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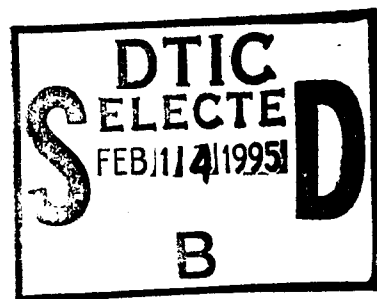
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in Fischer 344 Rats

PRINCIPAL INVESTIGATOR: Tirumuru V. Reddy, Ph.D.

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ORGANIZATION: Environmental Monitoring Systems Laboratory
U.S. Environmental Protection Agency
26 W. Martin Luther King Drive
Cincinnati, Ohio 45268-0001

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PREPARED FOR: U.S. Army Medical Research and Materiel Command,
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13. ABSTRACT (<i>Maximum 200 words</i>) Toxic effects of 1,3-Dinitrobenzene (1,3-DNB) in male and female F344 rats were evaluated by feeding powdered certified laboratory chow diet supplemented with varied concentrations of 1,3-DNB (0, 2.5, 10, 25, 75 and 150 mg/kg diet) for fourteen days. The average daily 1,3-DNB doses consumed were 0.21, 0.87, 2.02, 6.28 and 11.82 mg/kg b.w. for females and 0.21, 0.80, 1.98, 5.77 and 10.56 for males. Food consumption was significantly decreased in high dose animals of both sexes. Final body weights were not altered but relative organ weights were significantly changed in the 150 and 75 mg dose groups involving the spleen (males and females) and testes (males). Hematology and clinical chemistry studies indicated significantly increased values in both sexes relating to reticulocytes and methemoglobin in the 150 and 75 mg/kg dose groups while the red blood cell count, hemoglobin level and % hematocrit were decreased in these same groups. In addition, the levels of bilirubin, protein and albumin were increased in high dose males. Histopathological evaluations suggested that the susceptible organs for 1,3-DNB toxicity were kidneys (hyaline droplets), spleen (erythroid cell hyperplasia), brain (malacia and microgliosis), testes (seminiferous tubular degeneration). These changes were noted mainly in the 150 and 75 mg/kg dose groups except those changes involving the brain (150 mg/kg group only).			
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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.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management and Study Director</u>
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09-22-94	Draft Report	09-22-94
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 Willa Fox, MA
 Quality Assurance Unit
 PAI-Cin

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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 J. 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.

Tirumuru V. Reddy
Tirumuru V. Reddy, Ph.D.
U.S. Environmental Protection Agency

12/30/94
Date

Greg R. Olson
Greg R. Olson, D.V.M., Ph.D.
Pathology Associates, Inc.

12/30/94
Date

Joni A. Torsella
Joni A. Torsella, Ph.D.
U.S. Environmental Protection Agency

12/30/94
Date

Barry E. Wiechman
Barry E. Wiechman, B.S., M.S.
Pathology Associates, Inc.

12-29-94
Date

Study Personnel

Principal Investigator: Tirumuru V. Reddy, Ph.D.

Co-Principal Investigator: F. Bernard Daniel, Ph.D.

Biochemist: Barry E. Wiechman, B.S., M.S.

Pathologist: Greg R. Olson, D.V.M., Ph.D.

Biostatistician: Joni A. Torsella, Ph.D.

Study Biological Technician: Bradley Peterson, A.S.

Histology Laboratory Supervisor: Sheree Lovelace, A.S.

Contract Officer Representative: Gunda Reddy, Ph.D.

Study Timetable:

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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 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 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/m³ 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 DNB when administered in the diet for 14 days and to provide data to select doses for a 90 day subchronic study.

MATERIALS AND METHODS

Test Material Preparation

1,3-Dinitrobenzene powder (CAS #99-65-0) was prepared by Fluka Chemical Corp. (Ronkonkoma, New York). The purity (99.0%) was confirmed by the U.S. EPA, Cincinnati. Certified powdered Purina Laboratory Chow 5002 was purchased (Ralston-Purina Co., St. Louis, MO) and stored at 4°C until used. DNB diets were prepared weekly. First, .225 g of DNB was added to 25 g of powdered diet in a mortar and thoroughly ground with a pestle. Afterwards 1475 g of the diet was added and mixed for 60 minutes in a mechanical mixer (Kitchen Aid, St. Joseph, MI) for uniform distribution of DNB in the diet. This was verified by determining the DNB concentration in the diet, taken from each of the 1 kg mixtures, by quantitative analysis done by HPLC. The premixed diet (150 mg/kg) was further diluted with fresh powdered diet to obtain the desired DNB concentration in the lower dose groups. The diet feeders were refilled twice a week and changed weekly.

Analyses of the DNB-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 245 nm. The entire chromatography system was interfaced with a Berthold HPLC computer program, Version 1.65 (Berthold, Nashua, NH). The DNB 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 present in Appendix H.

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, 6 weeks old and weighing approximately 120-125 g when delivered, were held for 2 weeks 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	Animal Nos.	Sex	Diet Concentration (mg DNB/kg diet)
1	5	1-5	F	150
2	5	6-10	F	75
3	5	11-15	F	25
4	5	16-20	F	10
5	5	21-25	F	2.5
6	5	26-30	F	0
7	5	31-35	M	150
8	5	36-40	M	75
9	5	41-45	M	25
10	5	46-50	M	10
11	5	51-55	M	2.5
12	5	56-60	M	0

Hematology and Clinical Chemistry

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, reticulocyte 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 (Roche, Nutley, NJ) 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, phosphorus, total bilirubin, blood urea nitrogen, creatinine, alanine aminotransferase, cholesterol, triglycerides, 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 b.w., 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	colon
mandibular and	cecum
mesenteric lymph nodes	rectum
mammary glands	liver
thigh muscle	pancreas
sciatic nerve	spleen
sternum	kidneys
femur with marrow	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs with bronchi	prostate
heart and aorta	testes, including epididymides
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity with turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord
ileum	eyes
harderian gland	

Subsequently, these tissues were trimmed, processed and embedded in paraffin. Blocks were sectioned at 5 μ 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 brain and spleen of both sexes and the testes and kidneys of males 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

Food and water consumption data are listed in Table 1, while individual data are presented in Appendix A. Food consumption was significantly ($p \leq 0.05$) decreased in both sexes receiving 150 mg DNB diet while water consumption was not significantly altered in any group.

Using the food consumption data, the average daily DNB dose levels received by group (see Experimental Design) are presented in Table 2. The average daily DNB doses consumed (mg/kg b.w.) were 12, 6, 2, 0.9 and 0.2 for females and 11, 6, 2, 0.8 and 0.2 for males.

Body Weights, Organ Weights and Weight Ratios

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

No significant decreases from control terminal body weights were noted in any of the treated groups.

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

Kidneys - The 25 mg DNB dose group (males) had an increased value.

Liver - The 150 mg DNB dose group of both sexes had increased values.

Spleen - The 150 and 75 mg DNB dose groups of both sexes had increased values along with the 25 mg DNB female group.

Testes - The 150 and 75 mg DNB dose groups had decreased values.

Hematology

Hematology analyses performed were total white blood cell count (WBC), platelet count, red blood count (RBC), methemoglobin, hemoglobin (HGB), hematocrit (HCT), reticulocytes, Heinz bodies and differential leukocyte count. Group data are summarized in Tables 8 (females) and 9 (males). Individual data are listed in Appendix D.

1. WBC and Differential:
There were no significant differences in total white cell count or differentials amongst the groups in either sex except for the 75 mg DNB dose group (females) which had a decreased WBC count.
2. RBC:
A significant decrease ($p \leq 0.05$) in red blood cell count was present in both sexes receiving 150 and 75 mg DNB diet and in the female 25 mg DNB dose group.
3. Hemoglobin:
A significant decrease ($p \leq 0.05$) was noted in hemoglobin levels in both sexes in the 150, 75 and 25 mg DNB dose groups.
4. Hematocrit:
A significant decrease ($p \leq 0.05$) was present in both sexes in the 150 and 75 mg DNB dose groups and in the female 25 mg DNB dose group.
5. Platelets:
There were no significant changes in total platelets in any treatment group except for a slight increase in the female 75 mg DNB dose group.
6. Reticulocytes:
A significant increase ($p \leq 0.05$) was noted only in both sexes in the 150 and 75 mg DNB dose groups and the female 25 mg DNB dose group.
7. Methemoglobin:
A significant increase ($p \leq 0.05$) was present in both sexes receiving 150, 75 and 25 mg DNB diet and the 10 mg DNB male group.
8. Heinz Bodies:
Heinz bodies were not evident in any treatment group.

Clinical Chemistry

The mean group values for each analyte are compiled in Tables 10 (females) and 11 (males). Individual data are present in Appendix E.

1. Total Protein:
The mean values for females ranged from 5.6 to 5.9 g/dl while in males the range was 6.2 to 6.8. Significant increases ($p \leq 0.05$) occurred in only the male 150 mg DNB dose group.

2. **Albumin:**
The mean values for females ranged from 4.2 to 4.3 g/dl while in males the range was 4.5 to 5.0. Significant increases ($p \leq 0.05$) were present in only the male 150 mg DNB dose group.
3. **Calcium:**
The mean values for females ranged from 10.3 to 10.5 mg/dl while in males the range was 10.5 to 11.3. Significant increases ($p \leq 0.05$) were evident in only the male 150 mg DNB dose group.
4. **Total Bilirubin:**
The mean values for females ranged from 0.10 to 0.18 mg/dl while in males the range was 0.10 to 0.16. Males receiving 150 and 75 mg DNB diet had significant increased ($p \leq 0.05$) values. No changes were evident in females.
5. **Blood Urea Nitrogen (BUN):**
The mean values for females ranged from 21.2 to 25.0 mg/dl while in males the range was 19.6 to 23.4. There were significant increases ($p \leq 0.05$) occurring in only the 75 and 25 mg DNB male dose groups.
6. **Creatinine:**
The mean values for females ranged from 0.50 to 0.60 mg/dl while in males the range was 0.58 to 0.66. There were no significant differences amongst the groups except for a slight increase in the female 75 mg DNB dose group.
7. **Aspartate Aminotransferase (AST):**
The mean values for females ranged from 110 to 152 IU/L while in males the range was 113 to 183. There were no significant differences amongst the groups except for a slight increase in the female 75 mg DNB dose group.
8. **Alanine Aminotransferase (ALT):**
The mean values for females ranged from 38 to 53 IU/L while in males the range was 46 to 81. There were no significant differences amongst the groups.
9. **Alkaline Phosphatase (ALK Phos):**
The mean values for females ranged from 150 to 189 IU/L while in males the range was 186 to 193. There were no significant changes amongst the groups.
10. **Sodium:**
The mean values for females ranged from 142 to 143 mmol/L while in males the range was 142 to 143. There were no significant differences amongst the groups.

11. Potassium:

The mean values for females ranged from 4.4 to 5.2 mmol/L while in males the range was 4.5 to 5.1. There were no significant differences amongst the groups.

12. Glucose:

The mean values for females ranged from 95 to 116 mg/dl while in males the range was 145 to 167. There were no significant differences amongst the groups.

13. Phosphorus:

The mean values for females ranged from 10.6 to 12.9 mg/dl while in males the range was 10.5 to 11.9. There were no significant changes amongst the groups.

14. Cholesterol:

The mean values for females ranged from 84 to 100 mg/dl while in males the range was 51 to 67. There were no significant differences amongst the groups except for a slight increase in the male 150 mg DNB dose group.

15. Triglycerides:

The mean values for females ranged from 28 to 38 mg/dl while in males the range was 56 to 79. There were no significant differences amongst the groups.

Clinical Observations

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

Mortality

There were no early deaths in any of the groups.

Gross Pathology

Gross changes noted at the terminal sacrifice were confined to the 150 and 75 mg/kg DNB dose groups. There changes included a dose related increase in spleen size or a decrease in testicular size.

Histopathology (Appendix G)

All tissues were histopathologically examined in control and high dose animals of both sexes while the brain, spleen, testes and kidneys (males only) were examined in all the remaining dose groups.

Significant changes were evident in the high dose (150 mg/kg DNB) group of both sexes involving bone marrow, spleen and brain. Brain lesions (cerebellar peduncles) featured prominent areas of cellular vacuolization, microgliosis and necrosis. The spleen and bone marrow were characterized by a minimal to moderate erythroid cell hyperplasia and pigment deposition (hemosiderin). 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. Similar splenic changes were noted in the 75 and 25 mg/kg groups but with a decreased severity.

Additional microscopic changes were apparent in the male 150 and 75 mg/kg DNB groups entailing the kidneys and testes. The kidneys exhibited an increase in hyaline droplet deposition along with an increased incidence an/or severity of tubular degeneration and regeneration. The testes were characterized 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 remaining diagnoses were considered spontaneous since their incidence levels were significantly low.

SUMMARY

The administration to Fischer 344 rats of 1,3-Dinitrobenzene at various doses in the diet for fourteen days resulted in the following significant findings:

1. A significant decrease in average daily food consumption in both sexes receiving 150 mg DNB diet.
2. Relative kidney weights were significantly increased in male rats receiving 25 mg DNB diet while relative liver weights were increased in both sexes in the 150 mg dose group.
3. Relative spleen weights were increased in both sexes in the 150 and 75 mg DNB diet groups and the female 25 mg dose group while testicular weights were decreased in the 150 and 75 mg DNB dose groups.
4. A significant decrease in red blood cell count, hemoglobin and hematocrit levels were apparent in both sexes receiving 150 and 75 mg DNB diet while reticulocyte levels were increased in these same groups. Methemoglobin levels were increased in both sexes receiving 150, 75 and 25 mg DNB diet and the male 10 mg dose group.
5. Microscopic examination revealed significant changes in the testes (seminiferous tubular degeneration), spleen (erythroid cell hyperplasia), kidneys (hyaline droplet deposition) and brain (vacuolization, microgliosis and necrosis). Brain changes were evident in both sexes in the 150 mg DNB

group with kidney and testicular changes present in the 150 and 75 mg male groups. The 150, 75 and 25 mg DNB groups of both sexes exhibited splenic changes of varying severity.

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Table 1: Food and Water Consumption

Dose (mg DNB/kg diet)	Food (g/kg b.w./day)	Water (g/kg b.w./day)
Females		
0	86.84±0.97	120.01±5.29
150	78.15±3.74 *	112.33±6.56
75	84.24±1.89	116.19±3.15
25	83.20±1.17	114.64±2.72
10	85.83±1.82	121.21±4.16
2.5	86.15±0.25	111.28±2.26
Males		
0	78.32±1.17	106.54±4.10
150	69.81±0.74 *	98.61±2.99
75	77.34±2.07	101.19±3.62
25	81.28±0.96	107.12±3.11
10	79.36±2.18	104.90±6.04
2.5	80.69±2.00	101.01±2.08

Mean ± Standard Error

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

Table 2: Calculated Daily DNB Consumption

Group	Sex	Dose Groups (mg DNB/kg diet)	Calculated Dose (mg DNB/kg b.w.)
1	F	150	11.82±0.57
2	F	75	6.28±0.14
3	F	25	2.02±0.03
4	F	10	0.87±0.02
5	F	2.5	0.22±0.00
6	F	0	
7	M	150	10.56±0.11
8	M	75	5.77±0.15
9	M	25	1.98±0.02
10	M	10	0.80±0.02
11	M	2.5	0.21±0.01
12	M	0	

Mean ± Standard Error

Table 3: Body Weights (grams)

Dose Groups (mg DNB/kg diet)	Weeks	
	1	2
Females		
0	132.93±3.24	140.92±3.87
150	129.42±0.91	134.97±1.57
75	135.07±2.54	144.67±2.54
25	134.74±2.76	143.68±3.30
10	133.63±1.50	143.21±1.78
2.5	134.21±2.14	143.25±2.61
Males		
0	199.21±4.92	222.40±4.77
150	198.01±2.58	212.03±2.74
75	196.13±2.92	216.53±2.88
25	198.07±5.27	221.45±5.92
10	195.35±8.36	217.27±9.60
2.5	195.29±5.13	216.84±5.79

Mean ± Standard Error

Table 4: Organ Weights (grams)/Females

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
Kidneys	1.10±0.01	1.07±0.04	1.14±0.04	1.12±0.04	1.15±0.01	1.12±0.02
Lungs	0.82±0.04	0.81±0.03	0.88±0.05	0.84±0.04	0.89±0.07	0.77±0.04
Liver	4.17±0.13	4.63±0.33	4.61±0.18	4.50±0.19	4.26±0.11	4.39±0.08
Heart	0.57±0.02	0.54±0.04	0.58±0.04	0.56±0.02	0.61±0.03	0.57±0.02
Brain	1.68±0.04	1.69±0.02	1.68±0.02	2.26±0.64	1.70±0.03	1.69±0.02
Spleen	0.36±0.01	0.68±0.05 *	0.74±0.03 *	0.45±0.03	0.37±0.01	0.38±0.01
Adrenals	0.08±0.01	0.06±0.00	0.14±0.07	0.07±0.00	0.07±0.00	0.08±0.00
Thymus	0.29±0.03	0.28±0.02	0.36±0.03	0.31±0.01	0.31±0.02	0.30±0.04
Gonad	0.13±0.01	0.11±0.01	0.15±0.01	0.12±0.02	0.15±0.01	0.13±0.01

Mean ± Standard Error

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

Table 5: Organ Weights (grams)/Males

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
Kidneys	1.69±0.06	1.64±0.06	1.69±0.05	1.82±0.06	1.70±0.08	1.68±0.04
Lungs	1.09±0.08	1.10±0.05	0.96±0.04	1.04±0.06	1.11±0.05	1.08±0.04
Liver	7.70±0.20	7.91±0.36	7.58±0.20	7.77±0.30	7.39±0.45	7.13±0.22
Heart	0.78±0.01	0.72±0.03	0.75±0.02	0.78±0.03	0.78±0.04	0.75±0.02
Brain	1.82±0.02	1.79±0.01	1.81±0.03	1.78±0.03	1.78±0.05	1.83±0.03
Spleen	0.51±0.02	1.05±0.02 *	0.98±0.03 *	0.58±0.02	0.51±0.02	0.47±0.01
Adrenals	0.06±0.01	0.06±0.00	0.05±0.00	0.05±0.01	0.06±0.00	0.06±0.01
Thymus	0.32±0.02	0.30±0.02	0.33±0.04	0.40±0.03	0.35±0.02	0.36±0.02
Gonad	3.91±0.22	1.98±0.21 *	1.78±0.05 *	3.77±0.18	4.05±0.32	4.00±0.25

Mean ± Standard Error

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

Table 6: Organ-to-Body Weight Ratios/Females

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
Body Weight(g)	139.68±3.38	132.88±3.87	141.68±3.37	139.68±3.29	136.22±5.16	141.37±2.12
Kidneys (%)	0.79±0.01	0.80±0.01	0.80±0.01	0.80±0.02	0.85±0.03	0.79±0.01
Lungs (%)	0.59±0.03	0.61±0.01	0.62±0.03	0.61±0.03	0.66±0.06	0.54±0.03
Liver (%)	2.98±0.05	3.47±0.15 *	3.25±0.05	3.21±0.07	3.14±0.09	3.10±0.04
Heart (%)	0.41±0.02	0.41±0.03	0.41±0.02	0.40±0.01	0.45±0.03	0.40±0.01
Brain (%)	1.20±0.03	1.27±0.03	1.19±0.02	1.62±0.45	1.26±0.05	1.19±0.02
Spleen (%)	0.26±0.00	0.51±0.03 *	0.52±0.01 *	0.32±0.01 *	0.28±0.01	0.27±0.01
Adrenals (%)	0.06±0.00	0.05±0.00	0.10±0.05	0.05±0.00	0.05±0.00	0.05±0.00
Thymus (%)	0.21±0.02	0.21±0.01	0.25±0.02	0.22±0.01	0.23±0.01	0.21±0.02
Gonad (%)	0.10±0.01	0.08±0.01	0.10±0.01	0.09±0.01	0.11±0.01	0.09±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/Males

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
Body Weight(g)	222.59±4.34	202.31±4.03	213.50±3.47	221.41±5.84	217.04±9.97	215.89±5.56
Kidneys (%)	0.76±0.02	0.81±0.02	0.79±0.01	0.82±0.02 *	0.78±0.01	0.78±0.02
Lungs (%)	0.49±0.04	0.54±0.02	0.45±0.02	0.47±0.03	0.51±0.01	0.50±0.02
Liver (%)	3.46±0.03	3.90±0.11 *	3.55±0.07	3.50±0.05	3.40±0.06	3.30±0.03
Heart (%)	0.35±0.01	0.35±0.01	0.35±0.01	0.35±0.01	0.36±0.01	0.35±0.01
Brain (%)	0.82±0.02	0.89±0.02	0.85±0.02	0.80±0.01	0.83±0.04	0.85±0.02
Spleen (%)	0.23±0.01	0.52±0.01 *	0.46±0.01 *	0.26±0.01	0.23±0.01	0.22±0.00
Adrenals (%)	0.03±0.00	0.03±0.00	0.02±0.00	0.02±0.00	0.03±0.00	0.03±0.00
Thymus (%)	0.14±0.01	0.15±0.01	0.15±0.02	0.18±0.01	0.16±0.01	0.17±0.01
Gonad (%)	1.76±0.11	0.97±0.09 *	0.83±0.03 *	1.71±0.11	1.87±0.14	1.86±0.14

Mean ± Standard Error

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

Table 8: Hematology Values/Females

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
RBC (x10 ⁶ /μl)	7.96 ±0.21	6.01* ±0.34	6.01* ±0.31	7.18* ±0.37	7.70 ±0.16	7.81 ±0.16
Hemoglobin (g/dl)	15.50 ±0.40	12.74* ±0.57	12.56* ±0.65	13.64* ±0.65	14.82 ±0.27	15.16 ±0.24
Hematocrit (%)	41.92 ±0.85	39.08* ±2.18	38.90* ±1.39	38.84* ±1.22	41.16 ±1.22	41.88 ±1.80
WBC (x10 ³ /μl)	4.36 ±1.13	3.12 ±0.37	2.94* ±0.67	3.92 ±0.99	3.24 ±0.75	3.42 ±0.69
Platelets (x10 ³ /μl)	747.00 ±30.21	773.40 ±83.53	877.40* ±79.36	786.25 ±35.45	811.67 ±29.74	776.00 ±59.29
Segmented Leukocytes (%)	17.12 ±4.43	12.22 ±1.58	15.40 ±5.74	17.14 ±5.13	18.30 ±3.51	17.15 ±3.66
Lymphocytes (%)	79.40 ±4.52	84.54 ±1.58	80.26 ±5.51	79.70 ±5.97	77.78 ±4.00	78.82 ±4.63
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
MCV (cumicr)	52.70 ±0.57	65.04* ±0.53	64.72* ±1.97	54.14 ±1.87	53.44 ±1.56	53.64 ±1.71
MCH (picogm)	19.50 ±0.29	21.20* ±0.34	20.88* ±0.27	18.96* ±0.30	19.28 ±0.15	19.44 ±0.24
MCHC (g/dl)	37.02 ±0.59	32.58* ±0.44	32.28* ±1.24	35.08* ±1.09	36.08 ±0.97	36.28 ±1.45
Reticulocytes (%)	1.62 ±0.11	9.24* ±1.12	12.54* ±0.65	4.28* ±0.41	2.38 ±0.17	2.05 ±0.22
MetHb (%)	0.62 ±0.25	7.24* ±1.20	4.70* ±0.27	2.90* ±0.31	1.40 ±0.19	0.82 ±0.31

Mean ± Standard Deviation

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

Table 9: Hematology Values/Males

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
RBC (x10 ⁶ /μl)	8.45 ±0.18	6.55* ±0.15	7.05* ±0.29	8.19 ±0.09	8.30 ±0.17	8.40 ±0.19
Hemoglobin (g/dl)	15.58 ±0.38	12.90* ±0.42	13.18* ±0.58	14.68* ±0.23	15.30 ±0.32	15.62 ±0.32
Hematocrit (%)	45.88 ±1.08	42.78* ±1.49	41.94* ±1.43	44.12 ±1.04	45.10 ±0.32	45.58 ±1.62
WBC (x10 ³ /μl)	4.52 ±0.75	4.42 ±1.39	4.98 ±0.93	4.66 ±0.79	4.10 ±1.39	4.02 ±0.70
Platelets (x10 ³ /μL)	849.40 ±28.06	947.00 ±60.51	984.00 ±66.98	945.80 ±59.84	883.00 ±52.05	899.00 ±14.53
Segmented Leukocytes (%)	20.40 ±4.03	15.78 ±4.36	15.00 ±2.97	17.60 ±2.55	16.14 ±3.10	18.70 ±2.11
Lymphocytes (%)	76.60 ±4.64	80.62 ±4.63	82.40 ±3.44	80.02 ±2.53	81.32 ±3.38	78.48 ±2.01
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
MCV (cumicr)	54.30 ±0.64	65.30* ±2.21	59.58* ±1.46	53.86 ±1.09	54.38 ±1.20	54.28 ±1.25
MCH (picogm)	18.44 ±0.21	19.70* ±0.24	18.72 ±0.24	17.92* ±0.11	18.48 ±0.26	18.58 ±0.18
MCHC (g/dl)	33.94 ±0.74	30.20* ±1.06	31.42* ±0.87	33.28 ±0.72	34.00 ±0.67	34.28 ±1.08
Reticulocytes (%)	2.62 ±0.40	10.90* ±2.00	9.12* ±1.54	4.12 ±0.29	2.66 ±0.23	2.30 ±0.27
MetHb (%)	0.74 ±0.34	8.78* ±0.74	6.28* ±0.74	3.34* ±0.59	1.78* ±0.47	0.62 ±0.29

Mean ± Standard Deviation

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

Table 10: Clinical Chemistry Values/Females

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	2.5	
Glucose (mg/dl)	113.60 ± 23.03	110.60 ± 30.91	94.60 ± 19.14	115.80 ± 25.61	103.20 ± 30.63	105.00 ± 18.75
BUN (mg/dl)	21.20 ± 1.79	24.00 ± 2.55	25.00 ± 2.35	23.00 ± 2.55	24.40 ± 4.16	23.80 ± 2.49
Creatinine (mg/dl)	0.50 ± 0.00	0.54 ± 0.05	0.60 ± 0.07*	0.52 ± 0.04	0.54 ± 0.05	0.50 ± 0.00
ALK Phos. (U/L)	170.40 ± 14.15	188.80 ± 58.64	150.40 ± 25.55	160.00 ± 21.51	154.20 ± 13.55	164.80 ± 22.62
AST (U/L)	116.80 ± 5.50	114.60 ± 16.10	152.00 ± 35.23*	109.60 ± 4.83	133.60 ± 12.54	126.40 ± 18.61
ALT (U/L)	46.80 ± 6.83	53.20 ± 15.14	41.80 ± 7.66	40.20 ± 5.07	38.00 ± 7.18	47.20 ± 8.87
Potassium (mmol/L)	4.58 ± 0.31	4.88 ± 0.63	5.24 ± 0.56	4.52 ± 0.48	4.42 ± 0.28	4.62 ± 0.22
Albumin (g/dl)	4.26 ± 0.15	4.44 ± 0.21	4.48 ± 0.26	4.36 ± 0.19	4.32 ± 0.16	4.26 ± 0.13
Calcium (mg/dl)	10.40 ± 0.23	10.48 ± 0.13	10.46 ± 0.36	10.36 ± 0.15	10.30 ± 0.12	10.42 ± 0.19
Sodium (mmol/dl)	142.00 ± 0.71	143.20 ± 1.92	141.40 ± 1.14	142.20 ± 0.84	143.00 ± 1.00	142.60 ± 0.55
Total Bilirubin (mg/dl)	0.12 ± 0.04	0.14 ± 0.05	0.18 ± 0.04	0.12 ± 0.04	0.12 ± 0.04	0.10 ± 0.00
Total Protein (g/dl)	5.64 ± 0.28	5.70 ± 0.20	5.90 ± 0.31	5.88 ± 0.29	5.84 ± 0.11	5.78 ± 0.22
Cholesterol (mg/dl)	89.20 ± 3.70	83.60 ± 5.55	89.60 ± 8.65	90.40 ± 9.61	94.20 ± 6.72	100.20 ± 3.11
Phosphorus (mg/dl)	10.60 ± 0.87	10.66 ± 1.27	12.94 ± 1.47	10.60 ± 1.56	10.74 ± 2.19	11.08 ± 1.55
Triglyceride (mg/dl)	38.00 ± 5.48	34.60 ± 15.95	31.40 ± 9.63	29.00 ± 1.87	28.20 ± 6.06	36.00 ± 9.11

Mean ± Standard Deviation

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

Table 11: Clinical Chemistry Values/Males

	Dose Groups (mg DNB/kg diet)					
	0	150	75	25	10	2.5
Glucose (mg/dl)	150.20 ± 19.25	144.80 ± 39.73	166.80 ± 27.67	156.60 ± 18.98	150.00 ± 27.18	152.20 ± 25.02
BUN (mg/dl)	20.00 ± 1.22	20.80 ± 1.30	23.40 ± 0.89*	22.60 ± 2.51*	19.60 ± 1.52	20.00 ± 1.00
Creatinine (mg/dl)	0.62 ± 0.04	0.60 ± 0.00	0.64 ± 0.05	0.66 ± 0.05	0.58 ± 0.04	0.58 ± 0.04
ALK Phos. (U/L)	193.40 ± 10.01	186.40 ± 32.07	189.40 ± 7.40	190.80 ± 4.60	190.40 ± 13.92	193.40 ± 13.74
AST (U/L)	141.00 ± 23.31	113.00 ± 15.30	133.00 ± 34.60	183.40 ± 84.99	123.60 ± 9.29	144.40 ± 27.69
ALT (U/L)	57.40 ± 10.14	49.60 ± 8.71	61.00 ± 22.27	81.20 ± 55.58	45.80 ± 9.73	51.00 ± 8.75
Potassium (mmol/L)	4.66 ± 0.30	5.14 ± 0.79	5.08 ± 0.48	4.84 ± 0.23	4.54 ± 0.26	4.90 ± 0.50
Albumin (g/dl)	4.54 ± 0.05	4.98 ± 0.08*	4.74 ± 0.19	4.62 ± 0.16	4.52 ± 0.16	4.52 ± 0.11
Calcium (mg/dl)	10.62 ± 0.23	11.26 ± 0.30*	10.90 ± 0.47	10.52 ± 0.23	10.78 ± 0.29	10.68 ± 0.40
Sodium (mmol/dl)	142.80 ± 1.10	142.20 ± 0.45	141.60 ± 1.14	142.60 ± 1.34	143.20 ± 1.30	143.40 ± 1.52
Total Bilirubin (mg/dl)	0.10 ± 0.00	0.16 ± 0.05*	0.16 ± 0.05*	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00
Total Protein (g/dl)	6.20 ± 0.19	6.76 ± 0.11*	6.36 ± 0.21	6.28 ± 0.18	6.22 ± 0.23	6.22 ± 0.11
Cholesterol (mg/dl)	52.40 ± 3.36	67.00 ± 4.85*	57.40 ± 6.11	51.20 ± 4.27	57.60 ± 1.95	52.20 ± 4.97
Phosphorus (mg/dl)	10.52 ± 0.61	11.88 ± 1.01	11.24 ± 1.27	11.30 ± 1.25	11.00 ± 0.73	11.24 ± 0.94
Triglyceride (mg/dl)	73.80 ± 22.63	56.40 ± 26.06	57.20 ± 21.18	65.60 ± 25.08	79.40 ± 16.68	68.40 ± 9.18

Mean ± Standard Deviation

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

APPENDIX A

FOOD AND WATER
CONSUMPTION

Weekly Food and Water Consumption

Dose (mg DNB/kg diet)	Food (g/wk)		Water (g/wk)	
	Week	Week	Week	Week
	1	2	1	2
Females				
0	82.94±2.82	84.60±1.15	117.92±5.08	113.10±5.09
150	76.28±1.58	68.96±5.30	106.00±4.60	103.48±6.62
75	85.06±4.35	81.68±1.60	116.40±4.79	112.26±5.44
25	81.16±1.65	82.54±1.94	113.36±3.02	110.64±2.29
10	82.24±1.35	85.30±2.25	119.30±4.25	115.88±5.40
2.5	82.00±1.95	87.08±1.22	110.38±3.05	105.88±2.65
Males				
0	100.20±3.47	133.22±4.20	137.28±5.16	175.78±7.94
150	93.38±1.52	106.86±3.42	130.44±2.28	149.76±5.85
75	97.43±2.80	127.74±3.08	125.45±5.66	166.10±7.44
25	103.42±3.95	137.20±3.37	137.40±4.85	175.72±6.27
10	99.80±4.95	131.20±7.15	134.54±10.43	166.84±12.81
2.5	102.32±2.85	131.62±3.87	125.84±3.76	162.38±4.49

Mean ± Standard Error

Individual Food and Water Consumption

Dose (mg DNB/kg diet)	Animal Number	Females				Males				
		Food (g/wk)		Water (g/wk)		Food (g/wk)		Water (g/wk)		
		Week 1	Week 2	Week 1	Week 2	Week 1	Week 2	Week 1	Week 2	
150	1	77.7	63.4	100.4	88.5	31	98.0	107.1	136.2	155.9
	2	74.3	52.7	105.2	104.0	32	91.0	115.0	124.5	151.3
	3	72.2	69.6	107.0	99.1	33	91.9	111.0	128.9	135.4
	4	81.5	84.1	122.4	128.0	34	95.9	94.6	127.3	138.7
	5	75.7	75.0	95.0	97.8	35	90.1	106.6	135.3	167.5
75	6	102.3	87.0	123.6	122.1	36	*	130.5	*	186.9
	7	81.2	83.1	125.8	124.9	37	96.5	126.0	128.8	171.4
	8	78.8	80.0	122.1	115.3	38	97.4	133.3	118.2	150.7
	9	80.4	77.5	109.6	99.9	39	91.1	116.5	114.9	147.5
	10	82.6	80.8	100.9	99.1	40	104.7	132.4	139.9	174.0
25	11	78.9	85.7	107.8	109.8	41	105.6	138.1	128.5	165.5
	12	87.6	85.2	120.3	113.4	42	106.2	146.0	148.9	174.0
	13	80.2	85.5	119.4	112.0	43	115.7	142.6	148.9	198.8
	14	78.7	75.8	114.1	115.7	44	95.3	127.9	126.6	163.7
	15	80.4	80.5	105.2	102.3	45	94.3	131.4	134.1	176.6
10	16	85.5	88.1	136.3	133.1	46	103.4	138.7	147.7	187.5
	17	79.7	77.6	115.1	115.4	47	105.7	139.7	148.0	177.6
	18	80.8	83.7	115.6	113.5	48	109.8	141.5	139.4	173.7
	19	85.5	90.8	114.5	99.3	49	81.3	103.2	93.3	116.4
	20	79.7	86.3	115.0	118.1	50	98.8	132.9	144.3	179.0
2.5	21	86.4	91.8	115.6	106.8	51	107.6	140.9	136.1	172.5
	22	85.2	86.5	111.5	111.7	52	109.3	139.8	128.0	163.2
	23	82.9	86.3	116.9	111.2	53	101.6	126.3	130.5	171.6
	24	79.9	84.7	99.9	98.3	54	93.5	120.8	115.8	149.8
	25	75.6	86.1	108.0	101.4	55	99.6	130.3	118.8	154.8
0	26	91.0	87.5	117.3	110.2	56	113.0	147.3	153.4	202.2
	27	87.7	84.3	126.5	123.5	57	98.9	136.8	131.6	171.3
	28	76.7	84.6	110.8	109.8	58	99.0	122.3	122.5	152.5
	29	82.0	86.0	131.5	124.8	59	98.3	129.4	137.0	177.1
	30	77.3	80.6	103.5	97.2	60	91.8	130.3	141.9	175.8

* Excess Spillage

APPENDIX B

BODY WEIGHTS

Weekly Body Weights (grams)

Dose (mg DNB/kg diet)	Animal Number	Weeks		Animal Number	Weeks		
		1	2		1	2	
		Females			Males		
150	1	131.47	137.20	31	204.50	218.43	
	2	128.23	129.40	32	203.37	218.83	
	3	130.17	137.17	33	195.23	207.83	
	4	126.47	133.53	34	196.03	208.97	
	5	130.77	137.53	35	190.90	206.07	
75	6	142.60	152.00	36	203.47	223.40	
	7	137.40	147.13	37	196.57	215.50	
	8	136.47	146.33	38	201.33	222.83	
	9	130.43	139.40	39	191.13	209.07	
	10	128.47	138.47	40	188.13	211.87	
25	11	140.87	150.57	41	202.17	224.70	
	12	140.27	150.10	42	208.33	234.37	
	13	135.80	145.73	43	207.73	232.33	
	14	129.57	137.80	44	191.20	212.27	
	15	127.20	134.20	45	180.93	203.57	
10	16	136.87	149.20	46	209.63	231.00	
	17	136.60	144.60	47	207.77	231.70	
	18	132.43	140.83	48	209.30	234.73	
	19	133.53	142.60	49	172.10	187.40	
	20	128.70	138.80	50	177.93	201.53	
2.5	21	140.73	151.93	51	211.07	236.03	
	22	136.60	145.37	52	198.73	220.77	
	23	134.50	143.10	53	193.23	215.67	
	24	130.33	138.17	54	194.27	210.57	
	25	128.87	137.70	55	179.17	201.17	
0	26	141.63	151.57	56	212.17	236.07	
	27	138.80	147.60	57	208.07	230.53	
	28	131.13	139.77	58	198.97	220.20	
	29	129.30	134.93	59	190.07	214.27	
	30	123.77	130.73	60	186.80	210.93	

APPENDIX C
ORGAN WEIGHTS

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER	
1	1	129.65	1.066	0.775	4.280	0.822	0.598	3.301
1	2	121.06	0.939	0.718	3.614	0.776	0.593	2.985
1	3	131.02	1.076	0.812	4.584	0.821	0.620	3.499
1	4	140.20	1.076	0.883	5.213	0.767	0.630	3.718
1	5	142.47	1.176	0.875	5.445	0.825	0.614	3.822
2	6	153.18	1.297	0.951	5.281	0.847	0.621	3.448
2	7	143.25	1.114	0.938	4.558	0.778	0.655	3.182
2	8	141.77	1.134	0.973	4.638	0.800	0.686	3.271
2	9	133.42	1.056	0.809	4.195	0.791	0.606	3.144
2	10	136.80	1.092	0.730	4.372	0.798	0.534	3.196
3	11	145.05	1.163	0.970	4.675	0.802	0.669	3.223
3	12	148.50	1.193	0.773	4.961	0.803	0.521	3.341
3	13	140.22	1.200	0.846	4.729	0.856	0.603	3.373
3	14	133.09	1.001	0.774	4.032	0.752	0.582	3.030
3	15	131.55	1.056	0.861	4.080	0.803	0.655	3.101
4	16	146.61	1.208	0.708	4.585	0.824	0.483	3.127
4	17	124.36	1.140	0.879	4.044	0.917	0.707	3.252
4	18	137.45	1.133	1.129	4.078	0.824	0.821	2.967
4	19	142.98	1.136	0.917	4.463	0.795	0.641	3.121
4	20	137.21	1.132	0.838	4.136	0.825	0.611	3.014
5	21	147.61	1.207	0.832	4.551	0.818	0.564	3.083
5	22	141.79	1.063	0.748	4.221	0.750	0.528	2.977
5	23	143.90	1.141	0.663	4.622	0.793	0.461	3.212
5	24	135.78	1.104	0.867	4.238	0.813	0.639	3.121
5	25	137.78	1.100	0.736	4.305	0.798	0.534	3.125
6	26	148.64	1.123	0.858	4.648	0.756	0.577	3.127
6	27	145.55	1.126	0.744	4.104	0.774	0.511	2.820
6	28	138.82	1.101	0.794	4.143	0.793	0.572	2.984
6	29	135.49	1.086	0.968	4.022	0.802	0.714	2.968
6	30	129.91	1.063	0.729	3.920	0.818	0.561	3.017

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER	
7	31	208.86	1.705	1.020	7.998	0.816	0.488	3.829
7	32	214.67	1.822	1.285	9.284	0.849	0.599	4.325
7	33	198.05	1.646	1.043	7.484	0.831	0.527	3.779
7	34	196.35	1.491	1.072	7.350	0.759	0.546	3.743
7	35	193.62	1.538	1.058	7.444	0.794	0.546	3.845
8	36	216.69	1.721	0.885	7.547	0.794	0.408	3.483
8	37	214.07	1.663	1.076	7.630	0.777	0.503	3.564
8	38	224.02	1.834	0.963	7.939	0.819	0.430	3.544
8	39	203.43	1.540	0.859	6.847	0.757	0.422	3.366
8	40	209.27	1.681	1.013	7.933	0.803	0.484	3.791
9	41	223.08	1.744	1.054	7.736	0.782	0.472	3.468
9	42	235.71	1.966	1.020	8.498	0.834	0.433	3.605
9	43	232.08	1.935	1.028	8.368	0.834	0.443	3.606
9	44	209.79	1.674	0.883	7.049	0.798	0.421	3.360
9	45	206.38	1.800	1.234	7.177	0.872	0.598	3.478
10	46	230.74	1.842	1.144	8.024	0.798	0.496	3.478
10	47	231.46	1.784	1.211	7.788	0.771	0.523	3.365
10	48	235.52	1.829	1.177	8.406	0.777	0.500	3.569
10	49	184.71	1.390	0.948	5.911	0.753	0.513	3.200
10	50	202.76	1.657	1.066	6.837	0.817	0.526	3.372
11	51	235.05	1.790	1.118	7.928	0.762	0.476	3.373
11	52	220.39	1.711	0.926	7.230	0.776	0.420	3.281
11	53	212.49	1.660	1.115	7.058	0.781	0.525	3.322
11	54	208.39	1.542	1.103	6.636	0.740	0.529	3.184
11	55	203.15	1.688	1.138	6.811	0.831	0.560	3.353
12	56	236.17	1.857	1.241	8.229	0.786	0.525	3.484
12	57	229.56	1.786	0.947	8.132	0.778	0.413	3.542
12	58	217.14	1.522	0.913	7.360	0.701	0.420	3.390
12	59	214.84	1.694	1.298	7.358	0.788	0.604	3.425
12	60	215.22	1.579	1.026	7.423	0.734	0.477	3.449

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN	
1	1	129.65	0.501	1.685	0.706	0.386	1.300	0.545
1	2	121.06	0.460	1.645	0.517	0.380	1.359	0.427
1	3	131.02	0.662	1.660	0.736	0.505	1.267	0.562
1	4	140.20	0.500	1.771	0.634	0.357	1.263	0.452
1	5	142.47	0.584	1.677	0.814	0.410	1.177	0.571
2	6	153.18	0.685	1.746	0.812	0.447	1.140	0.530
2	7	143.25	0.559	1.727	0.727	0.390	1.206	0.508
2	8	141.77	0.655	1.640	0.789	0.462	1.157	0.557
2	9	133.42	0.512	1.623	0.652	0.384	1.216	0.489
2	10	136.80	0.506	1.663	0.701	0.370	1.216	0.512
3	11	145.05	0.639	1.551	0.536	0.441	1.069	0.370
3	12	148.50	0.539	1.696	0.456	0.363	1.142	0.307
3	13	140.22	0.562	1.803	0.452	0.401	1.286	0.322
3	14	133.09	0.508	1.615	0.379	0.382	1.213	0.285
3	15	131.55	0.538	1.627	0.407	0.409	1.237	0.309
4	16	146.61	0.578	1.807	0.409	0.394	1.233	0.279
4	17	124.36	0.626	1.694	0.358	0.503	1.362	0.288
4	18	137.45	0.517	1.714	0.358	0.376	1.247	0.260
4	19	142.98	0.660	1.621	0.363	0.462	1.134	0.254
4	20	137.21	0.648	1.670	0.385	0.472	1.217	0.281
5	21	147.61	0.584	1.736	0.423	0.396	1.176	0.287
5	22	141.79	0.524	1.639	0.352	0.370	1.156	0.248
5	23	143.90	0.624	1.648	0.360	0.434	1.145	0.250
5	24	135.78	0.586	1.717	0.349	0.432	1.265	0.257
5	25	137.78	0.532	1.691	0.393	0.386	1.227	0.285
6	26	148.64	0.577	1.726	0.385	0.388	1.161	0.259
6	27	145.55	0.581	1.809	0.381	0.399	1.243	0.262
6	28	138.82	0.517	1.550	0.347	0.372	1.117	0.250
6	29	135.49	0.546	1.686	0.352	0.403	1.244	0.260
6	30	129.91	0.612	1.626	0.340	0.471	1.252	0.262

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN	
7	31	208.86	0.709	1.807	1.008	0.339	0.865	0.483
7	32	214.67	0.810	1.793	1.103	0.377	0.835	0.514
7	33	198.05	0.655	1.740	1.003	0.331	0.879	0.506
7	34	196.35	0.676	1.817	1.078	0.344	0.925	0.549
7	35	193.62	0.740	1.797	1.047	0.382	0.928	0.541
8	36	216.69	0.804	1.908	0.978	0.371	0.881	0.451
8	37	214.07	0.721	1.813	0.953	0.337	0.847	0.445
8	38	224.02	0.754	1.763	1.075	0.337	0.787	0.480
8	39	203.43	0.707	1.778	0.873	0.348	0.874	0.429
8	40	209.27	0.755	1.784	1.034	0.361	0.852	0.494
9	41	223.08	0.728	1.814	0.558	0.326	0.813	0.250
9	42	235.71	0.862	1.847	0.599	0.366	0.784	0.254
9	43	232.08	0.787	1.803	0.619	0.339	0.777	0.267
9	44	209.79	0.717	1.725	0.513	0.342	0.822	0.245
9	45	206.38	0.786	1.695	0.591	0.381	0.821	0.286
10	46	230.74	0.822	1.853	0.535	0.356	0.803	0.232
10	47	231.46	0.749	1.852	0.523	0.324	0.800	0.226
10	48	235.52	0.842	1.761	0.526	0.358	0.748	0.223
10	49	184.71	0.648	1.840	0.429	0.351	0.996	0.232
10	50	202.76	0.832	1.598	0.514	0.410	0.788	0.254
11	51	235.05	0.752	1.904	0.512	0.320	0.810	0.218
11	52	220.39	0.781	1.842	0.474	0.354	0.836	0.215
11	53	212.49	0.796	1.740	0.452	0.375	0.819	0.213
11	54	208.39	0.700	1.807	0.470	0.336	0.867	0.226
11	55	203.15	0.738	1.860	0.465	0.363	0.916	0.229
12	56	236.17	0.786	1.825	0.525	0.333	0.773	0.222
12	57	229.56	0.768	1.792	0.516	0.335	0.781	0.225
12	58	217.14	0.735	1.861	0.450	0.338	0.857	0.207
12	59	214.84	0.810	1.857	0.583	0.377	0.864	0.271
12	60	215.22	0.803	1.748	0.491	0.373	0.812	0.228

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	OVARIES WEIGHT	% ADRENAL	% THYMUS	% OVARIES	
1	1	129.65	0.058	0.262	0.110	0.045	0.202	0.085
1	2	121.06	0.059	0.222	0.101	0.049	0.183	0.083
1	3	131.02	0.072	0.259	0.149	0.055	0.198	0.114
1	4	140.20	0.067	0.356	0.084	0.048	0.254	0.060
1	5	142.47	0.066	0.319	0.107	0.046	0.224	0.075
2	6	153.18	0.069	0.419	0.141	0.045	0.274	0.092
2	7	143.25	0.058	0.404	0.109	0.040	0.282	0.076
2	8	141.77	0.065	0.413	0.181	0.046	0.291	0.128
2	9	133.42	0.420	0.250	0.152	0.315	0.187	0.114
2	10	136.80	0.063	0.301	0.146	0.046	0.220	0.107
3	11	145.05	0.071	0.327	0.174	0.049	0.225	0.120
3	12	148.50	0.070	0.310	0.123	0.047	0.209	0.083
3	13	140.22	0.074	0.305	0.136	0.053	0.218	0.097
3	14	133.09	0.057	0.251	0.082	0.043	0.189	0.062
3	15	131.55	0.067	0.336	0.102	0.051	0.255	0.078
4	16	146.61	0.080	0.333	0.158	0.055	0.227	0.108
4	17	124.36	0.068	0.276	0.141	0.055	0.222	0.113
4	18	137.45	0.078	0.375	0.159	0.057	0.273	0.116
4	19	142.98	0.079	0.289	0.115	0.055	0.202	0.080
4	20	137.21	0.065	0.272	0.152	0.047	0.198	0.111
5	21	147.61	0.081	0.438	0.154	0.055	0.297	0.104
5	22	141.79	0.081	0.300	0.136	0.057	0.212	0.096
5	23	143.90	0.075	0.231	0.116	0.052	0.161	0.081
5	24	135.78	0.067	0.247	0.152	0.049	0.182	0.112
5	25	137.78	0.071	0.307	0.103	0.052	0.223	0.075
6	26	148.64	0.082	0.330	0.146	0.055	0.222	0.098
6	27	145.55	0.074	0.337	0.124	0.051	0.232	0.085
6	28	138.82	0.068	0.309	0.112	0.049	0.223	0.081
6	29	135.49	0.099	0.184	0.135	0.073	0.136	0.100
6	30	129.91	0.072	0.285	0.156	0.055	0.219	0.120

INDIVIDUAL ORGAN WEIGHTS
(GRAMS)

GP-ANI NUMBER	BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	TESTES WEIGHT	% ADRENAL	% THYMUS	% TESTES
7 31	208.86	0.062	0.247	1.754	0.030	0.118	0.840
7 32	214.67	0.071	0.318	2.816	0.033	0.148	1.312
7 33	198.05	0.055	0.282	1.762	0.028	0.142	0.890
7 34	196.35	0.066	0.349	1.795	0.034	0.178	0.914
7 35	193.62	0.069	0.326	1.778	0.036	0.168	0.918
8 36	216.69	0.065	0.433	1.812	0.030	0.200	0.836
8 37	214.07	0.052	0.289	1.886	0.024	0.135	0.881
8 38	224.02	0.053	0.288	1.691	0.024	0.129	0.755
8 39	203.43	0.037	0.246	1.622	0.018	0.121	0.797
8 40	209.27	0.048	0.398	1.878	0.023	0.190	0.897
9 41	223.08	0.037	0.354	3.597	0.017	0.159	1.612
9 42	235.71	0.063	0.411	3.633	0.027	0.174	1.541
9 43	232.08	0.067	0.491	3.820	0.029	0.212	1.646
9 44	209.79	0.048	0.340	3.370	0.023	0.162	1.606
9 45	206.38	0.048	0.379	4.453	0.023	0.184	2.158
10 46	230.74	0.070	0.400	3.816	0.030	0.173	1.654
10 47	231.46	0.058	0.341	3.862	0.025	0.147	1.669
10 48	235.52	0.067	0.363	4.799	0.028	0.154	2.038
10 49	184.71	0.063	0.292	3.057	0.034	0.158	1.655
10 50	202.76	0.057	0.370	4.728	0.028	0.182	2.332
11 51	235.05	0.056	0.420	3.838	0.024	0.179	1.633
11 52	220.39	0.065	0.416	3.542	0.029	0.189	1.607
11 53	212.49	0.081	0.333	4.653	0.038	0.157	2.190
11 54	208.39	0.049	0.303	3.433	0.024	0.145	1.647
11 55	203.15	0.070	0.345	4.534	0.034	0.170	2.232
12 56	236.17	0.054	0.341	4.002	0.023	0.144	1.695
12 57	229.56	0.057	0.302	3.519	0.025	0.132	1.533
12 58	217.14	0.041	0.253	3.312	0.019	0.117	1.525
12 59	214.84	0.068	0.316	4.463	0.032	0.147	2.077
12 60	215.22	0.071	0.376	4.262	0.033	0.175	1.980

APPENDIX D
HEMATOLOGY DATA

Hematology Data/Females
14 Days

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	METHB %	WBC COUNT thsn/ cu mm	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	MCV cumicr
150	1	8.4	3.1	5.95	12.7	38.5	64.6
	2	7.0	3.2	6.57	13.7	42.6	64.9
	3	8.5	2.8	5.70	12.3	37.4	65.6
	4	5.7	2.8	5.79	12.3	37.3	64.5
	5	6.6	3.7	6.04	12.7	39.6	65.6
75	6	4.7	2.3	5.54	11.5	37.3	67.3
	7	4.6	3.3	6.22	13.1	38.5	61.8
	8	5.0	3.9	6.12	12.9	39.4	64.4
	9	4.9	2.8	6.31	12.9	41.0	64.9
	10	4.3	2.4	5.88	12.4	38.3	65.2
25	11	3.2	3.0	6.88	13.1	38.0	55.3
	12	2.7	3.7	6.97	13.0	37.7	54.1
	13	3.2	3.0	7.05	13.6	39.9	56.5
	14	2.5	5.1	7.80	14.6	40.4	51.7
	15	2.9	4.8	7.19	13.9	38.2	53.1
10	16	1.2	3.2	7.58	14.8	42.1	55.6
	17	1.7	2.9	7.81	15.1	40.3	51.6
	18	1.3	2.5	7.49	14.4	40.0	53.4
	19	1.4	4.5	7.74	14.8	40.6	52.4
	20	1.4	3.1	7.89	15.0	42.8	54.2
2.5	21	0.8	2.7	7.94	15.3	44.4	56.0
	22	0.6	2.9	7.92	15.5	41.4	52.2
	23	0.9	3.8	7.63	15.0	39.5	51.8
	24	1.3	4.4	7.92	15.1	42.6	53.8
	25	0.5	3.3	7.63	14.9	41.5	54.4
0	26	1.0	3.8	7.84	15.0	41.5	53.0
	27	0.4	4.4	7.86	15.6	41.6	53.0
	28	0.7	3.6	7.74	15.2	40.9	52.8
	29	0.4	6.3	8.26	16.0	42.7	51.7
	30	0.6	3.7	8.10	15.7	42.9	53.0

Hematology Data/Females
14 Days

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	MCH picogm	MCHC g/dl	PLAT thsn/ cu mm	NEUTRO- PHILS %	LYMPHO- CYTES %	RETIC %	HEINZ BODIES %
150	1	21.3	32.9	889	10.7	84.6	8.6	0.0
	2	20.8	32.1	779	10.3	86.9	7.6	0.0
	3	21.7	33.0	813	13.6	83.8	10.0	0.0
	4	21.2	32.8	696	13.2	84.8	9.7	0.0
	5	21.0	32.1	690	13.3	82.6	10.3	0.0
75	6	20.7	30.7	817	8.9	86.1	13.0	0.0
	7	21.0	34.0	977	23.2	72.7	11.9	0.0
	8	21.1	32.7	946	11.6	84.4	12.8	0.0
	9	20.5	31.6	800	19.0	76.8	11.8	0.0
	10	21.1	32.4	847	14.3	81.3	13.2	0.0
25	11	19.0	34.4	811	19.6	77.6	4.9	0.0
	12	18.6	34.5	805	16.7	81.0	4.0	0.0
	13	19.2	34.0	734	23.0	71.9	4.0	0.0
	14	18.7	36.1	*	17.3	79.6	4.0	0.0
	15	19.3	36.4	795	9.1	88.4	4.5	0.0
10	16	19.5	35.1	816	21.8	75.4	2.6	0.0
	17	19.3	37.4	780	16.2	80.1	2.2	0.0
	18	19.3	36.1	839	20.7	73.5	2.3	0.0
	19	19.2	36.6	*	14.5	82.1	2.4	0.0
	20	19.1	35.2	827	23.2	71.1	2.3	0.0
2.5	21	19.3	34.5	843	18.0	77.3	2.2	0.0
	22	19.6	37.5	715	17.4	78.7	1.9	0.0
	23	19.7	38.0	776	12.6	84.7	1.7	0.0
	24	19.1	35.5	719	14.2	82.1	2.1	0.0
	25	19.5	35.9	*	17.5	79.0	2.1	0.0
0	26	19.2	36.2	*	20.1	76.1	1.5	0.0
	27	19.9	37.6	759	11.5	84.9	1.7	0.0
	28	19.7	37.3	767	22.7	73.7	1.7	0.0
	29	19.3	37.4	760	14.5	82.1	1.7	0.0
	30	19.4	36.6	702	16.8	80.2	1.5	0.0

* = Quantity not sufficient

Hematology Data/Males
14 Days

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	METHB %	WBC COUNT thsn/ cu mm	RBC COUNT mill/ cu mm	HGB g/dl	HCT %	MCV cumicr
150	31	8.4	6.7	6.78	13.6	44.6	65.7
	32	7.9	3.9	6.38	12.7	42.6	66.7
	33	8.5	4.7	6.60	12.9	40.5	61.4
	34	9.6	3.2	6.52	12.8	43.3	66.3
	35	9.5	3.6	6.46	12.5	42.9	66.4
75	36	6.9	4.2	6.90	13.0	41.0	59.5
	37	6.3	5.0	7.36	13.6	44.0	59.8
	38	7.1	4.1	6.63	12.3	40.9	61.7
	39	5.4	5.2	7.23	13.8	42.9	59.3
	40	5.7	6.4	7.11	13.2	40.9	57.6
25	41	4.1	5.2	8.17	14.5	43.7	53.5
	42	3.4	3.8	8.09	14.4	44.0	54.4
	43	3.6	5.4	8.30	14.9	43.8	52.9
	44	2.5	3.8	8.26	14.9	45.9	55.5
	45	3.1	5.1	8.15	14.7	43.2	53.0
10	46	1.6	2.9	8.32	15.0	44.9	54.0
	47	2.1	3.2	8.25	15.2	44.7	54.2
	48	2.3	4.3	8.36	15.4	45.5	54.4
	49	1.1	6.4	8.52	15.8	45.1	53.0
	50	1.8	3.7	8.05	15.1	45.3	56.3
2.5	51	0.3	3.7	8.11	15.2	43.2	53.3
	52	0.9	4.9	8.60	16.0	46.6	54.2
	53	0.3	4.5	8.55	15.7	46.5	54.4
	54	0.8	3.9	8.39	15.8	44.6	53.2
	55	0.8	3.1	8.34	15.4	47.0	56.3
0	56	0.3	5.4	8.36	15.5	44.8	53.6
	57	0.7	3.5	8.34	15.1	46.1	55.3
	58	0.9	5.1	8.74	16.1	47.3	54.1
	59	1.2	4.4	8.50	15.8	46.4	54.5
	60	0.6	4.2	8.29	15.4	44.8	54.0

Hematology Data/Males
14 Days

DOSE GROUPS (mg DNB/kg) diet	ANIMALS #	MCH picogm	MCHC g/dl	PLAT thsn/ cu mm	NEUTRO- PHILS %	LYMPHO- CYTES %	RETIC %	HEINZ BODIES %
150	31	20.0	30.5	968	11.9	84.5	12.0	0.0
	32	19.9	29.8	962	14.1	82.9	10.4	0.0
	33	19.6	31.9	840	15.7	80.2	7.8	0.0
	34	19.6	29.6	980	23.2	72.8	13.1	0.0
	35	19.4	29.2	985	14.0	82.7	11.2	0.0
75	36	18.8	31.6	945	13.9	84.1	7.0	0.0
	37	18.5	30.9	*	19.6	76.9	9.9	0.0
	38	18.6	30.2	941	15.6	81.9	8.0	0.0
	39	19.1	32.1	967	11.5	86.1	10.5	0.0
	40	18.6	32.3	1083	14.4	83.0	10.2	0.0
25	41	17.8	33.2	970	17.3	80.2	4.5	0.0
	42	17.8	32.8	918	16.9	81.4	4.1	0.0
	43	18.0	34.0	1027	18.6	79.0	4.3	0.0
	44	18.0	32.4	866	21.1	76.4	3.8	0.0
	45	18.0	34.0	948	14.1	83.1	3.9	0.0
10	46	18.1	33.5	914	17.3	79.8	2.3	0.0
	47	18.4	34.0	878	18.6	78.8	2.8	0.0
	48	18.5	34.0	899	19.1	78.1	2.7	0.0
	49	18.6	35.1	796	12.3	85.4	2.6	0.0
	50	18.8	33.4	928	13.4	84.5	2.9	0.0
2.5	51	18.7	35.1	913	19.5	78.1	2.5	0.0
	52	18.6	34.4	*	17.5	79.0	2.6	0.0
	53	18.4	33.8	*	21.6	75.7	2.2	0.0
	54	18.8	35.4	900	16.0	81.3	1.9	0.0
	55	18.4	32.7	884	18.9	78.3	2.3	0.0
0	56	18.5	34.6	861	16.6	80.9	2.4	0.0
	57	18.1	32.7	818	24.4	71.3	2.3	0.0
	58	18.4	33.9	828	16.3	81.0	2.6	0.0
	59	18.6	34.1	851	20.1	77.6	2.5	0.0
	60	18.6	34.4	889	24.6	72.2	3.3	0.0

* = Quantity not sufficient

APPENDIX E

CLINICAL CHEMISTRY
DATA

Clinical Chemistries/Females
14 Days

DOSE GROUPS (mg DNB/kg)	ANIMALS #	GLUCOSE mg/dl	BUN mg/dl	CREAT mg/dl	SODIUM mmol/l	POTASSIUM mmol/l	CHOL mg/dl
150	1	111	21	0.5	141	5.4	86
	2	70	23	0.6	146	4.0	90
	3	140	24	0.6	142	5.0	86
	4	91	24	0.5	144	4.5	76
	5	141	28	0.5	143	5.5	80
75	6	117	29	0.6	141	4.8	79
	7	96	23	0.5	143	5.3	99
	8	97	24	0.6	141	6.0	97
	9	64	24	0.7	140	5.5	83
	10	99	25	0.6	142	4.6	90
25	11	106	25	0.5	142	4.8	81
	12	120	21	0.5	143	4.0	88
	13	77	23	0.6	142	5.0	92
	14	141	26	0.5	143	4.0	106
	15	135	20	0.5	141	4.8	85
10	16	97	24	0.6	144	4.5	96
	17	96	20	0.5	143	4.2	98
	18	73	21	0.5	142	4.1	85
	19	155	30	0.5	144	4.8	90
	20	95	27	0.6	142	4.5	102
2.5	21	100	22	0.5	142	4.7	102
	22	125	27	0.5	143	4.9	104
	23	119	22	0.5	142	4.3	101
	24	77	22	0.5	143	4.6	97
	25	104	26	0.5	143	4.6	97
0	26	114	21	0.5	143	4.3	92
	27	107	23	0.5	142	4.5	88
	28	82	20	0.5	142	5.0	94
	29	146	23	0.5	141	4.8	87
	30	119	19	0.5	142	4.3	85

Clinical Chemistries/Females
14 Days

DOSE GROUPS	ANIMALS	AST	ALT	PHOS	AP	Ca	TOTAL BILIRUBIN	TOTAL PROTEIN	ALB	TRIG
(mg DNB/kg) diet	#	U/L	U/L	mg/dl	U/L	mg/dl	mg/dl	g/dl	g/dl	mg/dl
150	1	121	40	10.6	139	10.6	0.1	5.8	4.3	31
	2	128	45	11.4	162	10.4	0.1	6.0	4.8	29
	3	101	43	12.1	147	10.5	0.2	5.6	4.3	18
	4	129	63	8.7	278	10.3	0.2	5.6	4.4	61
	5	94	75	10.5	218	10.6	0.1	5.5	4.4	34
75	6	171	45	12.0	190	10.3	0.2	5.5	4.1	22
	7	116	41	10.8	155	10.8	0.2	6.2	4.8	46
	8	174	40	13.9	131	10.9	0.2	6.2	4.6	36
	9	187	52	14.1	125	10.1	0.2	5.9	4.5	27
	10	112	31	13.9	151	10.2	0.1	5.7	4.4	26
25	11	104	38	11.7	151	10.3	0.1	5.9	4.5	29
	12	105	37	10.7	180	10.2	0.1	5.9	4.3	26
	13	112	35	12.4	133	10.6	0.2	6.0	4.3	31
	14	115	44	8.5	184	10.4	0.1	6.2	4.6	29
	15	112	47	9.7	152	10.3	0.1	5.4	4.1	30
10	16	126	39	14.2	161	10.4	0.1	5.7	4.2	18
	17	134	32	8.4	146	10.1	0.1	5.9	4.4	34
	18	148	35	10.5	136	10.3	0.1	5.8	4.1	31
	19	117	50	9.5	157	10.4	0.1	6.0	4.5	29
	20	143	34	11.1	171	10.3	0.2	5.8	4.4	29
2.5	21	125	35	12.1	158	10.2	0.1	5.7	4.2	24
	22	129	58	10.3	138	10.7	0.1	6.1	4.4	39
	23	98	51	9.0	195	10.3	0.1	5.6	4.2	49
	24	130	42	11.0	153	10.4	0.1	5.9	4.4	35
	25	150	50	13.0	180	10.5	0.1	5.6	4.1	33
0	26	113	40	10.5	155	10.6	0.1	5.9	4.4	36
	27	119	57	11.1	170	10.3	0.1	5.3	4.1	38
	28	125	41	11.5	187	10.7	0.1	5.9	4.4	44
	29	116	48	9.2	158	10.2	0.2	5.4	4.1	42
	30	111	48	10.7	182	10.2	0.1	5.7	4.3	30

Clinical Chemistries/Males
14 Days

DOSE GROUPS (mg DNB/kg)	ANIMALS #	GLUCOSE mg/dl	BUN mg/dl	CREAT mg/dl	SODIUM mmol/l	POTASSIUM mmol/l	CHOL mg/dl
150	31	207	22	0.6	142	6.3	72
	32	131	21	0.6	142	4.1	68
	33	113	22	0.6	142	4.9	71
	34	113	19	0.6	142	5.3	61
	35	160	20	0.6	143	5.1	63
75	36	158	23	0.7	142	5.0	55
	37	122	24	0.6	143	5.0	62
	38	181	22	0.6	141	5.9	48
	39	186	24	0.7	142	4.8	59
	40	187	24	0.6	140	4.7	63
25	41	153	23	0.7	144	4.6	53
	42	154	26	0.7	142	4.7	51
	43	186	23	0.7	141	4.8	55
	44	133	22	0.6	144	4.9	53
	45	157	19	0.6	142	5.2	44
10	46	122	18	0.6	144	4.6	55
	47	119	20	0.5	144	4.1	57
	48	164	18	0.6	144	4.8	59
	49	173	21	0.6	143	4.6	57
	50	172	21	0.6	141	4.6	60
2.5	51	160	21	0.5	141	4.1	58
	52	177	19	0.6	144	4.8	49
	53	156	19	0.6	144	5.4	57
	54	158	21	0.6	143	5.2	50
	55	110	20	0.6	145	5.0	47
0	56	159	20	0.6	143	4.4	48
	57	160	19	0.6	144	5.0	52
	58	161	22	0.7	143	4.8	51
	59	155	20	0.6	141	4.8	57
	60	116	19	0.6	143	4.3	54

Clinical Chemistries/Males
14 Days

DOSE GROUPS (mg DNB/kg)	ANIMALS	AST	ALT	PHOS	AP	Ca	TOTAL BILIRUBIN	TOTAL PROTEIN	ALB	TRIG
diet	#	U/L	U/L	mg/dl	U/L	mg/dl	mg/dl	g/dl	g/dl	mg/dl
150	31	102	61	12.3	162	11.6	0.2	6.8	4.9	44
	32	108	51	11.0	242	11.3	0.1	6.9	5.0	103
	33	135	52	11.0	170	10.8	0.2	6.8	5.0	45
	34	122	37	13.4	174	11.4	0.2	6.6	5.1	46
	35	98	47	11.7	184	11.2	0.1	6.7	4.9	44
75	36	130	59	10.9	187	10.7	0.1	6.3	4.8	34
	37	121	41	12.6	191	11.6	0.2	6.7	5.0	79
	38	193	99	12.5	187	11.0	0.2	6.2	4.5	54
	39	114	55	9.7	181	10.9	0.1	6.4	4.8	40
	40	107	51	10.5	201	10.3	0.2	6.2	4.6	79
25	41	151	62	10.7	186	10.8	0.1	6.3	4.7	86
	42	329	180	12.1	192	10.2	0.1	6.3	4.5	51
	43	121	47	9.5	188	10.4	0.1	6.5	4.8	99
	44	185	62	12.7	198	10.6	0.1	6.3	4.7	47
	45	131	55	11.5	190	10.6	0.1	6.0	4.4	45
10	46	139	38	12.1	200	10.8	0.1	6.4	4.6	68
	47	122	39	11.1	187	10.4	0.1	6.2	4.4	65
	48	115	43	11.0	191	11.2	0.1	6.5	4.7	100
	49	124	47	10.1	169	10.8	0.1	6.0	4.6	95
	50	118	62	10.7	205	10.7	0.1	6.0	4.3	69
2.5	51	139	60	9.8	174	10.3	0.1	6.1	4.4	81
	52	113	45	11.1	204	10.9	0.1	6.2	4.5	70
	53	131	43	11.6	205	11.1	0.1	6.4	4.7	61
	54	152	61	11.3	184	10.2	0.1	6.2	4.5	72
	55	187	46	12.4	200	10.9	0.1	6.2	4.5	58
0	56	149	55	9.6	187	10.4	0.1	6.0	4.5	72
	57	121	47	10.7	198	10.9	0.1	6.3	4.6	40
	58	119	49	10.3	209	10.6	0.1	6.4	4.6	101
	59	140	69	10.8	186	10.4	0.1	6.0	4.5	70
	60	176	67	11.2	187	10.8	0.1	6.3	4.5	86

APPENDIX F

CLINICAL OBSERVATIONS

Clinical Observations

Date

6-21-94	All animals appear normal.
6-22-94	All animals appear normal.
6-23-94	All animals appear normal.
6-24-94	All animals appear normal.
6-27-94	All animals appear normal.
6-28-94	All animals appear normal except animal number 10-50 who has a scab associated with the implant site.
6-29-94	All animals appear normal.
6-30-94	All animals appear normal.
7-1-94	All animals appear normal.
7-5-94	All animals appear normal.
7-6-94	All animals appear normal.
7-7-94	All animals appear normal.

APPENDIX G

GROSS AND
HISTOPATHOLOGY
DATA

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
BRAIN	# EX 5	5	5	5	5	5
Vacuolization	4 80.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Microgliosis	4 80.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Necrosis	3 60.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Hemorrhage	0 0.0	0 0.0	1 20.0	0 0.0	0 0.0	0 0.0
SCIATIC NERVE	# EX 5	0	0	0	0	5
SPINAL CORD	# EX 5	0	0	0	0	5
SALIVARY GLAND	# EX 5	0	0	0	0	5
Inflammation, Chronic/Active	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	1 20.0
PANCREAS	# EX 5	0	0	0	0	5
MANDIBULAR LYMPH NODE	# EX 5	0	0	0	0	5
ZYMBAL'S GLAND	# EX 5	0	0	0	0	5
PITUITARY	# EX 4	0	0	0	0	5
ADRENALS	# EX 5	0	0	0	0	5
THYROID	# EX 5	0	0	0	0	5
PARATHYROID	# EX 5	0	0	0	0	4
TRACHEA	# EX 5	0	0	0	0	5
ESOPHAGUS	# EX 5	0	0	0	0	5

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4	5	6						
NUMBER OF ANIMALS:	5	5	5	5	5	5						
	#	%	#	%	#	%	#	%	#	%		
THYMUS	# EX 5		0		0		0		0		5	
HEART	# EX 5		0		0		0		0		5	
COLON	# EX 5		0		0		0		0		5	
JEJUNUM	# EX 5		0		0		0		0		5	
AORTA	# EX 5		0		0		0		0		5	
LIVER	# EX 5		0		0		0		0		5	
SPLEEN	# EX 5		5		5		5		5		5	
Hyperplasia, Erythroid Cell	5	100.0	5	100.0	4	80.0	0	0.0	0	0.0	0	0.0
Pigmentation, NOS	5	100.0	5	100.0	0	0.0	0	0.0	0	0.0	0	0.0
Fibrosis	0	0.0	1	20.0	1	20.0	0	0.0	1	20.0	0	0.0
Depletion, Lymphoid	2	40.0	3	60.0	0	0.0	0	0.0	0	0.0	0	0.0
TONGUE	# EX 5		0		0		0		0		5	
SKELETAL MUSCLE	# EX 5		0		0		0		0		5	
LUNGS	# EX 5		0		0		0		0		5	
Inflammation, Chronic	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	20.0
KIDNEYS	# EX 5		0		0		0		0		5	
Mineralization, NOS	5	100.0	0	0.0	0	0.0	0	0.0	0	0.0	3	60.0
URINARY BLADDER	# EX 5		0		0		0		0		5	

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
STOMACH	# EX 5	0	0	0	0	5
DUODENUM	# EX 5	0	0	0	0	5
ILEUM	# EX 5	0	0	0	0	5
CECUM	# EX 5	0	0	0	0	4
RECTUM	# EX 5	0	0	0	0	5
MESENTERIC LYMPH NODE	# EX 5	0	0	0	0	4
OVARIES	# EX 5	1	0	0	0	5
Cyst, NOS	0 0.0	1 100.0	0 0.0	0 0.0	0 0.0	0 0.0
UTERUS	# EX 5	0	0	0	0	5
Dilatation, Bilateral	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
SKIN	# EX 5	0	0	0	0	5
CLITORAL GLAND	# EX 5	0	0	0	0	5
Inflammation, Chronic/Active	3 60.0	0 0.0	0 0.0	0 0.0	0 0.0	2 40.0
Lymphocytic Infiltrates	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	2 40.0
EYES	# EX 5	0	0	0	0	5
Microgranuloma, Cornea	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
HARDERIAN GLAND	# EX 5	0	0	0	0	5
Lymphocytic Infiltrates	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

SEX: FEMALE

DAYS ON TEST: ALL

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5

	#	%	#	%	#	%	#	%	#	%	#	%	
FEMUR/STERNUM	# EX	5	0	0	0	0	0	0	0	0.0	5		
Hyperplasia, Erythroid Cell		5	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NASAL	# EX	5	0	0	0	0	0	0	0		5		
MAMMARY GLAND	# EX	5	0	0	0	0	0	0	0		5		

Incidence Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
BRAIN	# EX 5	5	5	5	5	5
Vacuolization	4 80.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Microgliosis	4 80.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Necrosis	4 80.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
SCIATIC NERVE	# EX 5	0	0	0	0	5
SPINAL CORD	# EX 5	0	0	0	0	5
SALIVARY GLAND	# EX 5	0	0	0	0	5
PANCREAS	# EX 5	0	0	0	0	5
MANDIBULAR LYMPH NODE	# EX 5	2	0	0	0	5
Hyperplasia, Lymphoid	2 40.0	1 50.0	0 0.0	0 0.0	0 0.0	1 20.0
Hemorrhage	0 0.0	2 100.0	0 0.0	0 0.0	0 0.0	0 0.0
ZYMBAL'S GLAND	# EX 5	0	0	0	0	5
PITUITARY	# EX 3	0	0	0	0	5
ADRENALS	# EX 5	0	0	0	0	5
THYROID	# EX 5	0	0	0	0	5
PARATHYROID	# EX 2	0	0	0	0	4
TRACHEA	# EX 5	0	0	0	0	5
ESOPHAGUS	# EX 5	0	0	0	0	5

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12						
NUMBER OF ANIMALS:	5	5	5	5	5	5						
	#	%	#	%	#	%	#	%	#	%	#	%
THYMUS	# EX 5		0		0		0		0		5	
Hemorrhage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	20.0
HEART	# EX 5		0		0		0		0		5	
COLON	# EX 5		0		0		0		0		5	
JEJUNUM	# EX 5		0		0		0		0		5	
AORTA	# EX 5		0		0		0		0		5	
LIVER	# EX 5		0		0		0		0		5	
SPLEEN	# EX 5		5		5		5		5		5	
Hyperplasia, Erythroid Cell	5	100.0	5	100.0	4	80.0	0	0.0	0	0.0	0	0.0
Pigmentation, NOS	5	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Fibrosis	0	0.0	0	0.0	1	20.0	0	0.0	0	0.0	0	0.0
TONGUE	# EX 5		0		0		0		0		5	
SKELETAL MUSCLE	# EX 5		0		0		0		0		5	
LUNGS	# EX 5		0		0		0		0		5	
Inflammation, Chronic	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	20.0
KIDNEYS	# EX 5		5		5		5		5		5	
Mineralization, NOS	5	100.0	5	100.0	5	100.0	5	100.0	5	100.0	5	100.0
Hyaline Droplets	5	100.0	4	80.0	1	20.0	0	0.0	0	0.0	0	0.0
Regeneration, Tubular	3	60.0	3	60.0	4	80.0	3	60.0	1	20.0	1	20.0
Degeneration, Tubular	5	100.0	5	100.0	5	100.0	4	80.0	5	100.0	5	100.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
URINARY BLADDER	# EX 5	0	0	1	0	5
Urolith, NOS	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
PROSTATE	# EX 5	0	0	1	0	5
STOMACH	# EX 5	0	0	1	0	5
Inflammation, Chronic/Active	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
DUODENUM	# EX 5	0	0	1	0	5
ILEUM	# EX 5	0	0	1	0	5
CECUM	# EX 5	0	0	1	0	5
RECTUM	# EX 5	0	0	1	0	5
MESENTERIC LYMPH NODE	# EX 5	0	0	1	0	5
TESTES	# EX 5	5	5	5	5	5
Degeneration, Seminiferous Tubules	5 100.0	5 100.0	0 0.0	0 0.0	0 0.0	0 0.0
EPIDIDYMIDES	# EX 5	0	0	0	0	5
Hypospermia	5 100.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
SEMINAL VESICLE	# EX 5	0	0	0	0	5
SKIN	# EX 5	0	0	0	0	5
PREPUTIAL GLAND	# EX 5	0	0	0	0	5
Inflammation, Chronic/Active	1 20.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
Lymphocytic Infiltrates	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0	4 80.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# %	# %	# %	# %	# %	# %
EYES	# EX 5	0	0	0	0	5
Microgranuloma, Cornea	2 40.0	0 0.0	0 0.0	0 0.0	0 0.0	1 20.0
HARDERIAN GLAND	# EX 5	0	0	0	0	5
FEMUR/STERNUM	# EX 5	0	0	0	0	5
Hyperplasia, Erythroid Cell	5 100.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
NASAL	# EX 5	0	0	0	0	5
MAMMARY GLAND	# EX 5	0	0	0	0	5

Incidence Calculated by No. of Tissues Scored

(END OF REPORT)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
BRAIN	# EX 5	# SEV 5	# SEV 5	# SEV 5	# SEV 5	# SEV 5
Vacuolization	4 1.40	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Microgliosis	4 1.80	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Necrosis	3 0.80	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Hemorrhage	0 0.00	0 0.00	1 0.20	0 0.00	0 0.00	0 0.00
SCIATIC NERVE	# EX 5	0	0	0	0	5
SPINAL CORD	# EX 5	0	0	0	0	5
SALIVARY GLAND	# EX 5	0	0	0	0	5
Inflammation, Chronic/Active	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	1 0.20
PANCREAS	# EX 5	0	0	0	0	5
MANDIBULAR LYMPH NODE	# EX 5	0	0	0	0	5
ZYMBAL'S GLAND	# EX 5	0	0	0	0	5
PITUITARY	# EX 4	0	0	0	0	5
ADRENALS	# EX 5	0	0	0	0	5
THYROID	# EX 5	0	0	0	0	5
PARATHYROID	# EX 5	0	0	0	0	4
TRACHEA	# EX 5	0	0	0	0	5
ESOPHAGUS	# EX 5	0	0	0	0	5

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
THYMUS	# EX 5	0	0	0	0	5
HEART	# EX 5	0	0	0	0	5
COLON	# EX 5	0	0	0	0	5
JEJUNUM	# EX 5	0	0	0	0	5
AORTA	# EX 5	0	0	0	0	5
LIVER	# EX 5	0	0	0	0	5
SPLEEN	# EX 5	5	5	5	5	5
Hyperplasia, Erythroid Cell	5 2.80	5 3.20	4 1.00	0 0.00	0 0.00	0 0.00
Pigmentation, NOS	5 2.00	5 1.00	0 0.00	0 0.00	0 0.00	0 0.00
Fibrosis	0 0.00	1 0.20	1 0.40	0 0.00	1 0.20	0 0.00
Depletion, Lymphoid	2 0.60	3 1.00	0 0.00	0 0.00	0 0.00	0 0.00
TONGUE	# EX 5	0	0	0	0	5
SKELETAL MUSCLE	# EX 5	0	0	0	0	5
LUNGS	# EX 5	0	0	0	0	5
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	1 0.20
KIDNEYS	# EX 5	0	0	0	0	5
Mineralization, NOS	5 1.00	0 0.00	0 0.00	0 0.00	0 0.00	3 0.60
URINARY BLADDER	# EX 5	0	0	0	0	5
STOMACH	# EX 5	0	0	0	0	5

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
DUODENUM	# EX 5	0	0	0	0	5
ILEUM	# EX 5	0	0	0	0	5
CECUM	# EX 5	0	0	0	0	4
RECTUM	# EX 5	0	0	0	0	5
MESENTERIC LYMPH NODE	# EX 5	0	0	0	0	4
OVARIES	# EX 5	1	0	0	0	5
UTERUS	# EX 5	0	0	0	0	5
Dilatation, Bilateral	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
SKIN	# EX 5	0	0	0	0	5
CLITORAL GLAND	# EX 5	0	0	0	0	5
Inflammation, Chronic/Active	3 0.80	0 0.00	0 0.00	0 0.00	0 0.00	2 0.60
Lymphocytic Infiltrates	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	2 0.40
EYES	# EX 5	0	0	0	0	5
Microgranuloma, Cornea	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
HARDERIAN GLAND	# EX 5	0	0	0	0	5
Lymphocytic Infiltrates	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
FEMUR/STERNUM	# EX 5	0	0	0	0	5
Hyperplasia, Erythroid Cell	5 2.40	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
NASAL	# EX 5	0	0	0	0	5

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4	5	6
NUMBER OF ANIMALS:	5	5	5	5	5	5

	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
MAMMARY GLAND	# EX	5	0	5	0	5	0	5	0	5

 Severity Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX 5	5	5	5	5	5
Vacuolization	4 1.60	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Microgliosis	4 1.80	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Necrosis	4 1.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
SCIATIC NERVE	# EX 5	0	0	0	0	5
SPINAL CORD	# EX 5	0	0	0	0	5
SALIVARY GLAND	# EX 5	0	0	0	0	5
PANCREAS	# EX 5	0	0	0	0	5
MANDIBULAR LYMPH NODE	# EX 5	2	0	0	0	5
Hyperplasia, Lymphoid	2 0.80	1 1.00	0 0.00	0 0.00	0 0.00	1 0.40
Hemorrhage	0 0.00	2 1.50	0 0.00	0 0.00	0 0.00	0 0.00
ZYMBAL'S GLAND	# EX 5	0	0	0	0	5
PITUITARY	# EX 3	0	0	0	0	5
ADRENALS	# EX 5	0	0	0	0	5
THYROID	# EX 5	0	0	0	0	5
PARATHYROID	# EX 2	0	0	0	0	4
TRACHEA	# EX 5	0	0	0	0	5
ESOPHAGUS	# EX 5	0	0	0	0	5

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
	# SEV	# SEV	# SEV	# SEV	# SEV	# SEV
THYMUS	# EX 5	0	0	0	0	5
Hemorrhage	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	1 0.20
HEART	# EX 5	0	0	0	0	5
COLON	# EX 5	0	0	0	0	5
JEJUNUM	# EX 5	0	0	0	0	5
AORTA	# EX 5	0	0	0	0	5
LIVER	# EX 5	0	0	0	0	5
SPLEEN	# EX 5	5	5	5	5	5
Hyperplasia, Erythroid Cell	5 3.00	5 3.00	4 1.40	0 0.00	0 0.00	0 0.00
Pigmentation, NOS	5 1.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Fibrosis	0 0.00	0 0.00	1 0.20	0 0.00	0 0.00	0 0.00
TONGUE	# EX 5	0	0	0	0	5
SKELETAL MUSCLE	# EX 5	0	0	0	0	5
LUNGS	# EX 5	0	0	0	0	5
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	1 0.20
KIDNEYS	# EX 5	5	5	5	5	5
Mineralization, NOS	5 1.60	5 1.20	5 1.20	5 1.20	5 1.00	5 1.40
Hyaline Droplets	5 2.00	4 1.00	1 0.20	0 0.00	0 0.00	0 0.00
Regeneration, Tubular	3 1.00	3 0.60	4 0.80	3 0.60	1 0.20	1 0.20
Degeneration, Tubular	5 2.40	5 1.40	5 1.60	4 0.80	5 1.20	5 1.60

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5
URINARY BLADDER	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
PROSTATE	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
STOMACH	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
Inflammation, Chronic/Active	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
DUODENUM	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
ILEUM	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
CECUM	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
RECTUM	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
MESENTERIC LYMPH NODE	# EX 5	# SEV 0	# SEV 0	# SEV 1	# SEV 0	# SEV 5
TESTES	# EX 5	# SEV 5	# SEV 5	# SEV 5	# SEV 5	# SEV 5
Degeneration, Seminiferous Tubules	5 4.00	5 4.00	0 0.00	0 0.00	0 0.00	0 0.00
EPIDIDYMIDES	# EX 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0	# SEV 5
Hypospermia	5 4.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
SEMINAL VESICLE	# EX 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0	# SEV 5
SKIN	# EX 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0	# SEV 5
PREPUTIAL GLAND	# EX 5	# SEV 0	# SEV 0	# SEV 0	# SEV 0	# SEV 5
Inflammation, Chronic/Active	1 0.20	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
Lymphocytic Infiltrates	2 0.40	0 0.00	0 0.00	0 0.00	0 0.00	4 0.80

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	7	8	9	10	11	12
NUMBER OF ANIMALS:	5	5	5	5	5	5

	#	SEV	#	SEV	#	SEV	#	SEV	#	SEV
EYES	# EX	5	0	0	0	0	0	0	5	
Microgranuloma, Cornea		2 0.40	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	1 0.20		
HARDERIAN GLAND	# EX	5	0	0	0	0	0	5		
FEMUR/STERNUM	# EX	5	0	0	0	0	0	5		
Hyperplasia, Erythroid Cell		5 2.40	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00		
NASAL	# EX	5	0	0	0	0	0	5		
MAMMARY GLAND	# EX	5	0	0	0	0	0	5		

Severity Calculated by No. of Tissues Scored

(END OF REPORT)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 1
 SEX: FEMALE

ANIMAL ID:	1	2	3	4	5
BRAIN	N				
Vacuolization	-	2	2	1	2
Microgliosis	-	2	3	2	2
Necrosis	-	-	2	1	1
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	U	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	N	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 1
 SEX: FEMALE

ANIMAL ID:	1	2	3	4	5
HEART	N	N	N	N	N
COLON	N	N	N	N	N
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN					
Hyperplasia, Erythroid Cell	3	2	3	3	3
Pigmentation, NOS	2	2	2	2	2
Depletion, Lymphoid	2	-	1	-	-
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNGS	N	N	N	N	N
KIDNEYS					
Mineralization, NOS	1	1	1	1	1
URINARY BLADDER	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 1
 SEX: FEMALE

ANIMAL ID:	1	2	3	4	5
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N
OVARIES	N	N	N	N	N
UTERUS	N	N	N		N
Dilatation, Bilateral	-	-	-	1	-
SKIN	N	N	N	N	N
CLITORAL GLAND		N	N		
Inflammation, Chronic/Active	1	-	-	1	2
EYES		N	N	N	N
Microgranuloma, Cornea	1	-	-	-	-
HARDERIAN GLAND	N	N	N	N	
Lymphocytic Infiltrates	-	-	-	-	1
FEMUR/STERNUM					
Hyperplasia, Erythroid Cell	3	3	2	2	2
NASAL	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 2
 SEX: FEMALE

ANIMAL ID:	6	7	8	9	10
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 2
SEX: FEMALE

ANIMAL ID:	6	7	8	9	10
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN					
Hyperplasia, Erythroid Cell	4	3	3	3	3
Pigmentation, NOS	1	1	1	1	1
Fibrosis	-	1	-	-	-
Depletion, Lymphoid	2	2	1	-	-
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 2
 SEX: FEMALE

ANIMAL ID:	6	7	8	9	10
MESENTERIC LYMPH NODE	*	*	*	*	*
OVARIES	*	*		*	*
Cyst, NOS	-	-	P	-	-
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 3
 SEX: FEMALE

ANIMAL ID:	11	12	13	14	15
BRAIN		N	N	N	N
Hemorrhage	1	-	-	-	-
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 3
 SEX: FEMALE

ANIMAL ID:	11	12	13	14	15
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN					N
Hyperplasia, Erythroid Cell	2	1	1	1	-
Fibrosis	-	2	-	-	-
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 3
SEX: FEMALE

ANIMAL ID:	11	12	13	14	15
OVARIES	*	*	*	*	*
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 4
 SEX: FEMALE

ANIMAL ID:	16	17	18	19	20
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 4
 SEX: FEMALE

ANIMAL ID:	16	17	18	19	20
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	N	N	N	N	N
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
OVARIES	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 4
SEX: FEMALE

ANIMAL ID:	16	17	18	19	20
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 5
 SEX: FEMALE

ANIMAL ID:	21	22	23	24	25
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 5
 SEX: FEMALE

ANIMAL ID:	21	22	23	24	25
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN		N	N	N	N
Fibrosis	1	-	-	-	-
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS	*	*	*	*	*
URINARY BLADDER	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
OVARIES	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 5
SEX: FEMALE

ANIMAL ID:	21	22	23	24	25
UTERUS	*	*	*	*	*
SKIN	*	*	*	*	*
CLITORAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 6
 SEX: FEMALE

ANIMAL ID:	26	27	28	29	30
BRAIN	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND		N	N	N	N
Inflammation, Chronic/Active	1	-	-	-	-
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	U	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS	N	N	N	N	N
HEART	N	N	N	N	N
COLON	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 6
SEX: FEMALE

ANIMAL ID:	26	27	28	29	30
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN	N	N	N	N	N
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNGS Inflammation, Chronic	-	-	-	-	1
KIDNEYS Mineralization, NOS	1	1	-	-	1
URINARY BLADDER	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N
CECUM	N	N	N	A	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	U

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 6
 SEX: FEMALE

ANIMAL ID:	26	27	28	29	30
OVARIES	N	N	N	N	N
UTERUS	N	N	N	N	N
SKIN	N	N	N	N	N
CLITORAL GLAND			N		
Inflammation, Chronic/Active	2	-	-	-	1
Lymphocytic Infiltrates	-	1	-	1	-
EYES	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N
FEMUR/STERNUM	N	N	N	N	N
NASAL	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(Report Continued)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	31	32	33	34	35
BRAIN			N		
Vacuolization	1	2	-	3	2
Microgliosis	2	2	-	3	2
Necrosis	1	1	-	2	1
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N		N	
Hyperplasia, Lymphoid	-	-	2	-	2
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	U	U	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	U	N	U	N	U
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 7
 SEX: MALE

ANIMAL ID:	31	32	33	34	35
THYMUS	N	N	N	N	N
HEART	N	N	N	N	N
COLON	N	N	N	N	N
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN					
Hyperplasia, Erythroid Cell	3	3	3	3	3
Pigmentation, NOS	1	1	1	1	1
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNGS	N	N	N	N	N
KIDNEYS					
Mineralization, NOS	2	2	2	1	1
Hyaline Droplets	2	2	2	2	2
Regeneration, Tubular	2	-	2	-	1
Degeneration, Tubular	3	3	2	2	2
URINARY BLADDER	N			N	N
Urolith, NOS	-	P	P	-	-
PROSTATE	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 7
 SEX: MALE

ANIMAL ID:	31	32	33	34	35
STOMACH		N	N	N	N
Inflammation, Chronic/Active	1	-	-	-	-
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N
TESTES					
Degeneration, Seminiferous Tubules	4	4	4	4	4
EPIDIDYMIDES					
Hypospermia	4	4	4	4	4
SEMINAL VESICLE	N	N	N	N	N
SKIN	N	N	N	N	N
PREPUTIAL GLAND	N				N
Inflammation, Chronic/Active	-	1	-	-	-
Lymphocytic Infiltrates	-	-	1	1	-
EYES		N	N	N	
Microgranuloma, Cornea	1	-	-	-	1
HARDERIAN GLAND	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 7
SEX: MALE

ANIMAL ID:	31	32	33	34	35
FEMUR/STERNUM					
Hyperplasia, Erythroid Cell	2	3	2	2	3
NASAL	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 8
 SEX: MALE

ANIMAL ID:	36	37	38	39	40
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*			*
Hyperplasia, Lymphoid	-	-	2	-	-
Hemorrhage	-	-	1	2	-
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 8
 SEX: MALE

ANIMAL ID:	36	37	38	39	40
COLON	*	*	*	*	*
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN					
Hyperplasia, Erythroid Cell	3	3	3	3	3
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS					
Mineralization, NOS	1	1	2	1	1
Hyaline Droplets	1	1	2	1	-
Regeneration, Tubular	1	-	1	1	-
Degeneration, Tubular	1	2	2	1	1
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 8
 SEX: MALE

ANIMAL ID:	36	37	38	39	40
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
TESTES					
Degeneration, Seminiferous Tubules	4	4	4	4	4
EPIDIDYMIDES	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*
SKIN	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 9
 SEX: MALE

ANIMAL ID:	41	42	43	44	45
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 9
 SEX: MALE

ANIMAL ID:	41	42	43	44	45
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN					N
Hyperplasia, Erythroid Cell	2	2	2	1	-
Fibrosis	-	-	-	1	-
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS					
Mineralization, NOS	2	1	1	1	1
Hyaline Droplets	1	-	-	-	-
Regeneration, Tubular	1	1	1	-	1
Degeneration, Tubular	2	1	2	2	1
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 9
 SEX: MALE

ANIMAL ID:	41	42	43	44	45
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*
TESTES	N	N	N	N	N
EPIDIDYMIDES	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*
SKIN	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 10
 SEX: MALE

ANIMAL ID:	46	47	48	49	50
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 10
 SEX: MALE

ANIMAL ID:	46	47	48	49	50
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	N	N	N	N	N
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS					
Mineralization, NOS	1	1	2	1	1
Regeneration, Tubular	1	1	1	-	-
Degeneration, Tubular	1	1	1	-	1
URINARY BLADDER	*	*	*	N	*
PROSTATE	*	*	*	N	*
STOMACH	*	*	*	N	*
DUODENUM	*	*	*	N	*
ILEUM	*	*	*	N	*
CECUM	*	*	*	N	*
RECTUM	*	*	*	N	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 10
 SEX: MALE

ANIMAL ID:	46	47	48	49	50
MESENTERIC LYMPH NODE	*	*	*	N	*
TESTES	N	N	N	N	N
EPIDIDYMIDES	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*
SKIN	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 11
 SEX: MALE

ANIMAL ID:	51	52	53	54	55
BRAIN	N	N	N	N	N
SCIATIC NERVE	*	*	*	*	*
SPINAL CORD	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*
PANCREAS	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*
PITUITARY	*	*	*	*	*
ADRENALS	*	*	*	*	*
THYROID	*	*	*	*	*
PARATHYROID	*	*	*	*	*
TRACHEA	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*
THYMUS	*	*	*	*	*
HEART	*	*	*	*	*
COLON	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 11
 SEX: MALE

ANIMAL ID:	51	52	53	54	55
JEJUNUM	*	*	*	*	*
AORTA	*	*	*	*	*
LIVER	*	*	*	*	*
SPLEEN	N	N	N	N	N
TONGUE	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*
LUNGS	*	*	*	*	*
KIDNEYS					
Mineralization, NOS	1	1	1	1	1
Regeneration, Tubular	-	-	-	-	1
Degeneration, Tubular	2	1	1	1	1
URINARY BLADDER	*	*	*	*	*
PROSTATE	*	*	*	*	*
STOMACH	*	*	*	*	*
DUODENUM	*	*	*	*	*
ILEUM	*	*	*	*	*
CECUM	*	*	*	*	*
RECTUM	*	*	*	*	*

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 11
SEX: MALE

ANIMAL ID:	51	52	53	54	55
MESENTERIC LYMPH NODE	*	*	*	*	*
TESTES	N	N	N	N	N
EPIDIDYMIDES	*	*	*	*	*
SEMINAL VESICLE	*	*	*	*	*
SKIN	*	*	*	*	*
PREPUTIAL GLAND	*	*	*	*	*
EYES	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*
NASAL	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 12
 SEX: MALE

ANIMAL ID:	56	57	58	59	60
BRAIN	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N
SPINAL CORD	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N
PANCREAS	N	N	N	N	N
MANDIBULAR LYMPH NODE Hyperplasia, Lymphoid	N	N	N	N	2
ZYMBAL'S GLAND	N	N	N	N	N
PITUITARY	N	N	N	N	N
ADRENALS	N	N	N	N	N
THYROID	N	N	N	N	N
PARATHYROID	N	N	U	N	N
TRACHEA	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N
THYMUS Hemorrhage	N	N	1	N	N
HEART	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : DNB Study
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-003
 GROUP: 12
 SEX: MALE

ANIMAL ID:	56	57	58	59	60
COLON	N	N	N	N	N
JEJUNUM	N	N	N	N	N
AORTA	N	N	N	N	N
LIVER	N	N	N	N	N
SPLEEN	N	N	N	N	N
TONGUE	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N
LUNGS	N	N	N		N
Inflammation, Chronic	-	-	-	1	-
KIDNEYS					
Mineralization, NOS	2	1	2	1	1
Regeneration, Tubular	-	1	-	-	-
Degeneration, Tubular	1	1	2	2	2
URINARY BLADDER	N	N	N	N	N
PROSTATE	N	N	N	N	N
STOMACH	N	N	N	N	N
DUODENUM	N	N	N	N	N
ILEUM	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
 Study Number 94-003
 14 Day 1,3-Dinitrobenzene
 Exposure in Fischer 344 Rats

 TABULATED ANIMAL DATA

STUDY ID : DNB Study

STUDY NUMBER: 94-003

FATE: ALL

GROUP: 12

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	56	57	58	59	60
CECUM	N	N	N	N	N
RECTUM	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N
TESTES	N	N	N	N	N
EPIDIDYMIDES	N	N	N	N	N
SEMINAL VESICLE	N	N	N	N	N
SKIN	N	N	N	N	N
PREPUTIAL GLAND			N		
Lymphocytic Infiltrates	1	1	-	1	1
EYES	N	N	N	N	
Microgranuloma, Cornea	-	-	-	-	1
HARDERIAN GLAND	N	N	N	N	N
FEMUR/STERNUM	N	N	N	N	N
NASAL	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N

 See Reports Code Table for Symbol Definitions

(END OF REPORT)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 1
SEX: FEMALE

Animal ID: 5
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Mild

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 2
SEX: FEMALE

Animal ID: 6
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Mild

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

Animal ID: 8
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Mild

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

OVARIES - Left, Cyst, 3mm, Round, Yellowish, Liquid

OVARIES - Cyst, NOS

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 3
SEX: FEMALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 4
SEX: FEMALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 5
SEX: FEMALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 6
SEX: FEMALE

No Gross Observations for any animal in this group

(Report Continued)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 7
SEX: MALE

Animal ID: 31
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:

Related Histopathology:

SPLEEN - Enlarged, Moderate

SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in size, Moderate

TESTES - Degeneration, Seminiferous Tubules

Animal ID: 32
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:

Related Histopathology:

SPLEEN - Enlarged, Moderate

SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in size, Moderate

TESTES - Degeneration, Seminiferous Tubules

Animal ID: 33
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:

Related Histopathology:

SPLEEN - Enlarged, Moderate

SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in size, Moderate

TESTES - Degeneration, Seminiferous Tubules

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 7
SEX: MALE

Animal ID: 34
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Moderate

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in size, Moderate

TESTES - Degeneration, Seminiferous Tubules

Animal ID: 35
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Moderate

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in Size, Moderate

TESTES - Degeneration, Seminiferous Tubules

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 8
SEX: MALE

Animal ID: 36
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Moderate

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in Size, Moderate

TESTES - Degeneration, Seminiferous Tubules

Animal ID: 37
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Mild

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in Size, Moderate

TESTES - Degeneration, Seminiferous Tubules

Animal ID: 38
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:
SPLEEN - Enlarged, Moderate

Related Histopathology:
SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Bilateral, Decreased in size, Moderate

TESTES - Degeneration, Seminiferous Tubules

MANDIBULAR LYMPH NODE - Foci, >1mm, Multiple, Red

MANDIBULAR LYMPH NODE - Hemorrhage

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 8
SEX: MALE

Animal ID: 39
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:

TESTES - Bilateral, Decreased in size, Moderate

MANDIBULAR LYMPH NODE - Foci, >1mm, Multiple, Red

Related Histopathology:

TESTES - Degeneration, Seminiferous Tubules

MANDIBULAR LYMPH NODE - Hemorrhage

Animal ID: 40
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 14

Reference to Necropsy Record:

SPLEEN - Enlarged, Moderate

TESTES - Bilateral, Decreased in size, Moderate

Related Histopathology:

SPLEEN - Hyperplasia, Erythroid Cell

TESTES - Degeneration, Seminiferous Tubules

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 9
SEX: MALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 10
SEX: MALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 11
SEX: MALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-003
14 Day 1,3-Dinitrobenzene
Exposure in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : DNB Study
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-003
GROUP: 12
SEX: MALE

No Gross Observations for any animal in this group

(END OF REPORT)

APPENDIX H

CHEMICAL ANALYSES

Determination of Homogeneity
of DNB in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 1				
150	Top	152	151	0.97
	Middle	153		1.64
	Bottom	147		2.61
75	Top	75.7	75.0	0.93
	Middle	74.9		0.05
	Bottom	74.3		0.88
25	Top	24.0	23.8	0.90
	Middle	24.2		1.49
	Bottom	23.2		2.40
10	Top	10.2	10.1	0.81
	Middle	10.1		0.03
	Bottom	10.0		0.83
2.5	Top	2.69	2.58	4.29
	Middle	2.50		3.02
	Bottom	2.55		1.27

Determination of Homogeneity
of DNB in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 2				
150	Top	154	152	1.34
	Middle	155		2.01
	Bottom	147		3.35
75	Top	72.6	74.2	2.14
	Middle	75.0		1.11
	Bottom	74.9		1.03
25	Top	25.3	24.8	1.80
	Middle	25.2		1.67
	Bottom	23.9		3.47
10	Top	10.1	10.1	0.11
	Middle	10.1		0.13
	Bottom	10.1		0.24
2.5	Top	2.47	2.50	1.32
	Middle	2.61		4.43
	Bottom	2.42		3.12

Analysis of DNB
in the Feed Mixtures

Target Concentration (mg/kg diet)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg diet)	% Error
Week 1				
150	20 Jun 94	21 Jun 94	151	0.53
75	20 Jun 94	21 Jun 94	75.0	0.06
25	10 Jun 94	17 Jun 94	23.8	4.74
10	13 Jun 94	17 Jun 94	10.1	0.92
2.5	13 Jun 94	16 Jun 94	2.58	3.22
Week 2				
150	22 Jun 94	23 Jun 94	152	1.09
75	22 Jun 94	29 Jun 94	74.2	1.12
25	23 Jun 94	29 Jun 94	24.8	0.78
10	23 Jun 94	29 Jun 94	10.1	1.04
2.5	23 Jun 94	27 Jun 94	2.50	0.09

APPENDIX I
PROTOCOL AND
AMENDMENTS

PROTOCOL

14 Day Range Finding and Toxicity Evaluation of
1,3-Dinitrobenzene (DNB) in Fischer (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 6-3-94
Principal Investigator Date
T.V. Reddy, Ph.D.

G. Reddy 6-7-94
G. Reddy, Ph.D., Sponsor Date

G.R. Olson 6-3-94
Project Manager Date
G.R. Olson, DVM, Ph.D.
Pathology Associates, Inc.

W.R. Fox 6-3-94
Quality Assurance Date
W.R. Fox, MA
Pathology Associates, Inc.

**14 DAY RANGE FINDING AND TOXICITY EVALUATION OF
1,3-DINITROBENZENE (DNB) IN FISCHER (344)RATS.**

RESEARCH PROTOCOL

**TIRUMURU V.REDDY,PH.D.
PRINCIPAL INVESTIGAROR**

**F.BERNARD DANIEL,PH.D.
CO-PRINCIPAL INVESTIGATOR.**

**Ecological Monitoring Research Division,
Environmental Monitoring Systems Laboratory
U.S.Environmental Protection Agency
Cincinnati,Ohio 45268**

May 26,1994

**TITLE: 14 Day Range Finding and Toxicity Evaluation of
1,3-Dinitrobenzene(DNB) in Fischer (344)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 a 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 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 with blood proteins and tissue DNA in rats.

PROTOCOL

1. Study. 14 day range finding and toxicity evaluation of 1,3-dinitrobenzene (DNB) in F344 male and female rats. This study will be started on June 10,94.
2. Purpose. To evaluate subacute toxicity of DNB when administered in the diet for 14 days and to select an ideal doses for 90 days subchronic toxicity study.
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. Principal Investigator. T.V. Reddy, Ph.D., Research Chemist
Environmental Monitoring Systems Laboratory
U.S. Environmental Protection Agency
Cincinnati, Ohio 45268
6. CO-Principal Investigator. F.Bernard Daniel, Ph.D. Director, Ecological
Monitoring research division, Environmental
Monitoring Systems Laboratory, U.S. Environmental
Protection Agency, Cincinnati, Ohio. 45268.
7. Study Coordinator. Barry Wiechman, MS. Pathology associates(PAI),
West Chester, Ohio 45069.
8. Project Manager. G.R. Olson, DVM, Ph.D., Pathology
Associates(PAI), West Chester, Ohio 45069.
9. Regulatory Compliance. This study is conducted 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, histopathology 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-Dinitrobenzene (DNB) Powder (CAS #99-65-0), 99% pure, was obtained from Fluka Chemical Corp., 980 South Second Street, Ronkonkoma, NY. The purity was further confirmed by HPLC.

12. Experimental Design.

A. Selection of Dose: Toxikon Corporation, Woburn, MA 01801 has conducted acute toxicity studies on DNB. They administered DNB 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 59 mg/kg BW, as the LD50 dose for male and female rats. Based on the above report, we calculated the following 5 target dose levels to test in Fischer rats, for the 14 day range finding study. (15, 7.5, 2.5, 1, 0.25mg/kg BW). Control rats will be fed only certified 5000-2 powdered chow diet.

B. Preparation of the Diet: Certified powdered Purina laboratory chow(5000-2) will be purchased from Purina labs and stored at 4°C until use. DNB diets are prepared once a week. Just before the diet preparation DNB is removed from the explosion proof storage shelves (kept in designated carcinogen room) weighed in the carcinogen room and mixed with the powdered diet (150 mg/kg). First 150 mg DNB will be mixed with 250g powdered diet and mixed for 15 min. Then an additional 250 g powdered diet is added and mixed for an additional 15 min. Then the remaining diet will be added to bring the DNB concentration as 150 mg/kg; and then mixed for an additional 1 hr. in a mechanical stirrer (Hobart Model C-100 Columbus, OH) for uniform distribution of TNB in the diet. This is also verified by determining the DNB concentration in the diet, taken from three different depths (top, middle and bottom layer) of the mixing chamber soon after diet preparation. Quantitative analysis of DNB is done by HPLC.

The premixed diet (150 mg/kg) is further diluted to 2, 6, 15 and 60 times with fresh powdered diet to obtain the desired DNB concentrations in the diet as 75, 37.5, 25, 10 and 2.5 mg DNB/kg diet, and the expected target doses respectively are 7.50, 2.5, 1.0, and 0.25 mg/kg BW. Individual diet concentrations are determined as described before. The diet feeders are refilled twice and changed once weekly. DNB concentrations are manipulated in such a way that each rat (caged individually) will receive the desired amount of DNB. This is determined by calculating the daily average intake, followed by an adjustment of DNB content in the diet. Dietary intake and water consumption are measured twice a week. Body weights are recorded once a week. There are no known contaminants in the food or water that would interfere

with the purpose or the conduct of the study.

C. Animals: Forty male and female Fischer 344 rats (6 week of age or 120-125 g) will be obtained from Charles River Breeding Laboratory (Portage, MI) and are held for 1W for quarantine (by which time all the serological tests are evaluated). After quarantine 5 rats from each sex are sacrificed and used for necropsy quality controls or base line controls to ensure the animals are healthy and with in the normal limits for all measurements at the time of arrival and after quarantine. Male and female rats are housed individually in polycarbonate shoe boxes with aspen bedding(San I chips supplied by P.J. Murphy, Forest Products Corporation, NJ),and are identified by electronic implants(Bio Medic Data systems Inc., Maywood,NJ.). Food and watere is provided ad libitum. Water is provided in 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 a relative humidity range of 40-60%. All cages are sequentially numbered for identification(5 rats/sex/dose group). Groups of rats are fed 150 mg DNB/kg diet(Gp 1), followed by 75 mg/kg (Gp 2), 25 mg/kg (Gp 3), 10mg/kg(Gp 4),and 2.5 mg DNB/kg diet (Gp 5) daily for 14 days. Group 6 will be given only powered purina chow diet(control). Food and water consumption are recorded 2 times a week. Food spills are taken into account while recording food consumption. Body weights are recorded once a week.

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 SD 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. Group designation and dose levels for 14 day toxicity study.

Group	No. of Animals		Dose Levels mgDNB/kg diet
	Male	Female	
1	5	5	150
2	5	5	75
3	5	5	25
4	5	5	10
5	5	5	2.5
6	5	5	0

G. Analysis of the Diet: The stability of DNB in the diet was determined by keeping the DNB diet at 4°C for one or two weeks and was established that the DNB diet is stable atleast for two weeks. The DNB diets are prepared once a week. The homogeneity of DNB in the freshly prepared diet is determined weekly once, by analyzing the DNB content in the diet by HPLC.

H. 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.

I. Clinical Pathology:

(1) Frequency: At termination.

(2) Number of Animals: All animals (samples per SOP following phenobarbital anesthetic.

J. Tests:

(1) Hematology:

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

(2) Blood Chemistry:

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

K. 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 14 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.

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

L. Postmortem Procedures:

(1) Gross Necropsy

The necropsy will include examination of :

External surface

All orifices

Cranial cavity

Carcass

External surface of the brain (at necropsy); Thoracic, abdominal and pelvic cavities and their viscera.

(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	colon
mesenteric lymph nodes	cecum
mammary glands	rectum
thigh muscle	liver
sciatic nerve	pancreas

sternum with marrow
femur with marrow
larynx
thymus
trachea
lungs and bronchi
heart and aorta
thyroid
parathyroids
esophagus
stomach
duodenum
jejunum
tongue
salivary gland

spleen
kidneys
adrenals
urinary bladder
seminal vesicles
prostate
testes, including epididymis
ovaries
uterus
nasal cavity and nasal turbinates
brain
pituitary
preputial or clitoral glands
Zymbal's gland
thoracic spinal cord

M. 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 the animals. Male and female from highest dose group and (150 mgDNB/kg/diet groups) and untreated controls. The tissues examined under light microscope are as follows:

cerebrum
cerebellum
trachea
thyroid
parathyroid
esophagus
salivary gland
harderian gland

heart
aorta
lung
thymus
spleen
mesenteric lymph node

pancreas
cecum
colon
rectum
stomach
skeletal muscle
sciatic nerve
tongue
skin
mammary gland
nasal region
sternum
femur
vertebrae
spinal cord

liver
kidney
urinary bladder
duodenum

adrenals
pituitary
eye(s)
jejunum
auditory sebaceous gland

ileum

MALE

FEMALE

accessory sex glands
epididymis
testes

uterus
ovaries

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). Approximately 240 slides from 20 rats (5 male and 5 female from 150 mg DNB/kg dose group and 5 rats each from control group). Based on the results from dose group tissues from other dose groups will be examined as needed. Following completion of each study all wet tissues, paraffin blocks and slides and all raw data will be stored in EPA archives.

N. 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

clinical observations

body weights

food and liquid consumption

clinical pathology tests

organ weights and organ/body

weight ratios

gross pathology

histopathology

O. Statistical Evaluation: Stat view computer software will be used for statistical analysis in 14-day and 90-day study for statistical analysis. Analysis will be done by Dr. Jonie Torsella, Okridge institute of science and education. 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.

P. Schedule: The study start and completion dates will be added by amendment.

Amendment 1
for
United States Army Study 94-003
14-DAY TOXICITY EVALUATION OF
1,3-DINITROBENZENE 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 to correct a typographical error in the protocol.

1. Page 4 of the protocol:

B. Line 10: Change TNB to DNB.

Reason: Typographical error.

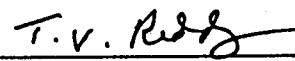
Amendment 1 Approval

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


AW Breidenbach Environmental
Research Center
U.S. Environmental Protection Agency
Cincinnati, Ohio 45268

 10-27-94

G. Reddy, Ph.D., Sponsor Date

 10-14-94

T.V. Reddy, Ph.D., Pi Date

 9-23-94

Willa Fox, MA, QA Date

Deviations from GLP's and Protocol

1. Preparation of the test diet stock was changed in order to obtain a more uniform mixture.
2. Sampling for homogeneity was changed due to the depth of the diet in the container. Samples were taken from different areas of the container and not top, middle and bottom as stated in the analysis section.

Tirumuru V. Reddy

Tirumuru V. Reddy, Ph.D.

DISTRIBUTION LIST

Commander
ATTN: SGRD-UBZ-C
U.S. Army Biomedical Research and Development Laboratory
Fort Detrick, Frederick, MD 21702-5010

Commander
ATTN: MCMR-RMI-S
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, MD 21702-5012

Commander/Director
U.S. Army Corps of Engineers
Construction Engineering Research Laboratory
Environmental Division
P.O. Box 4005
Champaign, IL 61820

Commandant
Academy of Health Sciences, U.S. Army
ATTN: DRXTH-ES
Aberdeen Proving Ground, MD 21010-5000

Commander
U.S. Army Environmental Hygiene Agency
ATTN: Library
Aberdeen Proving Ground, MD 21020-5000

Commander
U.S. Army Environmental Center
ATTN: S-FIM-AEC-TSS (Mr. R. L. Muhly)
Aberdeen Proving Ground, MD 21010-5401