplasia, Plasma Cell		0		0		0		0		1	(10)	1	(10)	0		0	
ZYMBAL'S GLAND	# Ex	0		0		0		0		8		10		0		0	
PITUITARY	# Ex	0		0		0		0		10		10		0		0	
Cyst, NOS, Pars Distalis		0		0		0		0		1	(10)	0	(0)	0		0	
ADRENALS	# Ex	0		0		0		0		10		10		0		0	
Accesory Cortical Nodule		0		0		0		0		1	(10)	0	(0)	0		0	
THYROID	# Ex	0		0		0		0		10		10		0		0	
PARATHYROID	# Ex	0		0		0		0		10		8		0		0	
TRAC[illegible]	# Ex	0		0		0		0		10		10		0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 FATES: ALL PAGE 6
DAYS : ALL SEX: MALE

GROUP: NUMBER OF ANIMALS:		0		0		0		0		5 10		6 10		7 10		8 10	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
ESOPHAGUS	# Ex	0		0		0		0		10		10		0		0	
THYMUS	# Ex	0		0		0		0		10		10		0		0	
Hemorrhage		0		0		0		0		2	(20)	1	(10)	0		0	
HEART	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic		0		0		0		0		6	(60)	1	(10)	0		0	
Inflammation, Subacute Artery		0		0		0		0		0	(0)	1	(10)	0		0	
Degeneration, Myocardial		0		0		0		0		2	(20)	1	(10)	0		0	
COLON	# Ex	0		0		0		0		10		10		0		0	
JEJUNUM	# Ex	0		0		0		0		10		10		0		0	
AORTA	# Ex	0		0		0		0		10		10		0		0	
LIVER	# Ex	0		0		0		0		10		10		1		0	
Bile Duct Hyperplasia		0		0		0		0		1	(10)	0	(0)	0	(0)	0	
Inflammation, Chronic		0		0		0		0		1	(10)	1	(10)	0	(0)	0	
Inflammation, Subacute		0		0		0		0		1	(10)	2	(20)	0	(0)	0	
Necrosis, Hepatocellular		0		0		0		0		1	(10)	3	(30)	1	(100)	0	
SPLEEN	# Ex	0		0		0		0		10		10		10		10	
Pigment, NOS		0		0		0		0		0	(0)	10	(100)	6	(60)	0	(0
Hyperplasia, Erythroid Cell		0		0		0		0		0	(0)	10	(100)	10	(100)	1	(10
Fibrosis		0		0		0		0		1	(10)	1	(10)	0	(0)	0	(0
TONGUE	# Ex	0		0		0		0		10		10		0		0	
SKELETAL MUSCLE	# Ex	0		0		0		0		10		10		0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 FATES: ALL
DAYS : ALL SEX: MALE

GROUP:		5		6		7		8	
NUMBER OF ANIMALS:		10		10		10		10	
		#	%	#	%	#	%	#	%
LUNG	# Ex	10		10		0		0	
Inflammation, Chronic		2	(20)	1	(10)	0		0	
Inflammation, Chronic/Acute		1	(10)	0	(0)	0		0	
Alveolar/Bronchial Hyperplasia		0	(0)	1	(10)	0		0	
KIDNEYS	# Ex	10		10		10		10	
Mineralization, NOS		10	(100)	10	(100)	10	(100)	9	(90)
Lymphocytic Infiltrates		0	(0)	0	(0)	0	(0)	1	(10)
Pigment, NOS		0	(0)	10	(100)	10	(100)	0	(0)
Regeneration, Tubular		10	(100)	10	(100)	10	(100)	10	(100)
Hyaline Droplets		0	(0)	10	(100)	10	(100)	10	(100)
Degeneration, Tubular		10	(100)	10	(100)	10	(100)	10	(100)
Hyaline Casts		0	(0)	0	(0)	1	(10)	0	(0)
URINARY BLADDER	# Ex	10		10		0		0	
Urolith, NOS		1	(10)	0	(0)	0		0	
Hyperplasia, Epithelial		1	(10)	0	(0)	0		0	
PROSTATE	# Ex	10		10		0		0	
Inflammation, Acute		1	(10)	0	(0)	0		0	
Inflammation, Subacute		0	(0)	1	(10)	0		0	
STOMACH	# Ex	10		10		0		0	
DUODENUM	# Ex	10		10		0		0	
ILEUM	# Ex	10		10		0		0	
CECUM	# Ex	10		10		0		0	
RECTUM	# Ex	10		10		0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Project Summary Table
SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 92-003 | DATES: ALL | PAGE 8
DAYS : ALL | SEX: MALE

GROUP:		0		0		0		0		5		6		7		8	
NUMBER OF ANIMALS:		10		10		10		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
MESENTERIC LYMPH NODE	# Ex	0		0		0		0		10		10		0		0	
TESTES	# Ex	0		0		0		0		10		10		10		10	
Degen., Seminiferous Tubule		0		0		0		0		0	(0)	10	(100)	8	(80)	0	(0)
EPIDIDYMIS	# Ex	0		0		0		0		10		10		0		0	
Hypospermia		0		0		0		0		0	(0)	10	(100)	0		0	
SEMINAL VESICLE	# Ex	0		0		0		0		10		10		0		0	
SKIN	# Ex	0		0		0		0		10		10		0		0	
MAMMARY GLAND	# Ex	0		0		0		0		9		10		0		0	
PREPUTIAL GLANDS	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic/Active		0		0		0		0		4	(40)	2	(20)	0		0	
Lymphocytic Infiltrates		0		0		0		0		3	(30)	5	(50)	0		0	
EYES	# Ex	0		0		0		0		10		10		0		0	
Microgranuloma, Cornea		0		0		0		0		6	(60)	5	(50)	0		0	
HARDERIAN GLAND	# Ex	0		0		0		0		10		10		0		0	
Lymphocytic Infiltrates		0		0		0		0		0	(0)	1	(10)	0		0	
FEMUR	# Ex	0		0		0		0		10		10		0		0	
Hyperplasia, Erythroid Cell		0		0		0		0		0	(0)	7	(70)	0		0	
NASAL CAVITY	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic/Active		0		0		0		0		1	(10)	0	(0)	0		0	
Fungus, NOS		0		0		0		0		1	(10)	0	(0)	0		0	
Squamous Metaplasia		0		0		0		0		1	(10)	0	(0)	0		0	

(End of Report)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: FEMALE

GROUP:	1	2	3	4				
NUMBER OF ANIMALS:	10	10	10	10	0	0	0	0

		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
BRAIN	# Ex	10		10		0		0		0		0		0	
SCIATIC NERVE	# Ex	10		10		0		0		0		0		0	
SPINAL CORD	# Ex	10		10		0		0		0		0		0	
SALIVARY GLAND	# Ex	10		10		0		0		0		0		0	
PANCREAS	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		0		1	0.10	0		0		0		0		0	
Degeneration, Acinar		0		1	0.10	0		0		0		0		0	
MANDIBULAR LYMPH NODE	# Ex	10		10		0		0		0		0		0	
ZYMBAL'S GLAND	# Ex	10		10		0		0		0		0		0	
PITUITARY	# Ex	10		10		0		0		0		0		0	
ADRENALS	# Ex	10		10		0		0		0		0		0	
THYROID	# Ex	10		10		0		0		0		0		0	
PARATHYROID	# Ex	10		9		0		0		0		0		0	
TRACHEA	# Ex	10		10		0		0		0		0		0	
ESOPHAGUS	# Ex	10		10		0		0		0		0		0	

(Report Continued)

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
THYMUS	# Ex	9		10		0		0		0		0		0	
Hemorrhage		1	0.22	0		0		0		0		0		0	
HEART	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		1	0.10	0		0		0		0		0		0	
COLON	# Ex	10		10		0		0		0		0		0	
JEJUNUM	# Ex	10		10		0		0		0		0		0	
AORTA	# Ex	10		10		0		0		0		0		0	
LIVER	# Ex	10		10		0		1		0		0		0	
Inflammation, Chronic		1	0.10	1	0.10	0		0		0		0		0	
Congestion		1	0.20	0		0		0		0		0		0	
SPLEEN	# Ex	10		10		10		10		0		0		0	
Pigment, NOS		0		10	2.10	10	2.10	2	0.20	0		0		0	
Hyperplasia, Erythroid Cell		0		10	2.20	9	1.80	2	0.30	0		0		0	
Fibrosis		0		0		1	0.10	0		0		0		0	
TONGUE	# Ex	10		10		0		0		0		0		0	
SKELETAL MUSCLE	# Ex	10		10		0		0		0		0		0	
LUNG	# Ex	10		10		0		0		0		0		0	
Inflammation, Chronic		3	0.40	1	0.10	0		0		0		0		0	
KIDNEYS	# Ex	10		10		0		0		0		0		0	
Mineralization, NOS		6	0.60	4	0.50	0		0		0		0		0	

(Report Continued)

Severity Summary Table

PROJECT ID. NO: 92-003 DAYS: ALL
RATES: ALL SEX: FEMALE

GROUP:		1		2		3		4		0		0		0	
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
Lymphocytic Infiltrates		1	0.10	0		0		0		0		0		0	
Pigment, NOS		3		10	2.30	0		0		0		0		0	
URINARY BLADDER	# Ex	10		10		0		0		0		0		0	
STOMACH	# Ex	10		10		0		0		0		0		0	
DUODENUM	# Ex	10		10		0		0		0		0		0	
ILEUM	# Ex	10		10		0		0		0		0		0	
CECUM	# Ex	10		10		0		0		0		0		0	
RECTUM	# Ex	10		10		0		0		0		0		0	
MESENTERIC LYMPH NODE	# Ex	10		10		0		0		0		0		0	
OVARIES	# Ex	10		10		0		0		0		0		0	
UTERUS	# Ex	10		10		0		0		0		0		0	
Dilatation		1	0.20	1	0.30	0		0		0		0		0	
SKIN	# Ex	10		10		0		0		0		0		0	
MAMMARY GLAND	# Ex	9		10		0		0		0		0		0	
CLITORAL GLANDS	# Ex	10		10		0		0		0		0		0	
Lymphocytic Infiltrates		3	0.30	7	0.80	0		0		0		0		0	

(Report Continued)

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: FEMALE

GROUP:		1		2		3		4							
NUMBER OF ANIMALS:		10		10		10		10		0		0		0	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
Inflammation, Acute		1	0.20	0		0		0		0		0		0	
Dilatation, Ductal		0		1	0.20	0		0		0		0		0	
EYES	# Ex	10		10		0		0		0		0		0	
Microgranuloma, Cornea		3	0.40	3	0.40	0		0		0		0		0	
HARDERIAN GLAND	# Ex	10		10		0		0		0		0		0	
Lymphocytic Infiltrates		4	0.70	8	1.60	0		0		0		0		0	
Inflammation, Chronic/Active		0		2	0.40	0		0		0		0		0	
Inflammation, Chronic		0		1	0.20	0		0		0		0		0	
FEMUR	# Ex	10		10		0		0		0		0		0	
Pigment, NOS		0		4	0.50	0		0		0		0		0	
Hyperplasia, Erythroid Cell		0		9	1.10	0		0		0		0		0	
NASAL CAVITY	# Ex	10		10		0		0		0		0		0	

* Severity calculated by the number of tissues examined.

(Report Continued)

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: MALE

GROUP: NUMBER OF ANIMALS:		0		0		0		0		5 10		6 10		7 10		8 10	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
BRAIN	# Ex	0		0		0		0		10		10		0		0	
SCIATIC NERVE	# Ex	0		0		0		0		10		10		0		0	
SPINAL CORD	# Ex	0		0		0		0		10		10		0		0	
SALIVARY GLAND	# Ex	0		0		0		0		10		10		0		0	
PANCREAS	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic		0		0		0		0		1	0.10	1	0.20	0		0	
Degeneration, Acinar		0		0		0		0		1	0.10	1	0.20	0		0	
MANDIBULAR LYMPH NODE	# Ex	0		0		0		0		10		10		0		0	
Hyperplasia, Plasma Cell		0		0		0		0		1	0.20	1	0.20	0		0	
ZYMBAL'S GLAND	# Ex	0		0		0		0		8		10		0		0	
PITUITARY	# Ex	0		0		0		0		10		10		0		0	
ADRENALS	# Ex	0		0		0		0		10		10		0		0	
THYROID	# Ex	0		0		0		0		10		10		0		0	
PARATHYROID	# Ex	0		0		0		0		10		9		0		0	
TRACHEA	# Ex	0		0		0		0		10		10		0		0	
ESOPHAGUS	# Ex	0		0		0		0		10		10		0		0	

(Report Continued)

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: MALE

GROUP:		1		2		3		4		5		6		7		8	
NUMBER OF ANIMALS:		10		10		10		10		10		10		10		10	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
THYMUS	# Ex	0		0		0		0		10		10		0		0	
Hemorrhage		0		0		0		0		2	0.40	1	0.20	0		0	
HEART	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic		0		0		0		0		6	0.70	1	0.10	0		0	
Inflammation, Subacute Artery		0		0		0		0		0		1	0.10	0		0	
Degeneration, Myocardial		0		0		0		0		2	0.20	1	0.10	0		0	
COLON	# Ex	0		0		0		0		10		10		0		0	
JEJUNUM	# Ex	0		0		0		0		10		10		0		0	
AORTA	# Ex	0		0		0		0		10		10		0		0	
LIVER	# Ex	0		0		0		0		10		10		1		0	
Bile Duct Hyperplasia		0		0		0		0		1	0.10	0		0		0	
Inflammation, Chronic		0		0		0		0		1	0.10	1	0.10	0		0	
Inflammation, Subacute		0		0		0		0		1	0.10	2	0.20	0		0	
Necrosis, Hepatocellular		0		0		0		0		1	0.20	3	0.30	1	2.00	0	
SPLEEN	# Ex	0		0		0		0		10		10		10		10	
Pigment, NOS		0		0		0		0		0		10	1.80	6	0.80	0	
Hyperplasia, Erythroid Cell		0		0		0		0		0		10	2.10	10	1.90	1	0.1
Fibrosis		0		0		0		0		1	0.20	1	0.10	0		0	
TONGUE	# Ex	0		0		0		0		10		10		0		0	
SKELETAL MUSCLE	# Ex	0		0		0		0		10		10		0		0	
LUNG	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic		0		0		0		0		2	0.20	1	0.10	0		0	

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Severity Summary Table

PROJECT ID. NO: 92-003 DAYS: ALL
FATES: ALL SEX: MALE

GROUP: NUMBER OF ANIMALS:		1 0	2 0	3 0	4 0	5 10	6 10	7 10	8 10
Inflammation, Chronic/Active	#	0	0	0	0	1	0	0	0
	SEV					0.10			
Alveolar/Bronchial Hyperplasia	#	0	0	0	0	0	1	0	0
	SEV						0.20		
KIDNEYS	# Ex	0	0	0	0	10	10	10	10
Mineralization, NOS		0	0	0	0	10	10	10	9
	SEV					1.40	1.90	1.80	1.20
Lymphocytic Infiltrates		0	0	0	0	0	0	0	1
	SEV								0.20
Pigment, NOS		0	0	0	0	0	10	10	0
	SEV						2.00	1.20	
Regeneration, Tubular		0	0	0	0	10	10	10	10
	SEV					1.20	1.70	1.80	1.20
Hyaline Droplets		0	0	0	0	0	10	10	10
	SEV						2.90	2.60	2.20
Degeneration, Tubular		0	0	0	0	10	10	10	10
	SEV					1.50	2.60	2.10	1.60
Hyaline Casts		0	0	0	0	0	0	1	0
	SEV							0.20	
URINARY BLADDER	# Ex	0	0	0	0	10	10	0	0
Hyperplasia, Epithelial		0	0	0	0	1	0	0	0
	SEV					0.20			
PROSTATE	# Ex	0	0	0	0	10	10	0	0
Inflammation, Acute		0	0	0	0	1	0	0	0
	SEV					0.20			
Inflammation, Subacute		0	0	0	0	0	1	0	0
	SEV						0.20		
STOMACH	# Ex	0	0	0	0	10	10	0	0
DUODENUM	# Ex	0	0	0	0	10	10	0	0
ILEUM	# Ex	0	0	0	0	10	10	0	0
CECUM	# Ex	0	0	0	0	10	10	0	0
RECTUM	# Ex	0	0	0	0	10	10	0	0
MESENTERIC LYMPH NODE	# Ex	0	0	0	0	10	10	0	0

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Severity Summary Table

PROJECT ID. NO: 92-003 FATES: ALL
DAYS: ALL SEX: MALE

GROUP:		1		2		3		4		5		6		7		8	
NUMBER OF ANIMALS:		0		0		0		0		10		10		10		10	
		#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
TESTES	# Ex	0		0		0		0		10		10		10		10	
Degen., Seminiferous Tubule		0		0		0		0		0		10	4.00	8	2.60	0	
EPIDIDYMIS	# Ex	0		0		0		0		10		10		0		0	
Hypospermia		0		0		0		0		0		10	4.00	0		0	
SEMINAL VESICLES	# Ex	0		0		0		0		10		10		0		0	
SKIN	# Ex	0		0		0		0		10		10		0		0	
MAMMARY GLAND	# Ex	0		0		0		0		9		10		0		0	
PREPUTIAL GLANDS	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic/Active		0		0		0		0		4	0.80	2	0.50	0		0	
Lymphocytic Infiltrates		0		0		0		0		3	0.30	5	0.60	0		0	
EYES	# Ex	0		0		0		0		10		10		0		0	
Microgranuloma, Cornea		0		0		0		0		6	0.90	5	0.60	0		0	
HARDERIAN GLAND	# Ex	0		0		0		0		10		10		0		0	
Lymphocytic Infiltrates		0		0		0		0		0		1	0.10	0		0	
FEMUR	# Ex	0		0		0		0		10		10		0		0	
Hyperplasia, Erythroid Cell		0		0		0		0		0		7	1.00	0		0	
NASAL CAVITY	# Ex	0		0		0		0		10		10		0		0	
Inflammation, Chronic/Active		0		0		0		0		1	0.30	0		0		0	
Squamous Metaplasia		0		0		0		0		1	0.10	0		0		0	

* Severity calculated by the number of tissues examined.

(End of Report)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	01	02	05	08	09	10	R01	R02	R03	R04
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N		N	N	N	N	N	N	N
Cyst, Squamous	-	-	P	-	-	-	-	-	-	-
PARATHYROID	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	01	02	05	08	09	10	R01	R02	R03	R04
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	U	N		N	N	N	N	N	N	N
Hemorrhage	-	-	2	-	-	-	-	-	-	-
HEART	N	N	N	N	N	N	N	N	N	
Inflammation, Chronic	-	-	-	-	-	-	-	-	-	1
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N		N	N	N	N		N	N
Inflammation, Chronic	-	-	-	-	-	-	-	1	-	-
Congestion	-	-	2	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE
DAYS: ALL RATES: ALL

ANIMAL ID:	01	02	05	08	09	10	R01	R02	R03	R04
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNG	N		N	N			N	N	N	N
Inflammation, Chronic	-	2	-	-	1	3	-	-	-	-
KIDNEYS		N		N	N				N	
Mineralization, NOS	1	-	1	-	-	1	1	1	-	1
Lymphocytic Infiltrates	-	-	-	-	-	-	-	1	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N		N	N	N	N	N
Foreign Body, Glandular	-	-	-	-	P	-	-	-	-	-
DUODENUM		N	N	N	N	N	N	N	N	N
Ectopic Pancreas	P	-	-	-	-	-	-	-	-	-
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	01	02	05	08	09	10	R01	R02	R03	R04
OVARIES	N	N	N	N	N	N	N	N	N	N
UTERUS	N		N	N	N	N	N	N	N	N
Dilatation	-	2	-	-	-	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	U	N	N	N	N	N
CLITORAL GLANDS		N		N			N	N	N	N
Lymphocytic Infiltrates	1	-	-	-	1	1	-	-	-	-
Inflammation, Acute	-	-	2	-	-	-	-	-	-	-
EYES			N	N	N		N	N	N	N
Microgranuloma, Cornea	1	1	-	-	-	2	-	-	-	-
HARDERIAN GLAND	N		N	N		N	N		N	
Lymphocytic Infiltrates	-	1	-	-	1	-	-	3	-	2
FEMUR	N	N	N	N	N	N	N	N	N	N
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	11	12	13	14	15	16	17	18	19	20
BRAIN	M	M	M	M	M	M	M	M	M	M
SCIATIC NERVE	M	M	M	M	M	M	M	M	M	M
SPINAL CORD	M	M	M	M	M	M	M	M	M	M
SALIVARY GLAND	M	M	M	M	M	M	M	M	M	M
PANCREAS		M	M	M	M	M	M	M	M	M
Inflammation, Chronic	1	-	-	-	-	-	-	-	-	-
Degeneration, Acinar	1	-	-	-	-	-	-	-	-	-
MANDIBULAR LYMPH NODE	M	M	M	M	M	M	M	M	M	M
ZYMBAL'S GLAND	M	M	M	M	M	M	M	M	M	M
PITUITARY	M	M	M	M	M	M	M	M	M	M
ADRENALS	M	M	M	M	M	M	M	M	M	M
THYROID	M	M	M	M	M	M	M	M	M	M
PARATHYROID	U	M	M	M	M	M	M	M	M	M

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	11	12	13	14	15	16	17	18	19	20
TRACHEA	M	M	M	M	M	M	M	M	M	M
ESOPHAGUS	M	M	M	M	M	M	M	M	M	M
THYMUS	M	M	M	M	M	M	M	M	M	M
HEART	M	M	M	M	M	M	M	M	M	M
COLON	M	M	M	M	M	M	M	M	M	M
JEJUNUM	M	M	M	M	M	M	M	M	M	M
AORTA	M	M	M	M	M	M	M	M	M	M
LIVER	M	M		M	M	M	M	M	M	M
Inflammation, Chronic	-	-	1	-	-	-	-	-	-	-
SPLEEN										
Pigment, NOS	2	2	2	2	2	2	2	3	2	2
Hyperplasia, Erythroid Cell	3	2	2	1	2	3	2	3	2	2
TONGUE	M	M	M	M	M	M	M	M	M	M
SKELETAL MUSCLE	M	M	M	M	M	M	M	M	M	M

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	11	12	13	14	15	16	17	18	19	20
LUNG	M	M		M	M	M	M	M	M	M
Inflammation, Chronic	-	-	1	-	-	-	-	-	-	-
KIDNEYS										
Mineralization, NOS	2	-	-	-	-	1	1	-	1	-
Pigment, NOS	3	2	2	2	2	3	2	3	2	2
URINARY BLADDER	M	M	M	M	M	M	M	M	M	M
STOMACH	M	M	M	M	M	M	M	M	M	M
DUODENUM	M	M	M	M	M	M	M	M	M	M
ILEUM	M	M	M	M	M	M	M	M	M	M
CECUM	M	M	M	M	M	M	M	M	M	M
RECTUM	M	M	M	M	M	M	M	M	M	M
MESENTERIC LYMPH NODE	M	M	M	M	M	M	M	M	M	M
OVARIES	M	M	M	M	M	M	M	M	M	M

(Report Continued)

Tabulated Animal Data

ANIMAL ID:	11	12	13	14	15	16	17	18	19	20
UTERUS	N	N	N	N	N	N	N		N	N
Dilatation	-	-	-	-	-	-	-	3	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
CLITORAL GLANDS		N		N				N		
Lymphocytic Infiltrates	1	-	1	-	1	2	1	-	1	1
Dilatation, Ductal	-	-	2	-	-	-	-	-	-	-
EYES	N	N			N	N	N		N	N
Microgranuloma, Cornea	-	-	1	1	-	-	-	2	-	-
HARDERIAN GLAND				N						N
Lymphocytic Infiltrates	1	1	2	-	2	3	2	3	2	-
Inflammation, Chronic/Active	-	-	-	-	-	2	-	2	-	-
Inflammation, Chronic	-	-	-	-	-	-	-	-	2	-
FEMUR	N									
Pigment, NOS	-	2	-	1	-	1	-	1	-	-
Hyperplasia, Erythroid Cell	-	1	1	1	2	1	1	2	1	1
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-303 GROUP: 3 SEX: FEMALE PAGE 9
DAYS: ALL FATES: ALL

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
BRAIN	•	•	•	•	•	•	•	•	•	•
SCIATIC NERVE	•	•	•	•	•	•	•	•	•	•
SPINAL CORD	•	•	•	•	•	•	•	•	•	•
SALIVARY GLAND	•	•	•	•	•	•	•	•	•	•
PANCREAS	•	•	•	•	•	•	•	•	•	•
MANDIBULAR LYMPH NODE	•	•	•	•	•	•	•	•	•	•
ZYMBAL'S GLAND	•	•	•	•	•	•	•	•	•	•
PITUITARY	•	•	•	•	•	•	•	•	•	•
ADRENALS	•	•	•	•	•	•	•	•	•	•
THYROID	•	•	•	•	•	•	•	•	•	•
PARATHYROID	•	•	•	•	•	•	•	•	•	•
TRACHEA	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 3 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
ESOPHAGUS	•	•	•	•	•	•	•	•	•	•
THYMUS	•	•	•	•	•	•	•	•	•	•
HEART	•	•	•	•	•	•	•	•	•	•
COLON	•	•	•	•	•	•	•	•	•	•
JEJUNUM	•	•	•	•	•	•	•	•	•	•
AORTA	•	•	•	•	•	•	•	•	•	•
LIVER	•	•	•	•	•	•	•	•	•	•
SPLEEN										
Pigment, NOS	2	2	2	2	3	2	2	2	2	2
Hyperplasia, Erythroid Cell	3	3	2	3	2	1	1	2	1	-
Fibrosis	-	-	-	-	-	-	1	-	-	-
TONGUE	•	•	•	•	•	•	•	•	•	•
SKELETAL MUSCLE	•	•	•	•	•	•	•	•	•	•
LUNG	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 3 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
KIDNEYS	•	•	•	•	•	•	•	•	•	•
URINARY BLADDER	•	•	•	•	•	•	•	•	•	•
STOMACH	•	•	•	•	•	•	•	•	•	•
DUODENUM	•	•	•	•	•	•	•	•	•	•
ILEUM	•	•	•	•	•	•	•	•	•	•
CECUM	•	•	•	•	•	•	•	•	•	•
RECTUM	•	•	•	•	•	•	•	•	•	•
MESENTERIC LYMPH NODE	•	•	•	•	•	•	•	•	•	•
OVARIES	•	•	•	•	•	•	•	•	•	•
UTERUS	•	•	•	•	•	•	•	•	•	•
SKIN	•	•	•	•	•	•	•	•	•	•
MAMMARY GLAND	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
CLITORAL GLANDS	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR	*	*	*	*	*	*	*	*	*	*
NASAL CAVITY	*	*	*	*	*	*	*	*	*	*

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	31	32	33	34	35	36	37	38	40	R05
BRAIN	•	•	•	•	•	•	•	•	•	•
SCIATIC NERVE	•	•	•	•	•	•	•	•	•	•
SPINAL CORD	•	•	•	•	•	•	•	•	•	•
SALIVARY GLAND	•	•	•	•	•	•	•	•	•	•
PANCREAS	•	•	•	•	•	•	•	•	•	•
MANDIBULAR LYMPH NODE	•	•	•	•	•	•	•	•	•	•
ZYMBAL'S GLAND	•	•	•	•	•	•	•	•	•	•
PITUITARY	•	•	•	•	•	•	•	•	•	•
ADRENALS	•	•	•	•	•	•	•	•	•	•
THYROID	•	•	•	•	•	•	•	•	•	•
PARATHYROID	•	•	•	•	•	•	•	•	•	•
TRACHEA	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

ANIMAL ID:	31	32	33	34	35	36	37	38	40	R05
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*		*	*	*	*	*	*	*	*
Hepatodiapragmatic Nodule	-	P	-	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N		N		N
Pigment, NOS	-	-	-	-	-	-	1	-	1	-
Hyperplasia, Erythroid Cell	-	-	-	-	-	-	2	-	1	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNG	*	*	*	*	*	*	*	*	*	*

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	31	32	33	34	35	36	37	38	40	R05
KIDNEYS	•	•	•	•	•	•	•	•	•	•
URINARY BLADDER	•	•	•	•	•	•	•	•	•	•
STOMACH	•	•	•	•	•	•	•	•	•	•
DUODENUM	•	•	•	•	•	•	•	•	•	•
ILEUM	•	•	•	•	•	•	•	•	•	•
CECUM	•	•	•	•	•	•	•	•	•	•
RECTUM	•	•	•	•	•	•	•	•	•	•
MESENTERIC LYMPH NODE	•	•	•	•	•	•	•	•	•	•
OVARIES	•	•	•	•	•	•	•	•	•	•
UTERUS	•	•	•	•	•	•	•	•	•	•
SKIN	•	•	•	•	•	•	•	•	•	•
MAMMARY GLAND	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID:	31	32	33	34	35	36	37	38	40	ROS
CLITORAL GLANDS	•	•	•	•	•	•	•	•	•	•
EYES	•	•	•	•	•	•	•	•	•	•
HARDERIAN GLAND	•	•	•	•	•	•	•	•	•	•
FEMUR	•	•	•	•	•	•	•	•	•	•
NASAL CAVITY	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 5 SEX: MALE PAGE 17
DAYS: ALL FATES: ALL

ANIMAL ID:	41	42	44	45	46	47	48	49	R06	R07
BRAIN	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N		N	N	N	N	N
Inflammation, Chronic	-	-	-	-	1	-	-	-	-	-
Degeneration, Acinar	-	-	-	-	1	-	-	-	-	-
MANDIBULAR LYMPH NODE	N	N	N		N	N	N	N	N	N
Hyperplasia, Plasma Cell	-	-	-	2	-	-	-	-	-	-
ZYMBAL'S GLAND	U	N	N	N	N	N	N	N	U	N
PITUITARY	N	N	N		N	N	N	N	N	N
Cyst, NOS, Pars Distalis	-	-	-	P	-	-	-	-	-	-
ADRENALS	N	N	N		N	N	N	N	N	N
Accesory Cortical Nodule	-	-	-	P	-	-	-	-	-	-
THYROID	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 5 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	41	42	44	45	46	47	48	49	R06	207
PARATHYROID	M	M	M	M	M	M	M	M	M	M
TRACHEA	M	M	M	M	M	M	M	M	M	M
ESOPHAGUS	M	M	M	M	M	M	M	M	M	M
THYMUS	M	M	M	M	M	M	M		M	
Hemorrhage	-	-	-	-	-	-	-	2	-	2
HEART	M	M			M			M		
Inflammation, Chronic	-	-	2	1	-	1	1	-	1	1
Degeneration, Myocardial	-	-	1	-	-	-	1	-	-	-
COLON	M	M	M	M	M	M	M	M	M	M
JEJUNUM	M	M	M	M	M	M	M	M	M	M
AORTA	M	M	M	M	M	M	M	M	M	M
LIVER	M	M	M		M		M	M	M	M
Bile Duct Hyperplasia	-	-	-	-	-	1	-	-	-	-
Inflammation, Chronic	-	-	-	1	-	-	-	-	-	-
Inflammation, Subacute	-	-	-	-	-	1	-	-	-	-
Necrosis, Hepatocellular	-	-	-	-	-	2	-	-	-	-

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 5 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	41	42	44	45	46	47	48	49	R06	R07
SPLEEN	M	M	M	M	M		M	M	M	M
Fibrosis	-	-	-	-	-	2	-	-	-	-
TONGUE	M	M	M	M	M	M	M	M	M	M
SKELETAL MUSCLE	M	M	M	M	M	M	M	M	M	M
LUNG	M		M	M	M	M		M	M	
Inflammation, Chronic	-	1	-	-	-	-	-	-	-	1
Inflammation, Chronic/Acute	-	-	-	-	-	-	1	-	-	-
KIDNEYS										
Mineralization, NOS	2	1	1	1	1	2	1	2	1	2
Regeneration, Tubular	1	1	1	1	1	1	1	2	1	2
Degeneration, Tubular	2	1	2	1	1	2	1	2	1	2
URINARY BLADDER	M	M	M	M	M		M	M	M	M
Urolith, NOS	-	-	-	-	-	2	-	-	-	-
Hyperplasia, Epithelial	-	-	-	-	-	2	-	-	-	-
PROSTATE	M	M	M	M	M	M	M	M		M
Inflammation, Acute	-	-	-	-	-	-	-	-	2	-
STOMACH	M	M	M	M	M	M	M	M	M	M
DUODENUM	M	M	M	M	M	M	M	M	M	M

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 5 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	41	42	44	45	46	47	48	49	R06	R07
ILEUM	M	M	M	M	M	M	M	M	M	M
CECUM	M	M	M	M	M	M	M	M	M	M
RECTUM	M	M	M	M	M	M	M	M	M	M
MESENTERIC LYMPH NODE	M	M	M	M	M	M	M	M	M	M
TESTES	M	M	M	M	M	M	M	M	M	M
EPIDIDYMIS	M	M	M	M	M	M	M	M	M	M
SEMINAL VESICLES	M	M	M	M	M	M	M	M	M	M
SKIN	M	M	M	M	M	M	M	M	M	M
MAMMARY GLAND	M	M	M	M	M	M	U	M	M	M
PREPUTIAL GLANDS					M		M	M		
Inflammation, Chronic/Active	3	2	-	2	-	-	-	-	1	-
Lymphocytic Infiltrates	-	-	1	-	-	1	-	-	-	1
EYES		M	M	M				M		
Microgranuloma, Cornea	2	-	-	-	1	1	1	-	2	2

(Report Continued)

Tabulated Animal Data

ANIMAL ID:	41	42	44	45	46	47	48	49	R06	R07
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M
FEMUR	M	M	M	M	M	M	M	M	M	M
NASAL CAVITY	M	M	M		M	M	M	M	M	M
Inflammation, Chronic/Active	-	-	-	3	-	-	-	-	-	-
Fungus, NOS	-	-	-	P	-	-	-	-	-	-
Squamous Metaplasia	-	-	-	1	-	-	-	-	-	-

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	51	52	53	55	56	58	59	60	R08	R09
BRAIN	M	M	M	M	M	M	M	M	M	M
SCIATIC NERVE	M	M	M	M	M	M	M	M	M	M
SPINAL CORD	M	M	M	M	M	M	M	M	M	M
SALIVARY GLAND	M	M	M	M	M	M	M	M	M	M
PANCREAS	M	M	M	M	M		M	M	M	M
Inflammation, Chronic	-	-	-	-	-	2	-	-	-	-
Degeneration, Acinar	-	-	-	-	-	2	-	-	-	-
MANDIBULAR LYMPH NODE		M	M	M	M	M	M	M	M	M
Hyperplasia, Plasma Cell	2	-	-	-	-	-	-	-	-	-
ZYMBAL'S GLAND	M	M	M	M	M	M	M	M	M	M
PITUITARY	M	M	M	M	M	M	M	M	M	M
ADRENALS	M	M	M	M	M	M	M	M	M	M
THYROID	M	M	M	M	M	M	M	M	M	M
PARATHYROID	M	M	M	M	U	M	U	M	M	M

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	51	52	53	55	56	58	59	60	R08	R09
TRACHEA	M	M	M	M	M	M	M	M	M	M
ESOPHAGUS	M	M	M	M	M	M	M	M	M	M
THYMUS		M	M	M	M	M	M	M	M	M
Hemorrhage	2	-	-	-	-	-	-	-	-	-
HEART		M	M	M	M	M		M	M	M
Inflammation, Chronic	-	-	-	-	-	-	1	-	-	-
Inflammation, Subacute Artery	1	-	-	-	-	-	-	-	-	-
Degeneration, Myocardial	1	-	-	-	-	-	-	-	-	-
COLON	M	M	M	M	M	M	M	M	M	M
JEJUNUM	M	M	M	M	M	M	M	M	M	M
AORTA	M	M	M	M	M	M	M	M	M	M
LIVER	M		M		M		M	M	M	M
Inflammation, Chronic	-	-	-	-	-	1	-	-	-	-
Inflammation, Subacute	-	1	-	1	-	-	-	-	-	-
Necrosis, Hepatocellular	-	1	-	1	-	1	-	-	-	-
SPLEEN										
Pigment, NOS	1	1	2	2	2	2	2	2	2	2
Hyperplasia, Erythroid Cell	2	2	2	2	2	2	2	3	2	2
Fibrosis	-	-	-	-	1	-	-	-	-	-

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	51	52	53	55	56	58	59	60	R08	R09
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNG	N	N	N		N	N	N		N	N
Inflammation, Chronic	-	-	-	1	-	-	-	-	-	-
Alveolar/Bronchial Hyperplasia	-	-	-	-	-	-	-	2	-	-
KIDNEYS										
Mineralization, NOS	2	2	2	2	2	2	2	1	2	2
Pigment, NOS	2	2	2	2	2	2	2	2	2	2
Regeneration, Tubular	2	1	2	2	2	2	1	1	2	2
Hyaline Droplets	3	3	2	3	3	3	3	3	3	3
Degeneration, Tubular	2	2	3	3	3	3	2	2	3	3
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
PROSTATE	N	N	N	N	N	N	N		N	N
Inflammation, Subacute	-	-	-	-	-	-	-	2	-	-
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	51	52	53	55	56	58	59	60	R08	R09
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N
TESTES										
Degen., Seminiferous Tubule	4	4	4	4	4	4	4	4	4	4
EPIDIDYMIS										
Hypospermia	4	4	4	4	4	4	4	4	4	4
SEMINAL VESICLES	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
PREPUTIAL GLANDS						N		N	N	
Inflammation, Chronic/Active	-	-	-	-	3	-	-	-	-	2
Lymphocytic Infiltrates	2	1	1	1	-	-	1	-	-	-
EYES	N				N	N	N		N	
Microgranuloma, Cornea	-	1	2	1	-	-	-	1	-	1

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	51	52	53	55	56	58	59	60	R08	R09
HARDERIAN GLAND	N	N	N	N	N	N	N	N		N
Lymphocytic Infiltrates	-	-	-	-	-	-	-	-	1	-
FEMUR		N			N		N			
Hyperplasia, Erythroid Cell	2	-	1	1	-	2	-	1	1	2
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 7 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	62	63	64	65	66	67	68	69	70	R10
BRAIN	•	•	•	•	•	•	•	•	•	•
SCIATIC NERVE	•	•	•	•	•	•	•	•	•	•
SPINAL CORD	•	•	•	•	•	•	•	•	•	•
SALIVARY GLAND	•	•	•	•	•	•	•	•	•	•
PANCREAS	•	•	•	•	•	•	•	•	•	•
MANDIBULAR LYMPH NODE	•	•	•	•	•	•	•	•	•	•
ZYMBAL'S GLAND	•	•	•	•	•	•	•	•	•	•
PITUITARY	•	•	•	•	•	•	•	•	•	•
ADRENALS	•	•	•	•	•	•	•	•	•	•
THYROID	•	•	•	•	•	•	•	•	•	•
PARATHYROID	•	•	•	•	•	•	•	•	•	•
TRACHEA	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 7 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	62	63	64	65	56	67	68	69	70	R10
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*
LIVER	*	*	*	*	*	*	*	*		*
Necrosis, Hepatocellular	-	-	-	-	-	-	-	-	2	-
SPLEEN										
Pigment, NOS	-	-	1	-	2	1	2	1	1	-
Hyperplasia, Erythroid Cell	2	2	2	2	2	2	2	1	2	2
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNG	*	*	*	*	*	*	*	*	*	*

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 7 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	62	63	64	65	66	67	68	69	70	R10
KIDNEYS										
Mineralization, NOS	2	2	2	2	2	2	2	1	1	2
Pigment, NOS	1	1	1	2	1	2	1	1	1	1
Regeneration, Tubular	2	2	2	1	2	2	2	2	1	2
Hyaline Droplets	3	2	3	2	3	3	2	2	3	3
Degeneration, Tubular	2	2	2	2	2	2	2	2	2	3
Hyaline Casts	-	-	-	-	-	2	-	-	-	-
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
PROSTATE	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 7 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	62	63	64	65	66	67	68	69	70	R10
TESTES		M								M
Degen., Seminiferous Tubule	4	-	3	3	3	3	4	3	3	-
EPIDIDYMIS	•	•	•	•	•	•	•	•	•	•
SEMINAL VESICLES	•	•	•	•	•	•	•	•	•	•
SKIN	•	•	•	•	•	•	•	•	•	•
MAMMARY GLAND	•	•	•	•	•	•	•	•	•	•
PREPUTIAL GLANDS	•	•	•	•	•	•	•	•	•	•
EYES	•	•	•	•	•	•	•	•	•	•
HARDERIAN GLAND	•	•	•	•	•	•	•	•	•	•
FEMUR	•	•	•	•	•	•	•	•	•	•
NASAL CAVITY	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 8 SEX: MALE PAGE 31
DAYS: ALL FATES: ALL

ANIMAL ID:	71	72	73	74	75	76	77	78	80	R11
BRAIN	•	•	•	•	•	•	•	•	•	•
SCIATIC NERVE	•	•	•	•	•	•	•	•	•	•
SPINAL CORD	•	•	•	•	•	•	•	•	•	•
SALIVARY GLAND	•	•	•	•	•	•	•	•	•	•
PANCREAS	•	•	•	•	•	•	•	•	•	•
MANDIBULAR LYMPH NODE	•	•	•	•	•	•	•	•	•	•
ZYMBAL'S GLAND	•	•	•	•	•	•	•	•	•	•
PITUITARY	•	•	•	•	•	•	•	•	•	•
ADRENALS	•	•	•	•	•	•	•	•	•	•
THYROID	•	•	•	•	•	•	•	•	•	•
PARATHYROID	•	•	•	•	•	•	•	•	•	•
TRACHEA	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 8 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	71	72	73	74	75	76	77	78	80	R11
ESOPHAGUS	•	•	•	•	•	•	•	•	•	•
THYMUS	•	•	•	•	•	•	•	•	•	•
HEART	•	•	•	•	•	•	•	•	•	•
COLON	•	•	•	•	•	•	•	•	•	•
JEJUNUM	•	•	•	•	•	•	•	•	•	•
AORTA	•	•	•	•	•	•	•	•	•	•
LIVER	•	•	•	•	•	•	•	•	•	•
SPLEEN	M	M	M	M	M	M	M	M	M	
Hyperplasia, Erythroid Cell	-	-	-	-	-	-	-	-	-	1
TONGUE	•	•	•	•	•	•	•	•	•	•
SKELETAL MUSCLE	•	•	•	•	•	•	•	•	•	•
LUNG	•	•	•	•	•	•	•	•	•	•

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 0 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	71	72	73	74	75	76	77	78	80	R11
KIDNEYS										
Mineralization, NOS	1	-	1	2	2	1	1	1	1	2
Lymphocytic Infiltrates	-	2	-	-	-	-	-	-	-	-
Regeneration, Tubular	1	1	1	2	1	1	1	1	1	2
Hyaline Droplets	2	2	2	2	2	2	2	2	2	2
Degeneration, Tubular	1	1	2	2	2	1	1	2	2	2
URINARY BLADDER	•	•	•	•	•	•	•	•	•	•
PROSTATE	•	•	•	•	•	•	•	•	•	•
STOMACH	•	•	•	•	•	•	•	•	•	•
DUODENUM	•	•	•	•	•	•	•	•	•	•
ILEUM	•	•	•	•	•	•	•	•	•	•
CECUM	•	•	•	•	•	•	•	•	•	•
RECTUM	•	•	•	•	•	•	•	•	•	•
MESENTERIC LYMPH NODE	•	•	•	•	•	•	•	•	•	•
TESTES	M	M	M	M	M	M	M	M	M	M

(Report Continued)

Tabulated Animal Data

PROJECT ID: 92-003 GROUP: 8 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID:	71	72	73	74	75	76	77	78	80	R11
EPIDIDYMIS	•	•	•	•	•	•	•	•	•	•
SEMINAL VESICLES	•	•	•	•	•	•	•	•	•	•
SKIN	•	•	•	•	•	•	•	•	•	•
MAMMARY GLAND	•	•	•	•	•	•	•	•	•	•
PREPUTIAL GLANDS	•	•	•	•	•	•	•	•	•	•
EYES	•	•	•	•	•	•	•	•	•	•
HARDERIAN GLAND	•	•	•	•	•	•	•	•	•	•
FEMUR	•	•	•	•	•	•	•	•	•	•
NASAL CAVITY	•	•	•	•	•	•	•	•	•	•

(End of Report)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE PAGE 1
DAYS: ALL FATES: ALL

ANIMAL ID: 01 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 02 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 05 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Thymus - Discolored (>5), Red Areas	THYMUS- Hemorrhage, Multifocal
>Liver - All Lobes, Mottled, Moderate, Dark Red and Brown	LIVER- Congestion

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(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE PAGE 2
DAYS: ALL FATES: ALL

ANIMAL ID: 08 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 09 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 10 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R01 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 1 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID: R02 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R03 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R04 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE PAGE 4
DAYS: ALL FATES: ALL

ANIMAL ID: 11 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 12 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 13 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 14 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE PAGE 5
DAYS: ALL FATES: ALL

ANIMAL ID: 15 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 16 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 17 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 18 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 2 SEX: FEMALE PAGE 6
DAYS: ALL FATES: ALL

ANIMAL ID: 19 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 20 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 3 SEX: FEMALE
DAYS: ALL FATES: ALL

ANIMAL ID: 21 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 22 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 23 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 24 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 3 SEX: FEMALE PAGE 8
DAYS: ALL FATES: ALL

ANIMAL ID: 25 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 26 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 27 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 28 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 3 SEX: FEMALE PAGE 9
DAYS: ALL FATES: ALL

ANIMAL ID: 29 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 30 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE PAGE 10
DAYS: ALL FATES: ALL

ANIMAL ID: 31 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 32 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>Liver - Median Lobe, Nodule, 7x5x5mm, (1), Oval, Red — LIVER- Hepatodiapragmatic Nodule

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ANIMAL ID: 33 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 34 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE PAGE 11
DAYS: ALL FATES: ALL

ANIMAL ID: 35 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 36 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 37 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 38 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 4 SEX: FEMALE PAGE 12
DAYS: ALL FATES: ALL

ANIMAL ID: 40 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R05 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifica
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 5 SEX: MALE PAGE 13
DAYS: ALL FATES: ALL

ANIMAL ID: 41 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 42 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 44 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 45 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 5 SEX: MALE PAGE 14
DAYS: ALL FATES: ALL

ANIMAL ID: 46 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 47 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 48 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 49 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>Thymus - Foci, <1mm, (>5), Round, Red — THYMUS- Hemorrhage, Multifocal

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 5 SEX: MALE PAGE 15
DAYS: ALL FATES: ALL

ANIMAL ID: R06 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R07 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Thymus - Discolored, Foci, <1mm, (>5), Red	THYMUS- Hemorrhage, Multifocal

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(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 6 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID: 51 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 14x9x9mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 52 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 15x9x9mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 53 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 17x8x7mm and 20x10x7mm	TESTES- Degen., Seminiferous Tubule

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 6 SEX: MALE PAGE 17
DAYS: ALL FATES: ALL

ANIMAL ID: 55 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, Right - 20x10x5mm, Left - 19x10x7mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 56 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Spleen - Enlarged, 30x8x3mm, Moderate	SPLEEN- Pigment, NOS, SPLEEN- Hyperplasia, Erythroid Cell, SPLEEN- Fibrosis, Multifocal
>Testes - Decreased in Size, 14x10x10mm	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 58 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Spleen - Enlarged, 39x10x4mm, (1)	SPLEEN- Pigment, NOS, SPLEEN- Hyperplasia, Erythroid Cell

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 6 SEX: MALE PAGE 18
DAYS: ALL FATES: ALL

ANIMAL ID: 58 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 19x17x5m, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 59 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 16x8x8mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 60 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 14x9x9mm	TESTES- Degen., Seminiferous Tubule

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 6 SEX: MALE PAGE 19
DAYS: ALL FATES: ALL

ANIMAL ID: R08 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 18x10x10mm, (?)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: R09 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 14x8x8mm, (2)	TESTES- Degen., Seminiferous Tubule
>Spleen - Enlarged, 37x9x6mm, (1)	SPLEEN- Pigment, NOS, SPLEEN- Hyperplasia, Erythroid Cell

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 7 SEX: MALE PAGE 20
DAYS: ALL FATES: ALL

ANIMAL ID: 62 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 16x8x8mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 63 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:

ANIMAL ID: 64 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 19x9x5mm, (2)	TESTES- Degen., Seminiferous Tubule

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 7 SEX: MALE PAGE 21
DAYS: ALL FATES: ALL

ANIMAL ID: 65 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 17x10x10mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 66 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 15x7x5mm and 17x10x7mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 67 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 17x10x10mm, (2)	TESTES- Degen., Seminiferous Tubule

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 7 SEX: MALE PAGE 22
DAYS: ALL FATES: ALL

ANIMAL ID: 68 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, Right - 20x10x5mm, Left - 20x10x5mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 69 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Bilateral, Decreased in Size, 17x12x7mm and 15x7x5mm, (2)	TESTES- Degen., Seminiferous Tubule

ANIMAL ID: 70 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>Testes - Decreased in Size, Moderate, 14x8x8mm	TESTES- Degen., Seminiferous Tubule
>Liver - Left Median Lobe, Foci, <1mm, Round, Red	LIVER- Necrosis, Hepatocellular

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 7 SEX: MALE PAGE 23
DAYS: ALL FATES: ALL

ANIMAL ID: R10 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 8 SEX: MALE PAGE 24
DAYS: ALL FATES: ALL

ANIMAL ID: 71 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 72 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 73 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 74 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 8 SEX: MALE
DAYS: ALL FATES: ALL

ANIMAL ID: 75 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 76 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 77 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 78 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(Report Continued)

Pathology Associates, Inc.
Study No. 92-003
Fischer 344 Rats
90-Day Study

Correlation of Gross & Micro Findings

PROJECT ID: 92-003 GROUP: 8 SEX: MALE PAGE 26
DAYS: ALL FATES: ALL

ANIMAL ID: 80 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: R11 PATHOLOGIST: GRO
ANIMAL FATE: Terminal Sacrifice
DAYS ON TEST:90

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

(End of Report)

APPENDIX I

CHEMICAL ANALYSES

Determination of Homogeneity

Target Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
		Week 1		
600	Top	635	612	3.74
	Middle	608		0.64
	Bottom	584		4.66
300	Top	308	323	4.71
	Middle	333		3.05
	Bottom	321		0.74
50.0	Top	50.6	46.6	8.56
	Middle	47.8		2.44
	Bottom	43.5		6.67
		Week 2		
800	Top	842	855	1.49
	Middle	850		0.51
	Bottom	865		1.25
400	Top	423	411	2.95
	Middle	412		0.24
	Bottom	398		3.18
66.7	Top	69.0	64.6	6.70
	Middle	59.3		8.32
	Bottom	65.7		1.63
		Week 3		
800	Top	812	823	1.41
	Middle	852		3.52
	Bottom	794		3.52
400	Top	415	427	2.78
	Middle	432		1.31
	Bottom	433		1.47
66.7	Top	67.2	68.0	1.19
	Middle	67.0		1.47
	Bottom	70.6		3.82

Determination of Homogeneity

Target Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
		Week 4		
800	Top	821	827	0.81
	Middle	836		1.07
	Bottom	823		0.53
400	Top	427	422	1.27
	Middle	427		1.35
	Bottom	411		2.62
66.7	Top	71.8	71.9	0.16
	Middle	74.4		3.45
	Bottom	70.7		1.67
		Week 5		
800	Top	832	826	0.71
	Middle	826		0.00
	Bottom	822		0.49
400	Top	369	406	9.06
	Middle	418		2.93
	Bottom	412		1.64
66.7	Top	63.7	66.0	3.56
	Middle	67.4		2.12
	Bottom	67.0		1.45
		Week 6		
800	Top	839	856	1.95
	Middle	851		0.58
	Bottom	877		2.53
400	Top	421	405	4.04
	Middle	400		1.21
	Bottom	393		2.83
66.7	Top	66.0	64.7	2.06
	Middle	62.9		2.69
	Bottom	65.1		0.63

Determination of Homogeneity

Target Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
		Week 7		
800	Top	820	832	1.40
	Middle	805		3.21
	Bottom	870		4.60
400	Top	399	394	1.38
	Middle	397		0.67
	Bottom	386		2.04
66.7	Top	72.4	71.5	1.29
	Middle	71.2		0.37
	Bottom	70.8		0.92
		Week 8		
800	Top	803	804	0.07
	Middle	807		0.38
	Bottom	801		0.31
400	Top	409	421	2.89
	Middle	422		0.22
	Bottom	432		2.67
66.7	Top	67.1	67.6	0.77
	Middle	69.0		1.95
	Bottom	66.9		1.17
		Week 9		
800	Top	805	787	2.24
	Middle	823		4.47
	Bottom	735		6.70
400	Top	363	367	0.99
	Middle	365		0.53
	Bottom	372		1.52
66.7	Top	69.2	69.6	0.55
	Middle	68.3		1.86
	Bottom	71.3		2.40

Determination of Homogeneity

Target Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
		Week 10		
800	Top	836	851	1.80
	Middle	874		2.68
	Bottom	844		0.88
400	Top	410	415	1.04
	Middle	417		0.59
	Bottom	416		0.45
66.7	Top	70.9	67.6	4.98
	Middle	67.3		0.36
	Bottom	64.5		4.63
		Week 11		
800	Top	790	777	1.75
	Middle	749		3.50
	Bottom	790		1.75
400	Top	382	407	6.37
	Middle	412		1.07
	Bottom	429		5.29
66.7	Top	64.3	67.7	5.01
	Middle	69.3		2.47
	Bottom	69.4		2.55
		Week 12		
800	Top	803	808	0.67
	Middle	827		2.32
	Bottom	795		1.65
400	Top	412	403	2.26
	Middle	407		1.16
	Bottom	389		3.42
66.7	Top	68.6	67.4	1.77
	Middle	66.3		1.57
	Bottom	67.3		0.21

Determination of Homogeneity

Target Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
		Week 13		
800	Top	802	839	4.44
	Middle	872		3.90
	Bottom	843		0.54
400	Top	447	425	5.27
	Middle	413		2.84
	Bottom	415		2.43
66.7	Top	68.6	67.9	1.00
	Middle	64.2		5.49
	Bottom	71.0		4.49

Stability Determination

Target Concentration (mg TNB/kg diet)	Observed Concentration (mg TNB/kg diet) 9-Nov-92	30-Dec-92	Percent of Original Conc.
800	823	814	98.9
400	427	426	99.8
66.7	68.0	62.9	92.5

APPENDIX J

45 DAY HEMATOLOGY AND CLINICAL CHEMISTRY DATA

Additional animals were needed following the 90 day study because sample size for hematology and clinical chemistries at 45 days was inadequate for proper analysis (except for methemoglobin). All study methodology was consistent with original study.

Group Number	Dose Groups mg TNB/kg diet	Sex	# of Animals
1	0	F	5
2	800	F	5
3	400	F	5
4	66.67	F	5
5	0	M	5
6	800	M	5
7	400	M	5
8	66.67	M	5

The actual levels of TNB (mg/kg b.w.) consumed per day were:

Group (females)		Group (males)	
1	0	5	0
2	61.6±2.7	6	59.3 ±2.95
3	29.5±1.1	7	28.4±1.0
4	5.1±0.2	8	4.9±0.2

Results from these analyses are present in Tables 9, 10, 13 and 14 and Appendices D and E.

Weeks 1-7

Target Diet Concentration (mg TNB/kg diet)	Site of Sampling	Concentration by Analysis (mg TNB/kg diet)	Mean Concentration (mg TNB/kg diet)	Deviation from Mean (%)
800	Top	849	816	4.11
	Middle	875		7.27
	Bottom	723		11.38
400	Top	378	387	2.24
	Middle	397		2.67
	Bottom	385		0.43
66.7	Top	61.9	62.5	0.97
	Middle	64.8		3.75
	Bottom	60.7		2.78

Weekly Food and Water Consumption
Group Means

Group	Sex	Diet Concentration (mg TNB/kg)	Food (g/wk) Week 1	Week 2	Week 3	Week 4
1	F	0	81.62 ± 1.89	88.16 ± 2.36	86.46 ± 0.91	80.46 ± 1.06
2	F	800	64.10 ± 0.67	71.00 ± 1.54	71.62 ± 1.49	70.60 ± 2.55
3	F	400	73.64 ± 0.55	74.96 ± 1.75	77.70 ± 1.81	72.18 ± 1.65
4	F	66.67	79.80 ± 1.60	84.82 ± 1.30	82.34 ± 1.62	78.04 ± 2.17
5	M	0	110.72 ± 3.75	119.20 ± 2.71	115.14 ± 1.17	105.68 ± 1.95
6	M	800	80.30 ± 2.90	99.08 ± 5.43	92.64 ± 1.81	92.26 ± 0.99
7	M	400	87.64 ± 1.73	98.56 ± 3.25	100.30 ± 4.60	94.58 ± 3.12
8	M	66.67	105.78 ± 3.23	112.70 ± 1.76	112.78 ± 2.40	102.12 ± 3.12

Group	Sex	Diet Concentration (mg TNB/kg)	Water (g/wk) Week 1	Week 2	Week 3	Week 4
1	F	0	117.28 ± 4.84	118.70 ± 3.68	124.58 ± 2.73	118.56 ± 4.27
2	F	800	109.44 ± 3.72	122.24 ± 6.60	130.70 ± 6.54	124.14 ± 7.68
3	F	400	117.12 ± 2.80	122.50 ± 4.14	131.62 ± 3.68	124.08 ± 5.05
4	F	66.67	118.08 ± 10.08	119.16 ± 6.76	125.86 ± 7.35	117.60 ± 8.38
5	M	0	147.02 ± 4.86	147.56 ± 2.54	144.40 ± 2.87	136.68 ± 2.08
6	M	800	117.48 ± 4.72	136.04 ± 3.41	136.56 ± 3.64	136.26 ± 2.73
7	M	400	119.54 ± 3.03	132.68 ± 5.13	137.66 ± 5.84	132.74 ± 4.50
8	M	66.67	135.00 ± 3.79	144.92 ± 5.92	149.36 ± 7.19	137.02 ± 5.84

* Mean ± Standard Error

Weekly Food and Water Consumption
Group Means

Group	Sex	Diet Concentration (mg TNB/kg)	Food (g/wk) Week 5	Week 6	Week 7
1	F	0	87.28 ± 1.41	87.64 ± 0.85	12.66 ± 0.[illegible]
2	F	800	71.90 ± 2.95	72.24 ± 3.07	12.12 ± 0.45
3	F	400	75.88 ± 1.55	76.44 ± 1.42	11.98 ± 0.27
4	F	66.67	80.70 ± 3.39	82.06 ± 3.28	13.04 ± 0.38
5	M	0	111.84 ± 3.37	115.70 ± 3.01	17.64 ± 0.80
6	M	800	92.28 ± 1.66	97.58 ± 3.77	15.46 ± 1.96
7	M	400	96.02 ± 2.48	99.08 ± 3.35	15.64 ± 0.62
8	M	66.67	107.24 ± 2.64	110.18 ± 2.03	17.22 ± 0.57

Group	Sex	Diet Concentration (mg TNB/kg)	Water (g/wk) Week 5	Week 6	Week 7
1	F	0	124.90 ± 4.07	127.32 ± 4.43	28.30 ± 1.78
2	F	800	131.16 ± 8.82	129.10 ± 9.29	29.82 ± 4.20
3	F	400	131.30 ± 3.97	126.60 ± 5.75	26.08 ± 1.29
4	F	66.67	124.30 ± 7.02	126.86 ± 8.08	29.20 ± 2.33
5	M	0	143.12 ± 2.69	144.10 ± 2.90	34.20 ± 1.28
6	M	800	137.34 ± 3.91	135.94 ± 4.22	31.46 ± 1.49
7	M	400	136.26 ± 3.44	138.10 ± 4.12	34.62 ± 2.57
8	M	66.67	145.08 ± 6.70	144.82 ± 5.28	40.58 ± 3.75

* Mean ± Standard Error, Week 7 - Food intake was one day and water intake was two days

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk)				Water (g/wk)			
		Week 1	Week 2	Week 3	Week 4	Week 1	Week 2	Week 3	Week 4
1	151	87.0	89.5	87.3	81.4	130.8	122.8	124.5	114.4
	152	78.1	86.2	85.6	81.7	121.0	129.8	134.3	127.0
	153	76.7	82.5	86.3	80.9	101.3	110.0	122.5	124.0
	154	82.5	86.1	89.3	82.0	119.5	119.6	124.1	123.7
	155	83.8	96.5	83.8	76.3	113.8	111.3	117.5	103.7
2	156	64.8	71.4	73.5	68.8	105.3	117.7	121.1	118.0
	157	65.4	75.5	75.0	79.5	117.0	137.4	145.2	139.0
	158	63.6	71.9	67.8	71.1	119.6	138.3	148.1	145.0
	159	61.7	65.9	68.3	69.8	101.0	106.9	118.7	114.2
	160	65.0	70.3	73.5	63.8	103.8	110.9	120.4	104.5
3	161	75.6	78.8	84.7	74.4	126.6	132.6	132.4	123.8
	162	73.6	70.9	74.2	69.4	116.1	112.2	129.8	118.9
	163	72.8	78.7	76.2	72.2	116.6	120.6	123.0	119.2
	164	73.8	71.0	77.0	67.9	109.0	115.5	127.9	115.0
	165	72.4	75.4	76.4	77.0	117.3	131.6	145.0	143.5
4	166	85.2	85.2	86.9	86.0	129.2	128.3	129.4	131.4
	167	80.8	84.7	84.2	77.2	152.3	141.4	149.7	143.7
	168	79.6	80.5	81.0	74.6	107.3	107.2	112.9	104.3
	169	77.6	88.7	77.2	73.8	104.4	108.2	129.3	104.9
	170	75.8	85.0	82.4	78.6	97.2	110.7	108.0	103.7

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk) Week 5	Week 6	Week 7	Water (g/wk) Week 5	Week 6	Week 7
1	151	89.1	89.2	12.5	127.5	138.6	31.6
	152	88.1	87.4	13.0	130.6	134.5	33.0
	153	89.0	86.3	12.0	130.0	126.8	26.4
	154	88.5	89.9	12.7	127.6	123.5	23.2
	155	81.7	85.4	13.1	108.8	113.2	27.3
2	156	76.4	74.5	12.3	132.5	125.7	28.6
	157	78.3	83.2	13.2	148.6	154.2	36.8
	158	66.8	68.7	12.0	146.7	144.4	41.7
	159	74.9	68.8	12.6	128.5	119.7	22.6
	160	63.1	66.0	10.5	99.5	101.5	19.4
3	161	76.7	79.4	12.9	127.7	131.0	27.8
	162	71.8	74.3	11.6	126.0	120.9	22.9
	163	74.6	73.3	11.9	128.6	114.7	23.7
	164	75.1	74.9	12.2	127.1	119.4	26.1
	165	81.2	80.3	11.3	147.1	147.0	29.9
4	166	92.6	93.3	14.3	140.3	138.4	34.3
	167	82.0	84.1	12.3	142.5	153.1	35.4
	168	77.7	81.7	12.3	111.0	114.9	24.9
	169	72.0	74.9	12.9	112.8	115.7	26.3
	170	79.2	76.3	13.4	114.9	112.2	25.1

Note: On week 7, the food intake was one day and the water intake was two days.

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 1	Week 2	Week 3	Week 4	Water (g/wk) Week 1	Week 2	Week 3	Week 4
5	176	117.8	126.9	119.3	105.2	152.8	150.1	144.6	137.2
	177	119.2	124.2	112.7	100.3	159.8	154.5	143 2	134.9
	178	98.3	112.9	114.0	102.8	132.8	144.4	137.6	132.9
	179	108.9	117.1	113.7	110.6	139.2	139.7	141.7	133.9
	180	109.4	114.9	116.0	109.5	150.5	149.1	154.9	144.5
6	181	89.4	120.5	96.4	95.7	129.8	145.3	139.6	136.5
	182	76.1	92.7	92.3	90.6	106.9	134.8	137.2	137.0
	183	72.7	93.3	85.9	91.6	108.5	124.3	124.2	128.0
	184	79.8	91.9	93.8	90.3	115.0	138.1	135.2	134.7
	185	83.5	97.0	94.8	93.1	127.2	137.7	146.6	145.1
7	186	81.6	98.7	99.1	87.9	116.5	130.7	137.8	124.9
	187	88.8	104.6	105.6	100.5	120.5	143.6	145.8	141.5
	188	90.7	103.3	111.6	101.9	127.8	142.1	145.1	141.3
	189	90.9	99.9	101.2	95.8	123.0	133.1	144.6	136.6
	190	86.2	86.3	84.0	86.8	109.9	113.9	115.0	119.4
8	191	100.2	112.8	110.9	108.5	132.8	142.5	145.3	138.5
	192	102.0	116.7	121.1	108.7	136.2	161.4	168.6	153.2
	193	112.7	115.4	113.4	103.7	148.8	151.8	158.5	136.6
	194	114.5	112.1	112.2	93.7	130.6	125.6	125.7	116.8
	195	99.5	106.5	106.3	96.0	126.6	143.3	148.7	140.0

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk) Week 5	Week 6	Week 7	Water (g/wk) Week 5	Week 6	Week 7
5	176	120.1	119.8	20.1	147.6	150.0	34.6
	177	101.7	103.8	16.3	135.6	143.4	36.0
	178	107.9	109.2	15.7	138.7	133.3	30.2
	179	118.2	124.3	18.7	143.6	147.2	37.5
	180	111.3	116.4	17.4	150.1	146.6	32.7
6	181	93.2	110.8	22.1	135.4	138.5	37.3
	182	88.4	92.3	11.8	125.9	132.1	28.8
	183	90.9	88.6	16.9	135.4	124.4	30.1
	184	90.7	98.3	15.2	140.0	134.6	30.6
	185	98.2	97.9	11.3	150.0	150.1	30.5
7	186	97.0	101.8	15.4	141.7	145.0	30.9
	187	98.7	104.0	15.6	143.8	143.0	32.6
	188	100.5	104.0	17.6	134.3	144.2	28.8
	189	97.5	99.5	15.9	137.3	135.1	43.0
	190	86.4	86.1	13.7	124.2	123.2	37.8
8	191	112.3	109.5	16.9	144.2	137.2	32.7
	192	113.5	113.9	18.7	161.8	159.1	35.5
	193	106.8	110.5	16.3	145.8	146.9	51.2
	194	104.6	114.1	18.2	121.3	129.2	35.5
	195	99.0	102.9	15.5	152.3	151.7	48.0

Note: On week 7, the food intake was one day and the water intake was two days.

APPENDIX K

PROTOCOL AND AMENDMENTS

PROTOCOL

90 Day Range Subchronic Toxicity Evaluation of

1,3,5-Trinitrobenzene (TNB) in F344 Rats

This study will be conducted in agreement with Good Laboratory Practice Standards, Environmental Protection Agency, Toxic Substances Control Act (TSCA) 40 CFR Part 792 (Federal Register, Vol 54, No. 158, August 17, 1989, pp. 34034 - 34050). All aspects of the studies will be conducted in accordance with written Standard Operating Procedures (SOP) of the performing unit and all raw data and performance documents will be maintained in agreement with GLP. An administratively separate quality assurance unit (QAU from PAI) will monitor the studies to assure adherence to good laboratory practices and the approved SOPs. Any deviation from the protocol or GLP will be noted in the raw data and reflected in the final report.

Testing Facility
A.W. Breidenbach Environmental Research Center
U.S. Environmental Protection Agency
Cincinnati, OH 45268

Prime Contractor (Sponsor)
U.S. Army Biomedical Research and
Development Laboratory, Fort Detrick
Frederick, Maryland 21701-5010

T. V. Reddy 10.20.92
Principle Investigator Date
T.V. Reddy, Ph.D.

G. Reddy 10-26-92
G. Reddy, Ph.D., Sponsor Date

D.R. Olson 10/20/92
Project Manager Date
G.R. Olson, DVM, Ph.D.
Pathology Associates, Inc.

10-22-92
Quality Assurance Date
W.F. Fox, MA
Pathology Associates, Inc.

TITLE: 90 Day Subchronic Toxicity Evaluation of 1,3,5-Trinitrobenzene (TNB), 1,3-Dinitrobenzene (DNB) and N-Methyl-N-2,4,6-Tetranitroaniline (Tetryl) in F344 Rats.

BACKGROUND:

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. The wastewaters discharged from trinitrotoluene (TNT) manufacturing processes contain a variety of aromatic compounds, including DNB and TNB. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, Burlinson (1980) suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct. It is also found in aquatic systems and surface soils as by-products of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of tetryl. A recent estimate of tetryl in wastewaters generated from the production of tetryl at the Joliet Army Ammunition Plant was about 36 lb/per day of each production line.

Toxicity data on these compounds are limited. The oral LD50 of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD50 of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation potentials, but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs. Some of the toxicological and behavioral effects of DNB are: formation of methemoglobin, testicular degeneration and reproductive failure, and weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is rather toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin. Fetal doses (amount and route of administration are not given) of tetryl produced toxic degeneration (necrosis) in the kidneys of dogs and rabbits and liver necrosis in dogs (not in rabbits). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Hardy and Maloof (1950) reported effects from accidental exposure of 11 people to tetryl: 2 died, 1 was disabled and 8 did not detect permanent disability. They also reported irreversible liver damage, dermatitis, and upper respiratory irritation following tetryl exposure. The effects of tetryl exposure include gastrointestinal symptoms and epidermal, respiratory, nervous system, hematopoietic and circulatory injury. Atmospheric concentration of 1.5 mg/m3 or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in Salmonella mutagenesis assay. TNB has been shown to form adducts of blood proteins and tissue DNA in rats.

PROTOCOL (Phase - 1)

1. Study.	90 day subchronic toxicity evaluation with 1,3,5-trinitrobenzene (TNB) in F344 male and female rats.
2. Purpose.	To evaluate subchronic toxicity of TNB when administered in the diet for 90 days. This route was chosen because of the poor solubility of TNB.
3. Study Location.	A.W. Breidenbach Environmental Research Center U.S. Environmental Protection Agency Cincinnati, OH 45268
4. Sponsor and Address.	U.S. Army Biomedical Research and Development Laboratory, Fort Detrick Frederick, Maryland 21701-5010
5. Principle Investigator.	T.V. Reddy, Ph.D., Research Chemist Environmental Monitoring Systems Laboratory U.S. Environmental Protection Agency Cincinnati, Ohio 45268
6. Co-Principle Investigator.	F. Bernard Daniel, Ph.D. Environmental Monitoring Systems Laboratory U.S. Environmental Protection Agency Cincinnati, Ohio 45268
7. Study Coordinator.	Barry Wiechman, MS., Pathology Associates (PAI)
8. Project Manager.	G. R. Olson, DVM, Ph.D., Pathology Associates (PAI)
9. Regulatory Compliance.	This study is carried out according to U.S. EPA Health Effects testing guidelines (40 CFR 798) in compliance with GLP (40 CFR 792).
10. Quality Assurance.	The protocol in life phase and final report will be audited by the Quality Assurance Office in accordance with SOP's at Pathology Associates, West Chester, Ohio 45069.
11. Test Material.	1,3,5-Trinitrobenzene (TNB) Powder (CAS #99-35-4) is supplied by U.S. Army Biomedical research and Development Laboratory, Ft. Detrick, Frederick, Maryland 21702.
12. Experimental Design.	

A. Selection of Dose: Toxikon Corporation, Woburn, MA 01801 has conducted acute toxicity studies on TNB. They administered TNB in corn oil to rats at a single oral (Bolus) dose and observed the clinical signs for 14 days, following dosing. Based on the results they have established 298 mg/kg BW, and 275 mg/kg BW, as the LD50 dose for male and female rats, respectively. For combined sexes the reported LD50 dose was 284 mg/kg body weight. Based on the above report, we calculated the following 5 concentrations tested in rats for the 14 day range finding study (120, 80, 40, 20, 5 mg/kg BW). Selection of doses for the 90 day subchronic toxicity study was determined from the 14 day range finding experiment and are as follows. The doses selected are 60, 30 and 5 mg/kg BW. Control rats are fed only powdered chow diet.

B. Preparation of the Diet: Certified powdered Purina laboratory chow will be purchased from Purina labs and stored at 4°C until use. There were no known contaminants in the certified diet that could affect the outcome of the study. TNB diets are prepared once a week. Just before the diet preparation, TNB is removed from the explosion proof storage shelves, weighed for the desired concentration in the carcinogen room and mixed in the hood with appropriate powdered diet. The three desired doses for the 90 day study were selected from the 14 day range finding study.

C. Animals: 50 male F344 rats weighing 150-160 gm. 50 female F344 rats weighing 120-130 gm will be purchased from Charles River Laboratories and held for 1 week quarantine. After evaluation of the serological data and soon after release from quarantine, 5 rats from each sex are sacrificed and used for quality controls or base line control animals to ensure the animals are healthy and within normal limits for all measurements at the time of arrival and after quarantine. The animals will be individually identified with electronic implants. Male and female rats, after quarantine, are also housed individually in clear polycarbonate shoe boxes with aspen bedding (San I Chips supplied by P.J. Murphy, Forest Products Corporation, NJ). Shoe boxes and bedding are changed along with food and water (2 times a week). Food and water will be given ad libitum. Water is provided with 16 ounce bottles and stoppers and sipper tubes. At all times the animal rooms are maintained on a 12 hour light/dark cycle at 22-23°C with relative humidity range 40-60%.

D. Randomization: Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed ± 2 S.D. of the mean weight, and the mean body weights for each group of each sex will not be statistically different.

E. Justification: Rats historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies.

F. Analysis of the Diet: The purity of TNB was determined by HPLC and found to be more than 99%. The homogeneity and stability of TNB in the diet will be determined by analyzing the TNB content (by HPLC) in the diet, soon after each weekly diet preparation.

G. Observation of Animals:

(1) Clinical Observations:	Twice daily - mortality and morbidity check. Once daily - cageside observation for obvious indications of a toxic effect; these effects will be recorded as they are observed. Data for mortality and morbidity checks and cageside observations will be recorded on the same form. Because these are cageside animal checks, the observations will not be as specific as, and may not necessarily duplicate, those observations recorded on body weight days when thorough physical examinations are conducted.
(2) Physical Examinations:	At each weighing interval. These observations will include, but not be limited to, changes in: skin and fur; eyes and mucous membranes; respiratory, circulatory, autonomic and central nervous systems; some motor activity and behavior.
(3) Body Weight:	Prior to treatment and weekly, thereafter.
(4) Food Consumption:	Weekly - twice.
(5) Water Consumption:	Weekly - twice.
(6) Ophthalmoscopic Examination:	Prior to the treatment and at termination by a board certified veterinarian.

H. Clinical Pathology:

(1) Frequency	At 45 days (blood drawn only from 5 rats/group) and at termination.
(2) Number of Animals	All animals (samples per SOP following pentobarbital anesthetic).

I. Tests:

(1) Hematology

leukocyte count
heinz bodies
erythrocyte count
hemoglobin
methemoglobin
reticulocyte count
hematocrit
platelet count
differential leukocyte count

(2) Blood Chemistry

glucose
sodium
potassium
total protein
albumin
calcium
total bilirubin
urea nitrogen
creatinine
aspartate aminotransferase
alanine aminotransferase
alkaline phosphatase

J. Termination:

(1) Unscheduled Sacrifices and Deaths

Necropsies, by trained personnel using procedures approved by board-certified pathologists, will be conducted on all moribund animals and on all animals that die.

(2) Sacrifice

After 90 days of treatment, all surviving animals will be weighed and then fasted for 12 hrs. The following morning all rats will be anesthetized with sodium pentobarbital, and exsanguinated. Necropsies will be conducted on each animal by trained personnel using procedures approved by board-certified pathologists. Animals will be sacrificed in random order to eliminate bias.

A pathologist will be readily available for consultation (further participation by a pathologist is available).

K. Postmortem Procedures:

(1) Gross Necropsy

The necropsy will include examination of :
The external surface
All orifices
Cranial cavity
Carcass
External surface of the brain (at necropsy); cut surfaces of the brain
The thoracic, abdominal and pelvic cavities and their viscera
The cervical tissues and organs

(2) Organ Weights

For each terminally sacrificed animal, the following organs (when present) will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

brain	lungs
liver	thymus
spleen	testes with epididymides/ovaries
kidneys	heart
adrenals	

(3) Tissue Preservation

The following tissues (when present) from each animal will be preserved in 10% neutral buffered formalin:

skin	ileum
mandibular and mesenteric lymph nodes	colon
	cecum
mammary glands	rectum
thigh muscle	liver
sciatic nerve	pancreas
sternum with marrow	spleen
femur with marrow	kidneys
larynx	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs and bronchi	prostate
heart and aorta	testes, including epididymis
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity and nasal turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord

L. Histopathology:

1. Following necropsy, a list of all gross lesions recorded will be submitted to the project officer at U.S. Army Biomedical Research and Development Laboratory for his evaluation and for any additional histopathology than those described below.

Histopathological evaluations are to be done on the following tissues from all male and 5 female rats that are maintained on high dose and all rats from control diet and animals that die during the study. The tissues examined under light microscope are as follows:

cerebrum	pancreas
cerebellum	cecum
trachea	colon
thyroid	rectum
parathyroid	stomach
esophagus	skeletal muscle
salivary gland	sciatic nerve
harderian gland	tongue
skin	heart
mammary gland	
aorta	nasal region
lung	sternum
thymus	femur
spleen	vertebrae
mesenteric lymph node	spinal cord
liver	adrenals
kidney	pituitary
urinary bladder	eye(s)
duodenum	jejunum
auditory sebaceous gland	
ileum	

MALE	FEMALE
accessory sex glands	uterus
epididymis	ovaries
testes	

An average of 12 slides will be prepared for each rat covering all the tissues shown above (3 or 4 tissues are fixed on each slide). A total of 240 slides from 20 rats (5 male and 5 female from high dose group and 5 rats each from control group) from the 90 day study (high dose to be determined from 14 day study) will be examined. Based on the results from high dose group tissues from other doses, groups will be examined as needed. Following completion of each study all wet tissues, paraffin blocks and slides will be stored in PAI archives.

M. Final Report:

Four months after the termination of the in-life phase of the study, a final report which includes the following information (as appropriate) will be prepared and submitted to the Sponsor:

(1) Experimental Design and Methods

(2) Results

mortality	organ weights and organ/body weight ratios
clinical observations	gross pathology
body weights	histopathology
food and liquid consumption	
clinical pathology tests	

Statistical Evaluation:

Stat view computer software will be used for statistical analysis in 14-day and 90-day study for statistical analysis.

Dunnet's t-test will be used for comparing treatment group.

Kruskal-Wallis rank sums will be used to examine the differences among the treatment groups and Wilcoxon rank sum test was used to analyze pairwise differences between the control and each dose group.

Amendment 1
for
United States Army Study 92-003
90 DAY SUBCHRONIC TOXICITY EVALUATION OF 1,3,5-TRINITROBENZENE (TNB) IN FISCHER (F344) RATS

For
United States Army
Biomedical Research and Development Laboratory
Fort Detrick
Frederick, MD 21701-5010

The purpose of Amendment 1 is: 1) provide study start and completion dates and 2) to include an additional study to collect blood samples for hemotology analysis for methemoglobin.

1. Page 8, Add the following: N. Study Schedule:

   Study Start Date: October 29, 1992
   Necropsy Date: January 27, 1993
   Study Completion Date: June 30, 1993

Reason: These dates were not included in the protocol originally.

2. Page 5, I. (1) - Add the following paragraph: An additional study will be conducted at the same dosage levels (under as similar conditions of the original 90-Day study as possible) for 45 days to collect blood samples for hematological and clinical chemistry analysis with the exception of methemoglobin. The analysis will be performed by PAI, Arkansas personnel.

Reason: The samples from the original study could not be properly analyzed because of inadequate sample size.

Amendment 1 Approval

U.S. Army Medical Research and
Development Laboratory
Fort Detrick
Frederick, Maryland 21701-5010

AW Breidenbach Environmental Research Ctr
US Environmental Protection Agency
Cincinnati, Ohio 45268

G. Reddy 4-20-93
G. Reddy, Ph.D., Sponsor Date

T.V. Reddy 4.16.93
T.V. Reddy, Ph.D., PI Date

4.8.93
Willa Fox, MA, QA Date

Deviations from GLP's and Protocol

1. The 45 day hematology and clinical chemistry data from additional animals was required since the blood samples from the original animals lacked adequate sample size.

2. The diet concentrations were adjusted after the first week of the study from 600, 300 and 50 mg/kg to 800, 400 and 66.67 mg/kg. This was necessary in order to better achieve the target doses.

3. Clinical observations were performed twice daily but recorded once daily.

Tirumuru V. Reddy, Ph.D.

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