


**FINAL REPORT**

**28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO BLEND AND  
AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS**

**TESTING FACILITY:  
BATTELLE**

**SPONSOR:  
R.J. REYNOLDS TOBACCO COMPANY  
RESEARCH AND DEVELOPMENT  
BOWMAN GRAY TECHNICAL CENTER  
WINSTON-SALEM, NC 27102**

**APRIL 2009**

**SIGNATURE PAGE**  
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Milton R. Hejtmancik, Ph.D., D.A.B.T.

4/16/09  
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Date

  
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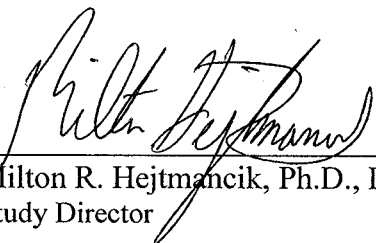
Allen W. Singer, D.V.M., D.A.B.T., D.A.C.V.P.

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**GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT**

This study was conducted in compliance with the Food and Drug Administration's (FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58), for the conduct of non-clinical laboratory studies with the following exceptions: plasma analysis was conducted using a non-validated bioanalytical method; characterization and stability analysis of bulk test articles was conducted, as intended, under non-GLP development procedures; and serology analyses were also conducted under non-GLP procedures ([Appendix I](#)).

  
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Milton R. Hejtmancik, Ph.D., D.A.B.T.  
Study Director

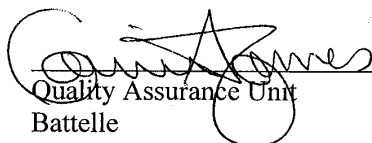
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### QUALITY ASSURANCE STATEMENT

This study was inspected by the Quality Assurance Unit and reports were submitted to the Study Director and management as follows:

<b>Phase Inspected</b>	<b>Date Inspected</b>	<b>Date Reported to Study Director and Management</b>
Protocol review	5/23/2008	5/23/2008
Test system receipt	6/5/2008	6/5/2008
Sexing	6/5/2008	6/5/2008
Formulation preparation	6/13/2008	6/13/2008
Dispensing	6/13/2008	6/13/2008
Formulation analysis	6/16/2008	6/16/2008
Protocol amendment review	6/17/2008	6/17/2008
Group assignment	6/18/2008	6/18/2008
Test system identification	6/18/2008	6/18/2008
Dispensing	6/19/2008	6/19/2008
Test article administration - dosed feed	6/19/2008	6/19/2008
Body weights	6/24/2008	6/24/2008
Clinical observations	6/24/2008	6/24/2008
Dispensing	6/24/2008	6/24/2008
Food consumption measurements	6/24/2008	6/24/2008
Test article administration - dosed feed	6/24/2008	6/24/2008
Food consumption measurements	6/26/2008	6/27/2008
Anesthetization	7/2/2008	7/2/2008
Blood collection	7/2/2008	7/2/2008
Centrifugation	7/2/2008	7/2/2008
Functional observational battery	7/9/2008	7/10/2008
Plasma analysis	7/9/2008	7/10/2008
Protocol amendment review	7/21/2008	7/21/2008
Fasting	7/22/2008	7/22/2008
Blood collection	7/22/2008	7/22/2008
Euthanasia	7/22/2008	7/22/2008
Necropsy/tissue collection	7/22/2008	7/22/2008
Organ weights	7/22/2008	7/22/2008
Clinical lab processing/analysis	7/22/2008	7/22/2008
Audit study file	7/24/2008	7/24/2008
Protocol amendment review	7/29/2008	7/29/2008
Animal room formulation analysis	7/29/2008	7/29/2008
Protocol amendment review	8/5/2008	8/05/2008
Audit study file	8/14/2008	8/14/2008
Audit analytical report	9/3/2008	9/03/2008
Audit study file	9/11/2008	9/11/2008
Audit neurobehavioral report	9/11/2008	9/11/2008
Audit study file	9/12/2008	9/12/2008

<b>Phase Inspected</b>	<b>Date Inspected</b>	<b>Date Reported to Study Director and Management</b>
Audit study file	10/3/2008	10/3/2008
Audit study file	10/10/2008	10/10/2008
Audit study file	11/10/2008	11/10/2008
Audit bioanalytical and kinetics report	11/13/2008	11/13/2008
Audit study file	11/20/2008	11/20/2008
Audit draft final report	11/20/2008	11/20/2008
Audit draft final report	3/16/2009	3/16/2009
Audit final report	4/15/2009	4/15/2009

 4/16/09  
Quality Assurance Unit Date  
Battelle

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## SUMMARY

The objective of this study was to compare the short-term toxicity of a tobacco blend, aqueous tobacco extract, and appropriate controls in rodents (nicotine tartrate positive control and diet negative control). The study also aimed to differentiate any palatability-related effects from toxic effects by including pairfed groups corresponding to the high dose groups from which food consumption was measured daily. Plasma concentrations of nicotine and cotinine were determined under continuous dose feed exposure. The following evaluations were performed: clinical observations, body weights, food consumption, clinical pathology, functional observational test battery (FOB), gross necropsy, and selected organ weights. Toxicokinetic evaluations of nicotine and cotinine in plasma were performed on Days 13, 14, and 28. The overall summary of the estimated nicotine doses and test article concentrations for nicotine tartrate, tobacco blend, and aqueous tobacco extract are listed below (Text Table 1):

**Text Table 1. Study Design for the 28-Day Repeated Dose Toxicity Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats**

Group	Target Dosage of Nicotine (mg/kg BW*/day)	Test Article Concentration** (mg/kg)	
		Males	Females
1 - Control	0	0	0
2 - Nicotine Tartrate (NT) High Dose	20	1026	855
3 - Control Diet Pair-fed to NT High Dose	0	0	0
4 - Tobacco Blend Low Dose	0.2	137	114
5 - Tobacco Blend Intermediate Dose 1	2	1370	1142
6 - Tobacco Blend Intermediate Dose 2	8	5479	4566
7 - Tobacco Blend High Dose	20	13698	11415
8 - Control Diet Pair-fed to Tobacco High Dose	0	0	0
9 - Tobacco Extract Low Dose	0.2	157	130
10 - Tobacco Extract Intermediate Dose 1	2	1566	1305
11 - Tobacco Extract Intermediate Dose 2	8	6264	5220
12 - Tobacco Extract High Dose	20	15659	13049
13 - Control Diet Pair-fed to Tobacco Extract High Dose	0	0	0
14 - Sentinels	0	0	0

\* BW = Body weight.

\*\* Quantity of test article or positive control per kg feed.

Dosing concentrations were derived based on the information provided in [Text Table 2](#).

**Text Table 2. Nicotine Concentrations in Tobacco Blend, Tobacco Extract, and Nicotine Tartrate Formulations**

Sex	Nicotine Dose (mg/kg BW <sup>a</sup> /day)	Food Consumption (kg/day)	Body Weight (kg)	Nicotine Needed (mg)	Nicotine <sup>b</sup> (mg/kg)	Tobacco Blend <sup>c</sup> (mg/kg)	Tobacco Extract <sup>c</sup> (mg/kg)	Nicotine Tartrate <sup>c</sup> (mg/kg)
M	0.2	0.02	0.36	0.072	3.6	137	157	
M	2	0.02	0.36	0.72	36	1370	1566	
M	8	0.02	0.36	2.88	144	5479	6264	
M	20	0.02	0.36	7.2	360	13698	15659	1026
F	0.2	0.014	0.21	0.042	3	114	130	
F	2	0.014	0.21	0.42	30	1142	1305	
F	8	0.014	0.21	1.68	120	4566	5220	
F	20	0.014	0.21	4.2	300	11415	13049	855

Tobacco = 26.28 mg/g of nicotine; 38.051 mg of tobacco blend for every mg of nicotine.

Extract = 22.99 mg/g of nicotine; 43.497 mg of extract for every mg of nicotine.

Nicotine Tartrate = 35% nicotine; 2.85 mg of nicotine hydrogen tartrate for every mg of nicotine.

a. BW = Body weight.

b. Quantity of nicotine per kg feed.

c. Quantity of test article or positive control per kg of feed.

Abbreviations used throughout this report to designate the dosage groups of male and female rats are listed below (Text Table 3):

**Text Table 3. Abbreviations Used Throughout this Report to Designate the Dose Groups for Male and Female Rats**

Group	Males	Females
1	CM	CF
2	NT20M	NT20F
3	PFCNTM	PFCNTF
4	B0.2M	B0.2F
5	B2M	B2F
6	B8M	B8F
7	B20M	B20F
8	PFCBM	PFCBF
9	E0.2M	E0.2F
10	E2M	E2F
11	E8M	E8F
12	E20M	E20F
13	PFCEM	PFCEF

## **1.0 INTRODUCTION**

The objective of this study was to evaluate the short-term toxicity of a tobacco blend and aqueous tobacco extract in comparison to the nicotine tartrate positive control and diet negative control in Wistar Han rats. The study also aimed to differentiate any palatability-related effects from toxic effects by including diet restricted groups corresponding to the high dose groups. Plasma was analyzed at the approximate mid-point of the study and Study Day 28 to measure nicotine and cotinine concentrations from animals fed nicotine containing test articles in the diet.

R.J. Reynolds Tobacco Company was the Sponsor of the study. Suzana Theophilus was designated as the Sponsor Monitor and approved the study protocol.

The study was conducted at Battelle under the direction of Milton R. Hejtmancik. The in-life portion of the study began on June 19, 2008 with exposure initiation and ended on July 25, 2008.

## 2.0 EXPERIMENTAL DESIGN

Three hundred eighty-eight male and female rats were randomized into 14 dose groups. The study consisted of a 28-day toxicity study that included a neurotoxicity component and a toxicokinetic study. Endpoints used to evaluate the potential toxicity of tobacco blend and aqueous tobacco extract were clinical observations, body weights, body weight changes, food consumption, clinical pathology, neurological and behavioral toxicology, gross necropsy, and selected organ weights. Toxicokinetic evaluations of nicotine tartrate, tobacco blend, and aqueous tobacco extract were performed on Days 13, 14, and 28. The general study design is listed below.

Group	Target Dosage of Nicotine (mg/kg/day)	Number of Rats			
		Males		Females	
		Core	TK <sup>a</sup>	Core	TK <sup>a</sup>
1 - Control	0	10	--	10	--
2 - Nicotine Tartrate (NT) High Dose	20	10	6	10	6
3 - Control Diet Pair-fed to NT High Dose	0	10	--	10	--
4 - Tobacco Blend Low Dose	0.2	10	6	10	6
5 - Tobacco Blend Intermediate Dose 1	2	10	6	10	6
6 - Tobacco Blend Intermediate Dose 2	8	10	6	10	6
7 - Tobacco Blend High Dose	20	10	6	10	6
8 - Control Diet Pair-fed to Tobacco Blend High Dose	0	10	--	10	--
9 - Tobacco Extract Low Dose	0.2	10	6	10	6
10 - Tobacco Extract Intermediate Dose 1	2	10	6	10	6
11 - Tobacco Extract Intermediate Dose 2	8	10	6	10	6
12 - Tobacco Extract High Dose	20	10	6	10	6
13 - Control Diet Pair-fed to Tobacco Extract High Dose	0	10	--	10	--

a. Nicotine/cotinine analysis.

TK = Toxicokinetic.

### **3.0 METHODS**

#### **3.1 Protocol and Amendments**

The study protocol, amendments to the protocol and deviations from the protocol are provided in [Appendix A](#). There were no deviations that occurred in the conduct of the study that were considered to significantly affect the quality or integrity of the study.

#### **3.2 Test Articles (Tobacco Blend, Aqueous Tobacco Extract) and Positive Control Article (Nicotine Hydrogen Tartrate Salt)**

Test articles, a natural tobacco blend containing no additives and an aqueous tobacco extract, were supplied by R.J. Reynolds Tobacco Company and were received on May 7, 2008 in good condition. A total of approximately 1278 lbs of tobacco blend was received as 71 containers (18 lbs per bucket) and a total of approximately 1105.5 lbs of tobacco extract was received as 33 containers (33.5 lbs per bucket). Test articles were provided by the Sponsor in plastic buckets and were stored frozen (-30 to -15°C). Nicotine hydrogen tartrate salt (Batch No. 028K0705) was supplied by Sigma-Aldrich. A total of approximately 1.8 kg of nicotine tartrate was received May 20, 2008 (expiration date May 20, 2009) in good condition and was stored at room temperature. The certificates of analysis for test articles and the nicotine tartrate positive control are provided in [Appendix B](#). The identity, strength, purity, composition, stability, and methods of production of test articles were the responsibility of the Sponsor.

Reserve samples of each set of the tobacco blend, aqueous tobacco extract, and the nicotine tartrate control article used to formulate the animal diets were collected under design form CN49730A-TASTAB. Reserve samples of the tobacco blend and tobacco extract will be maintained frozen (-30 to -15°C) and a reserve sample of the nicotine tartrate will be maintained at room temperature until submission of the chronic study final report.

#### **3.3 Chemical Analysis of Formulations**

##### **3.3.1 Pre-Dosing**

Samples of dose formulations from the dose preparation of tobacco blend, tobacco extract, and nicotine tartrate were analyzed at Battelle for verification of nicotine concentrations based on methods provided by the Sponsor. The detailed analytical results are provided in

[Appendix F](#). All pre-dose nicotine formulations that were analyzed for nicotine concentration met acceptance criteria (within 10 percent of the target concentrations; relative standard deviation [RSD] less than or equal to 10 percent).

Homogeneity studies were performed to support this 28-day study (CN49730A-FORMPRE). The tobacco extract and nicotine tartrate formulations met all design form acceptance criteria for homogeneity. The tobacco blend formulations met the design form acceptance criteria for homogeneity for grand % RSD (relative standard deviations were less than 10%). Relative errors (REs) were all more than 10% above target, suggesting the nicotine content of this test article may exceed the labeled concentration.

### **3.3.2 Post-Dosing**

Post-dose (animal room) nicotine formulations met the criteria for concentration (REs within 10% of target;  $RSD \leq 10\%$ ), except for the following:

- B0.2F (114 mg/kg) had an RSD of 12.5%.
- B0.2M (137 mg/kg) had an RE of 12.6%.
- B2F (1142 mg/kg) had an RE of 14.5%.
- B2M (1370 mg/kg) had an RE of 12.8%.

There was no impact of these failures to meet acceptance criteria on the study. Post-dose samples are taken from the animal room feeders. They have been exposed to the animal and are subject to the impact from this exposure on concentration. They may include selective eating of the feed or analyte from the formulation by the animal, contamination of the formulation by urine, feces, bedding, or other materials, and exposure of the formulation to the animal room environment. For these reasons, animal room samples should only be used to determine general trends that may result from the exposure of the formulation to the animal room environment.

Generally, the post-dose concentrations agreed with the pre-dose values.

## **3.4 Experimental Animals**

A total of 426 male and female Wistar Han rats were required for the study. A sufficient number of animals were obtained from Charles River Laboratories (Raleigh, NC) to provide

the required number of healthy animals for testing. The rats were approximately four to five weeks of age and ranged in body weight from approximately 131 to 230 grams at Day 1 of the toxicology study. The rats were housed in individual wire bottomed cages in Room 7C-074. During neurobehavioral exams, rats were housed individually in polycarbonate cages in Rooms 7C-089 and 7C-085.

The rat was chosen as the test system because considerable scientific documentation of the rat as a predictive animal model for humans exists, and there are no *in vitro* or computer models that can replace the integrative function of the whole animal model. The Battelle Institutional Animal Care and Use Committee approved the proposed activities before implementation.

#### **3.4.1 Animal Housing and Environmental Conditions**

All animals were received, quarantined, and housed individually in wire-bottomed cages according to testing facility standard operating procedures (SOPs). Animals subjected to neurobehavioral testing and animals fasted prior to necropsy were individually housed in polycarbonate cages with hardwood bedding. All housing and care conformed to the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) recommendations, current requirements stated in the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996), and the U.S. Department of Agriculture through the Animal Welfare Act, as amended.

The environmental conditions of the animal study rooms conformed to the following: (1) the light/dark cycle was held at approximately 12 hours of light and 12 hours of dark each day during the study using fluorescent lighting, starting at approximately 6:00 AM each day; (2) the room temperature and relative humidity controls were set to provide from 64 to 79°F and 30 to 70 percent, respectively, and were monitored for conformance; and (3) fresh air was supplied to the room at a rate providing a minimum of ten changes of room air per hour.

#### **3.4.2 Diet**

Animals were fed powdered NTP-2000 rodent diet *ad libitum*, according to facility SOP, except when fasted prior to scheduled necropsy and for the special paired groups. The

control group was fed the diet without test article and treated animals were fed the diet with the specified quantity of test article required to maintain their designated doses. Analysis reports of each feed lot were supplied by the vendor and were retained by Battelle.

### **3.4.3 Water**

Fresh water from the city of Columbus municipal water supply was provided *ad libitum* via automatic watering system except during neurobehavioral evaluations. The water supply is monitored under Battelle SOPs.

Water samples from Room 7C-074 were collected on October 23, 2008 for analysis. Results were available on October 31, 2008 and indicated there were no known or reported contaminants in the water that would have any impact on study results or interpretation.

## **3.5 Treatment Group Allocation and Animal Identification**

Animals were identified by pre-study numbers on cage cards during quarantine and acclimation. Following group assignment, the rats were individually identified by tail tattoo.

Prior to the initiation of dosing, animals were assigned to study groups using the PATH/TOX SYSTEM (version 4.2.2, Xybion Medical Systems Corporation, Cedar Knolls, NJ). The PATH/TOX SYSTEM software algorithm ensures homogeneity of group variances with respect to body weight across all groups. The following were the group assignments and animal identification numbers:

<b>Animal Identification Numbers</b>				
<b>Group</b>	<b>Males</b>		<b>Females</b>	
	<b>Core</b>	<b>TK</b>	<b>Core</b>	<b>TK</b>
1	101-110	--	151-160	--
2	201-210	211-216	251-260	261-266
3	301-310	--	351-360	--
4	401-410	411-416	451-460	461-466
5	501-510	511-516	551-560	561-566
6	601-610	611-616	651-660	661-666
7	701-710	711-716	751-760	761-766
8	801-810	--	851-860	--
9	901-910	911-916	951-960	961-966
10	1001-1010	1011-1016	1051-1060	1061-1066
11	1101-1110	1111-1116	1151-1160	1161-1166
12	1201-1210	1211-1216	1251-1260	1261-1266
13	1301-1310	--	1351-1360	--
14	1401-1410	--	1451-1460	--

Animals subjected to the FOB were identified such that the conduct of the FOB was blind. Therefore, these animals were identified by tail tattoos for which a unique number between 1 and 100 was randomly assigned to each animal in addition to each animal's identification number. Both the tail tattoo and the animal identification numbers were listed on the cage card for animals subjected to the FOB.

### 3.6 Experimental Design

Rats were randomized into 13 treatment groups and 1 sentinel group. The study consisted of a 28-day toxicity study including a neurotoxicity component and a toxicokinetic study. Endpoints used to evaluate potential toxicity of tobacco blend and aqueous tobacco extract were clinical observations, body weights and body weight changes, food consumption, neurological and behavioral toxicology, and clinical and anatomic pathology including organ weights. Toxicokinetic evaluations of plasma nicotine and cotinine concentrations were performed on toxicokinetic animals.

### 3.7 Clinical Observations

Cage-side observations for moribundity and mortality were made twice daily, once in the morning and once in the afternoon, throughout the study. Detailed clinical examinations

were conducted on all core animals at weekly intervals. A final detailed clinical examination was conducted for each core study rat on the day of its scheduled necropsy.

### **3.8 Body Weights (Core, TK, and Pairfed Animals)**

Individual body weights of animals were recorded on Day -3 (with respect to male TK's) for randomization and group assignment. After initiation of dosing, body weights for core study animals were recorded on Study Days 1, 4, 8, 11, 15, 18, 22, and 25. Body weights for TK study animals were recorded on Study Days 1, 8, 15, 22, and 28.

### **3.9 Food Consumption (Core Animals)**

Quantitative food consumption was measured for each animal bi-weekly starting on Day 1. A known amount of food was placed in the feed container and reweighed after three to four days. The difference in the weight of the food container was taken as a measurement of food consumed, and food consumption (g/day) was calculated.

#### **3.9.1 Food Allotments for Pairfed Groups**

Pair feeding was accomplished by measuring the individual food consumption daily for all animals in the high dose treatment groups and using that data to calculate the mean food consumption for the group. The corresponding pairfed groups were provided only the mean quantity of control feed calculated from high dose food consumption group means.

### **3.10 Neurobehavioral Toxicology (Core Animals)**

Five rats of each sex were randomly selected from each core study group, with the exception of pairfed control groups, and were identified such that the conduct of the FOB was blind. Animals subjected to the FOB were individually housed in polycarbonate cages with bedding the day prior to and the day of the neurobehavioral exam. At the completion of the FOB, animals were transported back to 7C-074 and housed in their home cages per protocol specifications.

### **3.11 Clinical Pathology (Core Animals)**

All animals were fasted overnight prior to the scheduled blood sampling for hematology, coagulation, and clinical chemistry determinations. Blood samples were collected under

CO<sub>2</sub>/O<sub>2</sub> anesthesia from the retro-orbital sinus for hematology and serum chemistry determinations and via vena cava for coagulation parameters. The tubes contained ethylene diamine tetraacetic acid (EDTA) as an anticoagulant for blood samples collected for hematology. The tubes used for serum chemistry determinations did not contain any anticoagulant, but did contain a serum separator gel. Sodium citrate was used as the anticoagulant for coagulation parameters.

### 3.11.1 Hematologic and Coagulation Parameters

Hematologic and coagulation parameters measured or calculated were as follows:

Erythrocyte count (RBC)	Mean corpuscular hemoglobin concentration (MCHC) (calculated)
Hemoglobin (HGB)	Reticulocyte count (RET) (absolute)
Hematocrit (HCT) (calculated)	Platelet count (PLT)
Mean corpuscular volume (MCV)	Total leukocyte count (WBC)
Mean corpuscular hemoglobin (MCH) (calculated)	WBC differential (absolute)
	Prothrombin time (PT)

### 3.11.2 Serum Chemistries

Serum chemistries measured or calculated were as follows (listed in order of priority):

Aspartate aminotransferase (AST)	Cholesterol (total) (CHOL)
Direct bilirubin	Creatinine (CREA)
Total bilirubin (TBIL)	Total protein (TP)
Gamma-glutamyl transferase (GGT)	Urea nitrogen (BUN)
Albumin (ALB)	Calcium (total) (CA)
Globulin (calculated) (GLOB)	Chloride (CL)
Albumin/globulin ratio (calculated) (AGR)	Phosphorus (PHOS)
Alkaline phosphatase (ALP)	Potassium (K)
Glucose (GLU)	Sodium (NA)
Triglycerides (TRIG)	

### 3.12 Toxicokinetic Blood Collections (TK Animals)

The toxicokinetic portion consisted of two phases. Phase I determined an appropriate time to sample plasma for nicotine and cotinine from animals fed nicotine containing test articles in the diet. This was accomplished by determining the time course of plasma nicotine and cotinine at the approximate mid-point of the study. At Study Days 13 and 14, six specified time points were spread over a 14-hour time interval to determine the observed C<sub>max</sub> and

$T_{\max}$  values for nicotine and cotinine in male and female rats from up to nine specified treatment groups. Phase 2 was based on the information obtained from Phase 1 data, in which the most appropriate (estimated  $C_{\max}$  and  $T_{\max}$ ) single collection time point was selected for collecting samples from male and female rats. The data from Phase 2 was used to evaluate dose proportionality by sex and group.

### **3.12.1 Phase 1 Collections**

From each dose group, six rats of each sex assigned to the toxicokinetics study were randomly subdivided into two subsets of animals. Each subset was used for blood collection at specific times in a manner that resulted in no more than two blood collections/animal and in a manner that distributes each subset over the 14-hour time course. Subset 1 consisted of three males and three females from each of the nine treatment groups from which blood was drawn at 10:00 PM, 4:00 AM, and 10:00 AM. Subset 2 consisted of three males and three females from each of the nine treatment groups from which blood was drawn at 12:00 AM, 6:00 AM, and 12:00 PM. This resulted in six time points for plasma nicotine and cotinine over a 14-hour time interval and allowed for the determination of the optimal time for collection in Phase 2 and subsequent studies.

TK study animals were anesthetized with  $\text{CO}_2/\text{O}_2$  and blood was collected from the retro-orbital cavity into tubes containing potassium EDTA as the anti-coagulant. Blood was placed on wet ice until centrifuged. Plasma was extracted, placed on dry ice, and stored in a freezer (-60 to -80°C). After each blood collection the animal was placed in its home cage supplied with feed and water until the next available blood draw.

### **3.12.2 Phase 2 Collections**

On Study Day 28, blood was collected from five male and five female TK animals in each of nine treatment groups at 12:00 AM based on the results from Phase 1 toxicokinetics. After plasma collection, all animals in the TK subset were terminated with no further data collection. From the five remaining male and five remaining female sentinels, plasma was collected at the TK Day 28 scheduled blood collection per sex to measure background nicotine and cotinine plasma levels among study animals not exposed to the test article.

### 3.13 Necropsy and Organ Weights

After at least 28 days of dosing, all surviving core animals, excluding sentinels, were fasted overnight and humanely terminated using CO<sub>2</sub>. Terminal body weights were determined and external features of the animals were evaluated prior to euthanasia, followed by necropsy.

Each necropsy included: examination of the external surface of the body; all orifices; the cranial, thoracic, abdominal and pelvic cavities and their contents; and collection of all tissues listed in the protocol, as well as gross findings. All scheduled necropsies were conducted under the supervision of a board-certified veterinary pathologist.

The following tissues were collected according to facility SOP. Tissues were fixed in 10 percent neutral buffered formalin (NBF), with the exception of testes, which were preserved in Bouin's fixative and subsequently transferred to 70 percent ethanol, and eyes with optic nerve which were fixed in Davidson's fixative and subsequently transferred to 10 percent NBF, per facility SOP.

#### Tissues Collected at Necropsy

Animal identification	Pituitary gland
Adrenal glands	Preputial glands
Bone and marrow (femur)	Prostate gland
Brain	Salivary gland (mandibular)
Clitoral gland	Sciatic nerve
Epididymides	Seminal vesicles
Esophagus, pharynx	Skeletal muscle (biceps femoris)
Eyes	Skin
Gross lesions	Spinal cord (cervical, thoracic, lumbar)
Harderian glands	Spleen
Heart	Sternum with bone marrow
Intestine, large (cecum, colon, rectum)	Stomach (fore-stomach and glandular)
Intestine, small (duodenum, jejunum, ileum)	Testes
Kidneys	Thymus
Liver (median lobe and left lateral lobe)	Thyroid gland (with parathyroids, if present in routine section)
Lungs with bronchi	Tongue
Lymph node (mesenteric)	Urinary bladder
Mammary gland (females only)	Uterus
Nose (nasal cavity and turbinates)	Vagina
Ovaries (without oviduct)	Zymbal glands
Oral cavity	
Pancreas	

The following organs were weighed for core rats euthanized at scheduled necropsy.

#### Organs Weighed at Necropsy

Adrenal glands <sup>a</sup>	Spleen
Brain	Ovaries (without oviduct) <sup>a</sup>
Epididymides <sup>a</sup>	Testes (without epididymides) <sup>a</sup>
Heart	Thymus
Kidneys <sup>a</sup>	Salivary glands (mandibular)
Liver	Uterus (with cervix)

a. Paired organs weighed together.

### 3.14 Computer Systems for Data Management

Computer System Name	Version #	Manufacturer	Data Type
Analyst	1.4.1 or 1.4.2	Applied Biosystems, Inc.	Chromatography/ Mass Spectrometry
Atlas	8.2	Thermo Fisher Scientific	Chromatography
Excel Building Supervisor	1.7	Honeywell	Animal Facility Environmental
PATH/TOX SYSTEM	4.2.2	Xybion Medical Systems Corporation	Animal Toxicology and Pathology
T-Track	1.0.0	Battelle	Environmental Storage

### 3.15 Data Analysis

(b) (4)



(b) (4)



## 4.0 RESULTS

### 4.1 Clinical Observations (Core Animals)

Several clinical signs were apparent over the course of this study. Clinical observations observed in the core study male (Table 1) and female (Table 2) extract exposure groups included minor abrasions (E0.2M), alopecia (E0.2M and E0.2F), and tremors (E8F). Clinical observations in the high dose male (Table 3) and high dose and pairfed female (Table 4) groups included rough hair coat (B20M, E20M, NT20F, PFCNTF, and B20F groups), thin appearance (NT20F, B20F, and E20F), lethargy (B20F), and tremors (E20F). These observations were sporadic in occurrence and did not follow a dose response relationship in any of the treatment groups. Treated rats not showing signs were similar to control (CM or CF) in overt behavior and in general health and appearance.

### 4.2 Body Weights (Core, TK, and Pairfed Animals)

The group mean absolute body weights for male and female core study rats are included in Tables 5 and 6. Treatment with the test articles and positive control was associated with a significant reduction in group mean body weight in the NT20M, B8M, B20M, E8M, and E20M exposure groups of 27.5, 17.2, 31.0, 14.9, and 30.7%, respectively, relative to control (CM) on Study Day 25 (Table 5). This decrease was apparent as early as Study Day 4, continued over the course of the study, and was both dose and time dependent in the tobacco blend and extract exposure groups. A similar trend occurred in the female exposure groups. Treatment with the test articles and positive control was associated with a significant reduction in group mean body weight in the NT20F, B8F, B20F, E8F, and E20F exposure groups relative to control (CF) of 21.1, 12.1, 27.3, 7.1, and 26.3%, respectively, on Study Day 25 (Table 6). This decrease occurred early (Study Day 4) and was generally dose and time dependent in the tobacco blend (TB) and tobacco extract (TE) exposure groups. Group mean body weights for the male and female core study rats group are also included in Figures 1 and 2 for the TB groups, Figures 5 and 6 for the TE groups, and Figures 9 and 10 for the nicotine tartrate (NT) groups, respectively. Group mean body weights for the pairfed male and female control groups in relation to their respective high dose groups are included in Figures 3 and 4 for the TB groups, Figures 7 and 8 for the TE groups, and Figures 11 and 12

for the NT groups. Group mean absolute body weight gain for the male and female TB groups are included in [Figures 13](#) and [14](#), respectively. Group mean absolute body weight gain for the TB high dose groups (B20M and B20F) and their paired control groups (PFCBM and PFCBF) are included in [Figures 15](#) and [16](#), respectively. Group mean absolute body weight gain for the male and female TE groups are included in [Figures 17](#) and [18](#), respectively. Group mean absolute body weight gain for the TE high dose groups (E20M and E20F) and their paired control groups (PFCEM and PFCEF) are included in [Figures 19](#) and [20](#), respectively. Group mean absolute body weight gain for the male and female NT groups are included in [Figures 21](#) and [22](#), respectively. Group mean absolute body weight gain for the NT high dose groups (NT20M and NT20F) and their paired control groups (PFCNTM and PFCNTF) are included in [Figures 23](#) and [24](#), respectively.

The group mean body weights for the paired control groups and the high dose groups are included in [Tables 7](#) and [8](#) for males and females, respectively. Exposure of the NT20M, B20M, and E20M high dose groups caused depressions in group mean body weight relative to CM of 27.5, 31.0, and 30.7%, respectively, when compared on Study Day 25. Diet restriction in the corresponding PFCNTM, PFCBM, and PFCEM groups caused somewhat similar reductions in group mean body weight relative to CM of 27.4, 24.5, and 23.0%, respectively, on Study Day 25. Comparative statistics have indicated that the magnitude of the reduction of body weight in the B20M and E20M groups was greater than in the corresponding PFCBM and PFCEM groups. Exposure of the NT20F, B20F, and E20F groups caused depressions in group mean body weight relative to CF of 21.2, 27.3, and 26.3%, respectively, on Study Day 25. Diet restriction in the corresponding PFCNTF, PFCBF, and PFCEF groups caused reductions relative to CF of 15.7, 11.1, and 14.3%, respectively, on Study Day 25. Comparative statistics have indicated the magnitude of the body weight reduction in the NT20F, B20F, and E20F groups was greater than in the corresponding PFCNTF, PFCBF, and PFCEF groups. Group mean body weights for male and female toxicokinetic group rats are included in [Tables 9](#) and [10](#), respectively.

### 4.3 Food Consumption (Core and Pairfed Animals)

The mean food consumption values for the core male and female groups are included in [Tables 11](#) and [12](#), respectively. The NT20M, B8M, B20M, E8M, and E20M dosage groups showed a decrease in grand mean food consumption of 38.4, 18.6, 39.7, 14.8, and 41.4% relative to the CM group. The NT20F, B20F, and E20F groups showed a decrease in grand mean food consumption of 28, 29.8, and 24.2% relative to the CF group. The food consumption of the pairfed control groups is included in [Table 13](#) for male rats and [Table 14](#) for female rats. The food consumption of the pairfed groups followed closely to that of the target high dose group. For males, the grand mean food consumption was 13.5 grams/day for the NT20M group and 14.0 grams/day for the PFCNTM group, 14.4 grams/day for the B20M group and 14.7 grams/day for the PFCBM group, and 15.1 grams/day for the E20M group and 15.4 grams/day for the PFCEM group. For females, the grand mean food consumption was 11.5 grams/day for the NT20F group and 11.7 grams/day for the PFCNTF group, 12.4 grams/day for the B20F group and 12.9 grams/day for the PFCBF group, and 12.5 grams/day for the E20F group and 12.8 grams/day for the PFCEF group. Group mean food consumption values for the male and female TB core rats are included in [Figures 25](#) and [26](#), respectively. Group mean food consumption values for the male and female TB high dose groups (B20M and B20F) and their respective pairfed control groups (PFCBM and PFCBF) are included in [Figures 27](#) and [28](#), respectively. Group mean food consumption values for the male and female TE core rats are included in [Figures 29](#) and [30](#), respectively. Group mean food consumption values for the male and female TE high dose groups (E20M and E20F) and their respective pairfed control groups (PFCEM and PFCEF) are included in [Figures 31](#) and [32](#), respectively. Group mean food consumption values for the male and female NT core rats are included in [Figures 33](#) and [34](#), respectively. Group mean food consumption values for the male and female NT high dose groups (NT20M and NT20F) and their respective pairfed control groups (PFCNTM and PFCNTF) are included in [Figures 35](#) and [36](#), respectively.

### 4.4 Neurobehavioral Toxicity (Core Animals)

The neurobehavioral effects narrative is provided in [Appendix G](#).

Male and female rats treated for a minimum of 28 days with feed containing the tobacco blend or tobacco extract test article generally exhibited a slightly reduced arousal level and emotionality, as compared to the CM/CF. In several cases, the NT20M/NT20F exhibited neurobehavioral effects similar to those seen in one or more tobacco blend or tobacco extract groups (as compared to the CM/CF group). In general, the effects of tobacco blend or tobacco extract treatment were slightly greater in female than in male rats, and the effects of the tobacco extract treatments were slightly greater than the effects of the tobacco blend treatments. For example, in female rats in the NT20F group, the B20F group or the E20F group, mean rectal temperature was significantly reduced as compared to the CF group. This effect can possibly be attributed to the hypothermic effect of nicotine ingestion in rodents (Ruskin *et al.*, 2007).

The results suggest that repeated oral ingestion of tobacco blend or tobacco extract, particularly at the high target dose (20 mg/kg/day) or ingestion of the nicotine tartrate high target dose positive control (20 mg/kg/day) resulted in slightly reduced arousal and emotionality, without significantly impacting other major neurobehavioral parameters including general physical appearance, postural integrity, spontaneous locomotor activity, muscular system integrity, equilibrium, sensory responsivity, pain thresholds or autonomic nervous system function. There was no evidence in male and female Wistar Hanover rats of the neurobehavioral effects (for example, increased spontaneous locomotor activity, tremor, stereotypy, etc.) that might be expected with treatments containing high levels of nicotine (Liang *et al.*, 2008).

From the results of the FOB testing, it cannot be concluded that tobacco blend or tobacco extract had a significant effect on any specific CNS systems, although the reduced mean rectal temperature effects observed in several groups of female rats might suggest a slight modulation of one or more CNS neurotransmitter systems (e.g., serotonin) (Knapp *et al.*, 2000).

#### 4.5 Toxicokinetics

The narrative for the toxicology study is included in [Appendix H](#). Phase 1 studies were conducted to determine the appropriate time to sample plasma for nicotine and cotinine from animals fed nicotine containing test articles in the diet. The  $T_{\max}$  was determined by selecting the most common Day 14  $T_{\max}$  among male and female rats of all dose groups. The

variability of the eating habits of the rats led to increased variability in the group mean  $C_{\max}$  determinations resulting in many dose groups with multiple time points that could be considered as potential  $T_{\max}$  values. A time of 12:00 AM was chosen as it occurred with the highest frequency among the male and female dose groups. Among the dose groups that had only one discernable  $T_{\max}$ , 12:00 AM again occurred with the highest frequency.

Evaluation of  $C_{\max}$  values on Day 28 revealed no gender effects as values were similar between the genders for all dose groups for nicotine and cotinine. There were no formulation effects as tobacco extract and tobacco blend with the same nicotine target dosages had similar  $C_{\max}$  values for both male and females. The  $C_{\max}$  values increased proportionally with an increase in dose for both the tobacco extract and blend except for the E2F group which was about two-fold higher than expected. However, this was not considered biologically relevant as the  $C_{\max}$  values for the female E8F and E20F dose groups both increased proportionally when compared with the E0.2F group.

#### **4.6 Clinical Pathology (Core Animals)**

Group mean hematology data are presented in [Table 15](#) for core male rats, [Table 16](#) for core female rats, [Table 17](#) for the pairfed male rats and [Table 18](#) for the pairfed female rats.

Although there were a few statistically significant differences as noted in these tables, there were no consistent dose-related trends that were indicative of any treatment-related effects.

Group mean absolute white blood cell differential count data are included in [Table 19](#) for core male rats, [Table 20](#) for core female rats, [Table 21](#) for pairfed male rats, and [Table 22](#) for pairfed female rats. There were no dose- or treatment-related trends in the differential white blood count data. There were no treatment-related differences in coagulation as indicated in [Table 23](#) for core male rats, [Table 24](#) for core female rats, [Table 25](#) for pairfed male rats, and [Table 26](#) for pairfed female rats.

Group mean clinical chemistry data are presented for core male rats ([Table 27](#)), core female rats ([Table 28](#)), pairfed male rats ([Table 29](#)), and pairfed female rats ([Table 30](#)). A number of trends in the clinical chemistry results were noted in the groups given the two test articles at the highest dose and the positive control (NT20M, NT20F, B20M, B20F, E20M and E20F group). These included: decreased total protein, albumin and globulin and decreased glucose

with increased alkaline phosphatase, total and direct bilirubin, blood urea nitrogen, albumin/globulin ratio, triglycerides and cholesterol. The alterations in these parameters were modest in magnitude and were of similar magnitude in all of the cited groups and in both sexes. Analysis of results in pairfed controls in comparison with the results of the NT20M, NT20F, B20M, B20F, E20M and E20F indicated that the alterations in cited parameters were not simply due to decreased food consumption. Other differences from control noted by the use of statistical methods were not interpreted to be related to test-article feeding, based on the small size of these differences in relation to variation that is found in untreated Wistar Han rats.

## **4.7 Pathology (Core Animals)**

### **4.7.1 Organ Weights**

Group mean absolute organ weights are included in [Table 31](#) for core male rats, [Table 32](#) for core female rats, [Table 33](#) for pairfed male rats, and [Table 34](#) for pairfed female rats. Male rats in the higher dosage groups (NT20M, B8M, B20M, E8M, and E20M) showed decreases in many absolute organ weights that were significantly different from the CM group. Female rats in the higher dosage groups (NT20F, B20F, and E20F) also showed a similar trend in decreased absolute organ weights. Group mean organ weight to body weight values are included in [Table 35](#) for core male rats, [Table 36](#) for core female rats, [Table 37](#) for pairfed male rats, and [Table 38](#) for pairfed rats. Most of the male treatment groups which showed decreased absolute organ weights now show organ-to-body weight values which were either similar to or slightly increased relative to the CM group. Female treatment groups showed group mean organ weight values that were similar to that of the CF group (Table 36). Group mean organ-to-brain weight values are included in [Table 39](#) for core male rats, [Table 40](#) for core female rats, [Table 41](#) for pairfed male rats, and [Table 42](#) for pairfed female rats. The high dose male (NT20M, B20M, and E20M) and female (NT20F, B20F, and E20F) showed a tendency for decreased organ-to-brain weight values when compared to those of their respective control group (CM or CF, respectively). These groups showed organ-to-brain weight values which were closer to that of their pairfed male (Table 41) and female (Table 42) control groups suggesting reduced organ weight (size) was related to the rather large reduction in body weight.

#### **4.7.2 Gross Findings**

A few findings were noted at necropsy to include liver nodule (Group CM, Animal 103), skin ulcer (Group E0.2M, Animal 905), skin alopecia (Group E0.2M, Animal 907), enlarged clitoral gland (Group E8F, Animal 1160), renal pelvis dilatation and small thymus (Group E20M, Animal 1204), and kidney cyst (Group PFCNTF, Animal 356). These findings were considered incidental and spontaneous in nature and unrelated to treatment. There were no treatment-related gross lesions.

## 5.0 DISCUSSION

No clinical signs of toxicity were observed during this study that could be directly attributed to the administration of any of the test or control articles. Some observations (thinness) may have occurred due to a lack of palatability for the diets at the higher nicotine concentration. Other observations (rough hair coat) may have resulted from stress associated with inanition.

Treated animals were generally similar to control in overt behavior and in general health and appearance. Neurobehavioral testing of the NT, TB, and TE 20 mg/kg test groups did reveal subtle changes in reduced arousal and emotionality without impairing other major neurobehavioral parameters including spontaneous locomotor activity, muscular system integrity, postural integrity, equilibrium, sensory responsivity, pain thresholds, or autonomic nervous system function. In general, the effects of TB and TE were slightly greater in female rats and the effects resulting from exposure to TE was slightly greater than that to TB.

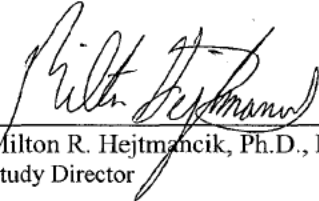
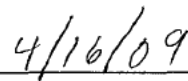
Nonetheless, there was no evidence of neurobehavioral effects associated with exposure to higher levels of nicotine including tremor, stereotypy, and spontaneous motor activity (Liang *et al.*, 2008). High dose female rats in the NT, TB, and TE treatment groups also showed a reduction in mean rectal temperature as compared to the CF group. This effect can be attributed to the hypothermic effect of nicotine ingestion in rodents (Ruskin *et al.*, 2007) and may be related to slight modification of one or more central nervous system neurotransmitter systems (e.g., serotonin) (Knapp *et al.*, 2000). Also, the neurobehavioral effects described above appear to be directly related to the nicotine component of each of the test articles since these effects were apparent with both test articles and the positive control.

No mortality occurred in any of the core test groups indicating the dosages over the course of this range finding study which indicated the doses were appropriate for the dosed feed route of administration. Toxicokinetic studies showed that the  $C_{\max}$  values increased proportionally with an increase in dose for the TB and TE groups with no gender effects, except for the E2F group which was about two-fold higher than expected. However, this increase was not considered biologically relevant as the  $C_{\max}$  values for the E8F and E20F groups both increased proportionally when compared to that of the E0.2F group. Also, a time of 12:00 AM was selected as the Day 14  $T_{\max}$  as it occurred with the highest frequency among the male and female dosage groups.

Clinical pathology studies at study termination revealed no treatment or dose-related trends. Trends in clinical chemistry occurred in groups given the test articles at the highest dose and the positive control and included: decreased total protein, albumin and globulin and decreased glucose with increased alkaline phosphatase, total and direct bilirubin, blood urea nitrogen, albumin/globulin ratio, triglycerides and cholesterol. The alterations in these parameters of these groups were of similar magnitude in both sexes. Comparison of results with paired controls indicated that the alterations were not simply due to decreased food consumption and were more likely associated with exposure. Changes in absolute organ weight and organ to body and/or brain weight values were attributed to treatment-related reductions in group mean body weight, since no gross lesions were detected at necropsy in any of the affected organs.

Exposure of rats to TB and TE at 8 and 20 mg/kg caused a dose-related reduction in group mean absolute body weight and food consumption relative to the respective control groups (CM and CF). Exposure to the test articles at 20 mg/kg caused profound decreases in both group mean body weight and food consumption which would preclude selection of this dose for the 90-day study. Moreover, the magnitude of the reduction in the high dose group for each test article was generally greater than that of their respective paired control group. Exposure to the test articles at 8 mg/kg caused more moderate reductions in group mean body weight and food consumption relative to control. Consequently, dosages of 0.3, 3, and 6 mg/kg are recommended for the 90-day studies.

Reports of deviations from the protocol are found in [Appendix A](#). The deviations were minor and had no impact on the data or interpretation of results.

**6.0 REQUIRED SIGNATURES**  
\_\_\_\_\_  
Milton R. Hejtmancik, Ph.D., D.A.B.T.  
Study Director  
\_\_\_\_\_  
Date

## 7.0 REFERENCES

Knapp, D.J., Sim-Selley, L.J., Breese, B.R., and Overstreet, D.H. (2000). Selective breeding of 5-HT(1A) receptor-mediated responses: application to emotion and receptor action. *Pharmacol. Biochem. Behav.* 67:701-708.

Liang, Y., Boules, M., Shaw, A.M., Williams, K., Fredrickson, P., and Richelson, E. (July 19, 2008). Effect of a novel neurotensin analog, NT69L, on nicotine-induced alterations in monoamine levels in rat brain. *Brain Res.* [Epub ahead of print].

Ruskin, D.N., Anand, R., and LaHoste, G.J. (2007). Menthol and nicotine oppositely modulate body temperature in the rat. *Eur. J. Pharmacol.* 559:161-164.

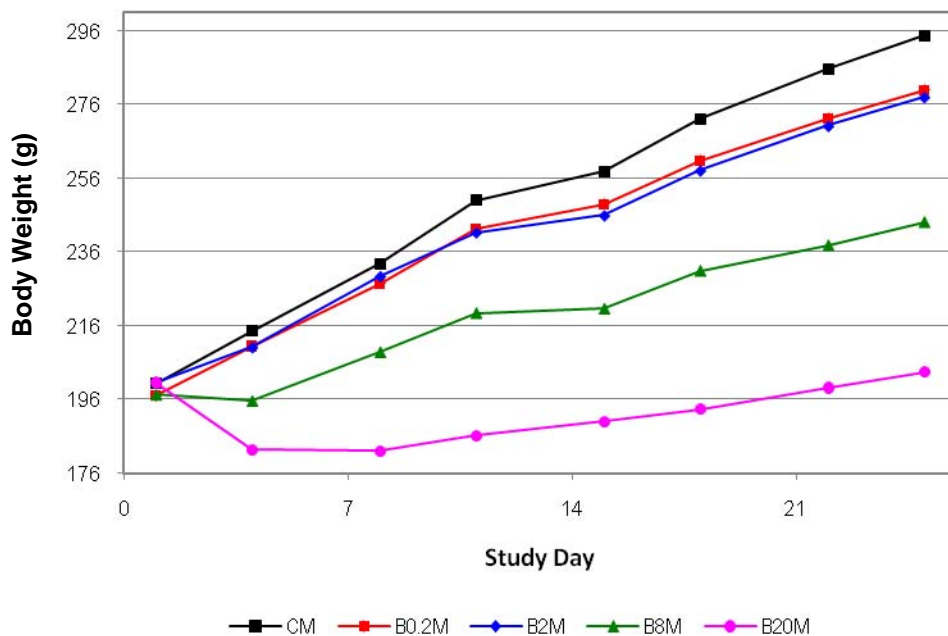
## **8.0 SPECIMEN STORAGE AND RECORD ARCHIVES**

The pertinent study records were maintained according to SOPs. The Battelle study records and final report were maintained under the direction of Battelle.

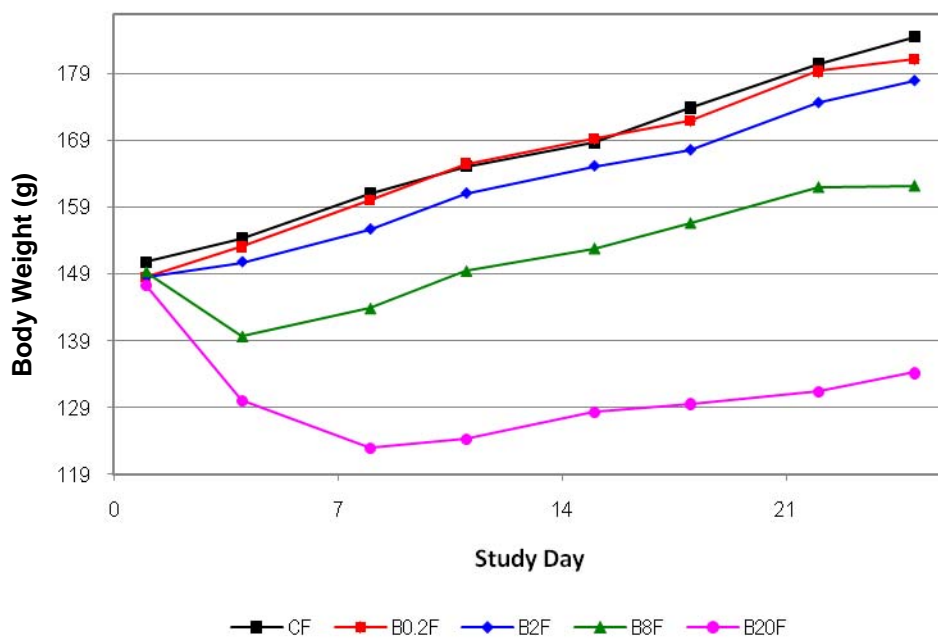
Wet tissues, clinical pathology slides, and archival samples will be maintained for a period of no less than one year after issuance of the final report. After one year, the Sponsor will provide authorization concerning the disposition of these items.

## 9.0 ACKNOWLEDGMENTS

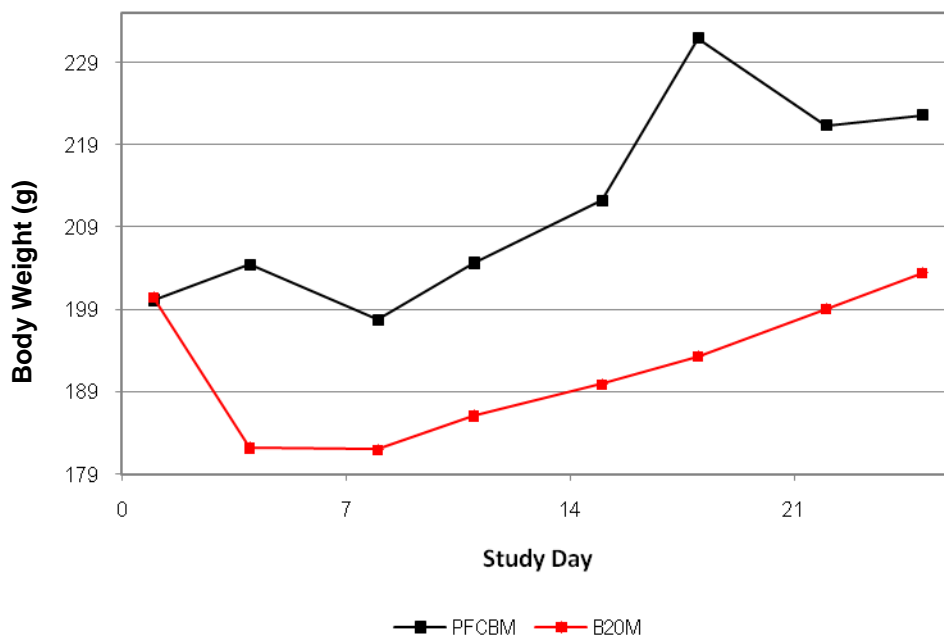
Participant	Role
Milton R. Hejtmancik, Ph.D., D.A.B.T.	Study Director
Dawn M. Fallacara, M.S.	Study Coordinator
Allen W. Singer, D.V.M., D.A.B.T., Diplomate, A.C.V.P.	Manager Toxicology Columbus
Nathanial Hale, B.S.	Primary Technician
Anthony J. Skowronek, D.V.M., Ph.D., Diplomate, A.C.V.P.	Study Pathologist
Michael J. Ryan, D.V.M., Ph.D., D.A.B.T., Diplomate, A.C.V.P.	Clinical Pathologist
Daphne Y. Vasconcelos, D.V.M., Ph.D., D.A.B.T., Diplomate, A.C.V.P.	Manager Pathology
Brian Burback, Ph.D.	Chemist
Edward A. Psurny, B.S.	Chemist
Kevin Carrico, B.A.	Dose Formulations
Seth T. Gibbs, Ph.D.	Toxicokineticist
Jerry D. Johnson, Ph.D., D.A.B.T.	Toxicokineticist
Glenn D. Ritchie, Ph.D.	Neurobehavioral Scientist



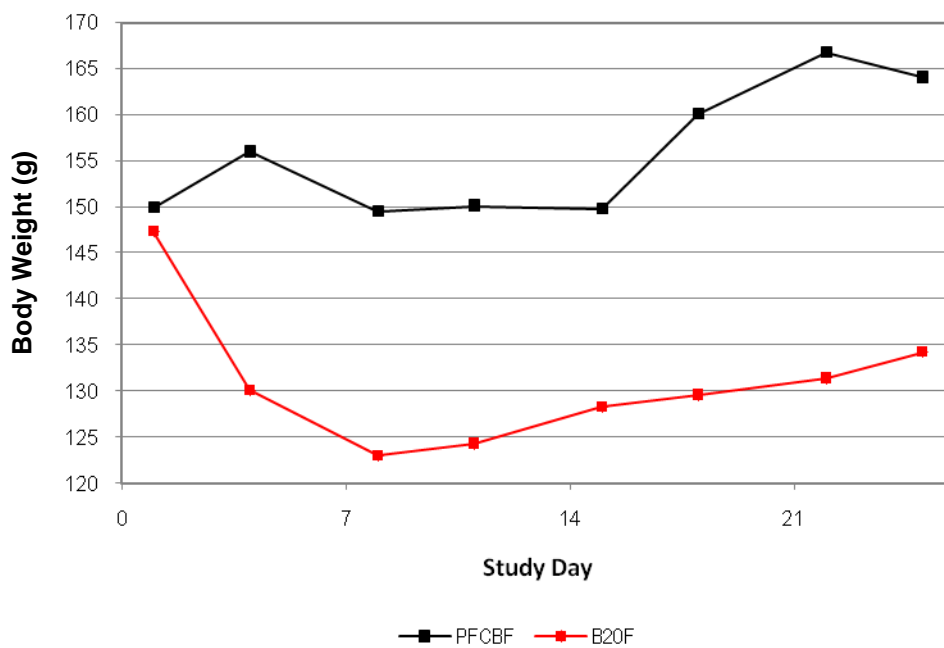
**Figure 1. Group Mean Body Weights (g) Tobacco Blend – Males**



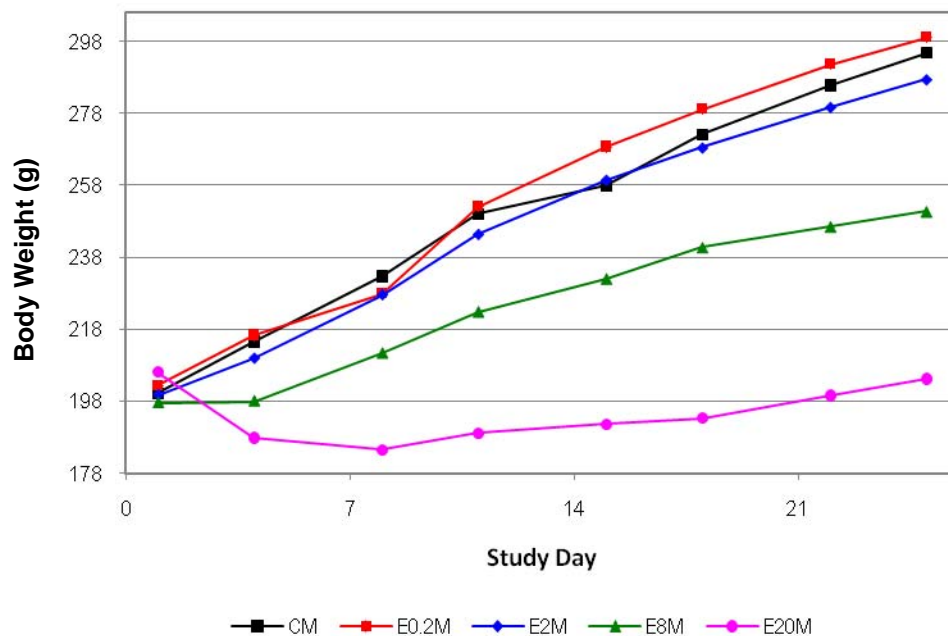
**Figure 2. Group Mean Body Weights (g) Tobacco Blend – Females**



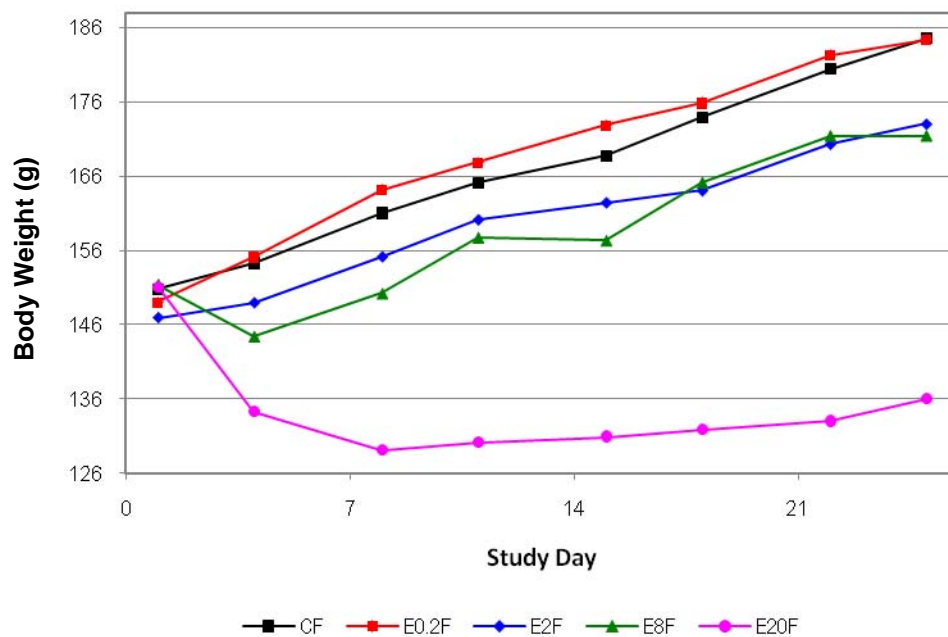
**Figure 3. Group Mean Body Weights (g) Tobacco Blend (High vs. Pairfed) – Males**



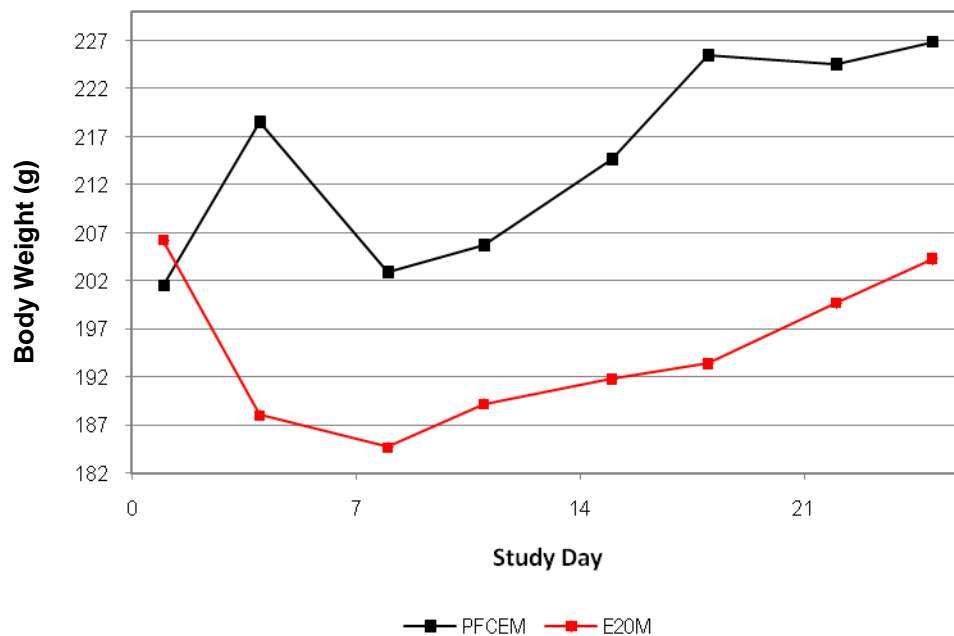
**Figure 4. Group Mean Body Weights (g) Tobacco Blend (High vs. Pairfed) – Females**



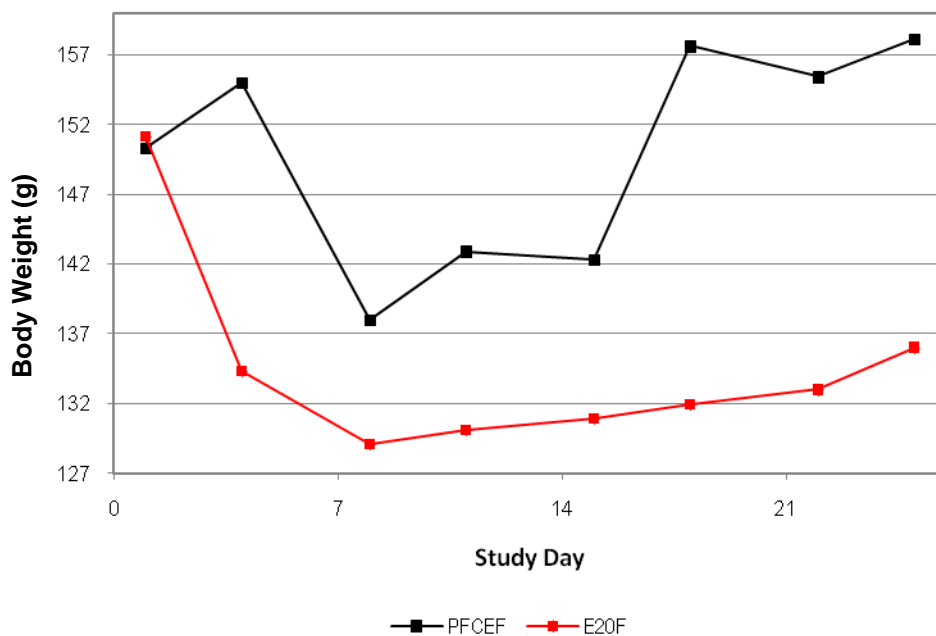
**Figure 5. Group Mean Body Weight (g) Tobacco Extract – Males**



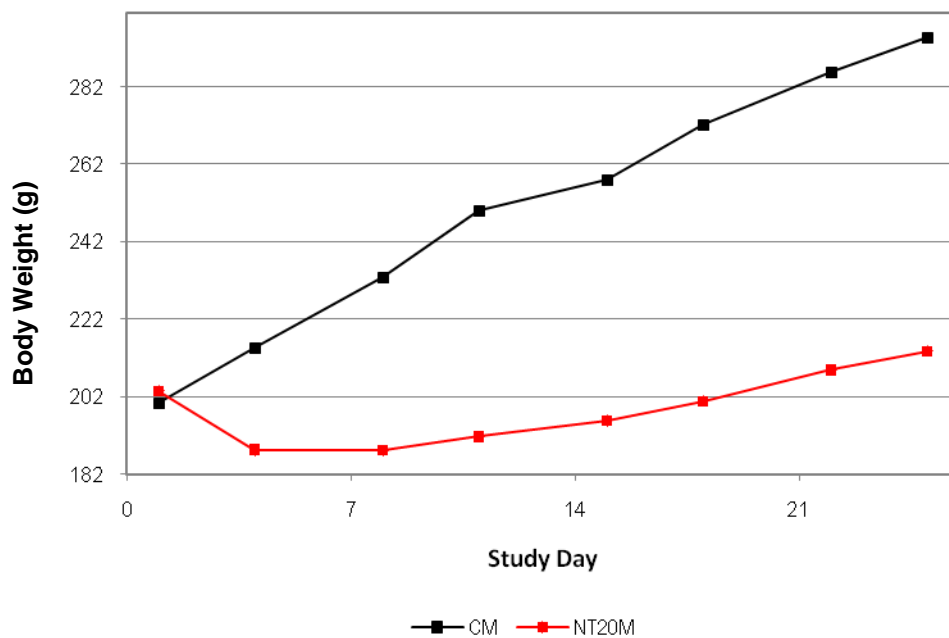
**Figure 6. Group Mean Body Weight (g) Tobacco Extract – Females**



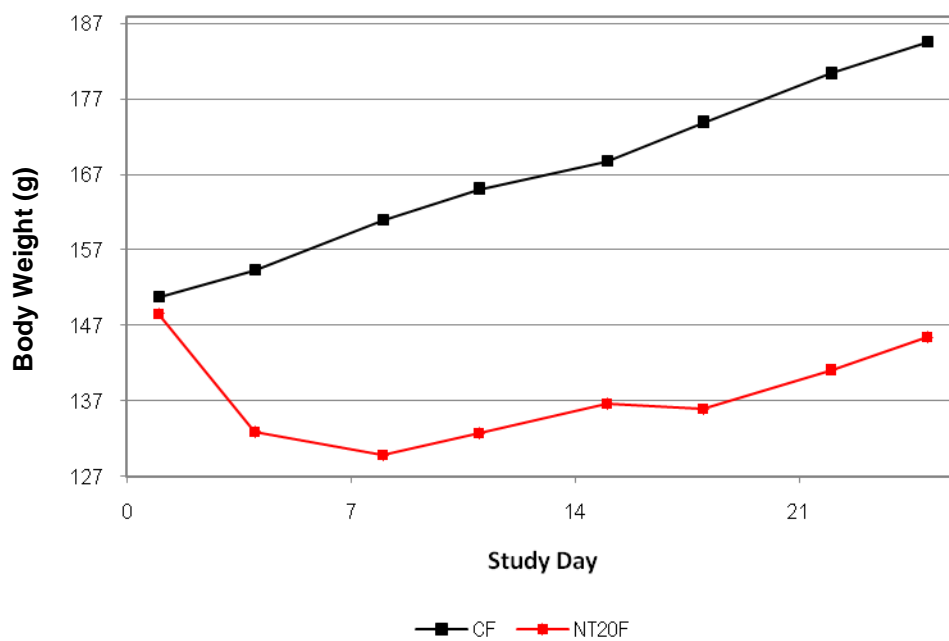
**Figure 7. Group Mean Body Weight (g) Tobacco Extract (High vs. Pairfed) – Males**



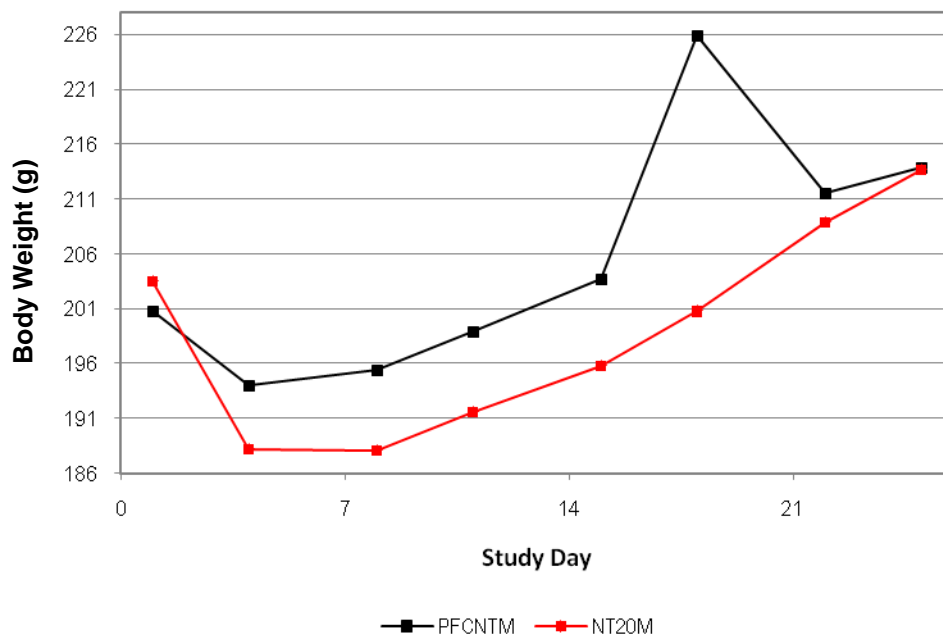
**Figure 8. Group Mean Body Weight (g) Tobacco Extract (High vs. Pairfed) – Females**



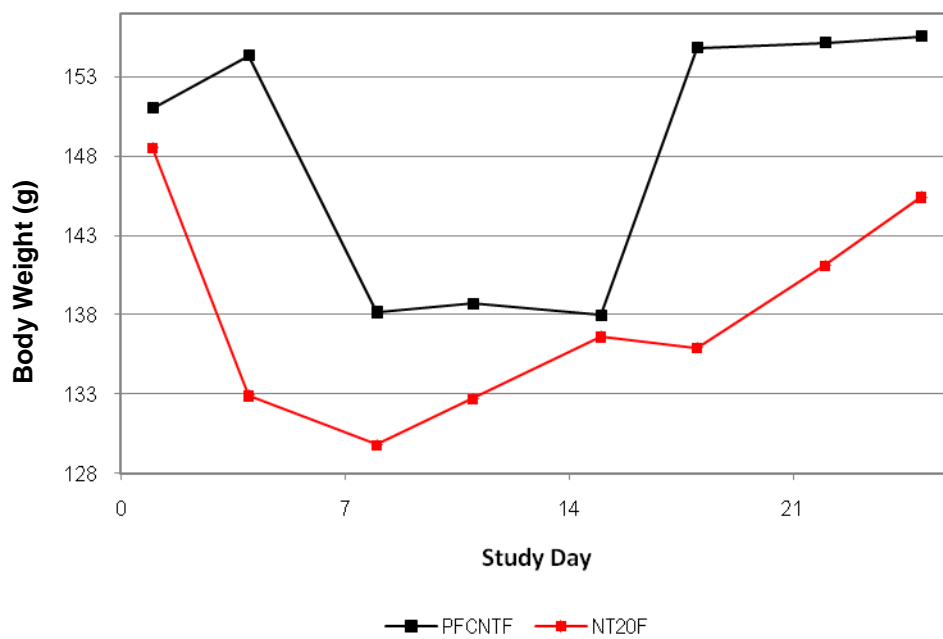
**Figure 9. Group Mean Body Weight (g) Nicotine Tartrate – Males**



**Figure 10. Group Mean Body Weight (g) Nicotine Tartrate – Females**



**Figure 11. Group Mean Body Weight (g) Nicotine Tartrate (High vs. Pairfed) – Males**



**Figure 12. Group Mean Body Weight (g) Nicotine Tartrate (High vs. Pairfed) – Females**

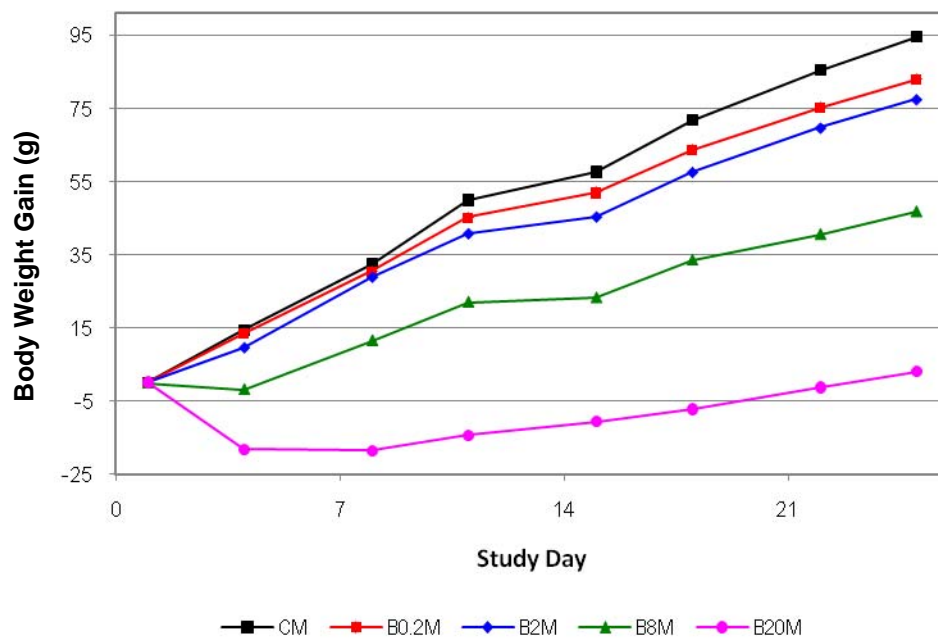


Figure 13. Group Mean Absolute Body Weight Gain (g) Tobacco Blend – Males

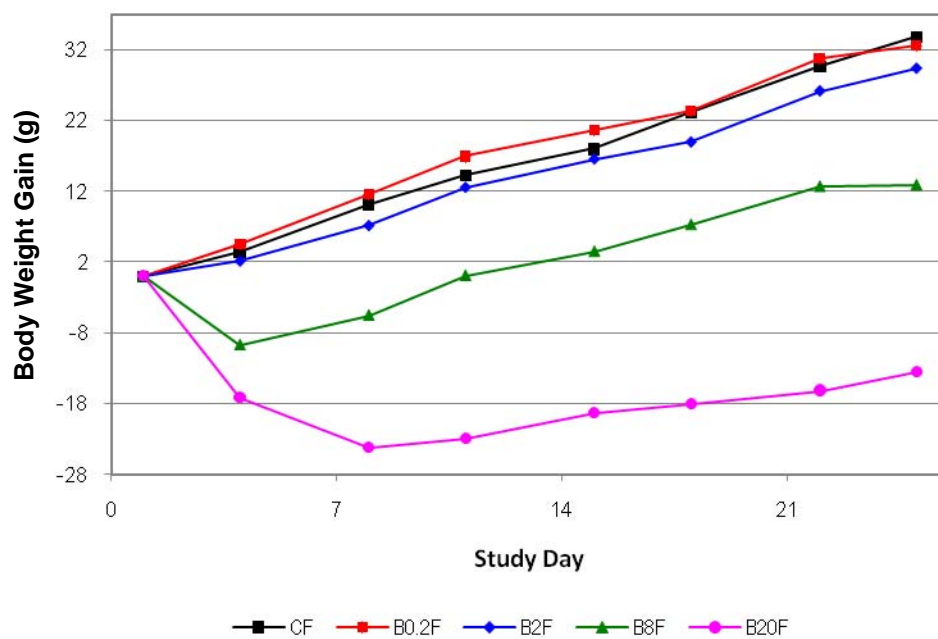
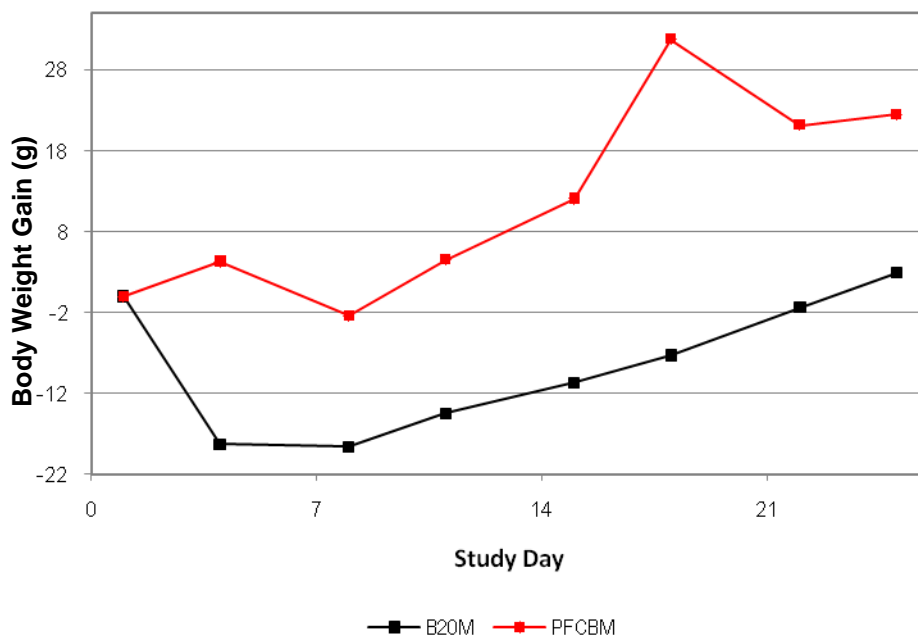
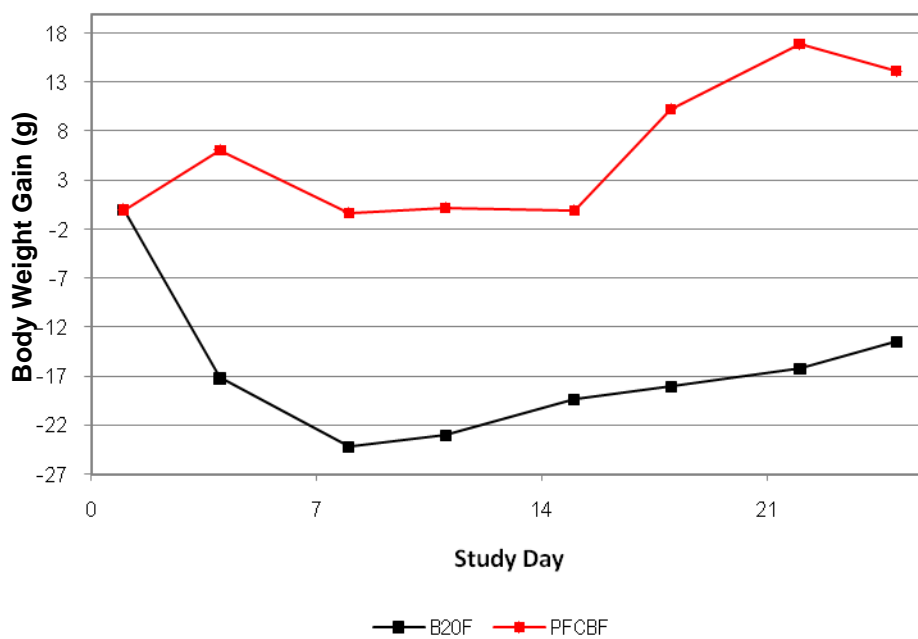


Figure 14. Group Mean Absolute Body Weight Gain (g) Tobacco Blend – Females



**Figure 15. Group Mean Absolute Body Weight Gain (g) Tobacco Blend (B20M vs. PFCBM) – Males**



**Figure 16. Group Mean Absolute Body Weight Gain (g) Tobacco Blend (B20F vs. PFCBF) – Females**

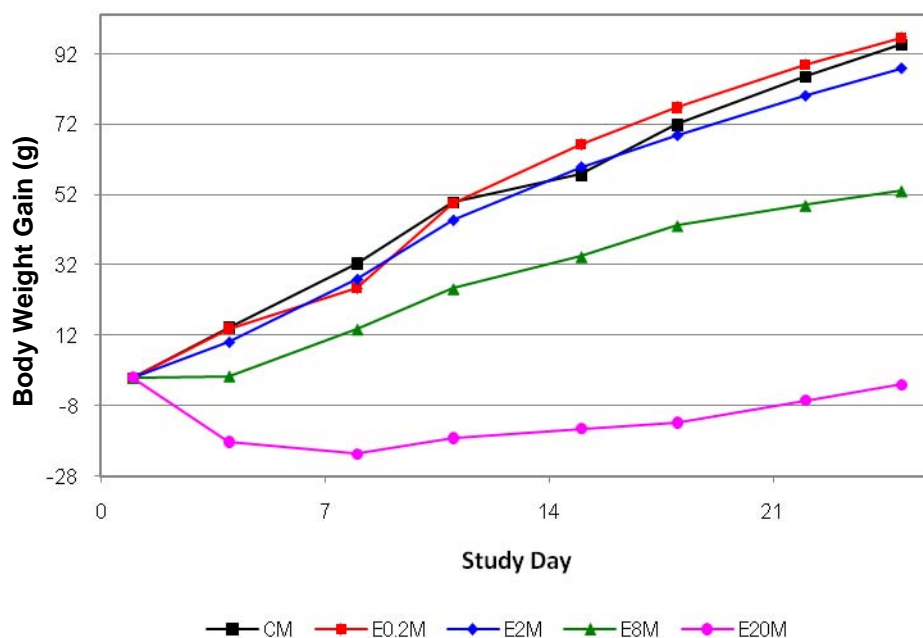


Figure 17. Group Mean Absolute Body Weight Gain (g) Tobacco Extract – Males

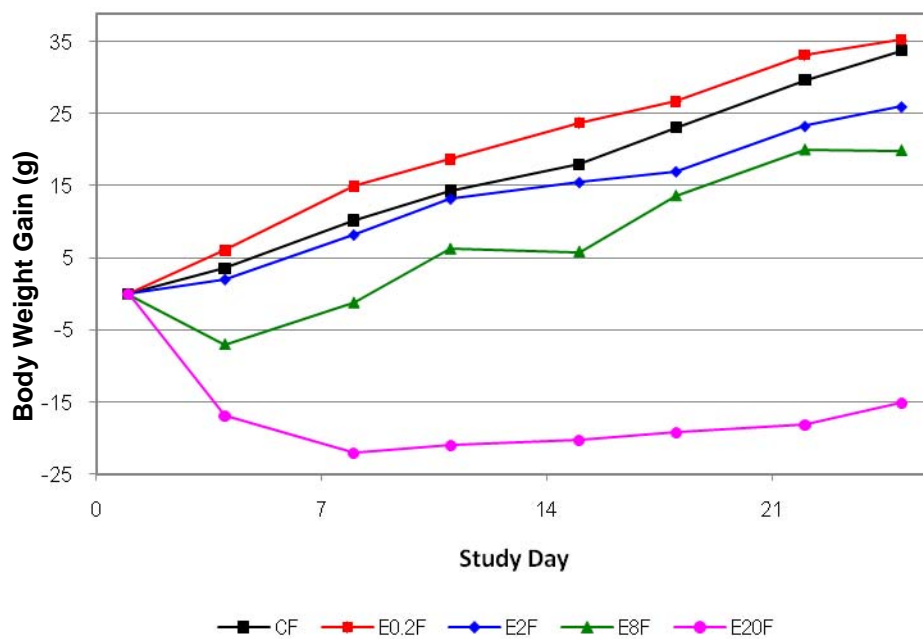
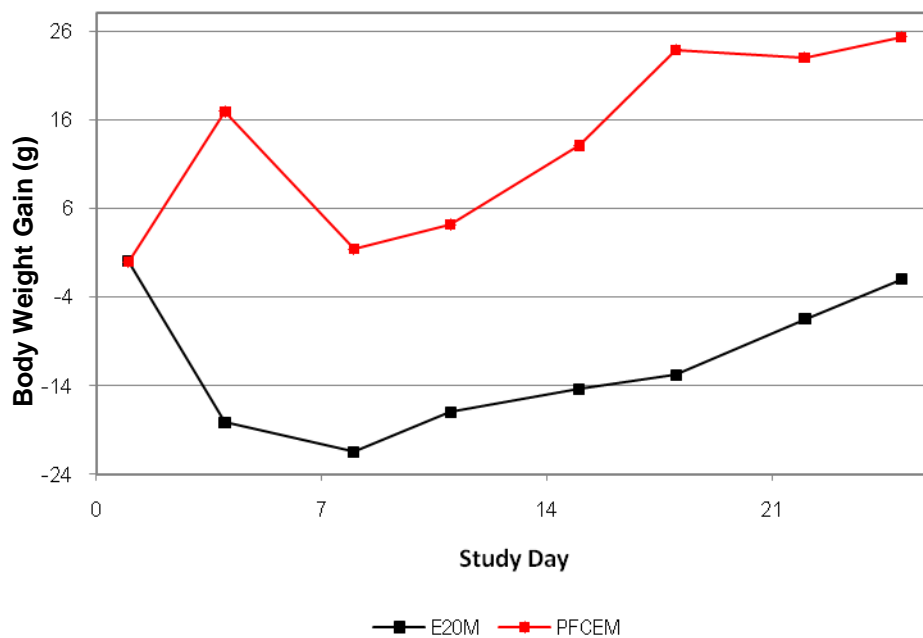
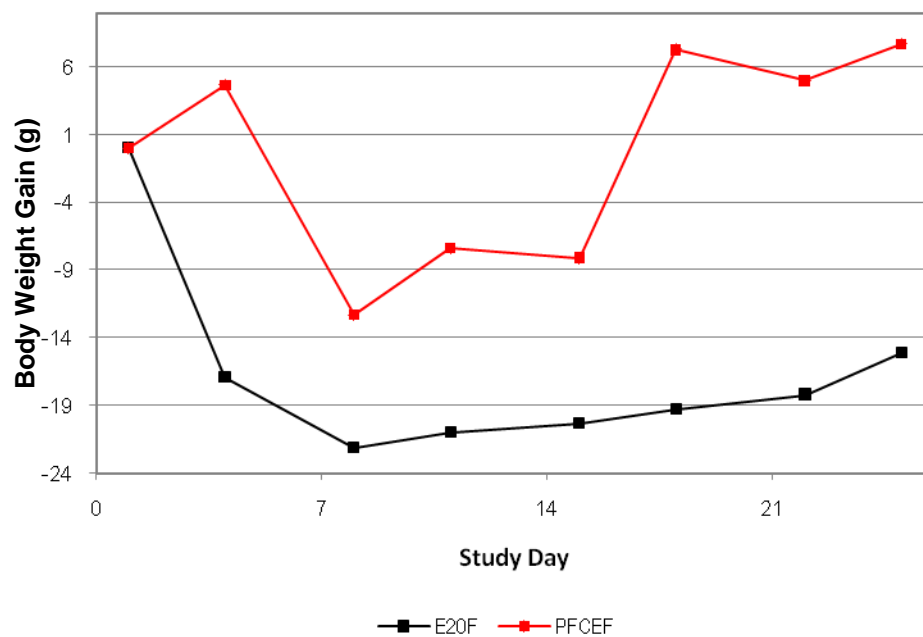


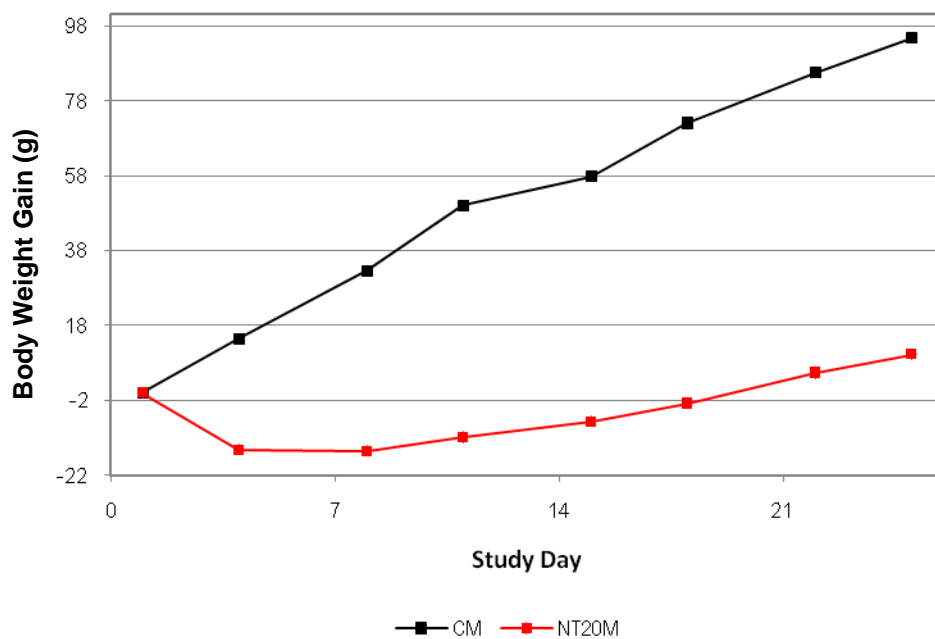
Figure 18. Group Mean Absolute Body Weight Gain (g) Tobacco Extract – Females



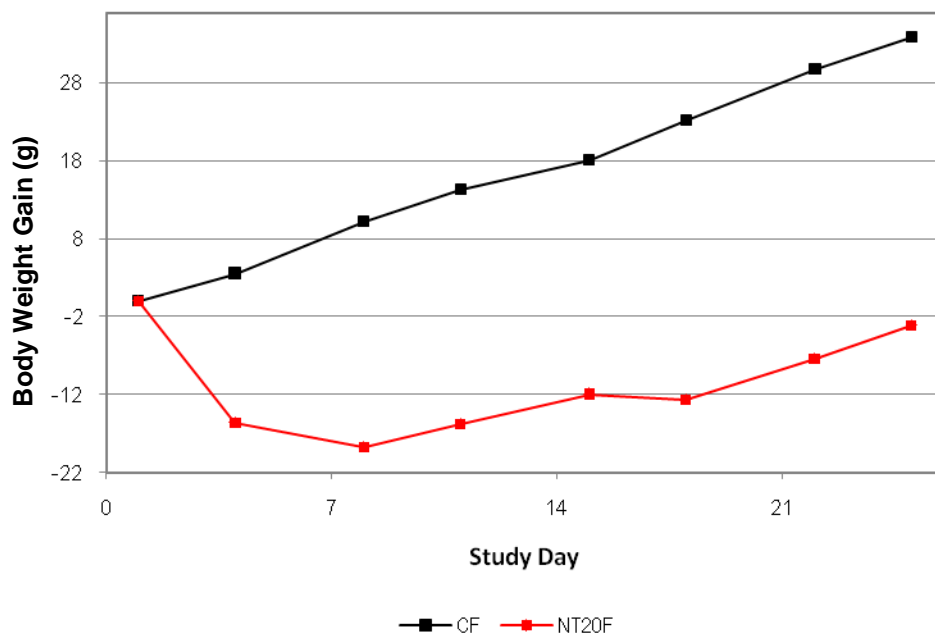
**Figure 19. Group Mean Absolute Body Weight Gain (g) Tobacco Extract (E20M vs. PFCEM) – Males**



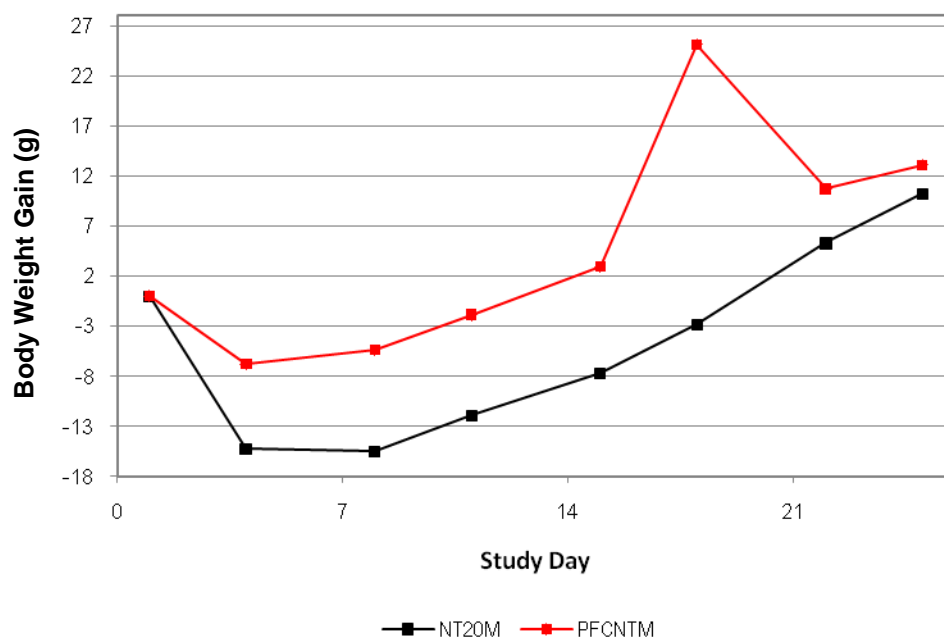
**Figure 20. Group Mean Absolute Body Weight Gain (g) Tobacco Extract (E20F vs. PFCEF) – Females**



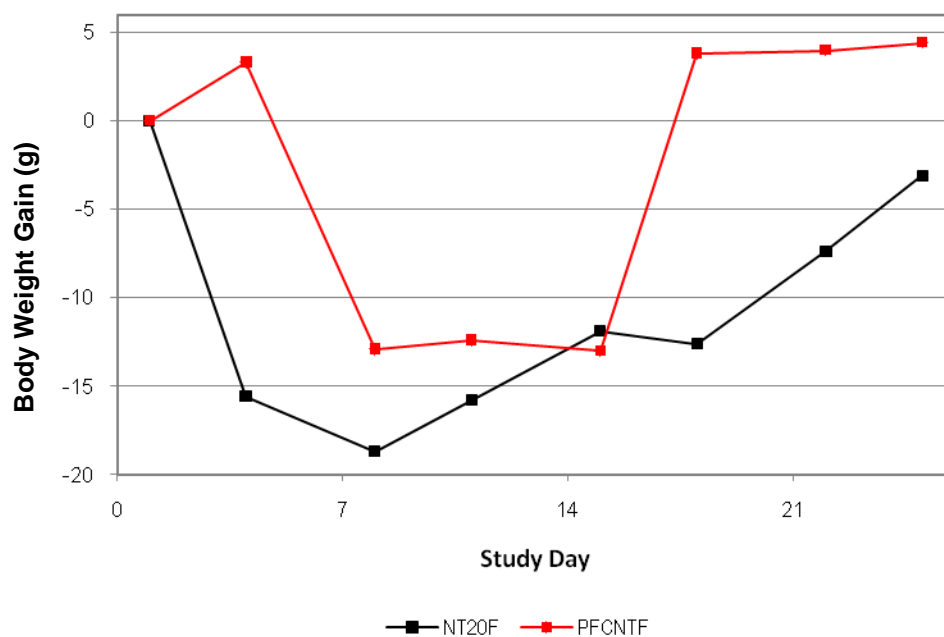
**Figure 21. Group Mean Absolute Body Weight Gain (g) Nicotine Tartrate – Males**



**Figure 22. Group Mean Absolute Body Weight Gain (g) Nicotine Tartrate – Females**



**Figure 23. Group Mean Absolute Body Weight Gain (g) Nicotine Tartate (NT20M vs. PFCNTM) – Males**



**Figure 24. Group Mean Absolute Body Weight Gain (g) Nicotine Tartate (NT20F vs. PFCNTF) – Females**

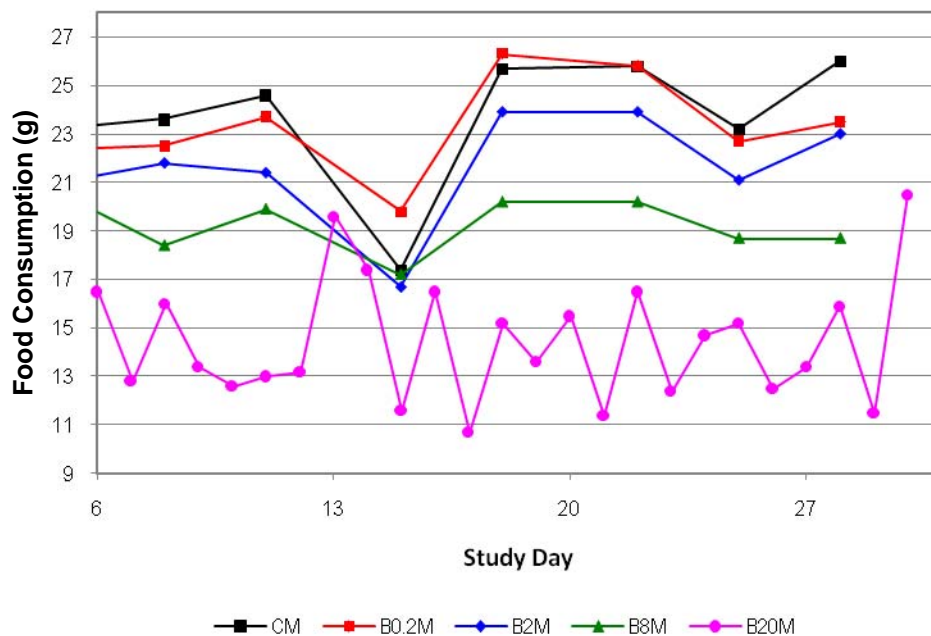


Figure 25. Group Mean Food Consumption (g) Tobacco Blend – Males

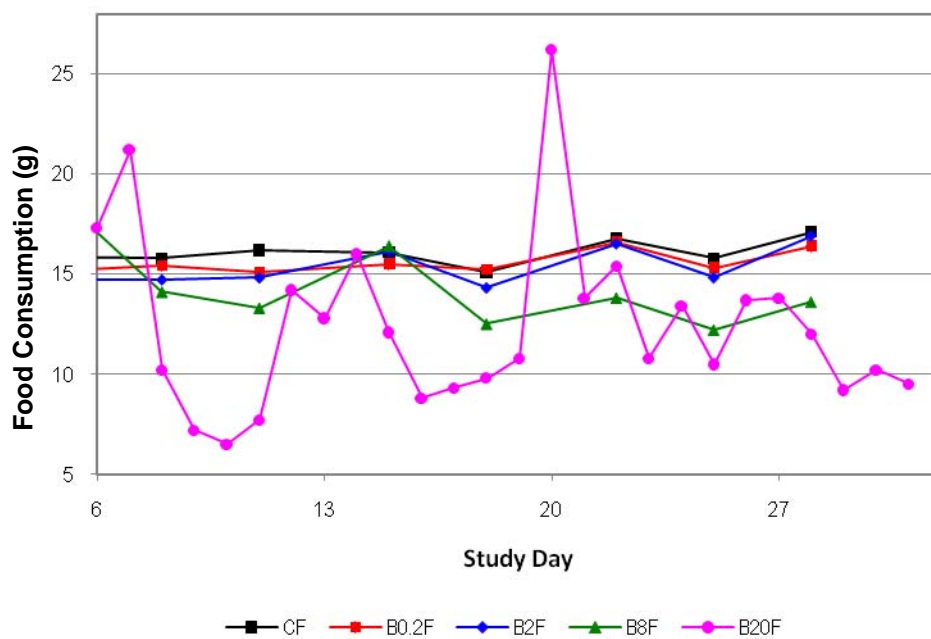
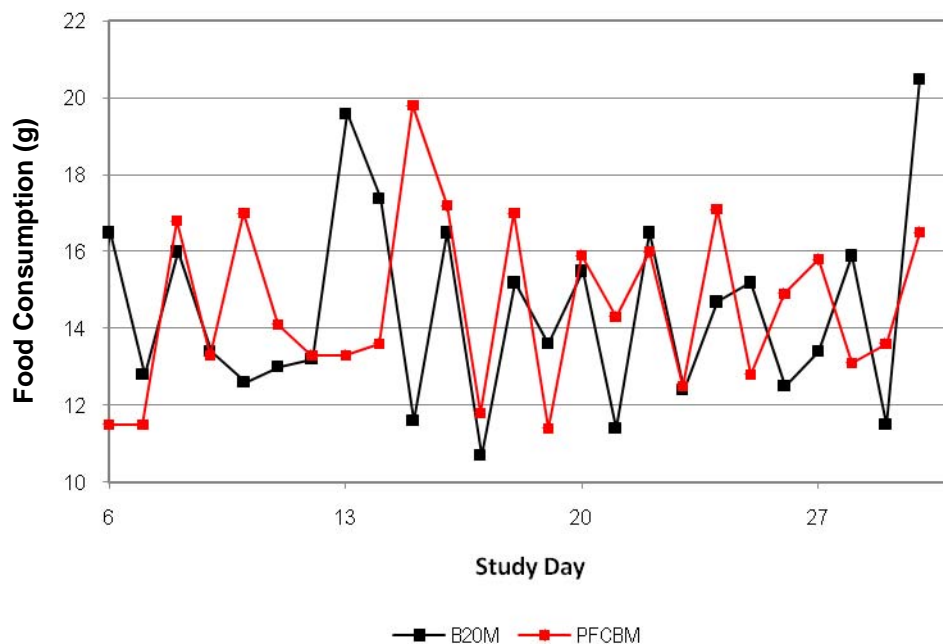
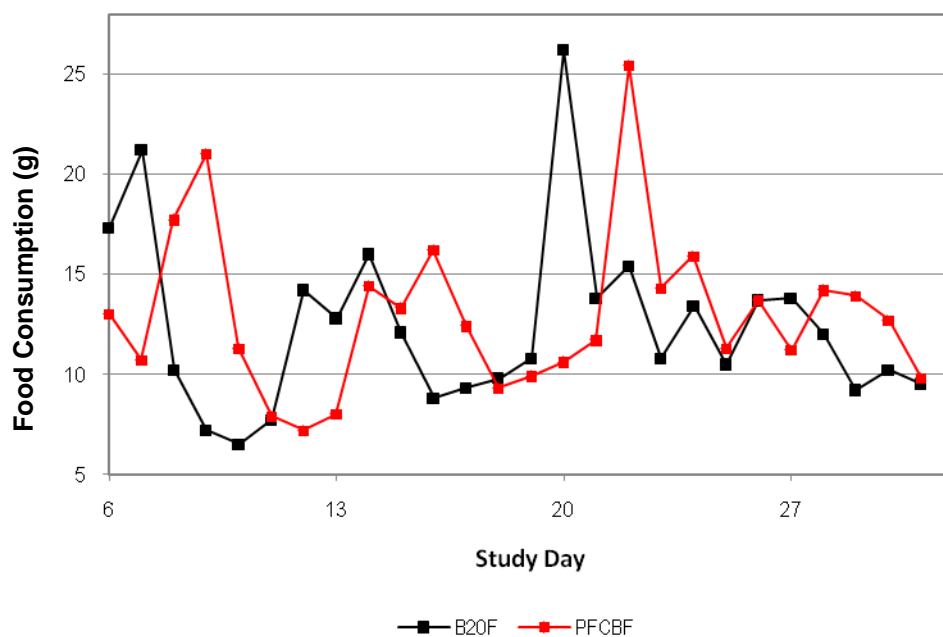


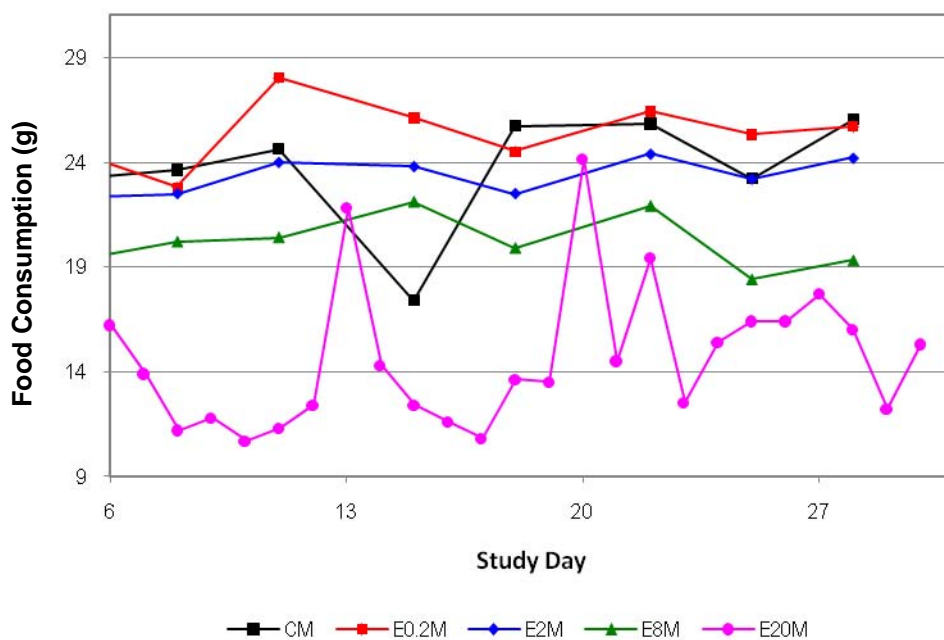
Figure 26. Group Mean Food Consumption (g) Tobacco Blend – Females



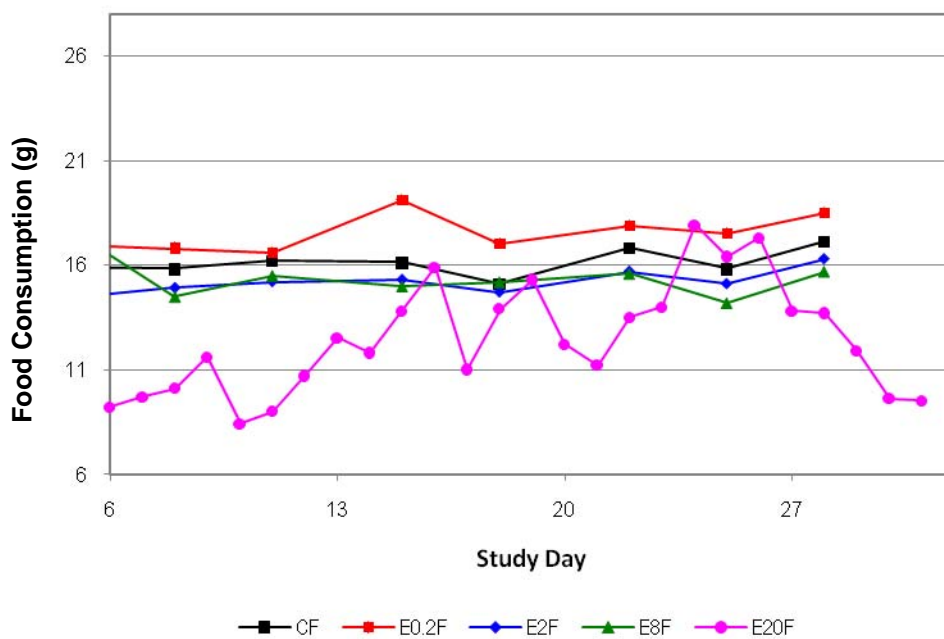
**Figure 27. Group Mean Food Consumption (g) Tobacco Blend (B20M vs. PFCBM) – Males**



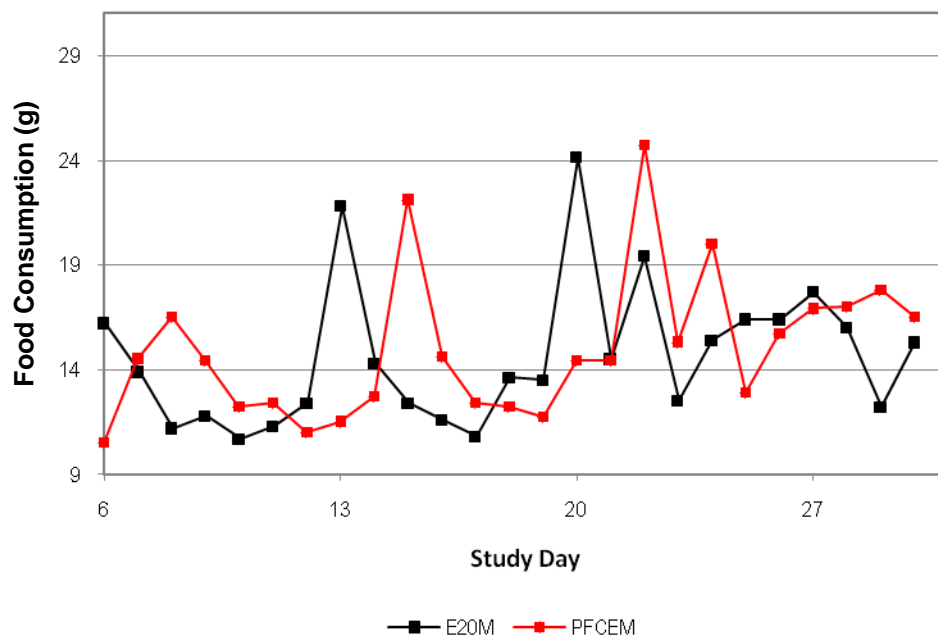
**Figure 28. Group Mean Food Consumption (g) Tobacco Blend (B20F vs. PFCBF) – Females**



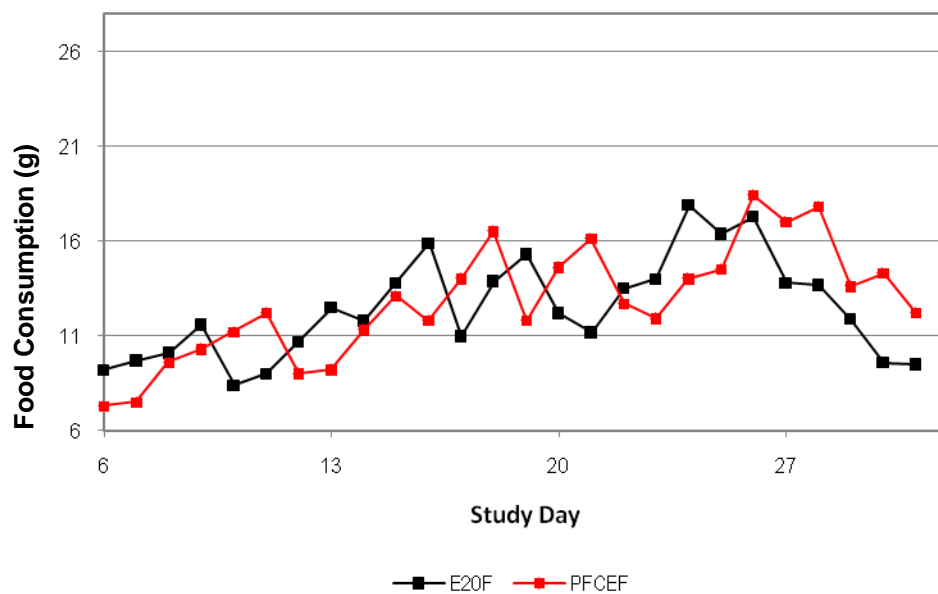
**Figure 29. Group Mean Food Consumption (g) Tobacco Extract – Males**



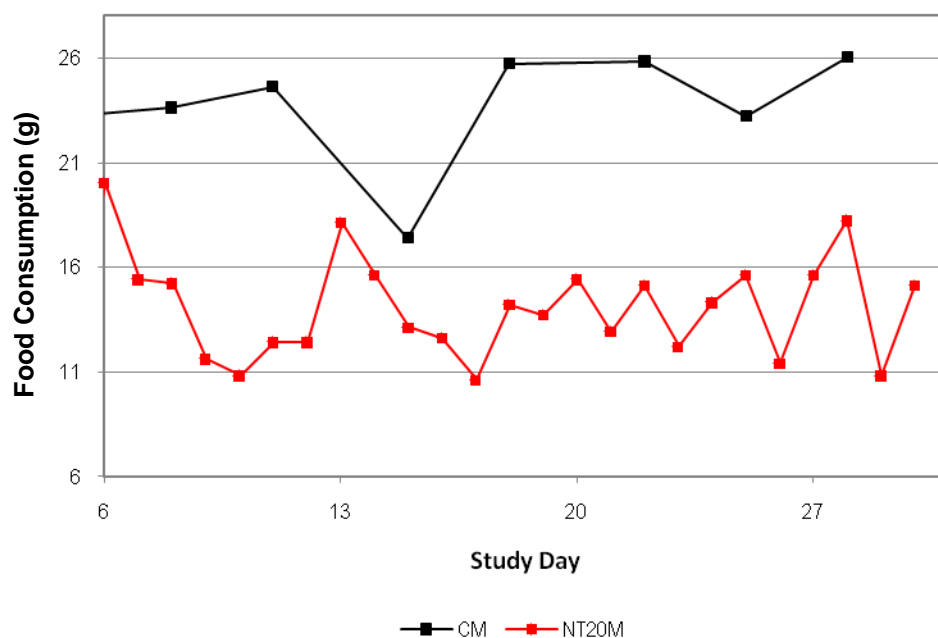
**Figure 30. Group Mean Food Consumption (g) Tobacco Extract – Females**



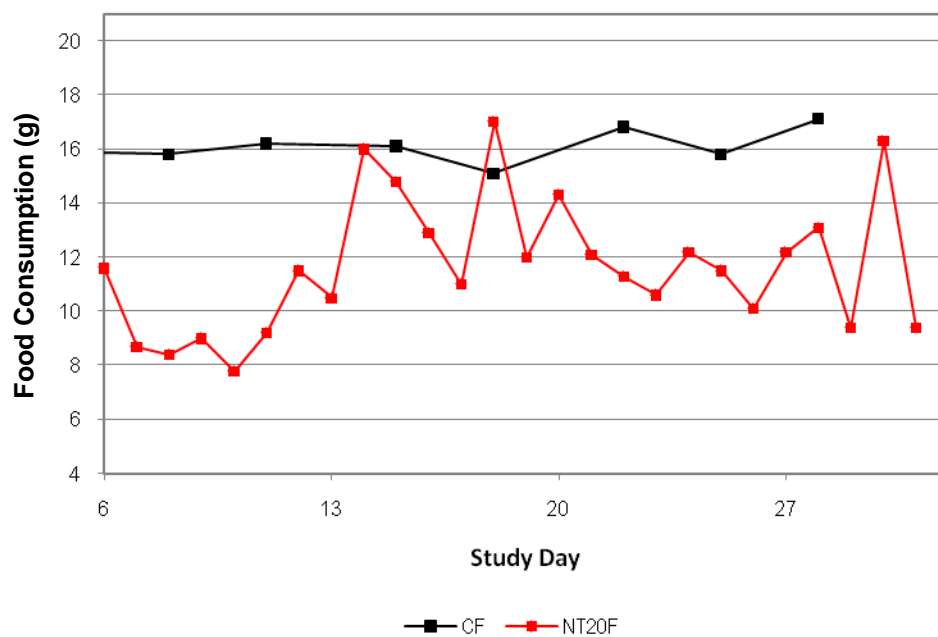
**Figure 31. Group Mean Food Consumption (g) Tobacco Extract (E20M vs. PFCEM) – Males**



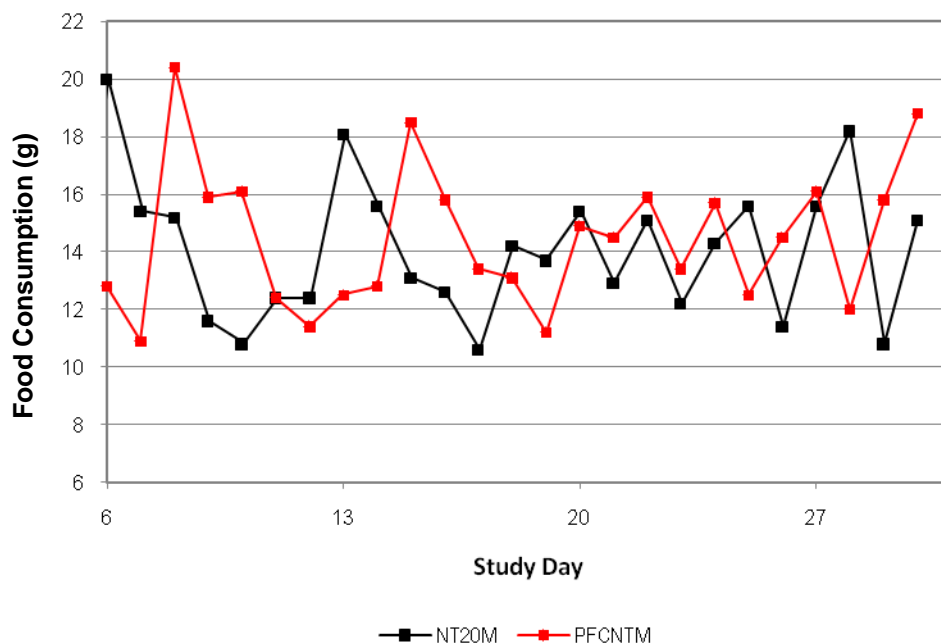
**Figure 32. Group Mean Food Consumption (g) Tobacco Extract (E20F vs. PFCEF) – Females**



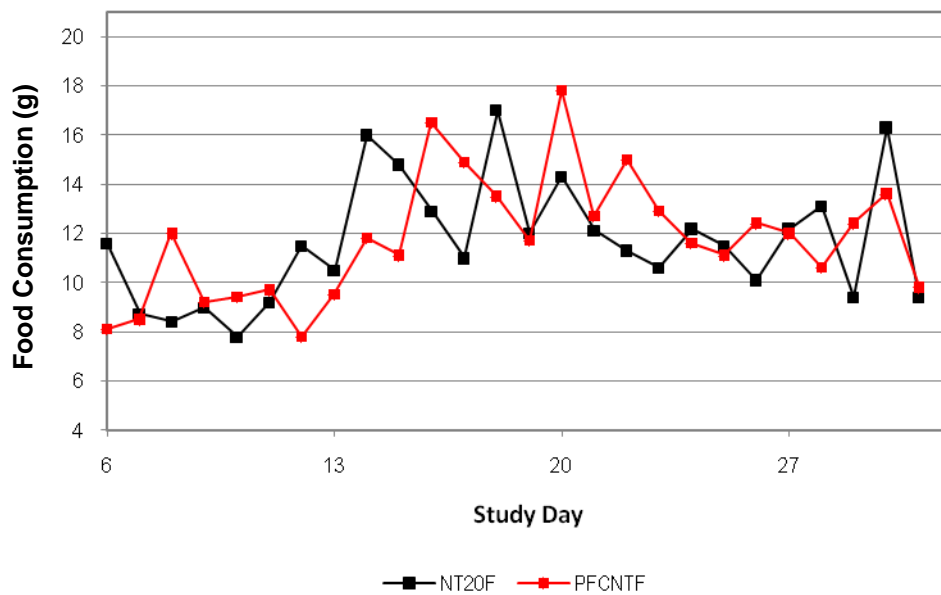
**Figure 33. Group Mean Food Consumption (g) Nicotine Tartrate – Males**



**Figure 34. Group Mean Food Consumption (g) Nicotine Tartrate – Females**



**Figure 35. Group Mean Food Consumption (g) Nicotine Tartrate (NT20M vs. PFCNTM) – Males**



**Figure 36. Group Mean Food Consumption (g) Nicotine Tartrate (NT20F vs. PFCNTF) – Females**

**Table 1. Group Summary of Clinical Observations – Males**

<b>Group</b>	<b>Observation</b>	<b>Animals Affected</b>	<b>Observed</b>		<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	
E0.2M	Abrasion, Body Lateral	2	8	29	6
	Abrasion, Neck	1	8	29	4
	Alopecia	1	22	29	2

**Table 2. Group Summary of Clinical Observations – Females**

<b>Group</b>	<b>Observation</b>	<b>Animals Affected</b>	<b>Observed</b>		<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	
E0.2F	Red Eye Discharge	1	1	30	5
	Alopecia	1	8	30	4
E8F	Tremors	2	15	22	2

**Table 3. Pairfed and High Dose Group Summary of Clinical Abnormalities – Males**

<b>Group</b>	<b>Observation</b>	<b>Animals Affected</b>	<b>Observed</b>		<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	
B20M	Rough Coat	1	8	31	4
E20M	Rough Coat	2	8	31	8

**Table 4. Paired and High Dose Group Summary of Clinical Abnormalities – Females**

<b>Group</b>	<b>Observation</b>	<b>Animals Affected</b>	<b>Observed</b>		<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	
NT20F	Rough Coat	1	8	32	4
	Thin Appearance	1	15	32	3
PFCNTF	Rough Coat	1	8	32	4
B20F	Red Eye Discharge	1	13	13	1
	Lethargic	1	13	13	1
	Rough Coat	1	22	32	2
	Thin Appearance	4	13	32	6
E20F	Thin Appearance	3	22	32	5
	Tremors	1	22	32	2

**Table 5. Group Mean Absolute Body Weight (g) Data – Males**

Group		Day							
		1	4	8	11	15	18	22	25
CM	Mean	200.3	214.6	232.8	250.1	257.9	272.2	285.8	294.8
	SD	13.2	12.9	15.0	13.8	15.9	15.7	17.4	18.4
	N	10	10	10	10	10	10	10	10
NT20M	Mean	203.5	188.2 <sup>A</sup>	188.1 <sup>A</sup>	191.6 <sup>A</sup>	195.8 <sup>A</sup>	200.8 <sup>A</sup>	208.9 <sup>A</sup>	213.7 <sup>A</sup>
	SD	11.2	8.8	10.5	11.1	10.3	10.6	11.5	11.3
	N	10	10	10	10	10	10	10	10
B0.2M	Mean	197.1	210.5	227.5	242.3	249.1	260.8	272.3	280.0
	SD	15.8	17.3	16.5	18.6	20.3	22.2	24.8	25.5
	N	10	10	10	10	10	10	10	10
B2M	Mean	200.6	210.2	229.5	241.4	246.0	258.2	270.3	278.1
	SD	11.9	10.0	11.9	12.7	13.4	18.2	19.1	18.9
	N	10	10	10	10	10	10	10	10
B8M	Mean	197.3	195.6 <sup>B</sup>	208.9 <sup>B</sup>	219.5 <sup>B</sup>	220.7 <sup>B</sup>	231.0 <sup>B</sup>	237.9 <sup>B</sup>	244.2 <sup>B</sup>
	SD	15.6	14.2	13.9	16.2	17.5	18.4	19.1	18.2
	N	10	10	10	10	10	10	10	10
B20M	Mean	200.5	182.2 <sup>B</sup>	182.0 <sup>B</sup>	186.1 <sup>B</sup>	189.9 <sup>B</sup>	193.3 <sup>B</sup>	199.1 <sup>B</sup>	203.4 <sup>B</sup>
	SD	16.8	13.6	13.1	13.9	13.1	13.5	13.2	14.1
	N	10	10	10	10	10	10	10	10
E0.2M	Mean	202.5	216.5	228.0	252.2	268.8 <sup>D</sup>	279.3 <sup>D</sup>	291.7 <sup>D</sup>	299.2
	SD	12.5	14.6	15.3	13.6	14.6	14.3	15.1	14.9
	N	10	10	10	10	10	10	10	10
E2M	Mean	199.7	209.9	227.6	244.4	259.5	268.5	279.8	287.5
	SD	14.2	14.5	16.6	17.2	19.3	20.9	25.0	26.9
	N	10	10	10	10	10	10	10	10

**Table 5. Group Mean Absolute Body Weight (g) Data – Males (Continued)**

Group		Day							
		1	4	8	11	15	18	22	25
E8M	Mean	197.6	198.1 <sup>B</sup>	211.4 <sup>B</sup>	222.9 <sup>B</sup>	232.1 <sup>B</sup>	240.8 <sup>B</sup>	246.6 <sup>B</sup>	250.8 <sup>B</sup>
	SD	13.7	12.3	11.4	11.2	11.3	13.3	13.3	15.7
	N	10	10	10	10	10	10	10	10
E20M	Mean	206.2	188.0 <sup>B</sup>	184.7 <sup>B</sup>	189.2 <sup>B</sup>	191.8 <sup>B</sup>	193.4 <sup>B</sup>	199.7 <sup>B</sup>	204.3 <sup>B</sup>
	SD	11.1	8.0	9.3	9.2	11.3	13.3	14.6	17.3
	N	10	10	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 6. Group Mean Absolute Body Weight (g) – Females**

Group		Day							
		1	4	8	11	15	18	22	25
CF	Mean	150.8	154.3	161.0	165.1	168.7	173.9	180.4	184.5
	SD	8.1	8.7	10.0	11.6	13.4	11.5	11.9	12.3
	N	10	10	10	10	10	10	10	10
NT20F	Mean	148.5	132.9 <sup>A</sup>	129.8 <sup>A</sup>	132.7 <sup>A</sup>	136.6 <sup>A</sup>	135.9 <sup>A</sup>	141.1 <sup>A</sup>	145.4 <sup>A</sup>
	SD	5.9	7.2	8.1	9.6	9.5	10.0	10.2	10.8
	N	10	10	10	10	10	10	10	10
B0.2F	Mean	148.6	153.1	160.1	165.5	169.2	171.9	179.3	181.1
	SD	6.4	6.9	7.9	8.4	10.4	8.9	9.9	10.1
	N	10	10	10	10	10	10	10	10
B2F	Mean	148.6	150.8	155.7	161.1	165.2	167.6	174.7	178.0
	SD	8.8	7.8	7.9	8.2	8.9	10.3	9.8	8.5
	N	10	10	10	10	10	10	10	10
B8F	Mean	149.3	139.6 <sup>B</sup>	143.8 <sup>B</sup>	149.4 <sup>B</sup>	152.8 <sup>B</sup>	156.6 <sup>B</sup>	162.0 <sup>B</sup>	162.2 <sup>B</sup>
	SD	8.5	8.2	8.0	8.7	8.0	9.0	7.5	8.6
	N	10	10	10	10	10	10	10	10
B20F	Mean	147.3	130.1 <sup>B</sup>	123.0 <sup>B</sup>	124.3 <sup>B</sup>	128.3 <sup>B</sup>	129.6 <sup>B</sup>	131.4 <sup>B</sup>	134.2 <sup>B,C</sup>
	SD	7.0	7.4	8.8	10.9	9.8	9.0	8.9	8.3
	N	10	10	10	10	9	9	9	9
E0.2F	Mean	149.0	155.1	164.1	167.8	172.8	175.8	182.3	184.3
	SD	7.9	8.0	9.8	11.1	9.9	12.0	11.7	10.9
	N	10	10	10	10	10	10	10	10
E2F	Mean	146.9	148.9	155.1	160.1	162.4	164.0	170.3	173.0
	SD	7.6	8.5	9.1	7.8	9.2	7.5	9.0	10.6
	N	10	10	10	10	10	10	10	10

**Table 6. Group Mean Absolute Body Weight (g) – Females (Continued)**

<b>Group</b>		<b>Day</b>							
		<b>1</b>	<b>4</b>	<b>8</b>	<b>11</b>	<b>15</b>	<b>18</b>	<b>22</b>	<b>25</b>
E8F	Mean	151.4	144.4 <sup>B</sup>	150.2 <sup>B</sup>	157.7 <sup>F</sup>	157.3 <sup>B</sup>	165.1 <sup>F</sup>	171.4 <sup>F</sup>	171.4 <sup>B,F</sup>
	SD	7.6	5.3	7.4	8.0	9.1	8.3	7.9	7.6
	N	10	10	10	10	10	10	10	10
E20F	Mean	151.1	134.3 <sup>B</sup>	129.1 <sup>B</sup>	130.1 <sup>B</sup>	130.9 <sup>B</sup>	131.9 <sup>B</sup>	133.0 <sup>B</sup>	136.0 <sup>B</sup>
	SD	8.3	7.1	7.6	6.5	7.5	8.6	9.5	9.8
	N	10	10	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 7. Pairfed and High Dose Group Mean Absolute Body Weight (g) Data – Males**

Group		Day							
		1	4	8	11	15	18	22	25
NT20M	Mean	203.5	188.2	188.1	191.6	195.8	200.8	208.9	213.7
	SD	11.2	8.8	10.5	11.1	10.3	10.6	11.5	11.3
	N	10	10	10	10	10	10	10	10
PFCNTM	Mean	200.8	194.0	195.4	198.9	203.7	225.9 <sup>A</sup>	211.5	213.9
	SD	11.2	12.2	11.6	10.8	10.6	12.2	11.7	12.0
	N	10	10	10	10	10	10	10	10
B20M	Mean	200.5	182.2	182.0	186.1	189.9	193.3	199.1	203.4
	SD	16.8	13.6	13.1	13.9	13.1	13.5	13.2	14.1
	N	10	10	10	10	10	10	10	10
PFCBM	Mean	200.2	204.5 <sup>B</sup>	197.8 <sup>B</sup>	204.7 <sup>B</sup>	212.3 <sup>B</sup>	232.0 <sup>B</sup>	221.4 <sup>B</sup>	222.7 <sup>B</sup>
	SD	13.4	13.2	11.3	10.7	10.4	11.9	9.9	9.9
	N	10	10	10	10	10	10	10	10
E20M	Mean	206.2	188.0	184.7	189.2	191.8	193.4	199.7	204.3
	SD	11.1	8.0	9.3	9.2	11.3	13.3	14.6	17.3
	N	10	10	10	10	10	10	10	10
PFCEM	Mean	201.6	218.6 <sup>C</sup>	203.0 <sup>C</sup>	205.8 <sup>C</sup>	214.7 <sup>C</sup>	225.5 <sup>C</sup>	224.6 <sup>C</sup>	226.9 <sup>C</sup>
	SD	13.8	14.7	11.7	11.4	11.4	13.0	9.6	10.1
	N	10	10	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 8. Pairfed and High Dose Group Mean Absolute Body Weight (g) Data – Females**

Group		Day							
		1	4	8	11	15	18	22	25
NT20F	Mean	148.5	132.9	129.8	132.7	136.6	135.9	141.1	145.4
	SD	5.9	7.2	8.1	9.6	9.5	10.0	10.2	10.8
	N	10	10	10	10	10	10	10	10
PFCNTF	Mean	151.0	154.3 <sup>A</sup>	138.2 <sup>A</sup>	138.7	138.0	154.8 <sup>A</sup>	155.1 <sup>A</sup>	155.5 <sup>A</sup>
	SD	9.2	8.4	8.0	8.1	7.5	8.0	6.4	6.7
	N	10	10	10	10	10	10	10	10
B20F	Mean	147.3	130.1	123.0	124.3	128.3	129.6	131.4	134.2
	SD	7.0	7.4	8.8	10.9	9.8	9.0	8.9	8.3
	N	10	10	10	10	9	9	9	9
PFCBF	Mean	149.9	156.0 <sup>B</sup>	149.5 <sup>B</sup>	150.1 <sup>B</sup>	149.8 <sup>b</sup>	160.1 <sup>B</sup>	166.8 <sup>B</sup>	164.1 <sup>B</sup>
	SD	7.4	6.9	5.6	5.8	4.7	5.4	5.3	5.2
	N	10	10	10	10	10	10	10	10
E20F	Mean	151.1	134.3	129.1	130.1	130.9	131.9	133.0	136.0
	SD	8.3	7.1	7.6	6.5	7.5	8.6	9.5	9.8
	N	10	10	10	10	10	10	10	10
PFCEF	Mean	150.3	155.0 <sup>C</sup>	138.0 <sup>C</sup>	142.9 <sup>C</sup>	142.3 <sup>C</sup>	157.6 <sup>C</sup>	155.4 <sup>C</sup>	158.1 <sup>C</sup>
	SD	9.0	10.0	7.5	6.2	5.9	5.5	6.5	6.0
	N	10	10	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 9. TK Group Mean Absolute Body Weight (g) Data – Males**

Group		Day				
		1	8	15	22	28
NT20M	Mean	169.1	161.1	164.8	175.3	186.5
	SD	11.6	6.4	6.6	4.1	7.4
	N	6	6	6	6	6
B0.2M	Mean	170.3	208.7	238.0	266.6	284.3
	SD	14.6	11.3	8.4	7.3	6.8
	N	6	6	6	6	6
B2M	Mean	165.1	200.2	228.3	253.9	270.7
	SD	13.3	14.9	16.8	17.7	22.0
	N	6	6	6	6	6
B8M	Mean	173.4	193.0	209.2	232.9	248.6
	SD	11.6	13.7	15.6	15.4	16.8
	N	6	6	6	6	6
B20M	Mean	176.3	160.8	160.7	171.0	179.8
	SD	8.6	17.3	21.2	25.0	29.4
	N	6	6	5	5	5
E0.2M	Mean	173.4	212.6	243.1	271.7	289.6
	SD	13.5	13.5	12.0	13.8	15.6
	N	6	6	6	6	6
E2M	Mean	174.4	208.7	234.4	264.3	284.9
	SD	12.1	13.2	16.0	14.1	14.7
	N	6	6	6	6	6
E8M	Mean	172.8	190.7	203.2	227.8	247.2
	SD	12.8	10.2	10.5	10.0	12.1
	N	6	6	5	5	5

**Table 9. TK Group Mean Absolute Body Weight (g) Data – Males (Continued)**

Group		Day				
		1	8	15	22	28
E20M	Mean	163.1 <sup>G</sup>	147.3	146.5	150.3 <sup>c</sup>	147.0 <sup>c</sup>
	SD	8.1	15.6	16.7	23.3	23.2
	N	6	6	6	6	6

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 10. TK Group Mean Absolute Body Weight (g) Data – Females**

Group		Day				
		1	8	15	22	28
NT20F	Mean	140.0	123.4	126.3	133.9	142.6
	SD	8.7	4.1	3.5	1.9	5.1
	N	6	6	6	6	6
B0.2F	Mean	140.8	158.9	167.4	177.7	189.9
	SD	7.4	7.7	8.8	9.4	10.5
	N	6	6	6	6	6
B2F	Mean	141.8	149.2	160.0	171.6	177.4
	SD	3.4	5.0	7.2	7.5	9.8
	N	6	6	6	6	6
B8F	Mean	139.2	132.9	141.6	154.9	162.5
	SD	8.2	6.0	10.1	11.8	11.5
	N	6	6	6	6	6
B20F	Mean	145.7	122.1	119.6	125.4 <sup>c</sup>	130.5 <sup>c</sup>
	SD	7.5	4.7	4.3	4.1	4.2
	N	6	6	6	6	6
E0.2F	Mean	141.8	154.5	163.2	173.3	183.1
	SD	8.8	9.3	6.2	9.8	7.9
	N	6	6	6	6	6
E2F	Mean	139.3	151.1	154.1	167.5	174.1
	SD	4.5	5.2	5.5	4.9	4.8
	N	6	6	6	6	6
E8F	Mean	135.3	132.2	141.4	154.8	160.5
	SD	6.8	5.6	4.6	7.8	4.6
	N	6	6	6	6	6

**Table 10. TK Group Mean Absolute Body Weight (g) Data – Females (Continued)**

Group		Day				
		1	8	15	22	28
E20F	Mean	140.6	120.5	123.0	129.3	131.0
	SD	10.7	4.4	7.1	11.8	13.4
	N	6	6	6	6	6

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 11. Group Mean Average Feed Consumed (g) Data – Males**

Group		Day								Grand Mean	Grand SD
		4	8	11	15	18	22	25	28		
CM	Mean	23.1	23.6	24.6	17.4	25.7	25.8	23.2	26.0	23.7	2.8
	SD	1.6	1.9	2.2	3.1	2.4	3.1	2.0	4.8		
	N	10	10	10	10	10	10	10	10		
NT20M	Mean	12.6 <sup>a</sup>	15.2 <sup>a</sup>	12.4 <sup>A</sup>	13.1 <sup>A</sup>	14.2 <sup>A</sup>	15.1 <sup>A</sup>	15.6 <sup>A</sup>	18.2 <sup>A</sup>	14.6	1.9
	SD	7.4	9.6	1.9	3.5	1.5	2.5	2.4	5.7		
	N	10	10	10	10	10	10	10	10		
B0.2M	Mean	22.3	22.5	23.7	19.8	26.3	25.7	22.7	23.5	23.3	2.0
	SD	2.8	2.0	3.6	6.4	2.9	3.7	2.8	3.1		
	N	10	10	10	10	10	10	10	10		
B2M	Mean	20.8 <sup>b</sup>	21.8	21.4	16.6	23.9	23.9	21.1	23.0	21.6	2.3
	SD	2.0	2.0	2.0	3.6	2.7	3.0	2.0	3.3		
	N	10	10	10	10	10	10	10	10		
B8M	Mean	21.1	18.4 <sup>b</sup>	19.9 <sup>B</sup>	17.2	20.2 <sup>b</sup>	20.1 <sup>b</sup>	18.7 <sup>B</sup>	18.7 <sup>B</sup>	19.3	1.3
	SD	7.0	2.4	4.1	4.7	2.9	6.4	2.8	2.6		
	N	10	10	10	10	10	10	10	10		
B20M	Mean	11.3 <sup>b</sup>	16.0 <sup>b</sup>	13.0 <sup>B</sup>	11.6 <sup>b</sup>	15.2 <sup>b</sup>	16.5 <sup>b</sup>	15.2 <sup>B</sup>	15.9 <sup>B</sup>	14.3	2.1
	SD	6.2	8.9	3.5	1.8	6.0	6.8	2.9	5.7		
	N	10	10	10	10	10	10	10	10		
E0.2M	Mean	25.0 <sup>b,D</sup>	22.8	28.0 <sup>b,D</sup>	26.1 <sup>B,d</sup>	24.5	26.4	25.3 <sup>D</sup>	25.7	25.5	1.5
	SD	1.8	2.2	4.0	2.3	1.7	2.2	2.6	2.4		
	N	10	10	10	10	10	10	10	10		
E2M	Mean	22.3	22.5	24.0 <sup>E</sup>	23.8 <sup>B,E</sup>	22.5 <sup>B</sup>	24.4	23.2	24.2	23.4	0.8
	SD	2.5	2.3	2.9	2.8	2.7	3.1	2.9	3.2		
	N	10	10	10	10	10	10	10	10		

**Table 11. Group Mean Average Feed Consumed (g) Data – Males (Continued)**

Group		Day								Grand Mean	Grand SD
		4	8	11	15	18	22	25	28		
E8M	Mean	19.0 <sup>b</sup>	20.1 <sup>B</sup>	20.4 <sup>b</sup>	22.1 <sup>B,F</sup>	19.9 <sup>B</sup>	21.9	18.5 <sup>b</sup>	19.4 <sup>B</sup>	20.2	1.3
	SD	4.2	2.3	2.2	4.0	2.5	4.9	2.2	2.2		
	N	10	10	10	10	10	10	10	10		
E20M	Mean	10.5 <sup>b</sup>	11.2 <sup>B</sup>	11.3 <sup>b</sup>	12.4 <sup>B</sup>	13.6 <sup>B</sup>	19.4 <sup>b</sup>	16.4 <sup>b</sup>	16.0 <sup>B</sup>	13.9	3.1
	SD	6.1	1.4	1.4	1.4	2.3	7.2	6.2	3.5		
	N	10	10	10	8	10	9	10	9		

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 12. Group Mean Average Feed Consumed (g) Data – Females**

Group		Day								Grand Mean	Grand SD
		4	8	11	15	18	22	25	28		
CF	Mean	15.9	15.8	16.2	16.1	15.1	16.8	15.8	17.1	16.1	0.6
	SD	1.9	1.5	1.2	1.8	1.6	1.4	1.6	1.7		
	N	10	10	10	10	10	10	10	10		
NT20F	Mean	7.8 <sup>a</sup>	8.4 <sup>A</sup>	9.2 <sup>A</sup>	14.8	17.0	11.2 <sup>A</sup>	11.5 <sup>A</sup>	13.1	11.6	3.2
	SD	6.9	1.4	2.1	10.5	14.2	1.5	1.6	5.5		
	N	10	10	10	10	10	10	10	10		
B0.2F	Mean	15.1	15.4	15.1	15.5	15.2	16.6	15.3	16.4	15.6	0.6
	SD	1.3	1.4	1.7	1.1	1.1	1.7	2.0	1.9		
	N	10	10	10	10	10	10	10	9		
B2F	Mean	14.7	14.7	14.8	16.1	14.3	16.5	14.8	16.9	15.4	1.0
	SD	3.1	1.0	1.4	2.2	0.7	1.5	1.0	2.3		
	N	10	10	10	10	10	10	10	10		
B8F	Mean	20.1	14.1	13.3 <sup>B</sup>	16.4	12.5 <sup>b</sup>	13.8 <sup>b</sup>	12.2 <sup>B</sup>	13.5 <sup>b</sup>	14.5	2.6
	SD	15.5	3.8	1.7	4.4	1.8	2.1	1.0	1.1		
	N	10	10	10	10	10	10	10	10		
B20F	Mean	12.9	10.2 <sup>b</sup>	7.7 <sup>B</sup>	12.1	9.8 <sup>b</sup>	15.4	10.5 <sup>B</sup>	12.0 <sup>b</sup>	11.3	2.3
	SD	15.5	6.4	1.9	8.1	2.5	10.4	1.8	4.9		
	N	10	10	10	9	9	8	8	9		
E0.2F	Mean	16.9 <sup>D</sup>	16.8 <sup>D</sup>	16.6	19.1 <sup>d</sup>	17.0 <sup>b,D</sup>	17.9	17.5	18.5 <sup>D</sup>	17.5	0.9
	SD	1.7	1.4	1.7	4.3	1.7	1.5	3.9	2.3		
	N	10	10	10	10	10	10	10	10		
E2F	Mean	14.3	14.9	15.2	15.3	14.7	15.7	15.1	16.3	15.2	0.6
	SD	1.7	1.6	1.7	1.8	1.4	1.6	1.8	1.8		
	N	10	10	10	10	10	10	10	10		

**Table 12. Group Mean Average Feed Consumed (g) Data – Females (Continued)**

Group		Day								Grand Mean	Grand SD
		4	8	11	15	18	22	25	28		
E8F	Mean	18.5	14.5	15.5 <sup>F</sup>	15.0	15.2 <sup>F</sup>	15.6	14.2	15.7	15.5	1.3
	SD	12.6	4.5	2.8	3.5	3.6	3.1	5.1	5.3		
	N	10	10	10	10	10	10	10	10		
E20F	Mean	7.5 <sup>b</sup>	10.1 <sup>b</sup>	9.0 <sup>B</sup>	13.8	13.9	13.5	16.4	13.7	12.2	3.0
	SD	6.5	5.3	2.8	8.8	8.3	6.5	12.3	4.5		
	N	10	10	10	9	10	10	9	10		

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 13. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Males**

Group		Day								
		2	3	4	5	6	7	8	9	10
NT20M	Mean	7.3	9.8	12.6	10.8	20.0	15.4	15.2	11.6	10.8
	SD	3.5	8.3	7.4	4.3	17.9	5.2	9.6	3.3	1.4
	N	10	10	10	10	10	10	10	10	10
PFCNTM	Mean			7.4	9.8	12.8	10.9 <sup>a</sup>	20.4	15.9 <sup>a</sup>	16.1 <sup>a</sup>
	SD			0.1	0.7	0.6	0.5	0.3	0.3	0.2
	N			10	10	10	10	10	10	10
B20M	Mean	17.1	15.1	11.3	11.7	16.5	12.8	16.0	13.4	12.6
	SD	18.7	12.8	6.2	4.5	15.3	3.1	8.9	6.9	5.1
	N	10	10	10	10	10	10	10	10	10
PFCBM	Mean			17.1 <sup>b</sup>	15.4 <sup>b</sup>	11.5	11.5	16.8	13.3	17.0 <sup>b</sup>
	SD			0.2	0.8	0.6	0.4	0.5	0.3	0.2
	N			10	10	10	10	10	10	10
E20M	Mean	29.7	17.7	10.5	14.5	16.2	13.9	11.2	11.8	10.7
	SD	30.5	14.0	6.1	11.9	9.7	4.4	1.4	3.1	2.0
	N	10	10	10	10	10	10	10	10	10
PFCEM	Mean			24.4 <sup>c</sup>	17.8	10.5	14.5	16.5	14.4 <sup>c</sup>	12.2 <sup>c</sup>
	SD			2.8	0.6	0.6	0.5	0.3	0.4	0.2
	N			10	10	10	10	10	10	10

**Table 13. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Males (Continued)**

[illegible]

**Table 13. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Males (Continued)**

[illegible]

**Table 13. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Males (Continued)**

Group		Day	
		29	30
NT20M	Mean	10.8	15.1
	SD	1.8	2.5
	N	10	10
PFCNTM	Mean	15.8 <sup>a</sup>	18.8 <sup>a</sup>
	SD	0.5	0.2
	N	10	10
B20M	Mean	11.5	20.5
	SD	2.1	17.3
	N	10	10
PFCBM	Mean	13.6 <sup>b</sup>	16.5
	SD	0.5	0.4
	N	10	10
E20M	Mean	12.2	15.3
	SD	4.7	6.9
	N	10	10
PFCEM	Mean	17.8 <sup>c</sup>	16.5
	SD	0.6	0.2
	N	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 14. Pairfed and High Dose Group Mean Average Feed Consumed (g) per Day Data – Females**

Group		Day								
		2	3	4	5	6	7	8	9	10
NT20F	Mean	19.6	4.8	7.8	8.6	11.6	8.7	8.4	9.0	7.8
	SD	34.9	2.4	6.9	6.6	11.1	2.2	1.4	2.5	1.4
	N	10	10	10	10	10	10	10	10	10
PFCNTF	Mean			15.9 <sup>a</sup>	4.8	8.1	8.5	12.0 <sup>a</sup>	9.2	9.4 <sup>a</sup>
	SD			2.9	0.6	0.6	0.6	0.4	0.3	0.1
	N			10	10	10	10	10	10	10
B20F	Mean	17.4	8.9	12.9	10.7	17.3	21.2	10.2	7.2	6.5
	SD	27.0	10.1	15.5	11.1	18.8	19.9	6.4	1.6	1.4
	N	10	10	10	10	10	10	10	10	10
PFCBF	Mean			16.4	8.9	13.0	10.7	17.7 <sup>b</sup>	21.0 <sup>B</sup>	11.2 <sup>b</sup>
	SD			1.2	0.7	0.7	0.5	0.2	1.2	0.2
	N			10	10	10	10	10	10	10
E20F	Mean	26.0	9.3	7.5	7.2	9.2	9.7	10.1	11.6	8.4
	SD	25.7	8.6	6.5	1.8	3.7	3.8	5.3	8.7	3.5
	N	10	10	10	10	10	10	10	10	10
PFCEF	Mean			17.7 <sup>c</sup>	9.6 <sup>c</sup>	7.3	7.5	9.6	10.3	11.2 <sup>c</sup>
	SD			1.5	0.5	0.5	0.6	0.3	0.2	0.1
	N			10	10	10	10	10	10	10

**Table 14. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Females (Continued)**

[illegible]

**Table 14. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Females (Continued)**

[illegible]

**Table 14. Paired and High Dose Group Mean Average Feed Consumed (g) per Day Data – Females (Continued)**

<b>Group</b>		<b>Day</b>		
		<b>29</b>	<b>30</b>	<b>31</b>
NT20F	Mean	9.4	16.3	9.4
	SD	2.3	11.9	1.6
	N	9	10	10
PFCNTF	Mean	12.4 <sup>a</sup>	13.6	9.8
	SD	0.4	0.3	0.2
	N	10	10	10
B20F	Mean	9.2	10.2	9.5
	SD	4.4	1.0	2.9
	N	9	9	9
PFCBF	Mean	13.9 <sup>b</sup>	12.7 <sup>b</sup>	9.8
	SD	0.5	0.1	0.3
	N	10	10	10
E20F	Mean	11.9	9.6	9.5
	SD	10.2	1.3	2.6
	N	10	10	10
PFCEF	Mean	13.6	14.3 <sup>c</sup>	12.2 <sup>c</sup>
	SD	0.4	0.3	0.6
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 15. Group Mean Hematology Data – Males**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
CM	Mean	8.67	15.7	49.3	56.9	18.1
	SD	0.54	1.0	3.2	1.2	0.6
	N	10	10	10	10	10
NT20M	Mean	8.49	14.9	45.0 <sup>A</sup>	52.9 <sup>A</sup>	17.6
	SD	0.57	0.9	3.3	1.1	0.6
	N	10	10	10	10	10
B0.2M	Mean	8.74	15.9	49.2	56.2	18.2
	SD	0.51	1.0	3.3	1.2	0.8
	N	10	10	10	10	10
B2M	Mean	8.79	15.9	49.3	56.1	18.1
	SD	0.37	0.6	1.8	1.5	0.7
	N	10	10	10	10	10
B8M	Mean	8.87	15.8	49.0	55.3 <sup>B</sup>	17.8
	SD	0.31	0.7	1.9	1.3	0.6
	N	10	10	10	10	10
B20M	Mean	8.61	15.3	46.0 <sup>B</sup>	53.4 <sup>B</sup>	17.8
	SD	0.45	0.8	2.4	0.9	0.3
	N	10	10	10	10	10
E0.2M	Mean	8.45	15.5	47.7	56.5	18.3
	SD	0.46	0.6	1.3	2.1	0.8
	N	10	10	10	10	10
E2M	Mean	8.83	16.0	50.1	56.8	18.1
	SD	0.67	1.0	3.5	1.2	0.7
	N	10	10	10	10	10

**Table 15. Group Mean Hematology Data – Males (Continued)**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
E8M	Mean	9.19	16.4	50.6	55.2	17.8
	SD	0.53	0.7	2.6	2.1	0.7
	N	10	10	10	10	10
E20M	Mean	8.81	15.7	47.0	53.4 <sup>B</sup>	17.8
	SD	0.49	0.7	2.1	1.1	0.6
	N	10	10	10	10	10

**Table 15. Group Mean Hematology Data – Males (Continued)**

Group		Mean Corpuscular Hemoglobin Concentration	Platelet Count	Reticulocytes
		(g/dL)	( $10^3/\mu\text{L}$ )	( $10^3/\mu\text{L}$ )
CM	Mean	31.8	916	202.8
	SD	0.8	91	21.5
	N	10	10	10
NT20M	Mean	33.2 <sup>A</sup>	865	169.2 <sup>A</sup>
	SD	0.8	73	40.2
	N	10	10	10
B0.2M	Mean	32.3	805	178.4
	SD	1.2	75	27.4
	N	10	10	10
B2M	Mean	32.2	864	191.9
	SD	0.7	141	23.0
	N	10	10	10
B8M	Mean	32.2	867	180.1
	SD	0.6	63	23.1
	N	10	10	10
B20M	Mean	33.3 <sup>B</sup>	756 <sup>B,C</sup>	151.6 <sup>B</sup>
	SD	0.6	116	36.8
	N	10	10	10
E0.2M	Mean	32.4	965 <sup>D</sup>	183.4
	SD	1.0	154	35.1
	N	10	10	10
E2M	Mean	32.0	817	201.4
	SD	0.8	69	40.6
	N	10	10	10

**Table 15. Group Mean Hematology Data – Males (Continued)**

Group		Mean Corpuscular Hemoglobin Concentration	Platelet Count	Reticulocytes
		(g/dL)	( $10^3/\mu\text{L}$ )	( $10^3/\mu\text{L}$ )
E8M	Mean	32.3	840	165.1
	SD	0.6	76	32.0
	N	10	10	10
E20M	Mean	33.4 <sup>B</sup>	853 <sup>G</sup>	133.8 <sup>B</sup>
	SD	0.7	71	44.0
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 16. Group Mean Hematology Data – Females**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
CF	Mean	8.34	15.0	46.0	55.2	18.0
	SD	0.28	0.6	1.8	1.2	0.5
	N	10	10	10	10	10
NT20F	Mean	8.35	14.8	44.5 <sup>A</sup>	53.4 <sup>A</sup>	17.7
	SD	0.30	0.4	1.2	1.1	0.7
	N	10	10	10	10	10
B0.2F	Mean	8.44	15.1	45.9	54.5	17.9
	SD	0.58	0.7	2.0	1.7	0.9
	N	10	10	10	10	10
B2F	Mean	8.63	15.6	47.6	55.2	18.0
	SD	0.62	0.9	2.6	1.3	0.6
	N	10	10	10	10	10
B8F	Mean	8.37	14.7	45.5	54.4	17.6
	SD	0.32	0.6	1.4	1.0	0.4
	N	10	10	10	10	10
B20F	Mean	8.45	15.1	45.1	53.4 <sup>B</sup>	17.9
	SD	0.47	0.8	2.8	1.6	0.8
	N	9	9	9	9	9
E0.2F	Mean	8.36	15.2	46.1	55.1	18.1
	SD	0.36	0.7	1.6	1.3	0.6
	N	10	10	10	10	10
E2F	Mean	8.37	15.3	46.4	55.5	18.3
	SD	0.37	0.5	1.6	1.2	0.6
	N	10	10	10	10	10

**Table 16. Group Mean Hematology Data – Females (Continued)**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
E8F	Mean	8.86	15.5	47.9	54.2	17.6
	SD	0.77	1.1	3.5	1.3	0.5
	N	10	10	10	10	10
E20F	Mean	8.47	15.3	44.8	52.8 <sup>B</sup>	18.0
	SD	0.37	0.9	2.4	1.8	0.7
	N	10	10	10	10	10

**Table 16. Group Mean Hematology Data – Females (Continued)**

		Mean Corpuscular Hemoglobin Concentration	Platelet Count	Reticulocytes
Group		(g/dL)	(10 <sup>3</sup> /μL)	(10 <sup>3</sup> /μL)
CF	Mean	32.6	886	213.3
	SD	0.7	92	35.9
	N	10	10	10
NT20F	Mean	33.2	755 <sup>A</sup>	195.4
	SD	0.9	85	31.7
	N	10	10	10
B0.2F	Mean	32.8	807	219.1
	SD	1.1	164	29.6
	N	10	10	10
B2F	Mean	32.7	827	218.5
	SD	0.7	93	30.9
	N	10	10	10
B8F	Mean	32.4	859	226.0
	SD	0.5	163	51.3
	N	10	10	10
B20F	Mean	33.4	731 <sup>B</sup>	154.0 <sup>B</sup>
	SD	0.9	107	56.0
	N	9	9	9
E0.2F	Mean	32.9	861	214.6
	SD	0.7	132	43.3
	N	10	10	10
E2F	Mean	33.0	823	226.9
	SD	0.8	174	43.6
	N	10	10	10

**Table 16. Group Mean Hematology Data – Females (Continued)**

		<b>Mean Corpuscular Hemoglobin Concentration</b>	<b>Platelet Count</b>	<b>Reticulocytes</b>
<b>Group</b>		<b>(g/dL)</b>	<b>(10<sup>3</sup>/μL)</b>	<b>(10<sup>3</sup>/μL)</b>
E8F	Mean	32.5	811	216.2
	SD	1.1	155	31.3
	N	10	10	10
E20F	Mean	34.1 <sup>B,C</sup>	713 <sup>B</sup>	132.4 <sup>B,C</sup>
	SD	0.7	88	35.6
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 17. Pairfed and High Dose Group Mean Hematology Data – Males**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
NT20M	Mean	8.49	14.9 <sup>A</sup>	45.0 <sup>A</sup>	52.9 <sup>A</sup>	17.6
	SD	0.57	0.9	3.3	1.1	0.6
	N	10	10	10	10	10
PFCNTM	Mean	8.73	15.8	47.8	54.7	18.1
	SD	0.31	0.9	2.6	1.8	0.6
	N	10	10	10	10	10
B20M	Mean	8.61	15.3	46.0	53.4	17.8
	SD	0.45	0.8	2.4	0.9	0.3
	N	10	10	10	10	10
PFCBM	Mean	8.95	15.8	47.9	53.5	17.6
	SD	0.42	0.7	2.8	0.9	0.4
	N	10	10	10	10	10
E20M	Mean	8.81	15.7	47.0	53.4 <sup>C</sup>	17.8
	SD	0.49	0.7	2.1	1.1	0.6
	N	10	10	10	10	10
PFCBM	Mean	8.58	15.4	46.8	54.5	17.9
	SD	0.34	0.5	2.0	0.7	0.3
	N	10	10	10	10	10

**Table 17. Paired and High Dose Group Mean Hematology Data – Males (Continued)**

		Mean Corpuscular Hemoglobin Concentration	Platelet Count	Reticulocytes
Group		(g/dL)	( $10^3/\mu\text{L}$ )	( $10^3/\mu\text{L}$ )
NT20M	Mean	33.2	865	169.2 <sup>A</sup>
	SD	0.8	73	40.2
	N	10	10	10
PFCNTM	Mean	33.1	937	131.9
	SD	0.5	97	23.6
	N	10	10	10
B20M	Mean	33.3	756	151.6
	SD	0.6	116	36.8
	N	10	10	10
PFCBM	Mean	33.0	842	133.2
	SD	1.1	73	16.8
	N	10	10	10
E20M	Mean	33.4	853	133.8
	SD	0.7	71	44.0
	N	10	10	10
PFCBM	Mean	32.9	887	150.3
	SD	0.7	96	27.6
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCBM vs. E20M.

**Table 18. Pairfed and High Dose Group Mean Hematology Data – Females**

<b>Group</b>		<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>
NT20F	Mean	8.35	14.8	44.5	53.4 <sup>A</sup>	17.7
	SD	0.30	0.4	1.2	1.1	0.7
	N	10	10	10	10	10
PFCNTF	Mean	8.18	15.0	44.9	54.8	18.3
	SD	0.42	0.6	2.1	1.4	0.6
	N	10	10	10	10	10
B20F	Mean	8.45	15.1	45.1	53.4	17.9
	SD	0.47	0.8	2.8	1.6	0.8
	N	9	9	9	9	9
PFCBF	Mean	8.29	15.0	44.9	54.2	18.1
	SD	0.30	0.6	1.6	1.5	0.7
	N	10	10	10	10	10
E20F	Mean	8.47	15.3	44.8	52.8 <sup>C</sup>	18.0
	SD	0.37	0.9	2.4	1.8	0.7
	N	10	10	10	10	10
PFCEF	Mean	8.17	14.7	45.0	55.1	18.0
	SD	0.41	0.5	2.1	1.4	0.6
	N	9	9	9	9	9

**Table 18. Paired and High Dose Group Mean Hematology Data – Females (Continued)**

		Mean Corpuscular Hemoglobin Concentration	Platelet Count	Reticulocytes
Group		(g/dL)	(10 <sup>3</sup> /μL)	(10 <sup>3</sup> /μL)
NT20F	Mean	33.2	755	195.4 <sup>A</sup>
	SD	0.9	85	31.7
	N	10	10	10
PFCNTF	Mean	33.4	837	163.4
	SD	0.7	114	30.1
	N	10	10	10
B20F	Mean	33.4	731 <sup>B</sup>	154.0
	SD	0.9	107	56.0
	N	9	9	9
PFCBF	Mean	33.4	889	189.6
	SD	0.4	111	43.1
	N	10	10	10
E20F	Mean	34.1 <sup>C</sup>	713 <sup>C</sup>	132.4 <sup>C</sup>
	SD	0.7	88	35.6
	N	10	10	10
PFCEF	Mean	32.6	951	208.3
	SD	0.7	118	31.1
	N	9	9	9

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 19. Group Mean Absolute WBC Differential Count Data – Males**

		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
<b>Group</b>	Mean	7.93	0.87	6.87	0.11	0.06
	SD	1.78	0.21	1.65	0.05	0.02
	N	10	10	10	10	10
CM	Mean	7.74	0.85	6.67	0.13	0.06
	SD	2.36	0.27	2.12	0.05	0.07
	N	10	10	10	10	10
NT20M	Mean	7.74	0.85	6.67	0.13	0.06
	SD	2.36	0.27	2.12	0.05	0.07
	N	10	10	10	10	10
B0.2M	Mean	6.37	0.78	5.42	0.09	0.05
	SD	2.17	0.36	1.84	0.05	0.04
	N	10	10	10	10	10
B2M	Mean	7.20	0.80	6.22	0.11	0.05
	SD	1.57	0.21	1.41	0.04	0.03
	N	10	10	10	10	10
B8M	Mean	5.69	0.76	4.79	0.08	0.04
	SD	2.86	0.30	2.82	0.03	0.01
	N	10	10	10	10	10
B20M	Mean	6.54	0.88	5.49	0.12	0.04
	SD	1.15	0.22	1.04	0.03	0.03
	N	10	10	10	10	10
E0.2M	Mean	7.58	1.11	6.28	0.12	0.05
	SD	1.57	0.59	1.28	0.03	0.01
	N	10	10	10	10	10
E2M	Mean	6.95	0.80	5.97	0.11	0.05
	SD	1.76	0.22	1.64	0.06	0.02
	N	10	10	10	10	10

**Table 19. Group Mean Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
E8M	Mean	7.33	0.75	6.42	0.10	0.04
	SD	2.17	0.19	2.00	0.05	0.02
	N	10	10	10	10	10
E20M	Mean	6.63	0.92	5.52	0.13	0.05
	SD	1.35	0.25	1.37	0.05	0.03
	N	10	10	10	10	10

**Table 19. Group Mean Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Basophils (10<sup>3</sup>/μL)</b>	
CM	Mean	0.03
	SD	0.01
	N	10
NT20M	Mean	0.02
	SD	0.01
	N	10
B0.2M	Mean	0.02
	SD	0.01
	N	10
B2M	Mean	0.02
	SD	0.01
	N	10
B8M	Mean	0.01 <sup>B</sup>
	SD	0.01
	N	10
B20M	Mean	0.02
	SD	0.01
	N	10
E0.2M	Mean	0.02
	SD	0.01
	N	10
E2M	Mean	0.02
	SD	0.02
	N	10

**Table 19. Group Mean Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Basophils (10<sup>3</sup>/μL)</b>	
E8M	Mean	0.02
	SD	0.01
	N	10
E20M	Mean	0.02 <sup>b</sup>
	SD	0.01
	N	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 20. Group Mean Absolute WBC Differential Count Data – Females**

		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
<b>Group</b>	Mean	5.40	0.82	4.40	0.10	0.05
	SD	1.65	0.30	1.39	0.06	0.03
	N	10	10	10	10	10
CF	Mean	6.43	0.88	5.32	0.15	0.05
	SD	1.48	0.29	1.20	0.06	0.01
	N	10	10	10	10	10
NT20F	Mean	4.82	0.70	3.95	0.10	0.06
	SD	1.31	0.36	1.17	0.03	0.03
	N	10	10	10	10	10
B0.2F	Mean	6.10	0.78	5.15	0.10	0.06
	SD	1.42	0.20	1.41	0.04	0.02
	N	10	10	10	10	10
B2F	Mean	6.12	0.79	5.15	0.12	0.05
	SD	2.05	0.34	1.93	0.04	0.02
	N	10	10	10	10	10
B8F	Mean	6.03	1.02	4.80	0.17 <sup>B</sup>	0.03 <sup>C</sup>
	SD	1.10	0.53	1.49	0.03	0.01
	N	9	9	9	9	9
B20F	Mean	5.19	0.91	4.14	0.09	0.04
	SD	1.92	0.53	1.63	0.04	0.01
	N	10	10	10	10	10
E0.2F	Mean	5.21	0.78	4.29	0.09	0.04
	SD	2.10	0.31	1.76	0.04	0.03
	N	10	10	10	10	10
E2F	Mean	5.19	0.91	4.14	0.09	0.04
	SD	1.92	0.53	1.63	0.04	0.01
	N	10	10	10	10	10

**Table 20. Group Mean Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
E8F	Mean	5.45	0.60	4.72	0.09	0.03
	SD	1.78	0.20	1.66	0.03	0.02
	N	10	10	10	10	10
E20F	Mean	6.25	0.81	5.25	0.13	0.03 <sup>c</sup>
	SD	2.37	0.30	2.05	0.07	0.01
	N	10	10	10	10	10

**Table 20. Group Mean Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>		<b>Basophils (10<sup>3</sup>/μL)</b>
CF	Mean	0.01
	SD	0.01
	N	10
NT20F	Mean	0.02
	SD	0.01
	N	10
B0.2F	Mean	0.01
	SD	0.01
	N	10
B2F	Mean	0.02
	SD	0.01
	N	10
B8F	Mean	0.02
	SD	0.01
	N	10
B20F	Mean	0.01
	SD	0.01
	N	9
E0.2F	Mean	0.01
	SD	0.01
	N	10
E2F	Mean	0.01
	SD	0.01
	N	10

**Table 20. Group Mean Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Basophils (10<sup>3</sup>/μL)</b>	
E8F	Mean	0.01
	SD	0.01
	N	10
E20F	Mean	0.02
	SD	0.01
	N	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 21. Paired and High Dose Group Mean Absolute WBC Differential Count Data – Males**

<b>Group</b>		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
NT20M	Mean	7.74 <sup>A</sup>	0.85	6.67 <sup>A</sup>	0.13 <sup>A</sup>	0.06
	SD	2.36	0.27	2.12	0.05	0.07
	N	10	10	10	10	10
PFCNTM	Mean	5.49	0.69	4.68	0.08	0.03
	SD	1.56	0.22	1.41	0.04	0.02
	N	10	10	10	10	10
B20M	Mean	6.54	0.88	5.49	0.12 <sup>B</sup>	0.04
	SD	1.15	0.22	1.04	0.03	0.03
	N	10	10	10	10	10
PFCBM	Mean	6.64	0.80	5.70	0.08	0.05
	SD	1.74	0.23	1.67	0.02	0.03
	N	10	10	10	10	10
E20M	Mean	6.63	0.92 <sup>C</sup>	5.52	0.13 <sup>C</sup>	0.05
	SD	1.35	0.25	1.37	0.05	0.03
	N	10	10	10	10	10
PFCM	Mean	6.83	0.71	5.96	0.09	0.04
	SD	1.36	0.16	1.25	0.03	0.02
	N	10	10	10	10	10

**Table 21. Paired and High Dose Group Mean Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>		<b>Basophils (10<sup>3</sup>/μL)</b>
NT20M	Mean	0.02
	SD	0.01
	N	10
PFCNTM	Mean	0.02
	SD	0.01
	N	10
B20M	Mean	0.02
	SD	0.01
	N	10
PFCBM	Mean	0.02
	SD	0.01
	N	10
E20M	Mean	0.02
	SD	0.01
	N	10
PFCM	Mean	0.02
	SD	0.01
	N	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCM vs. E20M.

**Table 22. Paired and High Dose Group Mean Absolute WBC Differential Count Data – Females**

<b>Group</b>		<b>White Blood Cell Count (10<sup>3</sup>/μL)</b>	<b>Neutrophils (10<sup>3</sup>/μL)</b>	<b>Total Lymphocytes (10<sup>3</sup>/μL)</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>
NT20F	Mean	6.43	0.88	5.32	0.15 <sup>A</sup>	0.05
	SD	1.48	0.29	1.20	0.06	0.01
	N	10	10	10	10	10
PFCNTF	Mean	5.74	0.78	4.80	0.09	0.07
	SD	2.63	0.38	2.25	0.05	0.04
	N	10	10	10	10	10
B20F	Mean	6.03	1.02	4.80	0.17 <sup>B</sup>	0.03
	SD	1.10	0.53	1.49	0.03	0.01
	N	9	9	9	9	9
PFCBF	Mean	5.60	0.67	4.78	0.07	0.06
	SD	2.27	0.21	2.10	0.03	0.05
	N	10	10	10	10	10
E20F	Mean	6.25	0.81	5.25	0.13 <sup>C</sup>	0.03 <sup>C</sup>
	SD	2.37	0.30	2.05	0.07	0.01
	N	10	10	10	10	10
PFCEF	Mean	5.35	0.64	4.57	0.07	0.06
	SD	1.49	0.21	1.32	0.02	0.02
	N	9	9	9	9	9

**Table 22. Paired and High Dose Group Mean Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>		<b>Basophils (10<sup>3</sup>/μL)</b>
NT20F	Mean	0.02
	SD	0.01
	N	10
PFCNTF	Mean	0.02
	SD	0.01
	N	10
B20F	Mean	0.01
	SD	0.01
	N	9
PFCBF	Mean	0.01
	SD	0.01
	N	10
E20F	Mean	0.02
	SD	0.01
	N	10
PFCEF	Mean	0.01
	SD	0.01
	N	9

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 23. Group Mean Coagulation Data – Males**

<b>Group</b>		<b>Prothrombin Time (Seconds)</b>
CM	Mean	15.1
	SD	0.5
	N	10
NT20M	Mean	15.4
	SD	0.6
	N	10
B0.2M	Mean	15.5
	SD	0.6
	N	8
B2M	Mean	15.7
	SD	0.5
	N	9
B8M	Mean	15.7
	SD	0.6
	N	6
B20M	Mean	15.6
	SD	0.7
	N	10
E0.2M	Mean	15.7
	SD	0.8
	N	10
E2M	Mean	16.1 <sup>B</sup>
	SD	0.9
	N	9

**Table 23. Group Mean Coagulation Data – Males (Continued)**

<b>Group</b>		<b>Prothrombin Time (Seconds)</b>
E8M	Mean	15.6
	SD	0.6
	N	8
E20M	Mean	16.1 <sup>B,C</sup>
	SD	0.6
	N	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 24. Group Mean Coagulation Data – Females**

<b>Group</b>		<b>Prothrombin Time (Seconds)</b>
CF	Mean	15.3
	SD	0.6
	N	10
NT20F	Mean	15.7
	SD	0.6
	N	6
B0.2F	Mean	15.2
	SD	0.6
	N	10
B2F	Mean	15.5
	SD	0.6
	N	7
B8F	Mean	15.0
	SD	0.6
	N	9
B20F	Mean	15.9
	SD	0.6
	N	7
E0.2F	Mean	15.5
	SD	0.6
	N	9
E2F	Mean	15.4
	SD	0.6
	N	8

**Table 24. Group Mean Coagulation Data – Females (Continued)**

<b>Group</b>		<b>Prothrombin Time (Seconds)</b>
E8F	Mean	15.3
	SD	0.7
	N	7
E20F	Mean	16.3
	SD	1.2
	N	5

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 25. Paired and High Dose Group Mean Coagulation Data – Males**

<b>Group</b>		<b>Prothrombin Time (Seconds)</b>
NT20M	Mean	15.4 <sup>A</sup>
	SD	0.6
	N	10
PFCNTM	Mean	16.1
	SD	0.6
	N	10
B20M	Mean	15.6
	SD	0.7
	N	10
PFCBM	Mean	16.2
	SD	0.8
	N	10
E20M	Mean	16.1
	SD	0.6
	N	10
PFCM	Mean	16.1
	SD	0.5
	N	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCM vs. E20M.

**Table 26. Paired and High Dose Group Mean Coagulation Data – Females**

<b>Group</b>	<b>Prothrombin Time (Seconds)</b>	
NT20F	Mean	15.7
	SD	0.6
	N	6
PFCNTF	Mean	16.0
	SD	0.5
	N	9
B20F	Mean	15.9
	SD	0.6
	N	7
PFCBF	Mean	16.2
	SD	0.6
	N	9
E20F	Mean	16.3
	SD	1.2
	N	5
PFCEF	Mean	15.9
	SD	0.5
	N	8

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 27. Group Mean Serum Chemistry Data – Males**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
CM	Mean	130	61	1	0.11
	SD	20	4	0	0.01
	N	10	10	10	10
NT20M	Mean	126	60	1	0.12
	SD	22	10	0	0.04
	N	10	10	10	10
B0.2M	Mean	127	67	1	0.11
	SD	23	12	0	0.02
	N	10	10	10	10
B2M	Mean	145	68	1	0.12
	SD	25	11	0	0.02
	N	10	10	10	10
B8M	Mean	125	66	1	0.11
	SD	28	14	0	0.02
	N	10	10	10	10
B20M	Mean	144	62	1	0.15
	SD	58	8	0	0.07
	N	10	10	10	10
E0.2M	Mean	109 <sup>b</sup>	61	1	0.11
	SD	20	7	0	0.02
	N	10	10	10	10
E2M	Mean	126	68 <sup>b</sup>	1	0.12
	SD	26	8	0	0.02
	N	10	10	10	10

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
E8M	Mean	126	65	1	0.11
	SD	26	5	0	0.02
	N	10	10	10	10
E20M	Mean	165 <sup>c</sup>	66	1	0.15
	SD	49	12	1	0.11
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
CM	Mean	0.04	6.3	100	4.2
	SD	0.01	0.2	27	0.2
	N	10	10	10	10
NT20M	Mean	0.06	5.7 <sup>A</sup>	71 <sup>a</sup>	4.0 <sup>A</sup>
	SD	0.03	0.1	5	0.2
	N	10	10	10	10
B0.2M	Mean	0.04	6.4	87	4.3
	SD	0.01	0.3	14	0.2
	N	10	10	10	10
B2M	Mean	0.04	6.3	89	4.2
	SD	0.01	0.3	11	0.2
	N	10	10	10	10
B8M	Mean	0.04	6.3	73 <sup>b</sup>	4.3
	SD	0.01	0.3	14	0.2
	N	10	10	10	10
B20M	Mean	0.10 <sup>b</sup>	5.7 <sup>B</sup>	76 <sup>b</sup>	4.1
	SD	0.05	0.4	7	0.2
	N	10	10	10	10
E0.2M	Mean	0.04	6.3	82	4.1
	SD	0.01	0.2	11	0.2
	N	10	10	10	10
E2M	Mean	0.04	6.4	80	4.3
	SD	0.01	0.4	15	0.2
	N	10	10	10	10

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
E8M	Mean	0.04	6.4	77 <sup>b</sup>	4.3
	SD	0.01	0.2	12	0.2
	N	10	10	10	10
E20M	Mean	0.09	5.9 <sup>b</sup>	73 <sup>b</sup>	4.2
	SD	0.08	0.4	14	0.2
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
CM	Mean	2.2	1.94	14	0.7
	SD	0.1	0.13	3	0.1
	N	10	10	10	10
NT20M	Mean	1.7 <sup>A</sup>	2.35 <sup>A</sup>	21 <sup>A</sup>	0.6 <sup>A</sup>
	SD	0.1	0.23	2	0.1
	N	10	10	10	10
B0.2M	Mean	2.1	2.03	14	0.7
	SD	0.2	0.24	3	0.1
	N	10	10	10	10
B2M	Mean	2.1	2.08	15	0.6
	SD	0.2	0.30	2	0.1
	N	10	10	10	10
B8M	Mean	2.0	2.21	17	0.7
	SD	0.2	0.24	3	0.1
	N	10	10	10	10
B20M	Mean	1.6 <sup>B</sup>	2.56 <sup>B</sup>	24 <sup>B</sup>	0.6
	SD	0.3	0.35	4	0.0
	N	10	10	10	10
E0.2M	Mean	2.2	1.92	14	0.6
	SD	0.2	0.19	3	0.1
	N	10	10	10	10
E2M	Mean	2.1	2.04	17	0.7
	SD	0.2	0.18	3	0.0
	N	10	10	10	10

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
E8M	Mean	2.1	2.07	17 <sup>B</sup>	0.7
	SD	0.1	0.16	2	0.1
	N	10	10	10	10
E20M	Mean	1.8 <sup>b</sup>	2.45 <sup>b</sup>	23 <sup>B</sup>	0.6 <sup>C</sup>
	SD	0.3	0.49	4	0.0
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
CM	Mean	36	76	11.3	10.8
	SD	11	14	0.2	0.8
	N	10	10	10	10
NT20M	Mean	52 <sup>A</sup>	86	11.1	11.0
	SD	10	13	0.3	1.4
	N	10	10	10	10
B0.2M	Mean	40	72	11.2	10.7
	SD	12	10	0.3	0.7
	N	10	10	10	10
B2M	Mean	32	77	11.4	11.4
	SD	7	12	0.3	1.3
	N	10	10	10	10
B8M	Mean	45	78	11.2	11.1
	SD	14	13	0.2	2.4
	N	10	10	10	10
B20M	Mean	80 <sup>b</sup>	83	11.1	10.1
	SD	44	15	0.4	1.5
	N	10	10	10	10
E0.2M	Mean	53 <sup>b,D</sup>	76	11.2	10.3
	SD	15	9	0.3	0.6
	N	10	10	10	10
E2M	Mean	48 <sup>E</sup>	73	11.5	11.4
	SD	13	11	0.3	1.3
	N	10	10	10	10

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
E8M	Mean	60 <sup>b</sup>	90	11.4	10.6
	SD	28	12	0.3	1.1
	N	10	10	10	10
E20M	Mean	78 <sup>b</sup>	87	11.3	9.9
	SD	42	18	0.4	1.8
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
CM	Mean	146	5.5	100
	SD	1	0.8	2
	N	10	10	10
NT20M	Mean	144 <sup>A</sup>	5.9	99
	SD	2	0.5	1
	N	10	10	10
B0.2M	Mean	146	5.9	100
	SD	1	0.4	1
	N	10	10	10
B2M	Mean	147	5.9	101
	SD	1	0.4	1
	N	10	10	10
B8M	Mean	147	6.0	101
	SD	1	0.5	1
	N	10	10	10
B20M	Mean	144 <sup>B</sup>	5.9	99
	SD	2	0.4	2
	N	10	10	10
E0.2M	Mean	147	5.9	100
	SD	1	0.3	1
	N	10	10	10
E2M	Mean	147	5.9	100 <sup>E</sup>
	SD	1	0.6	1
	N	10	10	10

**Table 27. Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
E8M	Mean	146	6.1	99 <sup>F</sup>
	SD	1	0.4	1
	N	10	10	10
E20M	Mean	145	5.9	101
	SD	2	0.3	3
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 28. Group Mean Serum Chemistry Data – Females**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
CF	Mean	65	67	1	0.10
	SD	16	9	0	0.02
	N	10	10	10	10
NT20F	Mean	123 <sup>a</sup>	74	3	0.20 <sup>a</sup>
	SD	33	10	1	0.06
	N	10	10	10	10
B0.2F	Mean	53	68	1	0.12
	SD	14	6	0	0.02
	N	10	10	10	10
B2F	Mean	63	73	1	0.11
	SD	15	12	0	0.02
	N	10	10	10	10
B8F	Mean	64	72	2	0.10
	SD	30	12	1	0.02
	N	10	10	10	10
B20F	Mean	131 <sup>b</sup>	69	3	0.28 <sup>b</sup>
	SD	36	9	1	0.14
	N	9	9	9	9
E0.2F	Mean	62	70	1	0.11
	SD	11	10	0	0.03
	N	10	10	10	10
E2F	Mean	60	67	1	0.10
	SD	14	6	0	0.02
	N	10	10	10	10

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
E8F	Mean	64	72	1	0.11
	SD	11	11	0	0.03
	N	10	10	10	10
E20F	Mean	117 <sup>b</sup>	71	3	0.23 <sup>b</sup>
	SD	30	10	1	0.08
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
CF	Mean	0.03	6.5	79	4.7
	SD	0.01	0.3	13	0.2
	N	10	10	10	10
NT20F	Mean	0.13 <sup>a</sup>	5.7 <sup>A</sup>	70	4.2 <sup>A</sup>
	SD	0.06	0.3	5	0.3
	N	10	10	10	10
B0.2F	Mean	0.04	7.0 <sup>B</sup>	73	5.1 <sup>B</sup>
	SD	0.01	0.3	7	0.3
	N	10	10	10	10
B2F	Mean	0.04	6.6	70	4.7 <sup>D</sup>
	SD	0.01	0.4	6	0.4
	N	10	10	10	10
B8F	Mean	0.04	6.3	68 <sup>B</sup>	4.4 <sup>B</sup>
	SD	0.01	0.1	8	0.2
	N	10	10	10	10
B20F	Mean	0.21 <sup>b</sup>	5.9 <sup>B</sup>	66 <sup>B</sup>	4.3 <sup>B</sup>
	SD	0.14	0.3	6	0.3
	N	9	9	9	9
E0.2F	Mean	0.04	6.8	76	4.7 <sup>D</sup>
	SD	0.01	0.4	11	0.3
	N	10	10	10	10
E2F	Mean	0.04	6.5	75	4.6
	SD	0.01	0.3	8	0.3
	N	10	10	10	10

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
E8F	Mean	0.03	6.2	73	4.4 <sup>B</sup>
	SD	0.01	0.2	12	0.2
	N	10	10	10	10
E20F	Mean	0.16 <sup>b</sup>	5.7 <sup>B</sup>	69	4.2 <sup>B</sup>
	SD	0.08	0.3	7	0.2
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
CF	Mean	1.8	2.62	16	0.7
	SD	0.2	0.28	2	0.0
	N	10	10	10	10
NT20F	Mean	1.6 <sup>A</sup>	2.72	24 <sup>A</sup>	0.6 <sup>A</sup>
	SD	0.2	0.28	2	0.0
	N	10	10	10	10
B0.2F	Mean	1.9	2.65	16	0.7
	SD	0.1	0.25	2	0.0
	N	10	10	10	10
B2F	Mean	1.9	2.49	18	0.7
	SD	0.2	0.34	2	0.0
	N	10	10	10	10
B8F	Mean	1.9	2.31	21 <sup>b</sup>	0.7
	SD	0.1	0.17	4	0.1
	N	10	10	10	10
B20F	Mean	1.5 <sup>B</sup>	2.83	30 <sup>b,C</sup>	0.6 <sup>B</sup>
	SD	0.2	0.33	5	0.0
	N	9	9	9	9
E0.2F	Mean	2.0	2.38	16	0.7
	SD	0.2	0.37	3	0.0
	N	10	10	10	10
E2F	Mean	1.9	2.47	17	0.7
	SD	0.1	0.18	2	0.0
	N	10	10	10	10

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
E8F	Mean	1.8 <sup>F</sup>	2.43	21 <sup>B</sup>	0.7
	SD	0.1	0.14	3	0.1
	N	10	10	10	10
E20F	Mean	1.5 <sup>b</sup>	2.77	30 <sup>B,C</sup>	0.6 <sup>B</sup>
	SD	0.2	0.39	4	0.1
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
CF	Mean	30	53	11.1	9.8
	SD	6	15	0.3	1.1
	N	10	10	10	10
NT20F	Mean	99 <sup>a</sup>	94 <sup>A</sup>	11.4 <sup>A</sup>	8.8
	SD	73	11	0.2	1.3
	N	10	10	10	10
B0.2F	Mean	34	55	11.1	8.7
	SD	10	11	0.4	0.9
	N	10	10	10	10
B2F	Mean	27	43	11.0	9.8
	SD	4	12	0.4	1.2
	N	10	10	10	10
B8F	Mean	44	68 <sup>B</sup>	11.2	9.6
	SD	29	16	0.3	1.0
	N	10	10	10	10
B20F	Mean	86 <sup>b</sup>	88 <sup>B</sup>	11.7 <sup>B</sup>	10.1
	SD	27	11	0.4	1.3
	N	9	9	9	9
E0.2F	Mean	30	52	11.0	9.4
	SD	7	8	0.3	1.2
	N	10	10	10	10
E2F	Mean	29	50	11.2	9.6
	SD	7	9	0.2	1.4
	N	10	10	10	10

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
E8F	Mean	45	66	11.1	9.5
	SD	24	15	0.2	0.9
	N	10	10	10	10
E20F	Mean	83 <sup>b</sup>	86 <sup>B</sup>	11.3	9.7
	SD	53	16	0.5	1.4
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
CF	Mean	146	5.4	102
	SD	1	0.2	2
	N	10	10	10
NT20F	Mean	146	5.8 <sup>A</sup>	101
	SD	1	0.3	2
	N	10	10	10
B0.2F	Mean	146	5.6 <sup>b</sup>	101
	SD	2	0.3	2
	N	10	10	10
B2F	Mean	146	5.9 <sup>b</sup>	101
	SD	1	0.3	2
	N	10	10	10
B8F	Mean	146	6.0 <sup>b</sup>	101
	SD	1	0.2	1
	N	10	10	10
B20F	Mean	147	5.6	99
	SD	2	0.6	3
	N	9	9	9
E0.2F	Mean	147	5.5	101
	SD	1	0.5	2
	N	10	10	10
E2F	Mean	147	5.8	102
	SD	1	0.4	1
	N	10	10	10

**Table 28. Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
E8F	Mean	147	5.8 <sup>B</sup>	101
	SD	1	0.4	1
	N	10	10	10
E20F	Mean	145	5.9 <sup>B</sup>	99 <sup>B</sup>
	SD	2	0.4	3
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 29. Paired and High Dose Group Mean Serum Chemistry Data – Males**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
NT20M	Mean	126	60	1	0.12
	SD	22	10	0	0.04
	N	10	10	10	10
PFCNTM	Mean	138	60	1	0.10
	SD	23	9	0	0.02
	N	10	10	10	10
B20M	Mean	144	62	1	0.15 <sup>b</sup>
	SD	58	8	0	0.07
	N	10	10	10	10
PFCBM	Mean	130	66	1	0.08
	SD	27	14	0	0.02
	N	10	10	10	10
E20M	Mean	165	66	1 <sup>c</sup>	0.15
	SD	49	12	1	0.11
	N	10	10	10	10
PFCEM	Mean	137	56	1	0.08
	SD	26	6	0	0.01
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 29. Paired and High Dose Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
NT20M	Mean	0.06 <sup>a</sup>	5.7 <sup>A</sup>	71 <sup>a</sup>	4.0 <sup>A</sup>
	SD	0.03	0.1	5	0.2
	N	10	10	10	10
PFCNTM	Mean	0.03	6.2	125	4.2
	SD	0.01	0.2	32	0.2
	N	10	10	10	10
B20M	Mean	0.10 <sup>b</sup>	5.7 <sup>B</sup>	76 <sup>B</sup>	4.1
	SD	0.05	0.4	7	0.2
	N	10	10	10	10
PFCBM	Mean	0.03	6.1	116	4.2
	SD	0.01	0.2	12	0.2
	N	10	10	10	10
E20M	Mean	0.09 <sup>c</sup>	5.9	73 <sup>C</sup>	4.2
	SD	0.08	0.4	14	0.2
	N	10	10	10	10
PFCEM	Mean	0.02	6.1	116	4.2
	SD	0.01	0.2	12	0.2
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 29. Paired and High Dose Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
NT20M	Mean	1.7 <sup>A</sup>	2.35	21 <sup>A</sup>	0.6 <sup>A</sup>
	SD	0.1	0.23	2	0.1
	N	10	10	10	10
PFCNTM	Mean	1.9	2.21	12	0.7
	SD	0.2	0.20	3	0.1
	N	10	10	10	10
B20M	Mean	1.6 <sup>B</sup>	2.56 <sup>B</sup>	24 <sup>b</sup>	0.6
	SD	0.3	0.35	4	0.0
	N	10	10	10	10
PFCBM	Mean	1.9	2.24	10	0.6
	SD	0.2	0.26	2	0.0
	N	10	10	10	10
E20M	Mean	1.8	2.45	23 <sup>c</sup>	0.6
	SD	0.3	0.49	4	0.0
	N	10	10	10	10
PFCEM	Mean	1.9	2.27	9	0.6
	SD	0.1	0.23	2	0.0
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 29. Paired and High Dose Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
NT20M	Mean	52	86	11.1	11.0 <sup>A</sup>
	SD	10	13	0.3	1.4
	N	10	10	10	10
PFCNTM	Mean	45	87	11.1	9.1
	SD	15	13	0.3	0.8
	N	10	10	10	10
B20M	Mean	80	83	11.1	10.1
	SD	44	15	0.4	1.5
	N	10	10	10	10
PFCBM	Mean	50	76	11.0	9.3
	SD	20	9	0.4	0.6
	N	10	10	10	10
E20M	Mean	78 <sup>c</sup>	87	11.3	9.9
	SD	42	18	0.4	1.8
	N	10	10	10	10
PFCEM	Mean	40	83	11.1	9.6
	SD	17	13	0.3	0.9
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 29. Paired and High Dose Group Mean Serum Chemistry Data – Males (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
NT20M	Mean	144 <sup>a</sup>	5.9	99 <sup>A</sup>
	SD	2	0.5	1
	N	10	10	10
PFCNTM	Mean	146	5.7	102
	SD	1	0.5	1
	N	10	10	10
B20M	Mean	144	5.9	99 <sup>B</sup>
	SD	2	0.4	2
	N	10	10	10
PFCBM	Mean	145	6.0	103
	SD	1	0.4	1
	N	10	10	10
E20M	Mean	145	5.9	101
	SD	2	0.3	3
	N	10	10	10
PFCM	Mean	145	6.0	103
	SD	1	0.3	1
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCM vs. E20M.

**Table 30. Paired and High Dose Group Mean Serum Chemistry Data – Females**

<b>Group</b>		<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>	<b>Total Bilirubin (mg/dL)</b>
NT20F	Mean	123	74 <sup>A</sup>	3 <sup>A</sup>	0.20 <sup>a</sup>
	SD	33	10	1	0.06
	N	10	10	10	10
PFCNTF	Mean	102	62	1	0.11
	SD	34	7	0	0.02
	N	10	10	10	10
B20F	Mean	131 <sup>b</sup>	69	3 <sup>b</sup>	0.28 <sup>b</sup>
	SD	36	9	1	0.14
	N	9	9	9	9
PFCBF	Mean	66	66	1	0.10
	SD	18	15	0	0.03
	N	10	10	10	10
E20F	Mean	117 <sup>C</sup>	71 <sup>C</sup>	3 <sup>C</sup>	0.23 <sup>c</sup>
	SD	30	10	1	0.08
	N	10	10	10	10
PFCEF	Mean	57	55	1	0.11
	SD	26	5	0	0.02
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 30. Paired and High Dose Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>
NT20F	Mean	0.13 <sup>a</sup>	5.7 <sup>A</sup>	70 <sup>a</sup>	4.2 <sup>A</sup>
	SD	0.06	0.3	5	0.3
	N	10	10	10	10
PFCNTF	Mean	0.04	6.6	99	4.8
	SD	0.01	0.3	18	0.2
	N	10	10	10	10
B20F	Mean	0.21 <sup>b</sup>	5.9 <sup>B</sup>	66 <sup>B</sup>	4.3 <sup>B</sup>
	SD	0.14	0.3	6	0.3
	N	9	9	9	9
PFCBF	Mean	0.04	6.5	91	4.7
	SD	0.01	0.3	12	0.2
	N	10	10	10	10
E20F	Mean	0.16 <sup>c</sup>	5.7 <sup>C</sup>	69 <sup>C</sup>	4.2 <sup>C</sup>
	SD	0.08	0.3	7	0.2
	N	10	10	10	10
PFCEF	Mean	0.03	6.7	85	4.8
	SD	0.01	0.3	10	0.2
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 30. Paired and High Dose Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Globulin (g/dL)</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
NT20F	Mean	1.6 <sup>A</sup>	2.72	24 <sup>A</sup>	0.6 <sup>A</sup>
	SD	0.2	0.28	2	0.0
	N	10	10	10	10
PFCNTF	Mean	1.8	2.62	12	0.7
	SD	0.2	0.34	3	0.0
	N	10	10	10	10
B20F	Mean	1.5 <sup>b</sup>	2.83	30 <sup>b</sup>	0.6 <sup>B</sup>
	SD	0.2	0.33	5	0.0
	N	9	9	9	9
PFCBF	Mean	1.8	2.64	12	0.7
	SD	0.1	0.14	2	0.0
	N	10	10	10	10
E20F	Mean	1.5 <sup>C</sup>	2.77	30 <sup>C</sup>	0.6
	SD	0.2	0.39	4	0.1
	N	10	10	10	10
PFCEF	Mean	1.9	2.55	12	0.7
	SD	0.2	0.33	3	0.1
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 30. Paired and High Dose Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>	<b>Phosphorus (mg/dL)</b>
NT20F	Mean	99	94 <sup>A</sup>	11.4 <sup>A</sup>	8.8
	SD	73	11	0.2	1.3
	N	10	10	10	10
PFCNTF	Mean	48	60	11.1	8.0
	SD	15	7	0.3	0.5
	N	10	10	10	10
B20F	Mean	86 <sup>b</sup>	88 <sup>B</sup>	11.7 <sup>B</sup>	10.1 <sup>B</sup>
	SD	27	11	0.4	1.3
	N	9	9	9	9
PFCBF	Mean	31	61	10.8	7.7
	SD	8	14	0.3	0.9
	N	10	10	10	10
E20F	Mean	83 <sup>c</sup>	86 <sup>C</sup>	11.3	9.7 <sup>C</sup>
	SD	53	16	0.5	1.4
	N	10	10	10	10
PFCEF	Mean	31	65	11.0	7.9
	SD	8	11	0.3	1.0
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 30. Paired and High Dose Group Mean Serum Chemistry Data – Females (Continued)**

<b>Group</b>		<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>	<b>Chloride (mmol/L)</b>
NT20F	Mean	146	5.8	101
	SD	1	0.3	2
	N	10	10	10
PFCNTF	Mean	146	5.9	102
	SD	1	0.4	2
	N	10	10	10
B20F	Mean	147 <sup>B</sup>	5.6	99 <sup>b</sup>
	SD	2	0.6	3
	N	9	9	9
PFCBF	Mean	145	5.8	103
	SD	1	0.5	1
	N	10	10	10
E20F	Mean	145	5.9	99 <sup>C</sup>
	SD	2	0.4	3
	N	10	10	10
PFCEF	Mean	146	5.9	102
	SD	1	0.3	2
	N	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 31. Group Mean Absolute Organ Weights (g) – Males**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
CM	Mean	0.067	1.938	0.9945	0.977	1.956	7.882
	SD	0.006	0.070	0.1191	0.092	0.131	0.825
	N	10	10	10	10	10	10
NT20M	Mean	0.045 <sup>A</sup>	1.839 <sup>A</sup>	0.8699 <sup>A</sup>	0.710 <sup>A</sup>	1.613 <sup>A</sup>	6.176 <sup>a</sup>
	SD	0.006	0.066	0.0735	0.064	0.126	0.358
	N	10	10	10	10	10	10
B0.2M	Mean	0.061	1.927	0.9670	0.902	1.916	7.006
	SD	0.007	0.073	0.0782	0.103	0.162	0.607
	N	10	10	10	10	10	10
B2M	Mean	0.065	1.932	0.9554	0.877 <sup>B</sup>	1.858	6.723 <sup>B</sup>
	SD	0.010	0.082	0.0623	0.086	0.218	0.919
	N	10	10	10	10	10	10
B8M	Mean	0.049 <sup>B</sup>	1.843 <sup>B</sup>	0.8928 <sup>B</sup>	0.763 <sup>B</sup>	1.678 <sup>B</sup>	6.264 <sup>B</sup>
	SD	0.008	0.083	0.0741	0.075	0.207	0.908
	N	10	10	10	10	10	10
B20M	Mean	0.047 <sup>B</sup>	1.758 <sup>B,C</sup>	0.8282 <sup>B</sup>	0.653 <sup>B</sup>	1.520 <sup>B</sup>	5.895 <sup>B</sup>
	SD	0.005	0.050	0.0508	0.065	0.143	0.644
	N	10	10	10	10	10	10
E0.2M	Mean	0.061	1.923	0.9337	0.948	2.001	7.498
	SD	0.012	0.065	0.1133	0.095	0.110	0.618
	N	10	10	10	10	10	10
E2M	Mean	0.061	1.932	0.9136	0.921	1.904	7.057
	SD	0.011	0.072	0.1012	0.124	0.215	0.946
	N	10	10	10	10	10	10

**Table 31. Group Mean Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
E8M	Mean	0.056 <sup>B</sup>	1.869	0.9206	0.810 <sup>B</sup>	1.660 <sup>B</sup>	6.356 <sup>B</sup>
	SD	0.006	0.046	0.1129	0.059	0.103	0.589
	N	10	10	10	10	10	10
E20M	Mean	0.044 <sup>B</sup>	1.793 <sup>B</sup>	0.7962 <sup>B,C</sup>	0.648 <sup>B</sup>	1.463 <sup>B,C</sup>	6.037 <sup>B</sup>
	SD	0.007	0.071	0.0784	0.061	0.146	0.621
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 31. Group Mean Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>	<b>Thymus</b>
CM	Mean	0.619	0.534	3.362	0.627
	SD	0.043	0.067	0.345	0.083
	N	10	10	10	10
NT20M	Mean	0.544 <sup>A</sup>	0.418 <sup>A</sup>	3.228	0.349 <sup>A</sup>
	SD	0.060	0.049	0.286	0.065
	N	10	10	10	10
B0.2M	Mean	0.569	0.551	3.266	0.566
	SD	0.058	0.086	0.170	0.095
	N	10	10	10	10
B2M	Mean	0.613	0.523	3.313	0.473 <sup>B</sup>
	SD	0.080	0.079	0.146	0.080
	N	10	10	10	10
B8M	Mean	0.549	0.412 <sup>B</sup>	3.139	0.427 <sup>B</sup>
	SD	0.043	0.092	0.144	0.090
	N	10	10	10	10
B20M	Mean	0.521 <sup>B</sup>	0.380 <sup>B</sup>	3.107	0.297 <sup>B</sup>
	SD	0.084	0.037	0.188	0.084
	N	10	10	10	10
E0.2M	Mean	0.596	0.536	3.221	0.565
	SD	0.079	0.071	0.286	0.113
	N	10	10	10	10
E2M	Mean	0.627	0.518	3.201	0.521
	SD	0.068	0.074	0.317	0.105
	N	10	10	10	10

**Table 31. Group Mean Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>	<b>Thymus</b>
E8M	Mean	0.577	0.469	3.267	0.507 <sup>B</sup>
	SD	0.048	0.063	0.246	0.093
	N	10	10	10	10
E20M	Mean	0.500 <sup>B</sup>	0.372 <sup>B</sup>	2.995 <sup>B</sup>	0.249 <sup>B,C</sup>
	SD	0.064	0.063	0.278	0.073
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 32. Group Mean Absolute Organ Weights (g) – Females**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Ovaries</b>
CF	Mean	0.072	1.796	0.625	1.263	4.672	0.108
	SD	0.007	0.051	0.049	0.102	0.279	0.025
	N	10	10	10	10	10	10
NT20F	Mean	0.043 <sup>A</sup>	1.665 <sup>A</sup>	0.481 <sup>A</sup>	0.985 <sup>a</sup>	4.419	0.055 <sup>A</sup>
	SD	0.005	0.062	0.037	0.046	0.340	0.013
	N	10	10	10	10	10	10
B0.2F	Mean	0.066	1.767	0.628	1.250	4.540	0.103
	SD	0.006	0.053	0.062	0.083	0.299	0.028
	N	10	10	10	10	10	10
B2F	Mean	0.072	1.818	0.614	1.195	4.369	0.101
	SD	0.010	0.065	0.045	0.074	0.306	0.020
	N	10	10	10	10	10	10
B8F	Mean	0.059 <sup>B</sup>	1.742	0.515 <sup>B</sup>	1.125 <sup>B</sup>	4.292 <sup>B</sup>	0.091
	SD	0.009	0.081	0.033	0.081	0.245	0.029
	N	10	10	10	10	10	10
B20F	Mean	0.045 <sup>B</sup>	1.691 <sup>B</sup>	0.461 <sup>B</sup>	0.985 <sup>B</sup>	4.044 <sup>B,C</sup>	0.055 <sup>b</sup>
	SD	0.006	0.060	0.033	0.046	0.247	0.009
	N	9	9	9	9	9	9
E0.2F	Mean	0.078 <sup>D</sup>	1.760	0.665	1.279	4.649	0.099
	SD	0.007	0.054	0.040	0.068	0.334	0.022
	N	10	10	10	10	10	10
E2F	Mean	0.078	1.778	0.593	1.227	4.308 <sup>B</sup>	0.101
	SD	0.019	0.037	0.049	0.083	0.367	0.018
	N	10	10	10	10	10	10

**Table 32. Group Mean Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Ovaries</b>
E8F	Mean	0.058 <sup>b</sup>	1.749	0.558 <sup>B,F</sup>	1.175	4.410	0.082 <sup>B</sup>
	SD	0.011	0.062	0.052	0.092	0.348	0.016
	N	10	10	10	10	10	10
E20F	Mean	0.041 <sup>b</sup>	1.661 <sup>B</sup>	0.464 <sup>B</sup>	1.000 <sup>B</sup>	4.021 <sup>B,C</sup>	0.057 <sup>B</sup>
	SD	0.008	0.074	0.031	0.061	0.237	0.011
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 32. Group Mean Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
CF	Mean	0.426	0.406	0.440	0.631
	SD	0.048	0.044	0.073	0.200
	N	10	10	10	10
NT20F	Mean	0.375 <sup>A</sup>	0.296 <sup>A</sup>	0.278 <sup>A</sup>	0.161 <sup>a</sup>
	SD	0.033	0.034	0.070	0.051
	N	10	10	10	10
B0.2F	Mean	0.406	0.379	0.425	0.523
	SD	0.035	0.059	0.069	0.164
	N	10	10	10	10
B2F	Mean	0.457	0.395	0.411	0.484
	SD	0.052	0.044	0.066	0.098
	N	10	10	10	10
B8F	Mean	0.450	0.348 <sup>B</sup>	0.377	0.496
	SD	0.028	0.039	0.041	0.214
	N	10	10	10	10
B20F	Mean	0.345 <sup>B</sup>	0.230 <sup>B,C</sup>	0.200 <sup>B,C</sup>	0.143 <sup>b</sup>
	SD	0.030	0.042	0.044	0.022
	N	9	9	9	9
E0.2F	Mean	0.437	0.421	0.416	0.641
	SD	0.058	0.060	0.065	0.172
	N	10	10	10	10
E2F	Mean	0.446	0.393	0.408	0.567
	SD	0.060	0.029	0.073	0.212
	N	10	10	10	10

**Table 32. Group Mean Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
E8F	Mean	0.444	0.397 <sup>F</sup>	0.376	0.524
	SD	0.035	0.056	0.062	0.238
	N	10	10	10	10
E20F	Mean	0.359 <sup>B</sup>	0.245 <sup>B,C</sup>	0.210 <sup>B,C</sup>	0.120 <sup>b,c,G</sup>
	SD	0.033	0.059	0.057	0.020
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 33. Paired and High Dose Group Mean Absolute Organ Weights (g) – Males**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
NT20M	Mean	0.045 <sup>A</sup>	1.839	0.8699 <sup>A</sup>	0.710	1.613	6.176
	SD	0.006	0.066	0.0735	0.064	0.126	0.358
	N	10	10	10	10	10	10
PFCNTM	Mean	0.050	1.870	0.9724	0.740	1.579	6.298
	SD	0.006	0.077	0.0769	0.042	0.105	0.505
	N	10	10	10	10	10	10
B20M	Mean	0.047	1.758 <sup>b</sup>	0.8282 <sup>B</sup>	0.653 <sup>B</sup>	1.520	5.895
	SD	0.005	0.050	0.0508	0.065	0.143	0.644
	N	10	10	10	10	10	10
PFCBM	Mean	0.050	1.877	0.9265	0.764	1.620	6.409
	SD	0.006	0.115	0.0636	0.061	0.151	0.607
	N	10	10	10	10	10	10
E20M	Mean	0.044 <sup>C</sup>	1.793	0.7962 <sup>C</sup>	0.648 <sup>C</sup>	1.463 <sup>C</sup>	6.037 <sup>C</sup>
	SD	0.007	0.071	0.0784	0.061	0.146	0.621
	N	10	10	10	10	10	10
PFCM	Mean	0.053	1.844	0.9507	0.782	1.644	6.794
	SD	0.009	0.085	0.0716	0.038	0.097	0.515
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCM vs. E20M.

**Table 33. Paired and High Dose Group Mean Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>	<b>Thymus</b>
NT20M	Mean	0.544 <sup>A</sup>	0.418	3.228	0.349
	SD	0.060	0.049	0.286	0.065
	N	10	10	10	10
PFCNTM	Mean	0.599	0.400	3.267	0.397
	SD	0.037	0.034	0.184	0.058
	N	10	10	10	10
B20M	Mean	0.521 <sup>B</sup>	0.380	3.107	0.297 <sup>B</sup>
	SD	0.084	0.037	0.188	0.084
	N	10	10	10	10
PFCBM	Mean	0.595	0.429	3.253	0.432
	SD	0.068	0.064	0.220	0.096
	N	10	10	10	10
E20M	Mean	0.500 <sup>C</sup>	0.372 <sup>C</sup>	2.995	0.249 <sup>C</sup>
	SD	0.064	0.063	0.278	0.073
	N	10	10	10	10
PFCM	Mean	0.606	0.489	3.247	0.431
	SD	0.056	0.061	0.259	0.099
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCM vs. E20M.

**Table 34. Paired and High Dose Group Mean Absolute Organ Weights (g) – Females**

<b>Group</b>		<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Ovaries</b>
NT20F	Mean	0.043 <sup>a</sup>	1.665	0.481 <sup>A</sup>	0.985 <sup>A</sup>	4.419	0.055 <sup>A</sup>
	SD	0.005	0.062	0.037	0.046	0.340	0.013
	N	10	10	10	10	10	10
PFCNTF	Mean	0.062	1.730	0.583	1.143	4.412	0.084
	SD	0.010	0.078	0.046	0.080	0.410	0.010
	N	10	10	10	10	10	10
B20F	Mean	0.045 <sup>B</sup>	1.691	0.461 <sup>B</sup>	0.985 <sup>B</sup>	4.044	0.055 <sup>B</sup>
	SD	0.006	0.060	0.033	0.046	0.247	0.009
	N	9	9	9	9	9	9
PFCBF	Mean	0.065	1.747	0.600	1.107	4.334	0.088
	SD	0.011	0.085	0.052	0.078	0.372	0.017
	N	10	10	10	10	10	10
E20F	Mean	0.041 <sup>C</sup>	1.661 <sup>C</sup>	0.464 <sup>C</sup>	1.000 <sup>C</sup>	4.021 <sup>C</sup>	0.057 <sup>C</sup>
	SD	0.008	0.074	0.031	0.061	0.237	0.011
	N	10	10	10	10	10	10
PFCEF	Mean	0.058	1.728	0.596	1.152	4.359	0.084
	SD	0.007	0.067	0.035	0.059	0.246	0.009
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 34. Paired and High Dose Group Mean Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>		<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
NT20F	Mean	0.375 <sup>A</sup>	0.296 <sup>a</sup>	0.278 <sup>A</sup>	0.161 <sup>a</sup>
	SD	0.033	0.034	0.070	0.051
	N	10	10	10	10
PFCNTF	Mean	0.420	0.398	0.393	0.491
	SD	0.047	0.077	0.068	0.339
	N	10	10	10	10
B20F	Mean	0.345 <sup>B</sup>	0.230 <sup>B</sup>	0.200 <sup>b</sup>	0.143 <sup>b</sup>
	SD	0.030	0.042	0.044	0.022
	N	9	9	9	9
PFCBF	Mean	0.424	0.391	0.452	0.559
	SD	0.040	0.034	0.109	0.369
	N	10	10	10	10
E20F	Mean	0.359 <sup>C</sup>	0.245 <sup>C</sup>	0.210 <sup>C</sup>	0.120 <sup>c</sup>
	SD	0.033	0.059	0.057	0.020
	N	10	10	10	10
PFCEF	Mean	0.445	0.376	0.425	0.506
	SD	0.048	0.039	0.111	0.211
	N	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 35. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males**

Group	Terminal Body Weight		Adrenal Glands	Brain	Epididymides	Heart	Kidneys
	Mean	SD					
CM	Mean	291.6	0.023	0.667	0.3416	0.335	0.672
	SD	20.5	0.002	0.047	0.0388	0.024	0.043
	N	10	10	10	10	10	10
NT20M	Mean	210.9 <sup>a</sup>	0.021	0.873 <sup>A</sup>	0.4128 <sup>A</sup>	0.337	0.765 <sup>A</sup>
	SD	9.9	0.003	0.027	0.0337	0.033	0.046
	N	10	10	10	10	10	10
B0.2M	Mean	274.2	0.022	0.708	0.3542	0.329	0.701
	SD	26.4	0.002	0.065	0.0287	0.030	0.050
	N	10	10	10	10	10	10
B2M	Mean	274.1	0.024	0.707	0.3499	0.320	0.676
	SD	19.2	0.003	0.041	0.0317	0.020	0.044
	N	10	10	10	10	10	10
B8M	Mean	237.2 <sup>B</sup>	0.021	0.781 <sup>B</sup>	0.3777 <sup>B</sup>	0.322	0.706
	SD	19.0	0.003	0.065	0.0350	0.029	0.047
	N	10	10	10	10	10	10
B20M	Mean	199.5 <sup>B</sup>	0.023	0.884 <sup>B</sup>	0.4158 <sup>B</sup>	0.327	0.763 <sup>B</sup>
	SD	13.6	0.002	0.059	0.0227	0.021	0.070
	N	10	10	10	10	10	10
E0.2M	Mean	291.8	0.021	0.661	0.3201 <sup>D</sup>	0.325	0.687
	SD	14.4	0.003	0.041	0.0362	0.026	0.045
	N	10	10	10	10	10	10
E2M	Mean	280.4	0.022	0.693	0.3279	0.328	0.679
	SD	25.5	0.004	0.057	0.0442	0.024	0.037
	N	10	10	10	10	10	10

**Table 35. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Terminal Body Weight		Adrenal Glands	Brain	Epididymides	Heart	Kidneys
	Mean	SD					
E8M	Mean	243.4 <sup>B</sup>	0.023	0.771 <sup>B</sup>	0.3788	0.333	0.684
	SD	15.9	0.002	0.063	0.0440	0.018	0.047
	N	10	10	10	10	10	10
E20M	Mean	198.9 <sup>B</sup>	0.022	0.911 <sup>B</sup>	0.4022 <sup>B</sup>	0.327	0.739 <sup>B</sup>
	SD	22.2	0.004	0.101	0.0310	0.023	0.064
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 35. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Terminal Body Weight		Liver	Salivary Gland	Spleen	Testes	Thymus
CM	Mean	291.6	2.701	0.213	0.183	1.155	0.215
	SD	20.5	0.181	0.015	0.022	0.113	0.024
	N	10	10	10	10	10	10
NT20M	Mean	210.9	2.931 <sup>A</sup>	0.258 <sup>A</sup>	0.199	1.532 <sup>A</sup>	0.165 <sup>A</sup>
	SD	9.9	0.165	0.022	0.023	0.136	0.029
	N	10	10	10	10	10	10
B0.2M	Mean	274.2	2.561	0.208	0.201	1.197	0.207
	SD	26.4	0.147	0.015	0.026	0.087	0.030
	N	10	10	10	10	10	10
B2M	Mean	274.1	2.447 <sup>B</sup>	0.224	0.191	1.212	0.172 <sup>B</sup>
	SD	19.2	0.238	0.024	0.024	0.063	0.020
	N	10	10	10	10	10	10
B8M	Mean	237.2 <sup>B</sup>	2.632	0.232 <sup>b</sup>	0.173	1.331 <sup>B</sup>	0.179 <sup>B</sup>
	SD	19.0	0.239	0.012	0.031	0.127	0.029
	N	10	10	10	10	10	10
B20M	Mean	199.5 <sup>B</sup>	2.955 <sup>B</sup>	0.262 <sup>b</sup>	0.191	1.560 <sup>B</sup>	0.148 <sup>B</sup>
	SD	13.6	0.263	0.043	0.017	0.076	0.037
	N	10	10	10	10	10	10
E0.2M	Mean	291.8	2.567	0.204	0.184	1.106 <sup>D</sup>	0.193
	SD	14.4	0.118	0.023	0.021	0.103	0.035
	N	10	10	10	10	10	10
E2M	Mean	280.4	2.509 <sup>B</sup>	0.224	0.184	1.147	0.185
	SD	25.5	0.147	0.017	0.018	0.124	0.033
	N	10	10	10	10	10	10

**Table 35. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Terminal Body Weight		Liver	Salivary Gland	Spleen	Testes	Thymus
E8M	Mean	243.4 <sup>B</sup>	2.609	0.237 <sup>B</sup>	0.192	1.345 <sup>B</sup>	0.207 <sup>F</sup>
	SD	15.9	0.121	0.015	0.020	0.099	0.030
	N	10	10	10	10	10	10
E20M	Mean	198.9 <sup>B</sup>	3.045 <sup>B</sup>	0.251 <sup>B</sup>	0.187	1.514 <sup>B</sup>	0.123 <sup>B,C</sup>
	SD	22.2	0.201	0.013	0.021	0.121	0.029
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 36. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females**

<b>Group</b>		<b>Terminal Body Weight</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
CF	Mean	177.1	0.041	1.018	0.353	0.715	2.642
	SD	11.3	0.004	0.063	0.025	0.057	0.119
	N	10	10	10	10	10	10
NT20F	Mean	141.6 <sup>A</sup>	0.030 <sup>A</sup>	1.181 <sup>A</sup>	0.341	0.698	3.125 <sup>A</sup>
	SD	10.3	0.002	0.090	0.028	0.049	0.190
	N	10	10	10	10	10	10
B0.2F	Mean	174.0	0.038	1.018	0.361	0.719	2.612
	SD	10.0	0.002	0.058	0.031	0.033	0.138
	N	10	10	10	10	10	10
B2F	Mean	169.6	0.042	1.074	0.363	0.705	2.578
	SD	9.2	0.006	0.046	0.026	0.035	0.154
	N	10	10	10	10	10	10
B8F	Mean	155.9 <sup>B</sup>	0.038	1.119 <sup>B</sup>	0.331	0.722	2.756
	SD	7.8	0.005	0.063	0.019	0.040	0.146
	N	10	10	10	10	10	10
B20F	Mean	128.2 <sup>B,C</sup>	0.035 <sup>B,c</sup>	1.321 <sup>B,C</sup>	0.360	0.768 <sup>B,C</sup>	3.153 <sup>B</sup>
	SD	6.7	0.005	0.064	0.025	0.022	0.081
	N	9	9	9	9	9	9
E0.2F	Mean	177.7	0.044 <sup>d</sup>	0.995	0.375	0.721	2.617
	SD	11.0	0.005	0.073	0.028	0.042	0.098
	N	10	10	10	10	10	10
E2F	Mean	165.6 <sup>B</sup>	0.047	1.076	0.359	0.742	2.608
	SD	8.9	0.012	0.051	0.035	0.055	0.252
	N	10	10	10	10	10	10

**Table 36. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Terminal Body Weight		Adrenal Glands	Brain	Heart	Kidneys	Liver
E8F	Mean	160.8 <sup>B</sup>	0.036	1.090	0.347	0.732	2.741
	SD	9.1	0.007	0.046	0.025	0.066	0.128
	N	10	10	10	10	10	10
E20F	Mean	132.6 <sup>B</sup>	0.031 <sup>b</sup>	1.257 <sup>B</sup>	0.351	0.756 <sup>C</sup>	3.040 <sup>b</sup>
	SD	8.8	0.007	0.090	0.023	0.055	0.190
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 36. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Terminal Body Weight		Ovaries	Salivary Gland	Spleen	Thymus	Uterus
	Mean						
CF	Mean	177.1	0.061	0.241	0.230	0.249	0.359
	SD	11.3	0.013	0.024	0.026	0.038	0.119
	N	10	10	10	10	10	10
NT20F	Mean	141.6 <sup>A</sup>	0.039 <sup>A</sup>	0.266 <sup>A</sup>	0.209	0.198 <sup>A</sup>	0.113 <sup>a</sup>
	SD	10.3	0.008	0.026	0.022	0.057	0.031
	N	10	10	10	10	10	10
B0.2F	Mean	174.0	0.060	0.233	0.217	0.244	0.303
	SD	10.0	0.018	0.009	0.026	0.033	0.103
	N	10	10	10	10	10	10
B2F	Mean	169.6	0.060	0.270 <sup>b</sup>	0.233	0.243	0.286
	SD	9.2	0.014	0.031	0.023	0.038	0.061
	N	10	10	10	10	10	10
B8F	Mean	155.9 <sup>B</sup>	0.058	0.289 <sup>b</sup>	0.223	0.242	0.318
	SD	7.8	0.018	0.016	0.019	0.027	0.137
	N	10	10	10	10	10	10
B20F	Mean	128.2 <sup>B,C</sup>	0.043 <sup>B</sup>	0.269 <sup>b</sup>	0.179 <sup>B</sup>	0.156 <sup>B</sup>	0.112 <sup>b</sup>
	SD	6.7	0.008	0.023	0.029	0.034	0.020
	N	9	9	9	9	9	9
E0.2F	Mean	177.7	0.055	0.247	0.237	0.235	0.363
	SD	11.0	0.010	0.037	0.034	0.039	0.106
	N	10	10	10	10	10	10
E2F	Mean	165.6 <sup>B</sup>	0.062	0.269	0.238	0.246	0.342
	SD	8.9	0.014	0.035	0.028	0.038	0.122
	N	10	10	10	10	10	10

**Table 36. Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

<b>Group</b>		<b>Terminal Body Weight</b>	<b>Ovaries</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
E8F	Mean	160.8 <sup>B</sup>	0.051	0.276 <sup>B</sup>	0.247	0.234	0.330
	SD	9.1	0.008	0.017	0.034	0.041	0.161
	N	10	10	10	10	10	10
E20F	Mean	132.6 <sup>B</sup>	0.043 <sup>B</sup>	0.271	0.186 <sup>B</sup>	0.157 <sup>B</sup>	0.091 <sup>b,G</sup>
	SD	8.8	0.009	0.024	0.048	0.034	0.018
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 37. Paired and High Dose Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males**

<b>Group</b>		<b>Terminal Body Weight</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>
NT20M	Mean	210.9	0.021	0.873 <sup>A</sup>	0.4128	0.337	0.765 <sup>A</sup>
	SD	9.9	0.003	0.027	0.0337	0.033	0.046
	N	10	10	10	10	10	10
PFCNTM	Mean	234.4 <sup>A</sup>	0.022	0.799	0.4164	0.316	0.675
	SD	14.2	0.003	0.031	0.0438	0.010	0.046
	N	10	10	10	10	10	10
B20M	Mean	199.5	0.023 <sup>B</sup>	0.884 <sup>B</sup>	0.4158 <sup>B</sup>	0.327	0.763 <sup>B</sup>
	SD	13.6	0.002	0.059	0.0227	0.021	0.070
	N	10	10	10	10	10	10
PFCBM	Mean	240.6 <sup>B</sup>	0.021	0.780	0.3855	0.317	0.672
	SD	11.1	0.002	0.039	0.0284	0.021	0.046
	N	10	10	10	10	10	10
E20M	Mean	198.9	0.022	0.911 <sup>c</sup>	0.4022	0.327	0.739 <sup>C</sup>
	SD	22.2	0.004	0.101	0.0310	0.023	0.064
	N	10	10	10	10	10	10
PFCEM	Mean	249.8 <sup>C</sup>	0.021	0.738	0.3807	0.313	0.659
	SD	11.2	0.004	0.031	0.0261	0.018	0.044
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test. For terminal body weight, the paired group was compared against the respective high dose. For percent organ-to-body weight ratios, the high dose was compared against the respective paired group.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 37. Paired and High Dose Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Terminal Body Weight		Liver	Salivary Gland	Spleen	Testes	Thymus
NT20M	Mean	210.9	2.931 <sup>A</sup>	0.258	0.199 <sup>A</sup>	1.532 <sup>A</sup>	0.165
	SD	9.9	0.165	0.022	0.023	0.136	0.029
	N	10	10	10	10	10	10
PFCNTM	Mean	234.4 <sup>A</sup>	2.687	0.256	0.171	1.398	0.170
	SD	14.2	0.143	0.020	0.018	0.104	0.027
	N	10	10	10	10	10	10
B20M	Mean	199.5	2.955 <sup>B</sup>	0.262	0.191	1.560 <sup>B</sup>	0.148
	SD	13.6	0.263	0.043	0.017	0.076	0.037
	N	10	10	10	10	10	10
PFCBM	Mean	240.6 <sup>B</sup>	2.664	0.247	0.178	1.355	0.179
	SD	11.1	0.231	0.022	0.022	0.117	0.035
	N	10	10	10	10	10	10
E20M	Mean	198.9	3.045 <sup>C</sup>	0.251	0.187	1.514 <sup>C</sup>	0.123 <sup>C</sup>
	SD	22.2	0.201	0.013	0.021	0.121	0.029
	N	10	10	10	10	10	10
PFCEM	Mean	249.8 <sup>C</sup>	2.719	0.243	0.196	1.300	0.172
	SD	11.2	0.154	0.023	0.023	0.092	0.034
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test. For terminal body weight, the paired group was compared against the respective high dose. For percent organ-to-body weight ratios, the high dose was compared against the respective paired group.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 38. Pairfed and High Dose Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females**

		<b>Terminal Body Weight</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
NT20F	Mean	141.6	0.030 <sup>a</sup>	1.181 <sup>a</sup>	0.341	0.698	3.125 <sup>A</sup>
	SD	10.3	0.002	0.090	0.028	0.049	0.190
	N	10	10	10	10	10	10
PFCNTF	Mean	166.7 <sup>A</sup>	0.037	1.039	0.350	0.686	2.645
	SD	10.0	0.007	0.044	0.017	0.045	0.171
	N	10	10	10	10	10	10
B20F	Mean	128.2	0.035	1.321 <sup>B</sup>	0.360	0.768 <sup>B</sup>	3.153 <sup>b</sup>
	SD	6.7	0.005	0.064	0.025	0.022	0.081
	N	9	9	9	9	9	9
PFCBF	Mean	169.0 <sup>B</sup>	0.038	1.034	0.355	0.655	2.562
	SD	5.2	0.006	0.048	0.022	0.034	0.168
	N	10	10	10	10	10	10
E20F	Mean	132.6	0.031	1.257 <sup>C</sup>	0.351	0.756 <sup>C</sup>	3.040 <sup>C</sup>
	SD	8.8	0.007	0.090	0.023	0.055	0.190
	N	10	10	10	10	10	10
PFCEF	Mean	170.3 <sup>C</sup>	0.034	1.016	0.350	0.677	2.559
	SD	6.3	0.004	0.052	0.023	0.036	0.104
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test. For terminal body weight, the pairfed group was compared against the respective high dose. For percent organ-to-body weight ratios, the high dose was compared against the respective pairfed group.

A = PFCNTF vs. NT20F.

B = PFCBM vs. B20F.

C = PFCEF vs. E20F.

**Table 38. Paired and High Dose Group Mean Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Terminal Body Weight		Ovaries	Salivary Gland	Spleen	Thymus	Uterus
	Mean	SD	N				
NT20F	Mean	141.6		0.039 <sup>A</sup>	0.266	0.209	0.198
	SD	10.3		0.008	0.026	0.022	0.057
	N	10		10	10	10	10
PFCNTF	Mean	166.7 <sup>A</sup>		0.051	0.252	0.239	0.235
	SD	10.0		0.007	0.021	0.048	0.031
	N	10		10	10	10	10
B20F	Mean	128.2		0.043 <sup>B</sup>	0.269	0.179 <sup>B</sup>	0.156 <sup>B</sup>
	SD	6.7		0.008	0.023	0.029	0.034
	N	9		9	9	9	9
PFCBF	Mean	169.0 <sup>B</sup>		0.052	0.250	0.232	0.267
	SD	5.2		0.009	0.021	0.019	0.063
	N	10		10	10	10	10
E20F	Mean	132.6		0.043	0.271	0.186	0.157 <sup>C</sup>
	SD	8.8		0.009	0.024	0.048	0.034
	N	10		10	10	10	10
PFCEF	Mean	170.3 <sup>C</sup>		0.050	0.261	0.221	0.250
	SD	6.3		0.006	0.024	0.018	0.063
	N	10		10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test. For terminal body weight, the paired group was compared against the respective high dose. For percent organ-to-body weight ratios, the high dose was compared against the respective paired group.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

**Table 39. Group Mean Percent Organ-to-Brain Weight Ratios – Males**

Group	Absolute Brain Weight (g)		Adrenal Glands	Epididymides	Heart	Kidneys	Liver
	Mean	SD					
CM	Mean	1.938	3.45	51.296	50.42	100.96	407.41
	SD	0.070	0.32	5.534	4.18	5.71	46.12
	N	10	10	10	10	10	10
NT20M	Mean	1.839	2.43 <sup>A</sup>	47.328	38.61 <sup>A</sup>	87.72 <sup>A</sup>	336.11 <sup>a</sup>
	SD	0.066	0.30	3.839	3.07	6.18	20.18
	N	10	10	10	10	10	10
B0.2M	Mean	1.927	3.15	50.179	46.80	99.46	364.07
	SD	0.073	0.39	3.573	5.18	7.70	35.09
	N	10	10	10	10	10	10
B2M	Mean	1.932	3.36	49.495	45.39 <sup>B</sup>	96.04	347.45 <sup>B</sup>
	SD	0.082	0.39	3.548	3.81	9.52	41.95
	N	10	10	10	10	10	10
B8M	Mean	1.843	2.67 <sup>B</sup>	48.623	41.41 <sup>B</sup>	91.02	340.06 <sup>B</sup>
	SD	0.083	0.46	5.582	3.71	10.27	49.34
	N	10	10	10	10	10	10
B20M	Mean	1.758	2.65 <sup>B</sup>	47.148	37.18 <sup>B</sup>	86.63 <sup>B</sup>	335.98 <sup>B</sup>
	SD	0.050	0.25	3.254	4.04	9.92	42.14
	N	10	10	10	10	10	10
E0.2M	Mean	1.923	3.15	48.575	49.31	104.04	390.25
	SD	0.065	0.59	5.777	4.69	4.34	33.58
	N	10	10	10	10	10	10
E2M	Mean	1.932	3.13	47.267	47.65	98.53	365.00
	SD	0.072	0.56	4.505	5.98	9.92	44.34
	N	10	10	10	10	10	10

**Table 39. Group Mean Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Adrenal Glands</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
E8M	Mean	1.869	2.99	49.298	43.41 <sup>B</sup>	88.89 <sup>B</sup>	340.88 <sup>B</sup>
	SD	0.046	0.37	6.246	4.01	5.97	38.96
	N	10	10	10	10	10	10
E20M	Mean	1.793	2.43 <sup>B</sup>	44.347 <sup>B</sup>	36.14 <sup>B</sup>	81.49 <sup>B</sup>	336.62 <sup>B</sup>
	SD	0.071	0.34	3.281	2.85	6.15	32.72
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 39. Group Mean Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>	<b>Thymus</b>
CM	Mean	1.938	31.97	27.50	173.25	32.38
	SD	0.070	2.30	2.69	13.62	4.20
	N	10	10	10	10	10
NT20M	Mean	1.839	29.54 <sup>A</sup>	22.80 <sup>A</sup>	175.60	19.02 <sup>A</sup>
	SD	0.066	2.59	2.91	14.92	3.69
	N	10	10	10	10	10
B0.2M	Mean	1.927	29.54	28.54	169.53	29.43
	SD	0.073	2.76	4.14	7.40	5.18
	N	10	10	10	10	10
B2M	Mean	1.932	31.70	27.12	171.59	24.42 <sup>B</sup>
	SD	0.082	3.79	4.32	7.42	3.36
	N	10	10	10	10	10
B8M	Mean	1.843	29.83	22.33 <sup>B</sup>	170.50	23.12 <sup>B</sup>
	SD	0.083	2.55	4.72	9.48	4.45
	N	10	10	10	10	10
B20M	Mean	1.758	29.61	21.67 <sup>B</sup>	176.85	16.93 <sup>B</sup>
	SD	0.050	4.39	2.54	11.50	4.97
	N	10	10	10	10	10
E0.2M	Mean	1.923	30.99	27.91	167.55	29.44
	SD	0.065	3.81	3.70	13.98	6.16
	N	10	10	10	10	10
E2M	Mean	1.932	32.45	26.79	165.70	26.99
	SD	0.072	3.24	3.60	14.62	5.50
	N	10	10	10	10	10

**Table 39. Group Mean Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>	<b>Thymus</b>
E8M	Mean	1.869	30.90	25.13	174.94	27.16
	SD	0.046	2.88	3.72	14.12	5.19
	N	10	10	10	10	10
E20M	Mean	1.793	27.82 <sup>B</sup>	20.72 <sup>B</sup>	166.94	13.85 <sup>B,C</sup>
	SD	0.071	3.12	3.19	13.25	4.01
	N	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CM vs. NT20M.

B = CM vs. B0.2M, B2M, B8M, B20M, E0.2M, E2M, E8M, E20M.

C = NT20M vs. B20M, E20M.

D = B0.2M vs. E0.2M.

E = B2M vs. E2M.

F = B8M vs. E8M.

G = B20M vs. E20M.

**Table 40. Group Mean Percent Organ-to-Brain Weight Ratios – Females**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Adrenal Glands</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Ovaries</b>
CF	Mean	1.796	4.03	34.79	70.31	260.26	5.98
	SD	0.051	0.37	2.68	5.16	16.15	1.30
	N	10	10	10	10	10	10
NT20F	Mean	1.665	2.56 <sup>A</sup>	28.92 <sup>A</sup>	59.25 <sup>A</sup>	265.79	3.32 <sup>A</sup>
	SD	0.062	0.30	2.37	3.30	22.43	0.84
	N	10	10	10	10	10	10
B0.2F	Mean	1.767	3.76	35.61	70.80	257.23	5.83
	SD	0.053	0.35	4.10	4.83	18.65	1.54
	N	10	10	10	10	10	10
B2F	Mean	1.818	3.96	33.81	65.76	240.44 <sup>B</sup>	5.57
	SD	0.065	0.54	2.75	3.93	17.04	1.21
	N	10	10	10	10	10	10
B8F	Mean	1.742	3.41 <sup>B</sup>	29.61 <sup>B</sup>	64.67 <sup>B</sup>	246.93	5.19
	SD	0.081	0.51	2.23	4.95	18.83	1.53
	N	10	10	10	10	10	10
B20F	Mean	1.691	2.67 <sup>B</sup>	27.31 <sup>B</sup>	58.27 <sup>B</sup>	239.23 <sup>B,C</sup>	3.23 <sup>B</sup>
	SD	0.060	0.37	2.14	2.77	13.99	0.60
	N	9	9	9	9	9	9
E0.2F	Mean	1.760	4.43 <sup>b,D</sup>	37.79 <sup>B</sup>	72.67	264.26	5.59
	SD	0.054	0.41	2.10	3.98	20.26	1.16
	N	10	10	10	10	10	10
E2F	Mean	1.778	4.40	33.39	69.02	242.38	5.68
	SD	0.037	1.04	2.78	4.30	20.17	1.05
	N	10	10	10	10	10	10

**Table 40. Group Mean Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Adrenal Glands</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Ovaries</b>
E8F	Mean	1.749	3.32 <sup>b</sup>	31.87 <sup>B</sup>	67.23	252.07	4.69 <sup>B</sup>
	SD	0.062	0.60	2.62	5.33	17.46	0.86
	N	10	10	10	10	10	10
E20F	Mean	1.661	2.50 <sup>b</sup>	27.99 <sup>B</sup>	60.26 <sup>B</sup>	242.52 <sup>C</sup>	3.42 <sup>B</sup>
	SD	0.074	0.55	2.28	3.69	17.61	0.68
	N	10	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 40. Group Mean Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
CF	Mean	1.796	23.68	22.63	24.53	35.23
	SD	0.051	2.46	2.37	4.21	11.22
	N	10	10	10	10	10
NT20F	Mean	1.665	22.53	17.81 <sup>A</sup>	16.75 <sup>A</sup>	9.65 <sup>a</sup>
	SD	0.062	1.83	2.18	4.33	2.98
	N	10	10	10	10	10
B0.2F	Mean	1.767	23.00	21.43	24.05	29.76
	SD	0.053	1.90	3.10	3.84	9.99
	N	10	10	10	10	10
B2F	Mean	1.818	25.12	21.74	22.63	26.70
	SD	0.065	2.89	2.61	3.62	5.95
	N	10	10	10	10	10
B8F	Mean	1.742	25.86	20.00	21.70	28.63
	SD	0.081	1.86	2.39	2.80	12.95
	N	10	10	10	10	10
B20F	Mean	1.691	20.41 <sup>B,C</sup>	13.61 <sup>B,C</sup>	11.82 <sup>B,C</sup>	8.48 <sup>b</sup>
	SD	0.060	1.59	2.46	2.57	1.37
	N	9	9	9	9	9
E0.2F	Mean	1.760	24.83	23.94	23.73	36.64
	SD	0.054	3.24	3.64	4.22	10.54
	N	10	10	10	10	10
E2F	Mean	1.778	25.05	22.12	22.92	32.04
	SD	0.037	3.21	1.79	3.98	12.31
	N	10	10	10	10	10

**Table 40. Group Mean Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>		<b>Absolute Brain Weight (g)</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Thymus</b>	<b>Uterus</b>
E8F	Mean	1.749	25.36	22.67 <sup>F</sup>	21.52	30.06
	SD	0.062	1.83	2.96	3.69	13.86
	N	10	10	10	10	10
E20F	Mean	1.661	21.63	14.88 <sup>B</sup>	12.65 <sup>B,C</sup>	7.22 <sup>b,c</sup>
	SD	0.074	2.06	4.01	3.49	1.24
	N	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = CF vs. NT20F.

B = CF vs. B0.2F, B2F, B8F, B20F, E0.2F, E2F, E8F, E20F.

C = NT20F vs. B20F, E20F.

D = B0.2F vs. E0.2F.

E = B2F vs. E2F.

F = B8F vs. E8F.

G = B20F vs. E20F.

**Table 41. Paired and High Dose Group Mean Absolute Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males**

Group		Absolute Brain Weight	Adrenal Glands	Epididymides	Heart	Kidneys	Liver
NT20M	Mean	1.839	2.43	47.328 <sup>A</sup>	38.61	87.72	336.11
	SD	0.066	0.30	3.839	3.07	6.18	20.18
	N	10	10	10	10	10	10
PFCNTM	Mean	1.870	2.70	52.072	39.57	84.59	336.84
	SD	0.077	0.34	4.613	1.80	6.88	24.35
	N	10	10	10	10	10	10
B20M	Mean	1.758	2.65	47.148	37.18 <sup>B</sup>	86.63	335.98
	SD	0.050	0.25	3.254	4.04	9.92	42.14
	N	10	10	10	10	10	10
PFCBM	Mean	1.877	2.68	49.440	40.76	86.45	342.87
	SD	0.115	0.33	3.094	3.09	8.23	41.43
	N	10	10	10	10	10	10
E20M	Mean	1.793	2.43 <sup>C</sup>	44.347 <sup>C</sup>	36.14 <sup>C</sup>	81.49 <sup>C</sup>	336.62 <sup>C</sup>
	SD	0.071	0.34	3.281	2.85	6.15	32.72
	N	10	10	10	10	10	10
PFCBM	Mean	1.844	2.86	51.570	42.44	89.35	368.70
	SD	0.085	0.56	3.221	2.03	6.77	24.66
	N	10	10	10	10	10	10

**Table 41. Paired and High Dose Group Mean Absolute Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group		Absolute Brain Weight	Salivary Gland	Spleen	Testes	Thymus
NT20M	Mean	1.839	29.54 <sup>A</sup>	22.80	175.60	19.02
	SD	0.066	2.59	2.91	14.92	3.69
	N	10	10	10	10	10
PFCNTM	Mean	1.870	32.04	21.42	174.91	21.26
	SD	0.077	2.17	2.13	11.21	3.31
	N	10	10	10	10	10
B20M	Mean	1.758	29.61	21.67	176.85	16.93 <sup>B</sup>
	SD	0.050	4.39	2.54	11.50	4.97
	N	10	10	10	10	10
PFCBM	Mean	1.877	31.79	22.95	173.85	23.10
	SD	0.115	3.78	3.62	14.44	5.38
	N	10	10	10	10	10
E20M	Mean	1.793	27.82 <sup>C</sup>	20.72 <sup>C</sup>	166.94	13.85 <sup>C</sup>
	SD	0.071	3.12	3.19	13.25	4.01
	N	10	10	10	10	10
PFCEM	Mean	1.844	32.91	26.60	176.07	23.40
	SD	0.085	3.24	3.61	10.83	5.15
	N	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTM vs. NT20M.

B = PFCBM vs. B20M.

C = PFCEM vs. E20M.

**Table 42. Pairfed and High Dose Group Mean Absolute Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females**

Group		Absolute Brain Weight	Adrenal Glands	Heart	Kidneys	Liver	Ovaries
NT20F	Mean	1.665	2.56 <sup>A</sup>	28.92 <sup>A</sup>	59.25 <sup>A</sup>	265.79	3.32 <sup>A</sup>
	SD	0.062	0.30	2.37	3.30	22.43	0.84
	N	10	10	10	10	10	10
PFCNTF	Mean	1.730	3.57	33.71	66.10	254.74	4.87
	SD	0.078	0.58	2.14	4.40	16.54	0.66
	N	10	10	10	10	10	10
B20F	Mean	1.691	2.67 <sup>B</sup>	27.31 <sup>B</sup>	58.27 <sup>B</sup>	239.23	3.23 <sup>B</sup>
	SD	0.060	0.37	2.14	2.77	13.99	0.60
	N	9	9	9	9	9	9
PFCBF	Mean	1.747	3.72	34.39	63.38	248.80	5.08
	SD	0.085	0.69	2.82	3.24	26.23	1.05
	N	10	10	10	10	10	10
E20F	Mean	1.661	2.50 <sup>C</sup>	27.99 <sup>C</sup>	60.26 <sup>C</sup>	242.52	3.42 <sup>C</sup>
	SD	0.074	0.55	2.28	3.69	17.61	0.68
	N	10	10	10	10	10	10
PFCEF	Mean	1.728	3.36	34.52	66.69	252.49	4.88
	SD	0.067	0.37	2.46	3.49	15.58	0.57
	N	10	10	10	10	10	10

**Table 42. Paired and High Dose Group Mean Absolute Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group		Absolute Brain Weight	Salivary Gland	Spleen	Thymus	Uterus
NT20F	Mean	1.665	22.53	17.81 <sup>a</sup>	16.75 <sup>A</sup>	9.65 <sup>a</sup>
	SD	0.062	1.83	2.18	4.33	2.98
	N	10	10	10	10	10
PFCNTF	Mean	1.730	24.26	23.05	22.71	28.26
	SD	0.078	1.94	4.82	3.79	18.98
	N	10	10	10	10	10
B20F	Mean	1.691	20.41 <sup>B</sup>	13.61 <sup>B</sup>	11.82 <sup>B</sup>	8.48 <sup>b</sup>
	SD	0.060	1.59	2.46	2.57	1.37
	N	9	9	9	9	9
PFCBF	Mean	1.747	24.25	22.47	25.77	31.53
	SD	0.085	2.05	2.46	5.32	18.91
	N	10	10	10	10	10
E20F	Mean	1.661	21.63 <sup>C</sup>	14.88 <sup>C</sup>	12.65 <sup>C</sup>	7.22 <sup>c</sup>
	SD	0.074	2.06	4.01	3.49	1.24
	N	10	10	10	10	10
PFCEF	Mean	1.728	25.77	21.81	24.60	29.34
	SD	0.067	2.65	2.35	6.22	12.47
	N	10	10	10	10	10

Multiple comparisons were made according to the letters listed below. Capital letters indicate the comparison was significantly different at  $p \leq 0.05$  with Dunnett's test of significance; lower case letters indicate comparisons were significantly different at  $p \leq 0.05$  with Modified T test.

A = PFCNTF vs. NT20F.

B = PFCBF vs. B20F.

C = PFCEF vs. E20F.

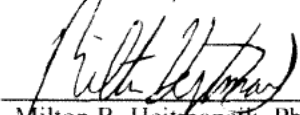
**APPENDIX A: PROTOCOL, AMENDMENTS, AND DEVIATIONS**

**STUDY PROTOCOL****28-DAY REPEATED DOSE TOXICITY STUDY OF  
TOBACCO BLEND AND AQUEOUS TOBACCO EXTRACT IN WISTAR HAN  
RATS****TESTING FACILITY:  
BATTELLE COLUMBUS  
505 KING AVENUE  
COLUMBUS, OH 43201****SPONSOR:  
R.J. REYNOLDS TOBACCO COMPANY  
RESEARCH AND DEVELOPMENT  
BOWMAN GRAY TECHNICAL CENTER  
WINSTON-SALEM, NC 27102**

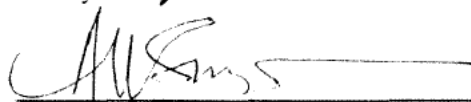
Page 2 of 19  
Battelle Study Number CN49730C  
Preparation Date: June 3, 2008

This protocol was approved by the Sponsor Study Monitor on 6/4/08 / M  
Date / Initials

**AP PROVED, BATTELLE:**

  
Milton R. Hejtmancik, Ph.D., D.A.B.T.  
Study Director

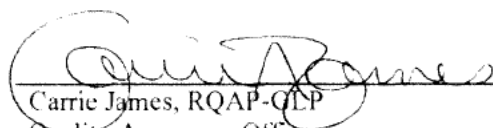
6/4/08  
Date

  
Allen W. Singer, D.V.M., D.A.C.V.P., D.A.B.T.  
Toxicology Columbus Manager

6-4-08  
Date

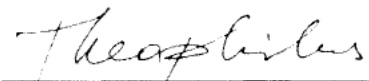
The protocol for the study, data, study conduct and the final report will be reviewed by Battelle's Quality Assurance Unit based upon current assurance principles and Good Laboratory Practices.

**REVIEWED, BATTELLE:**

  
Carrie James, RQAP-QLP  
Quality Assurance Officer

6/4/08  
Date

**AP PROVED, SPONSOR:**

  
Suzana Theophilus, Ph.D., D.A.B.T.  
Senior Staff Toxicologist

6/5/08  
Date

To the best of our knowledge, this study does not unnecessarily duplicate any previous experiments.

## **1.0 PURPOSE**

The purpose of this study is to compare the short-term toxicity of a tobacco blend, aqueous tobacco extract, and appropriate controls in rodents (nicotine tartrate positive control and diet negative control). The study will also determine plasma concentrations of nicotine and cotinine under the conditions of the study. The study will also aim to differentiate any palatability-related effects from toxic effects by including pair-fed groups corresponding to the high dose group. This data will be used in the design of long-term studies.

## **2.0 REGULATORY COMPLIANCE**

This study will be conducted in compliance with the current version of the United States Food and Drug Administration's (FDA) Good Laboratory Practice (GLP) Regulations, 21 CFR Part 58, for the conduct of nonclinical laboratory studies. This protocol will be listed in the Battelle total list of studies as "FDA GLP (non-regulated)."

All portions of this study to be performed at Battelle will adhere to the study protocol and any amendments, as well as to applicable Battelle facility Standard Operating Procedures (SOPs).

Portions of this study performed by the Sponsor or Sponsor's designee will be conducted according to SOPs of the performing laboratory. The conduct of such portions will be conducted in compliance with the current version of the United States Food and Drug Administration's (FDA) Good Laboratory Practice (GLP) Regulations, 21 CFR Part 58 for the conduct of nonclinical laboratory studies.

## **3.0 ROUTE AND DURATION OF ADMINISTRATION**

The test articles will be administered orally mixed in the feed, for a minimum of 28 days. This route of administration is chosen based upon human exposure via the oral route.

## **4.0 TESTING FACILITY**

### **4.1 Testing Facility**

Battelle Columbus  
505 King Avenue  
Columbus, Ohio 43201-2693

**4.2 Study Director**

Milton R. Hejtmancik, Ph.D., D.A.B.T.  
 Tel: 614-424-4465  
 Fax: 614-424-3171  
 E-mail: hejtman@battelle.org

**5.0 SPONSOR AND STUDY MONITOR****5.1 Sponsor:**

R.J. Reynolds Tobacco Company  
 Research and Development  
 Bowman Gray Technical Center  
 Winston-Salem, NC 27102

**5.2 Sponsor's Study Monitor**

Suzana Theophilus, Ph.D., D.A.B.T.  
 R.J. Reynolds Tobacco Company  
 Research and Development  
 Bowman Gray Technical Center  
 Winston-Salem, NC 27102  
 Tel: 336-741-1536  
 E-mail: theophe@rjrt.com

**6.0 PROPOSED STUDY SCHEDULE**

Proposed dates for the following study events are listed below. The actual dates will be documented in the study file.

Animal Receipt:	June 5, 2008
Animal Quarantine:	June 5, 2008 – June 18, 2008
Initiate Part I (TK Study):	June 19, 2008 (M), June 20, 2008 (F)
Phase 1 Collection:	July 1, 2008 – July 3, 2008
Phase 2 Collection:	July 16, 2008 (M), July 17, 2008 (F)
First Day of Dosing (Core Study):	June 24, 2008
Neurobehavioral Testing:	July [79] <sup>2</sup> , 2008 (M), July [810] <sup>2</sup> , 2008 (F)
Clinical/Pathology/Necropsy (Completion of In-Life):	July 22, 2008 – July 25, 2008
Unaudited Data Submitted to RJRT:	Week of August 8, 2008
RJRT Approval to Proceed to 90-Day Rat Study:	Week of August 18, 2008
Draft Final Report:	Week of November 21, 2008

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## 7.0 TEST SYSTEM

Species:	Rat
Strain:	Wistar Hanover
Source:	Charles River
Anticipated Age Range at Arrival:	4-5 weeks
Anticipated Body Weight Range at Arrival:	50-200 g
Number of Rats Required for Study:	388 rats (194/sex), including sentinels. A sufficient number of extra rats will be ordered to provide the required number of rats for the study.

### 7.1 Test System Justification

This is an accepted rodent species for use in toxicology studies of test articles intended for human use. At this time, studies in laboratory animals are required to support regulatory submissions. The number of rats is considered to be the minimum number necessary to yield meaningful results.

## 8.0 ANIMAL CARE, HOUSING, AND ENVIRONMENTAL CONDITIONS

General procedures for animal care and housing will meet or exceed current AAALAC recommendations, current requirements stated in the "Guide for Care and Use of Laboratory Animals" (National Research Council, 1996), and will conform to the Testing Facility Standard Operating Procedures (SOPs). The protocol will be reviewed and approved by Battelle's Institutional Animal Care and Use Committee (IACUC) and will be reviewed by the sponsor's IACUC, and Battelle will respond to any written comments and/or questions from the sponsor's IACUC regarding the protocol.

### 8.1 Quarantine and Acclimation

Rats will be quarantined and acclimated for not less than 7 days in accordance with facility SOP.

### 8.2 Animal Housing

All animal housing and environmental conditions will follow facility SOPs. All rats will be individually housed in wire-bottomed cages appropriate for the animals and the study [*with the exception of animals subjected to neurobehavioral testing (see Section 10.6) and when animals are fasted prior to necropsy, at which times animals will be individually housed in polycarbonate cages.*]<sup>3</sup> Sentinel rats for serological monitoring will be housed in the same room as the study rats.

### 8.3 Feed

Rats will be fed powdered NTP-2000 rodent diet *ad libitum*, according to facility SOP, except when fasted prior to scheduled necropsy and for the special pair fed groups (as described in Section 11.5, Food Consumption). The control group will be fed the diet without test article and the treated rats will be fed the diet with the specified quantity of test article required to maintain their designated doses. Analytical reports of each feed lot will be provided by the manufacturer. Analytical reports will be reviewed according to facility SOP to ensure acceptable standards, and freedom from levels of contaminants that may interfere with the purpose or conduct of the study. Copies of the analytical results will be retained in the study file.

### 8.4 Water

Fresh water from the Columbus municipal water supply will be provided *ad libitum* to the rats by an automatic watering system. The water supply will be analyzed within 6 months of the start of the study to ensure acceptable standards, and freedom from levels of contaminants that may interfere with the purpose or conduct of the study. A copy of the analytical results will be retained in the study file.

## 9.0 TEST ARTICLE AND CONTROL ARTICLE

Records of receipt and use of the test article and control article will be maintained.

### 9.1 Test Articles

#### 9.1.1 Tobacco Blend

Description:	Natural tobacco blend containing no additives
Supplier:	R.J. Reynolds Tobacco Company
Characterization:	A Certificate of Analysis (CoA) and/or equivalent documentation of test article identity, strength, purity, composition and other defining characteristics was provided by the Sponsor. Documentation of synthesis will be maintained by the Sponsor. Lot number(s) and expiration date(s), if any, will be included in the final report and study files.
Stability:	Test article stability was provided by the Sponsor for inclusion in the final report.
Storage Conditions:	Suitable quantities of the test article were provided by the sponsor in plastic buckets. The test article will be stored frozen (-30 to -15°C). Any test article from a single-use

container that is not used for the formulation task for which it was aliquoted will be saved for emergency use only.

#### 9.1.2 Aqueous Tobacco Extract

Description: Water extraction of tobacco test article

Supplier: R.J. Reynolds Tobacco Company

Characterization: A Certificate of Analysis (CoA) and/or equivalent documentation of test article identity, strength, purity, composition and other defining characteristics was provided by the Sponsor. Documentation of synthesis will be maintained by the Sponsor. Lot number(s) and expiration date(s) will be included in the final report.

Stability: Test article stability was provided by the Sponsor for inclusion in the final report.

Storage Conditions: Suitable quantities of the test article were provided by the sponsor in plastic buckets. The test article will be stored frozen (-30 to -15°C). Any test article from a single-use container that is not used for the formulation task for which it was aliquoted will be saved for emergency use only.

#### 9.2 Positive Control Article

Name: Nicotine hydrogen tartrate salt

Description: Positive control article containing nicotine. The nicotine free base is 35.1% of the bulk salt (2.85 g of salt contains 1 g of free nicotine). Animal dosing will be based upon nicotine and not the bulk salt.

Supplier: Sigma-Aldrich

Characterization: Identity, lot number(s), purity, composition, stability and other defining characteristics was provided by the Supplier. A Certificate of Analysis and a Material Safety Data Sheet was obtained from the supplier and will be maintained in the study file by the conducting laboratory and provided to the sponsor.

Storage Conditions: The control article will be stored under conditions recommended by the supplier.

### 9.3 Reserve Samples

Archival samples (~100 g) of each set of the tobacco blend, aqueous tobacco extract, and ~5g of the nicotine hydrogen tartrate positive control article used to formulate the animal diets were collected under design form CN49730 A-TASTAB. Reserve samples of the tobacco blend and tobacco extract shall be maintained frozen (-30 to -15 °C) and a reserve sample of the nicotine tartrate shall be maintained at room temperature until submission of the chronic study final report. At that time, reserve samples will be shipped to R.J. Reynolds Tobacco Company upon authorization by the Study Director. Samples will ship overnight on dry ice to:

R.J. Reynolds Tobacco Company  
Research and Development  
Bowman Gray Technical Center  
Winston Salem, NC 27102

The Study Monitor will be notified of the date of shipment.

#### 9.3.1. Disposition of Unused and Residual Test Articles

Following the completion of in-life dosing, the sponsor will provide the laboratory authorization to either dispose of or directions to store unused test article or positive control for potential use in further studies. If for any reason, the subsequent studies are cancelled, the sponsor will provide Battelle authorization to either dispose of these materials or have them returned to the sponsor.

### 9.4 Formulation Preparation and Analysis

#### 9.4.1 Formulation Preparation

Diet formulations will be prepared once according to a procedure developed by Battelle for this study, based on method(s) provided by the Sponsor. Exposure of the animals to the test articles and positive control will be by the NTP-2000 powdered feed. Formulations will be stored at room temperature prior to use and will be appropriately discarded on or after their expiration date.

#### 9.4.2 Retention Samples

~~[Duplicate samples, target 5 g, of the formulations~~ ***One formulation analysis sample, target 200 g, and one formulation retention sample, target 200 g, ]***<sup>1</sup> will be taken from the formulation batches prepared for each diet at each dose and will be stored ~~[frozen (-30 to -15°C) at room temperature.]~~<sup>1</sup> ~~[These retention samples will be discarded upon submission of the final report.~~ ***Formulation retention samples will be retained until the analysis is complete and acceptable to the Study Director or after the dose expires, whichever occurs first.]***<sup>1</sup>

#### **9.4.3 Formulation Analysis**

Nicotine will be used as the tracking compound for the formulation analysis. All prepared formulations will be analyzed for nicotine content. Animal room samples will be collected on the last day of use of the first and only formulation preparation.

Results of analyses for concentration and homogeneity and an audited formulation analysis report will be included in the final report.

### **10.0 EXPERIMENTAL DESIGN**

Three hundred eighty-eight rats will be assigned to 1 of 14 dose groups. The study will consist of a 28-day toxicity study including a neurotoxicity component and a toxicokinetic study.

Ten rats per sex will be maintained with the study rats as undosed sentinels for serological monitoring. Serological monitoring will be conducted before dose initiation and at study termination according to facility SOP.

Endpoints used to evaluate the potential toxicity of tobacco blend and aqueous tobacco extract will be clinical observations, body weights and body weight changes, food consumption, neurological and behavioral toxicology, and clinical and anatomic pathology including organ weights. A subset of 6 rats per sex is included in each treatment group for determinations of plasma nicotine and cotinine concentrations (TK study). No TK animals will be assigned to groups in which animals are fed the control diet (Groups 1, 3, 8, and 13).

The number of rats per group, and dosage levels, are as follows:

Group	Target Dosage of Nicotine (mg/kg/day)	Number of Rats			
		Males		Females	
		Core	TK <sup>a</sup>	Core	TK <sup>a</sup>
1 - Control	0	10	--	10	--
2 - Nicotine Tartrate (NT) High Dose	20	10	6	10	6
3 - Control Diet Pair-fed to NT High Dose	0	10	--	10	--
4 - Tobacco Blend Low Dose	0.2	10	6	10	6
5 - Tobacco Blend Intermediate Dose 1	2	10	6	10	6
6 - Tobacco Blend Intermediate Dose 2	8	10	6	10	6
7 - Tobacco Blend High Dose	20	10	6	10	6
8 - Control Diet Pair-fed to Tobacco High Dose	0	10	--	10	--
9 - Tobacco Extract Low Dose	0.2	10	6	10	6
10 - Tobacco Extract Intermediate Dose 1	2	10	6	10	6
11 - Tobacco Extract Intermediate Dose 2	8	10	6	10	6
12 - Tobacco Extract High Dose	20	10	6	10	6
13 - Control Diet Pair-fed to Tobacco Extract High Dose	0	10	--	10	--
14 - Sentinels	0	10	--	10	--

<sup>a</sup>Nicotine / cotinine analysis

## 10.1 Serology

The serology screen will be conducted according to facility SOP using 5 males and 5 females from the sentinel group soon after arrival. These animals will be necropsied to evaluate the internal organs for any signs of disease. Initiation of the study will be dependent on negative serology and no evidence of disease in the animals. This procedure will be repeated near or at termination of the study with the remaining 5 males and 5 females in the sentinel group.

Rat serology endpoints are as follows:

Sendai virus	Mouse adenovirus (MAV) 1 & 2
Pneumonia virus of mice (PVM)	Hantaviruses (HANT)
Sialodacryoadenitis virus (SDAV)	<i>Encephalitozoon cuniculi</i> (ECUN)
Kilham rat virus (KRV)	Cilia associated respiratory bacillus (CARB)
H-1 virus (H-1)	Mouse parvovirus (MPV) or PARV NS1
GDVII (murine encephalomyelitis virus)	Rat parvovirus (RPV)
REO	Rat minute virus (RMV)
<i>Mycoplasma pulmonis</i>	
Lymphocytic choriomeningitis virus (LCMV)	

## 10.2 Assignment to Groups

Rats will be assigned to dose groups by sex and body weight prior to the initiation of dosing using PATH/TOX SYSTEM 4.2.2. (Xybion Medical Systems Corp., Cedar Knolls, NJ), which ensures similar group mean body weights by sex. Rats whose body weights are outside a suitable range based on the mean body weights of the animals will not be assigned to the study upon the judgment of the study director. Animals whose behavior or clinical condition deviates from that typical of the species and strain will be eliminated from use on the study. After randomization, the mean body weights of each study group will not be significantly different ( $p \leq 0.05$ ). After assignment to groups, each rat will be identified by tail tattoo with an animal identification number unique within the study. Each cage card will contain information including but not limited to study number, group assignment, and animal identification number.

Animal identification numbers will be assigned as follows:

Group	Color Code	Males		Females	
		Core	TK	Core	TK
1 - Control	White	101-110	--	151-160	--
2 - Nicotine Tartrate (NT) High Dose	Gray	201-210	211-216	251-260	261-266
3 - Control Diet Pair-fed to NT High Dose	[Gray/Orange <i>White with Gray Stripes</i> ] <sup>1</sup>	301-310	--	351-360	--
4 - Tobacco Blend Low Dose	Lilac/Blue	401-410	411-416	451-460	461-466
5 - Tobacco Blend Intermediate Dose 1	Lilac/Green	501-510	511-516	551-560	561-566
6 - Tobacco Blend Intermediate Dose 2	Lilac/Yellow	601-610	611-616	651-660	661-666
7 - Tobacco Blend High Dose	Lilac/Red	701-710	711-716	751-760	761-766
8 - Control Diet Pair-fed to Tobacco High Dose	[Lilac/Orange <i>White with Lilac Stripes</i> ] <sup>1</sup>	801-810	--	851-860	--
9 - Tobacco Extract Low Dose	Tan/Blue	901-910	911-916	951-960	961-966
10 - Tobacco Extract Intermediate Dose 1	Tan/Green	1001-1010	1011-1016	1051-1060	1061-1066
11 - Tobacco Extract Intermediate Dose 2	Tan/Yellow	1101-1110	1111-1116	1151-1160	1161-1166
12 - Tobacco Extract High Dose	Tan/Red	1201-1210	1211-1216	1251-1260	1261-1266
13 - Control Diet Pair-fed to Tobacco Extract High Dose	[Tan/Orange <i>White with Tan Stripes</i> ] <sup>1</sup>	1301-1310	--	1351-1360	--
14 - Sentinels	Black	1401-1410	--	1451-1460	--

### 10.3 Clinical Observations

Cage-side observations for moribundity and mortality will be performed on all rats, twice daily, at least 6 hours apart, per facility SOP.

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Battelle Study Number CN49730C

Preparation Date: June 3, 2008

(Amended 6/08<sup>1</sup>)

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Detailed clinical examinations will be conducted on all rats, including those not subsequently assigned to study, prior to group assignment. During the in-life phase of the study detailed clinical examinations will be conducted weekly on all surviving core study rats. The final detailed clinical examination of each core study rat will be conducted on the day of its scheduled necropsy.

#### 10.4 Body Weight

Individual animal body weights will be recorded for all rats pre-study for randomization and group assignment. After initiation of dosing, body weights for all core study rats will be recorded biweekly on Tuesdays and Fridays and at necropsy. Weekly body weights will be recorded for animals in the TK plasma analysis groups.

#### 10.5 Food Consumption

Food consumption will be measured for all core animals on Tuesdays and Fridays with the exception of the pair fed control groups (Groups 3, 8, and 13) and their corresponding high dose treatment groups (Groups 2, 7, and 12, respectively) where food consumption will be measured daily (see below). Food consumption will not be measured on TK animals or sentinels.

Pair feeding will be accomplished by measuring the individual food consumption daily for all animals in the high dose treatment groups (Groups 2, 7, and 12) and using that data to calculate the mean food consumption for the group. The corresponding pair fed group will be provided only the mean quantity of control feed calculated from high dose food consumption group means. Therefore, the mean food consumed by Group 2 will be the amount offered to each animal in Group 3; Group 7 will determine the amount offered to Group 8; and Group 12 determines the food for Group 13. Food consumption shall be measured for pair fed groups and the amount of food adjusted daily, with the first adjustment made on Study Day [2 3]<sup>1</sup>. In order to accomplish this task, animals for this study will be housed individually.

#### 10.6 Neuro/Behavioral Toxicology

~~[At the approximate midpoint of the study (approximately Study Day 14), 5 Five]~~<sup>1</sup> rats of each sex will be randomly selected from each core study group with the exception of pair fed control groups (Groups 3, 8, and 13) ***[and will be identified such that the conduct of the functional observational test battery (FOB) will be blind. On Study Day [14 16]<sup>2</sup> (males) and Day [15 17]<sup>2</sup> (females), these]***<sup>1</sup> ~~[These]~~<sup>1</sup> rats will be subjected to ~~[a functional observational test battery the FOB]~~<sup>1</sup> to detect any signs of neuro/behavioral toxicology. ***[The day prior to their scheduled FOB, all rats will be individually housed on polycarbonate cages with bedding and feed to be acclimated prior to the conduct of the test. Upon completion of the FOB, rats will be returned to wire-bottomed cages. Food consumption will [not be measured on be continued through]<sup>2</sup> Day [14 16]<sup>2</sup> (males) and Day [15 17]<sup>2</sup> (females) for animals subjected to the FOB.]***<sup>1</sup> A copy of the neuro/behavioral findings will be included in the final report.

## 10.7 Toxicokinetics

Six rats per sex are included for each treatment group, excluding [*controls (Group 1)*],<sup>1</sup> pair fed control groups (Groups 3, 8, and 13) and sentinels (Group 14), for determinations of plasma nicotine and cotinine concentrations. [*From the 5 remaining male and 5 remaining female sentinels, plasma will be collected at the TK Day 28 scheduled blood collection per sex to measure background nicotine and cotinine plasma levels among study animals not exposed to the test article.*]<sup>2</sup> Methodology for plasma nicotine and cotinine analysis [~~have been~~ *will be*]<sup>1</sup> validated [~~previously~~]<sup>1</sup> under design form CN49730 A-BIOVAL.

The toxicokinetic portion will consist of 2 phases. Phase 1 will determine an appropriate time to sample plasma for nicotine and cotinine from animals fed nicotine containing test articles in the diet. This will be accomplished by determining the time

course of plasma nicotine and cotinine at the approximate mid-point of the study. At Study Days 13 and 14, 6 specified time points will be spread over a 14-hour time interval to determine the observed  $C_{max}$  and  $T_{max}$  values for nicotine and cotinine in male and female rats from up to nine specified treatment groups. No compartmental modeling or non-compartmental analysis will be performed on these concentration time profiles. Phase 2 will be based on the information obtained from the Study Day 13 and 14 data, in which the most appropriate (estimated  $C_{max}$  and  $T_{max}$ ) single collection time point will be selected for collecting samples for nicotine and cotinine analysis in male and female rats from up to 9 specified treatment groups. The data from both study days will be used to evaluate dose proportionality and nicotine metabolism by sex and group and, if possible or if necessary, evaluate changes in  $C_{max}$  and  $T_{max}$  between time periods.

#### 10.7.1 Phase 1 Toxicokinetics

For each dose group, 6 rats of each sex assigned to the toxicokinetics study will be randomly subdivided into 2 subsets of animals. Each subset will be used for blood collection at specific times in a manner that results in no more than 2 blood collections/animals and in a manner that distributes each subset over the 14-hour time course. Subset 1 consists of 3 males and 3 females from each of the nine treatment groups that will have blood drawn at 10 PM, 4 AM, and 10 AM (27 total TK samples per sex per time point). Subset 2 consists of 3 males and 3 females from each of the 9 treatment groups that will have blood drawn at 12 AM, 6 AM, and 12 PM (27 total TK samples per sex per time point). This will result in 6 time points for plasma nicotine and cotinine over a 14-hour time interval and allow a determination of the optimal time for collection in Phase 2 and subsequent studies.

TK study rats will be anesthetized with  $CO_2/O_2$  and blood will be collected from the retroorbital cavity into tubes containing potassium EDTA as the coagulant. The minimum quantity of blood required to yield 100  $\mu$ L of plasma for analysis will be drawn at each time point using techniques according to facility SOPs. Samples will be placed on wet ice until centrifuged. Plasma will be transferred into appropriately labeled tubes and placed on dry ice until stored in a freezer set to maintain -60 to -80°C. Samples will be analyzed for nicotine and cotinine by Battelle using a previously validated method.

After each blood collection the animal will be placed in its home cage supplied with feed and water until the next scheduled blood draw. These animals will remain on the study and be used for subsequent plasma nicotine and cotinine analysis. Toxicokinetic animals will be euthanized at termination of the study with no further data collected.

An audited bioanalytical report, together with appropriate QA documentation, will be provided to the Study Director for inclusion in the final report.

Toxicokinetic parameters to be evaluated will include but may not be limited to the observed  $C_{max}$ , and observed  $T_{max}$ . An audited toxicokinetic report, together with appropriate QA documentation, will be provided to the Study Director for inclusion in the final report.

#### 10.7.2 Phase 2 Toxicokinetics

On Study Day 28, blood will be collected from 5 TK males and 5 TK females in each of the 9 treatment groups (Groups 2, 4, 5, 6, 7, 9, 10, 11, and 12) at a time selected based on the results of the Phase 1 toxicokinetics (45 total TK samples per sex per time point). The blood will be used to harvest plasma and the plasma analyzed for nicotine and cotinine under the conditions described for the Phase 1 Toxicokinetics. After plasma collection, all animals in the Toxicokinetic subset will be terminated with no further data collection.

#### 10.8 Clinical Pathology

Clinical chemistry, hematology and coagulation assessments will be performed on all surviving core study rats on the day of their scheduled necropsy.

All rats will be fasted overnight prior to scheduled blood sampling for hematology, coagulation, and clinical chemistry determinations. Rats will be anesthetized and blood will be collected using an appropriate method. The tubes for hematology will contain EDTA as an anticoagulant. The tubes used for clinical chemistry determinations will not contain anticoagulant, but may contain serum separator gel. Sodium citrate will be used as an anticoagulant for the coagulation assay. Target volumes of blood collections for clinical chemistry, hematology and coagulation are 1.3, 0.5, and  $[1 \pm 0.675]^3$  mL, respectively. In the event that blood volumes do not meet these suggested values clinical chemistry and coagulation parameters will be given highest and lowest priority, respectively. Further prioritization may be assigned to clinical chemistry parameters based upon anticipated target organs (see below).

Clinical pathology results, and the clinical pathologist's report, will be included in the final report.

### 10.8.1 Clinical Chemistry Parameters

Clinical chemistry parameters to be evaluated are (listed in order of priority):

Aspartate aminotransferase	Cholesterol
Bilirubin, direct	Creatinine
Bilirubin, total	Protein, total
Gamma glutamyl transferase	Urea nitrogen
Albumin	Electrolytes:
Globulin	Calcium
Albumin/globulin ratio	Chloride
Alkaline phosphatase	Phosphorus
Glucose	Potassium
Triglycerides	Sodium

### 10.8.2 Hematologic Parameters

Hematologic parameters to be evaluated are:

Erythrocyte count	Mean corpuscular hemoglobin concentration
Hematocrit	Mean corpuscular volume
Hemoglobin	Platelet count
Leukocyte count, total	Reticulocyte count
Leukocyte differential	
Mean corpuscular hemoglobin	

### 10.8.3 Coagulation Parameters

Prothrombin time will be evaluated.

## 10.9 Necropsy

### 10.9.1 Unscheduled Necropsy

Complete necropsies will be performed on all core study rats that die or are terminated at an unscheduled interval. Terminal body weights will be recorded for moribund rats prior to euthanasia. Moribund rats will be euthanized using CO<sub>2</sub>. Organ weights will not be recorded for unscheduled deaths, and preservation of selected tissues will be at the discretion of the Study Director. Sentinel rats will not be necropsied.

### 10.9.2 Scheduled Necropsy

After at least 28 days of dosing, all surviving animals will be fasted overnight and humanely terminated using CO<sub>2</sub>. Terminal body weights will be determined and the external features of the animals will be evaluated, followed by necropsy.

All scheduled necropsies will be conducted under the supervision of a board-certified veterinary pathologist. Each necropsy will include examination of the external surface of the body and all orifices; the cranial, thoracic, abdominal and pelvic cavities and their contents; and collection of tissues.

Tissues listed below, when present, will be collected from all rats according to facility SOP. Tissues will be placed in 10% neutral buffered formalin (NBF), with the exception of testes, which will be preserved in Bouin's fixative and subsequently transferred to 70% ethanol, and eyes with optic nerve which will be fixed in Davidson's fixative and subsequently transferred to 10% NBF, per facility SOP.

Animal identification	Pituitary gland
Adrenal glands	Preputial glands
Bone and marrow (femur)	Prostate gland
Brain	Salivary gland (mandibular)
Clitoral gland	Sciatic nerve
Epididymides	Seminal vesicles
Esophagus, pharynx	Skeletal muscle (biceps femoris)
Eyes	Skin
Gross lesions	Spinal cord (cervical, thoracic, lumbar)
Harderian glands	Spleen
Heart	Sternum with bone marrow
Intestine, large (cecum, colon, rectum)	Stomach (fore-stomach and glandular)
Intestine, small (duodenum, jejunum, ileum)	Testes
Kidneys	Thymus
Liver (median lobe and left lateral lobe)	Thyroid gland (with parathyroids, if present in routine section)
Lungs with bronchi	Tongue
Lymph node (mesenteric)	Urinary bladder
Mammary gland (females only)	Uterus
Nose (nasal cavity and turbinates)	Vagina
Ovaries (without oviduct)	Zymbal glands
Oral cavity	
Pancreas	

**10.10 Organ Weights**

The following organs, when present, will be weighed for all scheduled necropsies. Paired organs will be weighed together. Absolute weight, organ-to-body weight and organ-to-brain-weight will be reported. Organ weights will not be conducted on sentinel or rats found dead or euthanized in moribund condition.

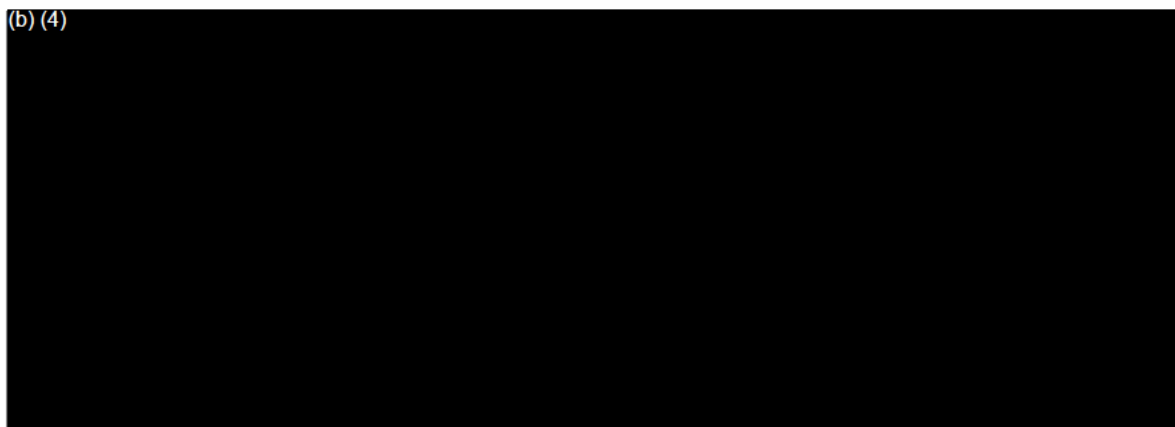
Adrenal glands	Spleen
Brain	Ovaries (without oviduct)
Epididymides	Testes (without epididymides)
Heart	Thymus
Kidneys	Salivary glands (mandibular)
Liver	Uterus (with cervix)

**11.0 COMPUTER SYSTEMS FOR DATA MANAGEMENT**

Computer System Name	Version	Manufacturer	Data Type
Analyst	1.4.1 or 1.4.2	Applied Biosystems Inc.	Chromatography/ Mass Spectrometry
Atlas	8.2	Thermo Fisher Scientific	Chromatography
Excel Building Supervisor	1.7	Honeywell	Animal Facility Environmental
PATH/TOX SYSTEM	4.2.2	Xybion Medical Systems Corp.	Animal Toxicology and Pathology
T-Track	1.0.0	Battelle	Environmental Storage

**12.0 STATISTICAL ANALYSIS**

(b) (4)



(b) (4)



### **13.0 REPORTING**

A draft final report will be prepared and submitted to the Sponsor as a .pdf file via email. The Sponsor shall submit final comments, if any, on the draft report to the Study Director. After review and acceptance of the draft final report by the sponsor, Battelle will submit to the Sponsor a bound final report along with a .pdf file.

### **14.0 STORAGE OF STUDY MATERIALS AND RECORDS RETENTION**

Except for analyses performed by the Sponsor or Sponsor's designated laboratory, all records required to reconstruct the study and the final report will be maintained under the direction of Battelle according to facility SOPs. The final report, study files, records and specimens will be stored in Battelle's archives for a period of no less than one year after issue of the final report. At the end of 1 year, the sponsor will provide authorization concerning the disposition of these items.

**AMENDMENT NUMBER 1 TO THE PROTOCOL FOR THE 28-DAY REPEATED  
DOSE TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO  
EXTRACT IN WISTAR HAN RATS (CN49730C)**

1. a. Page 12, Section 10.2, Assignment to Groups. The color code for Group 3 is changed from:  
  
“Gray/Orange”  
  
to:  
  
“White with Gray Stripes”  
  
b. Page 12, Section 10.2, Assignment to Groups. The color code for Group 8 is changed from:  
  
“Lilac/Orange”  
  
to:  
  
“White with Lilac Stripes”  
  
c. Page 12, Section 10.2, Assignment to Groups. The color code for Group 13 is changed from:  
  
“Tan/Orange”  
  
to:  
  
“White with Tan Stripes”  
  
d. The reasons for these changes are to provide technical staff with clearer identification of pair fed groups on cage cards.  
  
e. The effective date for theses changes is June 16, 2008.
2. a. Page 13, Section 10.6, Neuro/Behavioral Toxicology. The following paragraph has changed from:  
  
“At the approximate midpoint of the study (approximately Study Day 14), 5 rats of each sex will be randomly selected from each core study group with the exception of pair fed control groups (Groups 3, 8, and 13). These rats will be

subjected to a functional observational test battery to detect any signs of neuro/behavioral toxicology. A copy of the neuro/behavioral findings will be included in the final report.”

to:

“Five rats of each sex will be randomly selected from each core study group, with the exception of pair fed control groups (Groups 3, 8, and 13), and will be identified such that the conduct of the functional observational test battery (FOB) will be blind. On Study Day 14 (males) and Day 15 (females), these rats will be subjected to the FOB to detect any signs of neuro/behavioral toxicology. The day prior to their scheduled FOB, all rats will be individually housed in polycarbonate cages with bedding and feed to be acclimated prior to the conduct of the test. Upon completion of the FOB, rats will be returned to wire-bottomed cages. Food consumption will not be measured on Day 14 (males) and Day 15 (females) for animals subjected to the FOB. A copy of the neuro/behavioral findings will be included in the final report.”

- b. The reason for this change is to describe the change in caging and identification of animals subjected to the FOB in order to keep neuro/behavioral technicians blind during testing, and to indicate food consumption will not be measured for animals on the day of their scheduled FOB.
- c. The effective date for this change is June 16, 2008.

- 3. a. Page 13, Section 10.7, Toxicokinetics. The following paragraph has changed from:

“Six rats per sex are included for each treatment group, excluding pair fed control groups (Groups 3, 8, and 13) and sentinels (Group 14), for determinations of plasma nicotine and cotinine concentrations. Methodology for plasma nicotine and cotinine analysis has been validated previously under design form CN49730 A-BIOVAL.”

to:

“Six rats per sex are included for each treatment group, excluding controls (Group 1), pair fed control groups (Groups 3, 8, and 13) and sentinels (Group 14), for determinations of plasma nicotine and cotinine concentrations. Methodology for plasma nicotine and cotinine analysis will be validated under design form CN49730 A-BIOVAL.”

- b. The reason for this change is to exclude the control group (Group 1) from toxicokinetic determinations.
  - c. The effective date for this change is June 16, 2008.
- 4.
  - a. Page 8, Section 9.4.2., Retention Samples. The following paragraph has changed from:

“Duplicate samples, target 5 g, of the formulations will be taken from the formulation batches prepared for each diet at each dose and will be stored frozen (-30 to -15°C). These retention samples will be discarded upon submission of the final report.”

to:

“One formulation analysis sample, target 200 g, and one formulation retention sample, target 200 g, will be taken from the formulation batches prepared for each diet at each dose and will be stored at room temperature. Formulation retention samples will be retained until the analysis is complete and acceptable to the Study Director or after the dose expires, whichever occurs first.”
  - b. The reason for this change is to change the target quantity and storage conditions and duration of formulation analysis and retention samples.
  - c. The effective date for this change is June 11, 2008.
- 5.
  - a. Page 13, Section 10.5, Food Consumption. The following sentence has changed from:

“Food consumption shall be measured for pair fed groups and the amount of food adjusted daily, with the first adjustment made on Study Day 2.”

to:

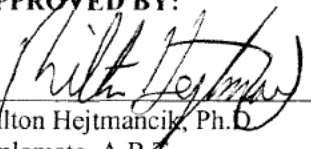
“Food consumption shall be measured for pair fed groups and the amount of food adjusted daily, with the first adjustment made on Study Day 3.”
  - b. The reason for this change is to correct an error.
  - c. The effective date for this change is June 16, 2008.

Battelle Study Number CN49730C

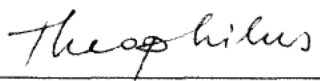
Page 4 of 4

6. Revised pages 8, 12 and 13 of the protocol as changed in this amendment are attached.

**APPROVED BY:**

  
Milton Hejtmancik, Ph.D.  
Diplomate, A.B.T.  
Study Director

6/17/08  
Date

  
Suzana Theophilus, Ph.D.  
Diplomate, A.B.T.  
Study Monitor  
R.J. Reynolds Tobacco Company

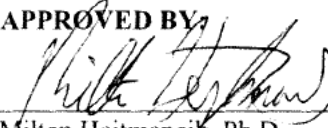
6/18/08  
Date

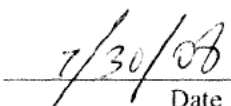
**AMENDMENT NUMBER 2 TO THE PROTOCOL FOR THE 28-DAY REPEATED  
DOSE TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO  
EXTRACT IN WISTAR HAN RATS (CN49730C)**

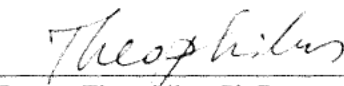
1. a. Page 4, Section 6.0, Proposed Study Schedule. The dates for the functional observational test battery (FOB) for male and female rats has changed from:  
“July 7, 2008 (M) and July 8, 2008 (F)”  
to:  
“July 9, 2008 (M) and July 10, 2008 (F)”  
b. The reason for the change is to conduct neurobehavioral exams on days other than Tuesday and/or Friday, when other critical events are scheduled at weekly intervals.  
c. The effective date for this change is July 2, 2008
2. a. Page 13a, Section 10.6, Neuro/Behavioral Toxicology. The study day on which male and female rats will be subjected to the functional observational test battery (FOB) has changed from:  
“Study Day 14 (males) and Study Day 15 (females)”  
to:  
“Study Day 16 (males) and Study Day 17 (females)”  
b. The reason for the change is to conduct neurobehavioral exams on days other than Tuesday and/or Friday, when other critical events are scheduled at weekly intervals.  
c. The effective date for this change is July 2, 2008
3. a. Page 13a, Section 10.6, Neuro/Behavioral Toxicology. Food consumption measurement of rats subjected to the functional observational test battery (FOB) has changed from:  
“Food consumption will not be measured on Day 14 (males) and Day 15 (females) for animals subjected to the FOB.”  
to:  
“Food consumption will be continued through Day 16 (males) and Day 17 (females) for animals subjected to the FOB.”

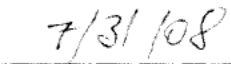
- b. The reason for this change is to continue food consumption measurements during the week of the functional observational test battery.
- c. The effective date for this change is July 2, 2008
4. a. Page 13b, Section 10.7, Toxicokinetics. The following paragraph has changed from: "Six rats per sex are included for each treatment group, excluding controls (Group 1), pair fed control groups (Groups 3, 8, and 13) and sentinels (Group 14), for determinations of plasma nicotine and cotinine concentrations. Methodology for plasma nicotine and cotinine analysis will be validated under design form CN49730 A-BIOVAL."
- to:
- "Six rats per sex are included for each treatment group, excluding controls (Group 1), pair fed control groups (Groups 3, 8, and 13) and sentinels (Group 14), for determinations of plasma nicotine and cotinine concentrations. From the 5 remaining male and 5 remaining female sentinels, plasma will be collected at the TK day 28 scheduled blood collections per sex to measure background nicotine and cotinine plasma levels among study animals not exposed to the test article. Methodology for plasma nicotine and cotinine analysis will be validated under design form CN49730 A-BIOVAL."
- b. The reason for this change is to measure background nicotine and cotinine plasma levels among study animals not exposed to test article.
- c. The effective date for this change is June 30, 2008.
5. Revised pages 4, 13a and 13b of the protocol as changed in this amendment are attached.

**APPROVED BY:**

  
Milton Hejtmancik, Ph.D.  
Diplomate, A.B.T.  
Study Director

  
Date

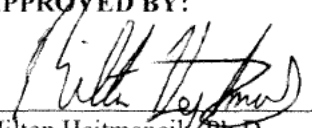
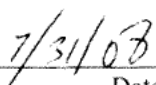
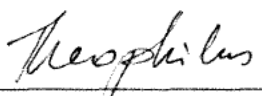
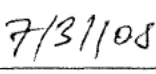
  
Suzana Theophilus, Ph.D.  
Diplomate, A.B.T.  
Study Monitor  
R.J. Reynolds Tobacco Company

  
Date

**AMENDMENT NUMBER 3 TO THE PROTOCOL FOR THE 28-DAY REPEATED  
DOSE TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO  
EXTRACT IN WISTAR HAN RATS (CN49730C)**

1. a. Page 5, Section 8.2, Animal Housing. The following sentence has changed from:  
  
"All rats will be individually housed in wire-bottomed cages appropriate for the animals and the study."  
  
to:  
  
"All rats will be individually housed in wire-bottomed cages appropriate for the animals and the study, with the exception of animals subjected to neurobehavioral testing (see Section 10.6) and when animals are fasted prior to necropsy, at which times animals will be individually housed in polycarbonate cages."  
  
b. The reason for the change is to allow technicians to have visual observations of animals for the functional observational battery (FOB), and for ease in transport to necropsy.  
  
c. The effective dates for these changes are June 16, 2008 and July 16, 2008 (pre-necropsy meeting)
2. a. Page 15, Section 10.8, Clinical Pathology. The target volume of blood collection for coagulation has changed from:  
  
"1.1 mL"  
  
to:  
  
"0.675 mL"  
  
b. The reason for the change is to allow for a smaller volume of whole blood to be collected from the vena cava for analysis of coagulation parameters.  
  
c. The effective date for this change is July 18, 2008
3. Revised pages 5 and 15 of the protocol as changed in this amendment are attached.

## APPROVED BY:

  
\_\_\_\_\_  
Milton Hejtmancik, Ph.D.  
Diplomate, A.B.T.  
Study Director  
\_\_\_\_\_  
7/31/08  
Date  
\_\_\_\_\_  
Suzana Theophilus, Ph.D.  
Diplomate, A.B.T.  
Study Monitor  
R.J. Reynolds Tobacco Company  
\_\_\_\_\_  
7/31/08  
Date

Battelle Study Number CN49730C

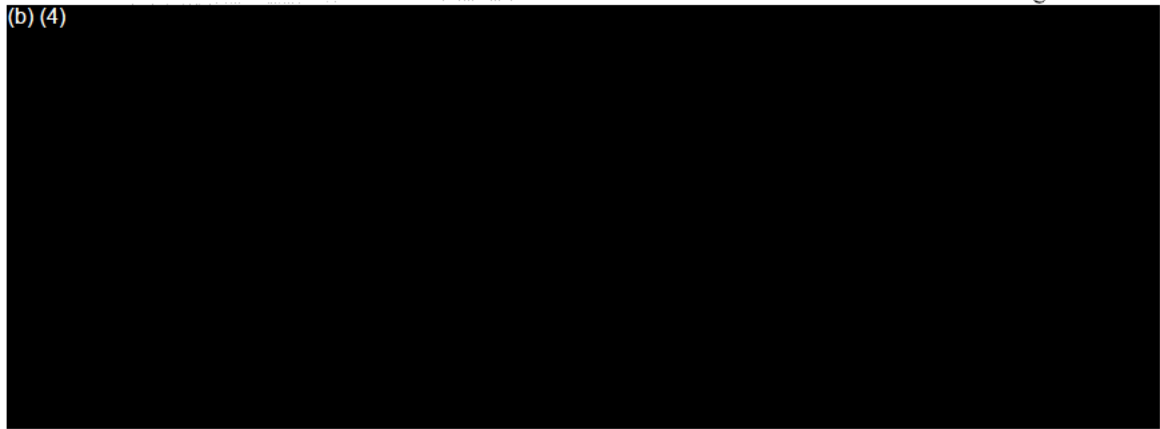
Page 1 of 2

**AMENDMENT NUMBER 4 TO THE PROTOCOL FOR THE 28-DAY REPEATED DOSE  
TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO EXTRACT IN  
WISTAR HAN RATS (CN49730C)**

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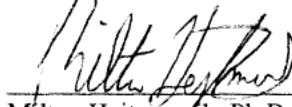


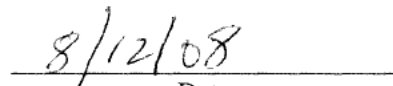
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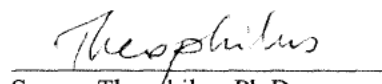


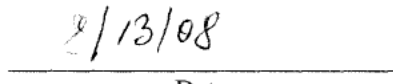
3. Revised pages 18 and 19 as changed in this amendment are attached.

**APPROVED BY:**

  
\_\_\_\_\_  
Milton Hejtmank, Ph.D.  
Diplomate, A.B.T.  
Study Director

  
\_\_\_\_\_  
Date

  
\_\_\_\_\_  
Suzana Theophilus, Ph.D.  
Diplomate, A.B.T.  
Study Monitor  
R.J. Reynolds Tobacco Company

  
\_\_\_\_\_  
Date

## DEVIATION REPORT

CN49730C

28-Day Repeated Dose Toxicity Study of Tobacco Blend and Aqueous Tobacco Extract in  
Wistar Han Rats

Type of Deviation: Protocol

Date of Deviation: June 19, 2008 (males) and June 20, 2008 (females)

Nature of Deviation: Serological monitoring was not completed prior to dose initiation for the toxicokinetic treatment groups

Cause of Deviation: Although blood samples had been collected for serology, serological testing was not completed until June 23, 2008.

Impact on the Study: None. Serology testing was completed prior to the initiation of the core study rats.

Corrective Action: A serology report from Charles River Laboratories, Inc. for Wistar Hans rat colony indicated no viral titers were present. A copy of this report was included in the study file. Rats for the toxicokinetic groups were released from quarantine on the basis of these results.

Prepared By: Dawn Fallacara

Approved By:   
Study Director

Date: 7/10/08

Original: Study File  
Copies: M. Hejtmancik  
Study Supervisor  
C. James  
N. Hale  
8835 Files

## DEVIATION REPORT

CN49730C

28-Day Repeated Dose Toxicity Study of Tobacco Blend and Aqueous Tobacco Extract in  
Wistar Han Rats

Type of Deviation: GLP

Date of Deviation: July 1, 2008 – July 17, 2008

Nature of Deviation: Methodology for plasma nicotine and cotinine analysis were not validated  
under design form CN49730A-BIOVAL

Cause of Deviation: Technical difficulties with the blank samples

Impact on the Study: No adverse effect

Corrective Action: A non-validated method was used for this 28-day study. Subsequent work  
was required to get the desired 1 ng/ml LOQ but only by increasing the  
acceptance criteria for the blank (from approximately 20-50% of the low  
standard).

Prepared By: Dawn Fallacara

Approved By:   
Study Director

Date: 11/12/08

Original: Study File

Copies: M. Hejtmancik  
Study Supervisor  
C. James  
B. Burback  
8835 Files



## Deviation Report

Study: CN49730C

Deviation classification: ☐ Protocol, Section: \_\_\_\_\_

☒ SOP: PATH.I-001 Section V.D.5.

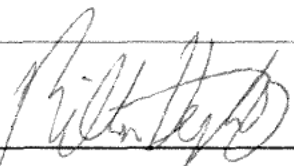
**Description of deviation:** Animal # 1410, a sentinel, was reported as having tattoo reading "14010". This was not documented on the IAPR as verified at necropsy. Animal was discarded at necropsy, in accordance with SOP.

	11/17/08		11/17/08
Signature	Date	Supervisor's signature	Date

**Study Director's assessment.**

**Impact on Study:** None.

**Corrective Action:** None required.

	11/19/08
Study Director's Signature	Date

**Deviation Report**

Study: <u>CN49730 C</u>	
Deviation classification:	<input checked="" type="checkbox"/> Protocol, Section: <u>10.9.2 Scheduled Necropsy</u>
	<input type="checkbox"/> SOP: _____

**Description of deviation:**

Animal 960: gross findings were not directly entered into XYBion on the day of necropsy, thus Gross Findings could not be documented.

<u>A. Smith</u>	<u>11/18/08</u>	<u>Michael J. Ryan</u>	<u>11/18/08</u>
Signature	Date	Supervisor's signature	Date

**Study Director's assessment.**

**Impact on Study:** None. There are a sufficient number of core females remaining in the E0.2F group for assessment of gross changes at necropsy.

**Corrective Action:** None required.

<u>Phil Stephens</u>	<u>11/19/08</u>
Study Director's Signature	Date

**APPENDIX B: CERTIFICATES OF ANALYSIS AND TEST ARTICLE  
CHARACTERIZATION AND STABILITY**

# RJReynolds

Bowman Gray Technical Center  
960 Reynolds Boulevard  
Winston-Salem, NC 27106  
(336) 741-1836

## CERTIFICATE OF ANALYSIS

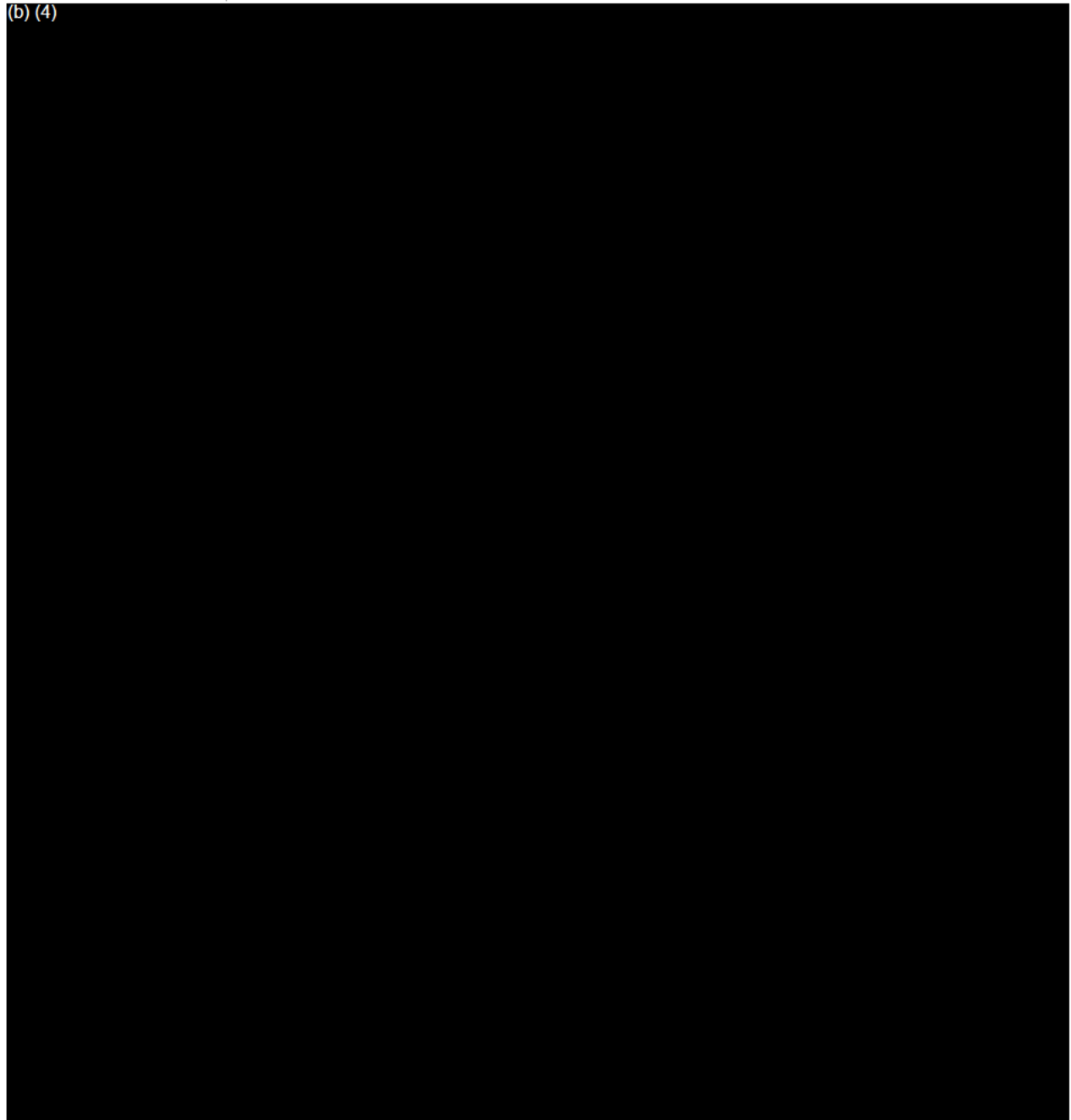
(b) (4)



THE INFORMATION CONTAINED HEREIN IS, TO THE BEST OF OUR KNOWLEDGE, CORRECT. THE DATA OUTLINED AND THE STATEMENTS MADE ARE INTENDED AS A SOURCE OF INFORMATION.

**CERTIFICATE OF ANALYSIS**

(b) (4)



THE INFORMATION CONTAINED HEREIN IS, TO THE BEST OF OUR KNOWLEDGE, CORRECT. THE DATA OUTLINED AND THE STATEMENTS MADE ARE INTENDED AS A SOURCE OF INFORMATION.

# *RJReynolds*

Bowman Gray Technical Center  
950 Reynolds Boulevard  
Winston-Salem, NC 27106  
(336) 741-1836

## **CERTIFICATE OF ANALYSIS**

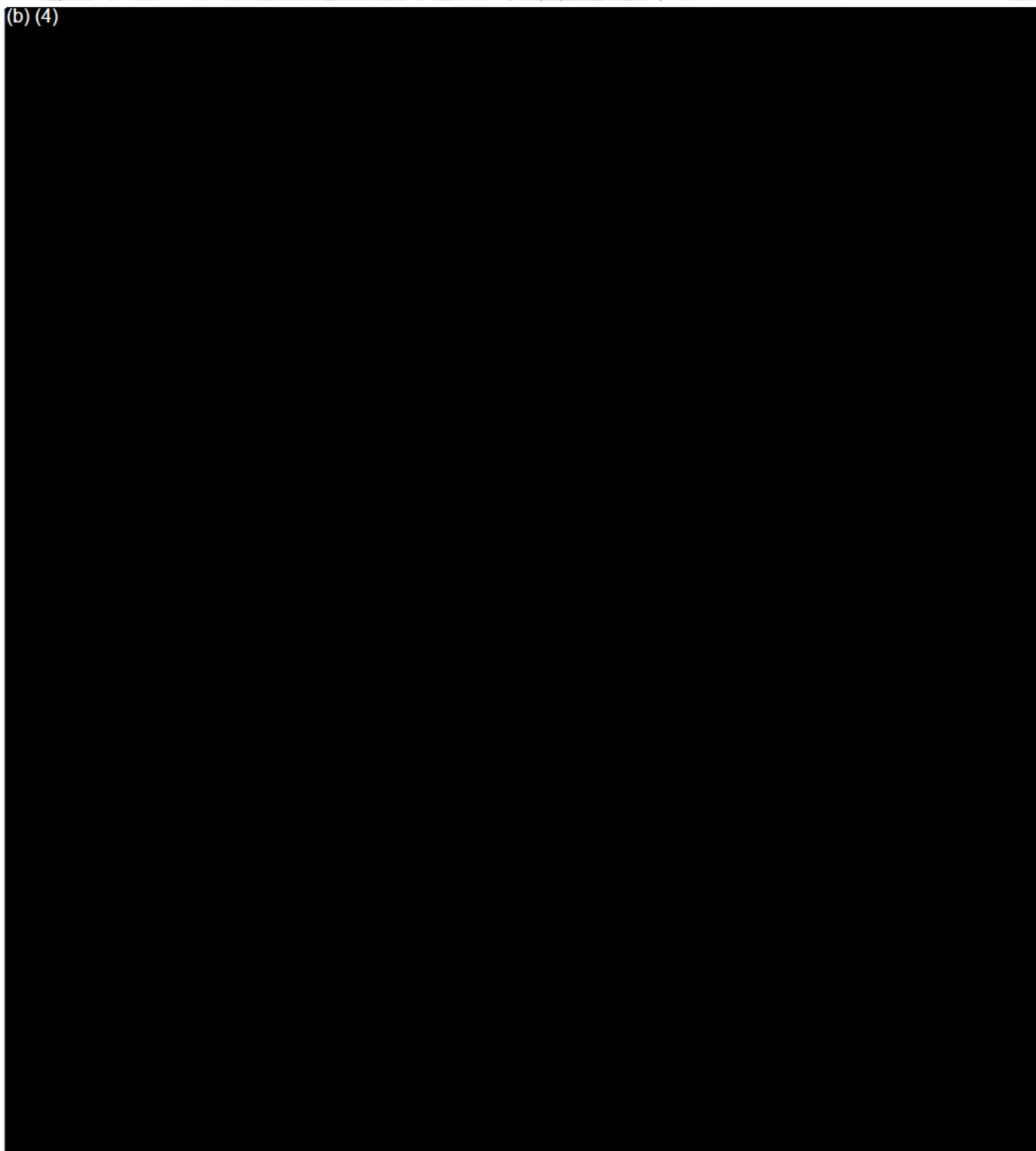
(b) (4)



THE INFORMATION CONTAINED HEREIN IS, TO THE BEST OF OUR KNOWLEDGE, CORRECT. THE DATA OUTLINED AND THE STATEMENTS MADE ARE INTENDED AS A SOURCE OF INFORMATION.

**CERTIFICATE OF ANALYSIS**

(b) (4)



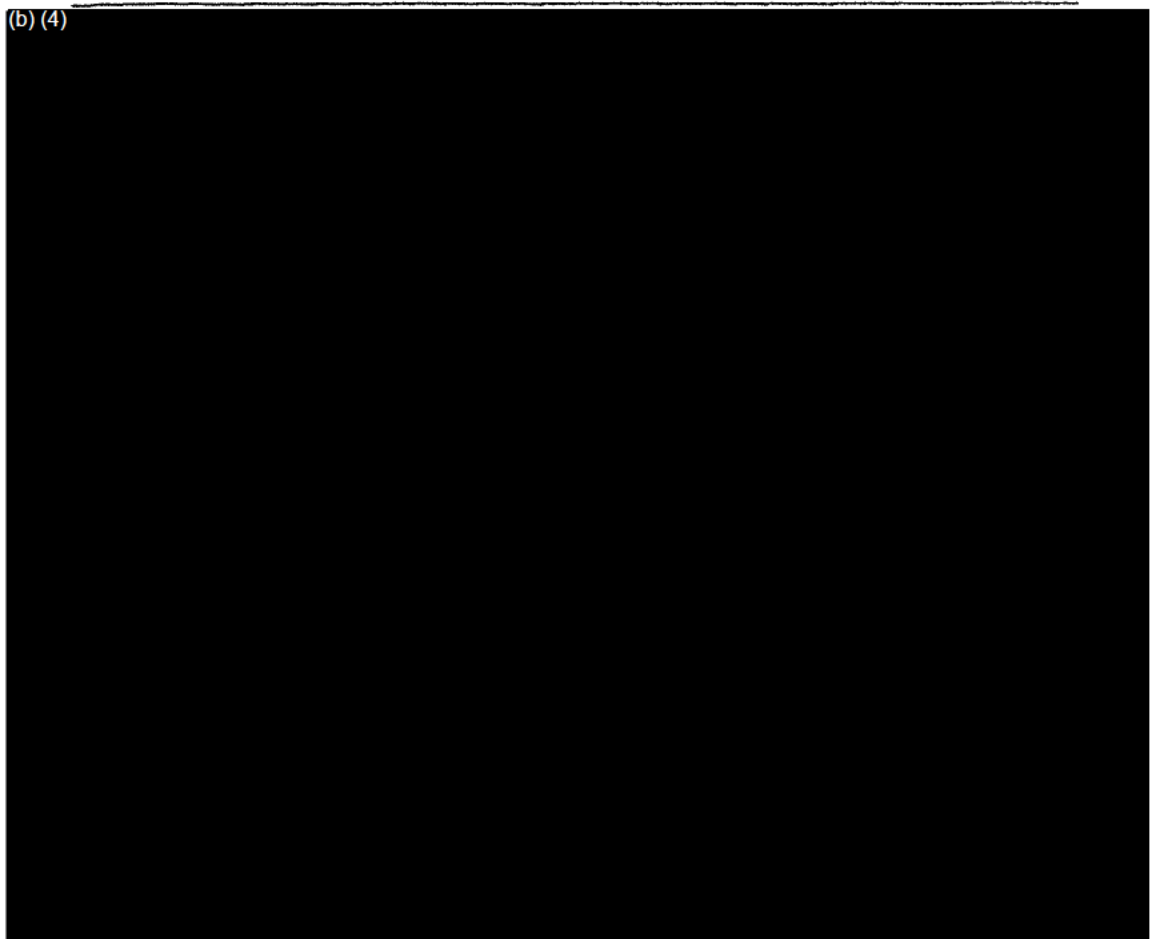
THE INFORMATION CONTAINED HEREIN IS, TO THE BEST OF OUR KNOWLEDGE, CORRECT. THE DATA OUTLINED AND THE STATEMENTS MADE ARE INTENDED AS A SOURCE OF INFORMATION.

## Certificate Of Analysis

Page 1 of 1

**SIGMA-ALDRICH**

(b) (4)



**RJRT Summary of  
Initial Test Article Characterization and  
Stability Data**

**Smokeless Tobacco and Extract  
Feeding Studies**

**8/27/08**

Initial test article characterization-smokeless tobacco and extract toxicology feeding studies 8/27/08  
RJRT Confidential

2

## Summary

(b) (4)



## Test article characterization

## Test design

(b) (4)



Initial test article characterization-smokeless tobacco and extract toxicology feeding studies 8/27/08  
 RJRT Confidential

3

The chemical and microbiological test article characterization and stability studies were designed to analyze various chemicals of interest and microbiological endpoints to determine the evolution of the test articles over time. The chemistry endpoints that were planned to be measured are presented in Table 1.

**Table 1. Chemistry endpoints by evaluation site**

Analyte	Site
pH	RJRT
% Dry matter	RJRT
% Moisture/water	RJRT
Nicotine	RJRT
Normicotine	RJRT
Anabasine	RJRT
Myosamine	RJRT
Anatabine	RJRT
N'-Nitrosonornicotine (NNN)	RJRT
4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	RJRT
N'-nitrosoanatabine (NAT)	RJRT
N'-nitrosoanabasine (NAB)	RJRT
Chloride	RJRT
Sugars (sucrose, fructose, glucose)	RJRT
Ammonia	RJRT
Hydroquinone	RJRT
Catechol	RJRT
Phenol	RJRT
M+p-Cresol	RJRT
Arsenic	RJRT
Cadmium	RJRT
Chromium	RJRT
Nickel	RJRT
Lead	RJRT
Formaldehyde	Labstat
Acrolein	Labstat
Benzo[a]pyrene	Labstat
Benzo[a]anthracene	Labstat
Benzo[b]fluoranthene	Labstat
Benzo[j]fluoranthene	Labstat
Benzo[k]fluoranthene	Labstat
Dibenz[a,h]anthracene	Labstat
Indeno[1,2,3-cd]pyrene	Labstat
Fluorene	Labstat
Acenaphthylene	Labstat
Fluoranthene	Labstat
Acenaphthene	Labstat
Naphthalene	Labstat
Chrysene	Labstat

Initial test article characterization-smokeless tobacco and extract toxicology feeding studies 8/27/08  
RJRT Confidential

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Analyte	Site
N-Nitrosodimethylamine (NDMA)	Labstat
N-Nitrosoethylmethylamine (NEMA)	Labstat
N-Nitrosopyrrolidine (NPYR)	Labstat
N-Nitrosodimethylpropylamine (NDPA)	Labstat
N-nitrosodimethylethylamine (NDEA)	Labstat
N-Nitrosodimethylbutylamine (NDBA)	Labstat
N-Nitrosopiperidine (NPIP)	Labstat
Nitrite	Labstat
Organochlorines	Microbac
Organophosphates	Microbac
Maleic hydrazide	Microbac
Dithiocarbamates (reported as mancozeb)	Microbac
N-methylcarbamates	Microbac
N-containing pesticides	Microbac
Herbicides	Microbac

The microbiological endpoints planned to be measured are presented in Table 2.

**Table 2. Microbial endpoints by evaluation site**

Endpoint	Site
Total bacteria	RJRT
Enteric bacteria (coliforms)	RJRT
Total yeast	RJRT
Total mold	RJRT
Water activity	RJRT
<i>Escherichia coli</i> type I	RJRT
<i>Streptococcus faecalis</i>	RJRT
<i>Thermophilic actinomycetes</i>	RJRT
<i>Aspergillus fumigatus</i> and other yeast/mold	RJRT
<i>Staphylococcus sp.</i> including <i>aureus</i>	RJRT
<i>Klebsiella spp.</i>	RJRT
<i>Salmonella</i>	RJRT
Aflatoxin B1	Trilogy
Aflatoxin B2	Trilogy
Aflatoxin G1	Trilogy
Aflatoxin G2	Trilogy
Ochratoxin A	Trilogy
T-2 toxin	Trilogy
Zearelenone	Trilogy
Sterigmatocystin	Trilogy
Deoxynivalenol	Trilogy
Diacetoxyscirpenol	Trilogy

(b) (4)

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(b) (4)



**Initial test article characterization**  
**Results summary: March-July 2008**

**1) Chemistry results**

**a) RJRT analyses**

**Full production test article characterization (initial time point)**

(b) (4)



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**Table 3. RJRT analyses-full production test articles (blend, extract) and reference**

Analyte, Measurement unit	Test Articles			Comparisons			
	2S3 (R)	Blend (B)	Extract (E)	R vs. B	R vs. E	B vs. E	Ranking
Total Solids, %			37.8	NA	NA	NA	NA
pH	7.32	5.45	5.19	B < R	E < R	E < B	E < B < R
Moisture, %	53.7	10.1		B < R	NA	NA	B < R
Nicotine, mg/g	15.1	26.3	23.0	R < B	R < E	E < B	R < E < B
Nicotine (colorimetric), %		2.57	2.40		NA	NA	NA
Nicotine, %	1.51	2.63	2.30	R < B	R < E	E < B	R < E < B
Nornicotine, %	<0.010	0.068	0.057	R < B	R < E	E < B	R < E < B
Myosmine, %	0.0010	0.0015	0.0010	NA	NA	NA	NA
Anabasine, %	0.003	0.010	0.009	R < B	R < E	E < B	R < E < B
Anatabine, %	0.024	0.065	0.056	R < B	R < E	E < B	R < E < B
Total Alkaloids, %	<1.55	2.77	2.42	R < B	R < E	E < B	R < E < B
2 <sup>nd</sup> Total Alkaloids, %	<0.038	0.15	0.12	R < B	R < E	E < B	R < E < B
Fructose, %	0.16	1.01	0.96	R < B	R < E	E < B	R < E < B
Sucrose, %	<0.10	0.19	<0.08	R < B	NA	E < B	R, E < B
Glucose, %	<0.10	0.29	0.37	R < B	R < E	B < E	R < B < E
Ammonia, %	0.27	0.30	0.26	R < B	NS	E < B	R, E < B
Chloride, %	5.53	2.71	2.55	B < R	E < R	E < B	E < B < R
Hydroquinone, µg/g	BDL	BDL	BDL	NA	NA	NA	NA
Catechol, µg/g	12.30	14.42	21.06	R < B	R < E	B < E	R < B < E
Phenol, µg/g	5.35	BDL	BDL	B < R	E < R	NA	B, E < R
p,m-Cresol, µg/g	7.98	BDL	BDL	B < R	E < R	NA	B, E < R
NNN, µg/g	1.57	1.02	1.00	B < R	E < R	NS	B, E < R
NNK, µg/g	0.43	0.40	0.36	NS	NS	NS	NS
NAT, µg/g	1.09	0.68	0.68	B < R	E < R	NS	B, E < R
NAB, µg/g	<0.43	<0.43	<0.49	NA	NA	NA	NS
Arsenic, µg/g	0.252	0.308	0.111	R < B	E < R	E < B	E < R < B
Cadmium, µg/g	0.77	0.74	0.30	B < R	E < R	E < B	E < B < R
Chromium, µg/g	0.44	0.71	0.23	R < B	E < R	E < B	E < R < B
Lead, µg/g	0.220	0.283	0.065	R < B	E < R	E < B	E < R < B
Nickel, µg/g	1.38	1.89	0.99	R < B	E < R	E < B	E < R < B

<indicates <LOD except for cumulative endpoints like total alkaloids, where at least one component of the sum was <LOD (e.g., nornicotine)

NA indicates non-applicable cases (e.g., only one replicate run such as nicotine, colorimetric assay; no significance test could be conducted for SD=0; comparisons of means with <LOD results)

NS indicates not statistically significant

#### b) Labstat analyses

The results for the analytes measured in the test articles and 2S3 reference (R) of the initial test article characterization work (2008 analysis) are presented in Table 4. The general trend for measured analytes is as follows: E < B < R. It is noteworthy that many PAHs are present at much lower levels in the blend and extract than in the reference tobacco.

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**Table 4. Labstat analyses-full test article production: blend, extract, and reference**

Analyte, Measurement unit	Mean SD	Test Articles			Comparisons (% difference)			Ranking
		2S3 (R)	Blend (B)	Extract (E)	B vs. R	E vs. R	E vs. B	
Formaldehyde, µg/g	Mean	0.860	0.309	0.023	-64.0	-97.3	-92.4	E < B < R
	SD	0.144	0.071	0.002				
Acrolein, µg/g	Mean	<0.016	<0.008	<0.001	NA	NA	NA	NA
	SD	0.000	0.000	0.000				
Nitrite, µg/g	Mean	9.182	2.808	* 0.125	-69.4	-98.6	-95.5	E < B < R
	SD	2.167	0.000	0.000				
NDMA, ng/g	Mean	* 7.553	* 2.835	<0.071	NA	-99.1	-97.5	E < B, R
	SD	1.745	0.000	0.000				
NPYR, ng/g	Mean	* 7.213	* 4.010	* 0.216	NA	NA	-94.6	E < B < R
	SD	0.000	0.000	0.000				
NEMA, ng/g	Mean	<2.980	<1.510	<0.081	NA	NA	NA	NA
	SD	0.000	0.745	0.000				
NDEA, ng/g	Mean	<3.080	* 1.864	<0.084	NA	NA	NA	NA
	SD	0.000	0.000	0.000				
NDPA, ng/g	Mean	<3.330	<1.690	<0.091	NA	NA	NA	NA
	SD	0.000	0.000	0.000				
NDBA, ng/g	Mean	<4.650	<2.360	<0.127	NA	NA	NA	NA
	SD	0.000	0.000	0.000				
NPIP, ng/g	Mean	<5.040	<2.560	<0.137	NA	NA	NA	NA
	SD	0.378	0.089	0.051				
Naphthalene, ng/g	Mean	80.257	28.462	4.289	-64.5	-94.7	-84.9	E < B < R
	SD	20.285	4.634	1.243				
Acenaphthylene, ng/g	Mean	58.486	2.003	0.074	-96.6	-99.9	-96.3	E < B < R
	SD	7.660	0.247	0.008				
Acenaphthene, ng/g	Mean	77.822	5.960	0.723	-92.3	-99.1	-87.9	E < B < R
	SD	11.786	0.625	0.207				
Fluorene, ng/g	Mean	495.400	8.973	0.409	-98.2	-99.9	-95.4	E < B < R
	SD	53.837	0.933	0.076				
Phenanthrene, <sup>&amp;</sup> ng/g	Mean	4747.210	65.110	2.760	-98.6	-99.9	-95.8	E < B < R
	SD	268.135	8.068	0.586				
Fluoranthene, ng/g	Mean	1806.850	44.870	2.950	-97.5	-99.8	-93.4	E < B < R
	SD	55.967	4.987	0.329				
Pyrene, <sup>&amp;</sup> ng/g	Mean	1750.400	32.170	2.340	-98.2	-99.9	-92.7	E < B < R
	SD	53.727	4.879	0.415				
Benzo(a)anthracene, <sup>&amp;</sup> ng/g	Mean	343.677	4.041	0.290	-98.8	-99.9	-92.8	E < B < R
	SD	17.607	0.691	0.053				
Chrysene, ng/g	Mean	496.849	10.707	0.947	-97.8	-99.8	-91.2	E < B < R
	SD	21.811	1.381	0.119				
Benzo(b)fluoranthene, ng/g	Mean	77.915	2.983	0.276	-96.2	-99.6	-90.7	E < B < R
	SD	4.635	0.273	0.030				
Benzo(k)fluoranthene, ng/g	Mean	27.482	1.536	0.137	-94.4	-99.5	-91.1	E < B < R
	SD	2.343	0.128	0.029				
Benzo(j)fluoranthene, ng/g	Mean	38.042	1.792	0.176	-95.3	-99.5	-90.2	E < B < R
	SD	1.997	0.151	0.029				
Benzo(c)pyrene, <sup>&amp;</sup> ng/g	Mean	69.059	2.102	0.211	-97.0	-99.7	-90.0	E < B < R
	SD	3.814	0.203	0.023				

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Analyte, Measurement unit	Mean SD	Test Articles			Comparisons (% difference)			Ranking
		2S3 (R)	Blend (B)	Extract (E)	B vs. R	E vs. R	E vs. B	
Benzo(a)pyrene, ng/g	Mean	62.696	1.599	0.140	-97.5	-99.8	-91.2	E < B < R
	SD	4.234	0.228	0.020				
Perylene, <sup>&amp;</sup> ng/g	Mean	8.572	* 0.172	0.031	-98.0	-99.6	-81.9	E < B < R
	SD	1.608	0.000	0.005				
Indeno(1,2,3,-cd)pyrene, ng/g	Mean	25.273	1.362	0.120	-94.6	-99.5	-91.2	E < B < R
	SD	2.102	0.218	0.017				
Dibenz(a,h)anthracene, ng/g	Mean	7.131	* 0.310	* 0.033	-95.7	-99.5	-89.3	E < B < R
	SD	1.324	0.104	0.013				
Benzo(g,h,i)perylene, <sup>&amp;</sup> ng/g	Mean	27.156	1.612	0.170	-94.1	-99.4	-89.4	E < B < R
	SD	2.003	0.256	0.024				
Dry Matter, %	Mean	45.462	89.589		97.1			R < B
	SD	0.057	0.071					
Moisture, %	Mean	54.538	10.411		-80.9			B < R
	SD	0.057	0.071					

< indicates all LOD values; \* indicates some LOQ values, with midpoint value assigned

& indicates additional analytes not requested to be measured but measured and, therefore, reported

For the available values, the analyte levels measured for the 2S3 reference indicated that the methods worked as expected.

### c) Microbac analyses

The following pesticides were measured (GN75387AB-blend, AC-extract): alachlor, aldrin, benfluralin, bifenthrin, butralin, camphechlor, captan, chinomethionate, chlordane, chlorothalonil, cyfluthrin,  $\lambda$ -cyhalothrin, cypermethrin, o,p-DDD, p,p-DDD, o,p-DDE, o,p-DDT, p,p-DDT, deltamethrin, dichloran, dieldrin, dinocap, endosulfan I, endosulfan II, endosulfan SO<sub>4</sub>, endrin, esfenvalerate, fenvalerate, flucytrinate, flumetralin, folpet,  $\alpha$ -HCH,  $\beta$ -HCH,  $\delta$ -HCH, heptachlor, heptachlor epoxide, hexachlorobenzene, isopropalin, lindane ( $\gamma$ -HCH), methoxychlor, nitrofen, pendimethalin, permethrin, pyrethrins, trifluoralin, EBDC (as mancozeb), maleic hydrazide, acephate, ethyl azinphos, methyl azinphos, methyl bromophos, chlorfenvinphos, chlorpyrifos, S-methyl demeton, diazinon, dichlorvos, dimefox, dimethoate, disulfoton, disulfoton sulfone, disulfoton sulfoxide, ethoprophos, fenamiphos, fenamiphos sulfoxide, fenamiphos sulfone, fenclorophos, fenitrothion, fensulfothion, fenthion, fenthion sulfone, fenthion sulfoxide, fenophos, formothion, malathion, methamidophos, methidathion, mevinphos, monocrotophos, naled, parathion, methyl parathion, phorate, phosalone, phosphamidon, phoxim, methyl pirimiphos, profenofos, trebufos, trebufos sulfone, trebufos sulfoxide, tetrachlorvinphos, thionazin, trichlorfon, vamidothion, vamidothion sulfoxide, dicamba, 2,4-D, 2,4,5-T, aldicarb, aldicarb sulfone, aldicarb sulfoxide, benalaxyl, butylate, carbaryl, carbofuran, clomazone, diflubenzuron, dimethomorph, diphenamid, ethiofencarb, ethiofencarb sulfone, ethiofencarb sulfoxide, 3-hydroxycarbofuran, metalaxyl, methiocarb, methiocarb sulfone, methiocarb sulfoxide, methomyl, 1-naphtol, oxadixyl, oxamyl, pebulate, piperonyl butoxide, pirimicarb, and propoxur.

With the exception of metalaxyl and butralin, all measured pesticides were below the limit of quantitation. However, based on mouse and rat-specific toxicology data and

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exposure assessments, the presence of these two pesticides at such low levels in the tobacco test articles is not expected to contribute in any substantial way to subchronic/chronic toxicity in rats and mice in the feeding studies.

## 2) Microbiology results

### a) RJRT microbial analyses

Figures 1 and 2 indicate the progress of the irradiated test articles with time in terms of microbial endpoints (for the initial samples stored under RJRT conditions at  $-7^{\circ}\text{C}$ ). Except for total bacterial counts and water activity (which showed changes from the beginning of the study to month 3), there were no other targeted organisms detected at month 3. By month 3, total bacterial counts were slightly increased for the blend and decreased for the extract. However, the water activity for the blend was still below the level where significant growth would be expected, and, although there was a slight increase in the total bacterial counts for the blend, the average values are still within acceptable limits.

Figure 1. Total bacterial counts (RJRT samples)

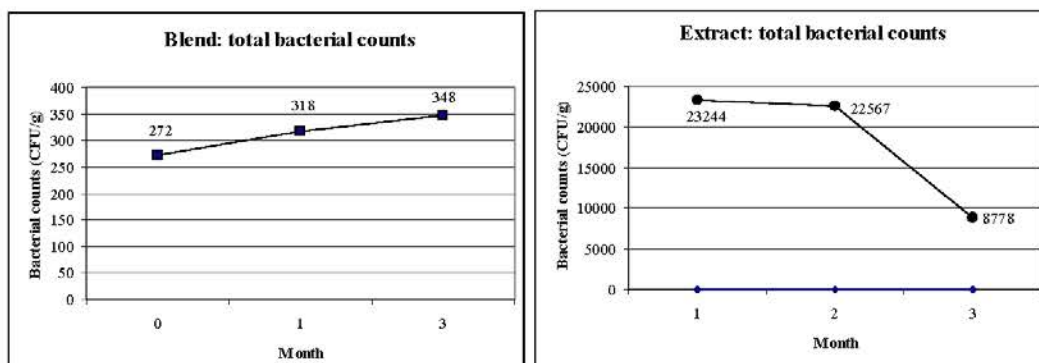
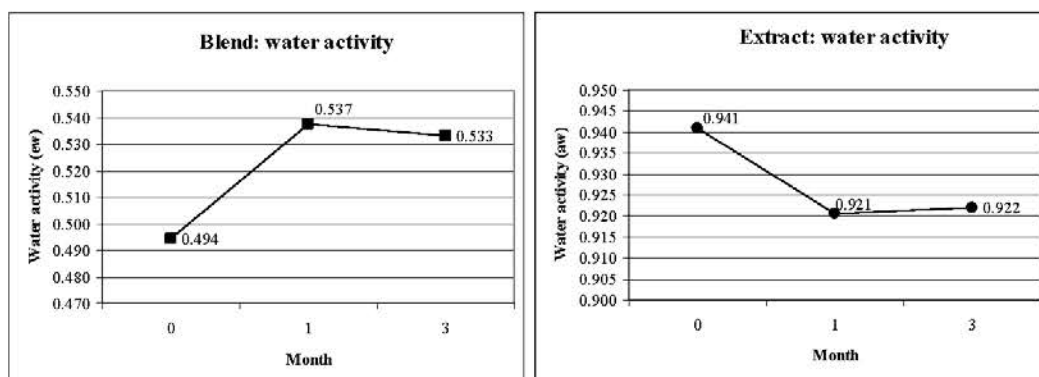


Figure 2. Water activity (RJRT samples)



**b) Trilogy toxin analyses**

Test articles were tested in April-May 2008 to determine the presence of toxins. No toxins were detected in the blend or extract except for Ochratoxin A. The presence of Ochratoxin A was confirmed by repeating the analysis. However, based on mouse and rat-specific toxicology data and exposure assessments, the presence of Ochratoxin A at such low levels would not be expected to induce Ochratoxin-specific toxicity in the rat and mouse feeding studies.

**3) Additional analyses****a) 1-Month stability study: March vs. April 2008 analysis (effects of storage conditions on chemistry endpoints)**

A 1-month stability study was conducted using an abbreviated list of compounds to obtain a preliminary read on the stability of key analytes under applicable storage conditions (GN76582). Results from this analysis are presented in Table 5.

**Table 5. Test article 1-month stability data (abbreviated analyte list)**

Analyte, Measurement unit	2S3			Blend			Extract		
	March	April	April vs. March	March	April	April vs. March	March	April	April vs. March
pH	7.32	7.28	-0.6%	5.45	5.34	-1.9%	5.19	5.45	5.1%
Moisture, %	53.71	54.12	0.8%	10.10	10.06	NS			
Nicotine, mg/g	15.15	15.13	NS	26.28	26.66	NS	22.99	22.80	NS
Nicotine, %	1.51	1.51	NS	2.63	2.67	NS	2.30	2.28	NS
Nornicotine, %	<0.010	0.016	NS	0.068	0.065	NS	0.057	0.055	NS
Myosmine, %	0.001	<0.001	NS	0.002	0.001	NS	0.001	0.001	NS
Anabasine, %	0.003	0.005	NS	0.010	0.011	NS	0.009	0.009	NS
Anatabine, %	0.024	0.026	NS	0.065	0.071	NS	0.056	0.058	NS
Total Alkaloids, %	<1.55	<1.56	NA	2.77	2.81	NS	2.42	2.40	NS
2 <sup>nd</sup> Total Alkaloids, %	<0.038	<0.049	NA	0.145	0.148	NS	0.123	0.122	NS
Fructose, %	0.16	0.13	NS	1.01	1.29	NS	0.96	1.21	NS
Sucrose, %	<0.10	<0.10	NA	0.19	<0.10	NS	<0.08	<0.09	NA
Glucose, %	<0.10	<0.10	NA	0.29	0.35	NS	0.37	0.38	NS
NNN, µg/g	1.57	1.68	NS	1.02	1.25	NS	1.00	1.02	NS
NNK, µg/g	0.43	0.43	NS	0.40	0.62	NS	0.36	0.39	NS
NAT, µg/g	1.09	1.13	NS	0.68	0.84	NS	0.68	0.69	NS
NAB, µg/g	<0.43	<0.42	NA	<0.43	<0.44	NA	<0.49	<0.49	NA
Total Solids, %							37.76	37.17	-1.6%

NA indicates comparisons of means that include only <LOD values (not applicable)

NS indicates not statistically significant

March and April sample means were compared using z-tests based on test method uncertainty for alkaloids, nitrosamines, and specific sugars. Comparisons of means for pH, moisture, and total solids were made using analysis of variance based on observed variation among replicates which are especially sensitive. P-values were adjusted using Bonferroni's method to control experimental error at a 5% significance level. Total and

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secondary alkaloids were calculated by substituting LOD for < LOD quantities. In all other cases, LOD was substituted for < LOD values, with means reported as "<" the calculated mean. Small differences in pH and moisture were statistically significant because little variation was observed among replicates. Otherwise, there were no significant differences for the 2S3, blend, and extract.

For the available values, the analyte levels measured for the 2S3 reference indicated that the methods worked as expected. Overall, these results confirm the stability of the test articles and 2S3 reference during the one month analysis period. This is directly applicable to the formulation regimen employed in the rat and mouse feeding studies.

#### b) Blend ground vs. non-ground (effects of grinding on chemistry endpoints)

Due to the fact that the blend-diet mixes were not sufficiently homogenous, the blend had to be ground further to achieve a smaller particle size. An additional study was designed to demonstrate that the non-ground and ground blends are equivalent in terms of the analytes selected for analyses (GN77727). Tables 6 and 7 summarize the results from these analyses.

**Table 6. Blend ground and non-ground (RJRT data)**

Analyte	Mean SD	Test Articles			Comparisons (% Difference)		
		Ground	Non-ground	2S3	Ground vs. Non-Ground	Ground vs. 2S3	Non-Ground vs. 2S3
Ammonia, %	Mean	0.282	0.287	0.253	NS	11.2	13.2
	SD	0.004	0.005	0.005			
pH	Mean	5.37	5.39	7.33	-0.2	-26.7	-26.5
	SD	0.008	0.005	0.008			
Moisture, %	Mean	9.37	9.30	52.50	NS	-82.1	-82.3
	SD	0.038	0.102	0.228			
Total Alkaloids, %	Mean	2.96	2.90	<1.56	21	90.3	86.5
	SD	0.038	0.043	0.016			
Secondary Alkaloids, %	Mean	0.163	0.162	<0.053	NS	208.2	206.0
	SD	0.002	0.003	0.001			
Nicotine, %	Mean	2.80	2.74	1.50	NS	86.2	82.3
	SD	0.037	0.042	0.016			
Nornicotine, %	Mean	0.074	0.074	0.018	NS	315.2	317.1
	SD	0.001	0.002	0.001			
Myosmine, %	Mean	0.002	0.002	<0.001	NS	NS	NS
	SD	0.000	0.000	0.000			
Anabasine, %	Mean	0.012	0.012	0.006	NS	111.8	107.1
	SD	0.001	0.000	0.000			
Anatabine, %	Mean	0.075	0.074	0.028	NS	164.8	161.4
	SD	0.001	0.002	0.000			
Nicotine, mg/g	Mean	28.0	27.4	15.0	NS	86.2	82.3
	SD	0.37	0.42	0.17			
Chloride, %	Mean	2.53	2.56	5.50	NS	-53.9	-53.4
	SD	0.004	0.035	0.024			
NNN, µg/g	Mean	1.46	1.38	1.61	NS	NS	NS

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Analyte	Mean SD	Test Articles			Comparisons (% Difference)		
		Ground	Non-ground	2S3	Ground vs. Non-Ground	Ground vs. 2S3	Non-Ground vs. 2S3
	SD	0.046	0.048	0.038			
NNK, µg/g	Mean	0.60	0.54	0.57	NS	NS	NS
	SD	0.071	0.083	0.067			
NAT, µg/g	Mean	1.13	1.07	1.18	NS	NS	NS
	SD	0.069	0.076	0.052			
NAB, µg/g	Mean	<0.43	<0.43	<0.43	NA	NA	NA
	SD						
Fructose, %	Mean	0.90	0.91	<0.10	NS	798.3	811.7
	SD	0.013	0.020	0.000			
Sucrose, %	Mean	<0.10	<0.10	<0.10	NA	NA	NA
	SD	0.000	0.000	0.000			
Glucose, %	Mean	0.17	0.22	<0.10	NS	66.7	118.3
	SD	0.008	0.045	0.000			
Hydroquinone, mg/g	Mean	BQL	BQL	BQL	NA	NA	NA
	SD						
Catechol, mg/g	Mean	15.36	14.25	12.38	7.8	24.1	15.1
	SD	0.230	0.232	0.163			
Phenol, mg/g	Mean	BQL	BQL	5.46	NA	NA	NA
	SD			0.052			
p,m-Cresol, mg/g	Mean	BQL	BQL	7.14	NA	NA	NA
	SD			0.060			
Arsenic, µg/g	Mean	0.34	0.36	0.48	NS	-27.8	NS
	SD	0.107	0.080	0.029			
Cadmium, µg/g	Mean	0.76	0.73	0.73	4.1	4.1	NS
	SD	0.020	0.010	0.000			
Chromium, µg/g	Mean	0.95	0.81	0.48	NS	97.9	68.8
	SD	0.190	0.190	0.010			
Lead, µg/g	Mean	0.38	0.37	0.30	NS	NS	NS
	SD	0.110	0.040	0.050			
Nickel, µg/g	Mean	1.80	1.60	1.15	12.5	56.5	39.1
	SD	0.060	0.080	0.020			

**Table 7. Blend ground and non-ground (Labstat data)**

Analyte	Mean SD	Test Articles			Comparisons (% Difference)		
		2S3	Non-Ground	Ground	Non-Ground vs. 2S3	Ground vs. 2S3	Non-Ground vs. Ground
Formaldehyde, µg/g	Mean	0.680	0.351	0.373	-48.4	-45.2	NS
	SD	0.074	0.020	0.053			
Acrolein, µg/g	Mean	* 0.019	<0.008	* 0.010	NA	NA	NA
	SD	0.007	0.000	0.004			
Nitrite, µg/g	Mean	* 1.492	* 0.755	<0.634	NA	NA	NA
	SD	0.592	0.302	0.000			
NDMA, ng/g	Mean	* 6.133	* 3.785	* 4.285	NA	NA	NA
	SD	1.331	1.063	1.138			
NPYR, ng/g	Mean	* 7.930	* 4.010	9.180	NA	NA	128.9

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Analyte	Mean SD	Test Articles			Comparisons (% Difference)		
		2S3	Non- Ground	Ground	Non- Ground vs. 2S3	Ground vs. 2S3	Non- Ground vs. Ground
	SD	0.000	0.000	0.532			
NEMA, ng/g	Mean	* 3.548	<1.510	* 1.805	NA	NA	NA
	SD	1.417	0.000	0.723			
NDEA, ng/g	Mean	* 3.682	<1.560	* 2.180	NA	NA	NA
	SD	1.474	0.000	0.945			
NDPA, ng/g	Mean	<3.330	<1.690	* 2.086	NA	NA	NA
	SD	0.000	0.000	0.885			
NDBA, ng/g	Mean	<4.640	<2.360	* 2.820	NA	NA	NA
	SD	0.000	0.000	1.127			
NPIP, ng/g	Mean	<5.040	<2.550	<2.560	NA	NA	NA
	SD	0.000	0.000	0.000			
Naphthalene, ng/g	Mean	67.585	38.348	41.454	-43.3	-38.7	NS
	SD	6.944	4.722	5.994			
Acenaphthylene, ng/g	Mean	44.799	2.185	3.715	-95.1	-91.7	NS
	SD	3.872	0.234	0.525			
Acenaphthene, ng/g	Mean	54.838	6.489	7.552	-88.2	-86.2	NS
	SD	3.585	0.991	1.470			
Fluorene, ng/g	Mean	391.164	11.193	14.544	-97.1	-96.3	NS
	SD	24.009	1.834	1.197			
Phenanthrene, <sup>&amp;</sup> ng/g	Mean	4762.500	73.180	68.910	-98.5	-98.6	NS
	SD	263.216	8.239	8.367			
Fluoranthene, ng/g	Mean	1845.940	47.190	50.130	-97.4	-97.3	NS
	SD	61.742	3.214	2.591			
Pyrene, ng/g	Mean	1737.980	29.980	31.860	-98.3	-98.2	NS
	SD	54.955	2.835	2.507			
Benzo(a)anthracene, <sup>&amp;</sup> ng/g	Mean	348.165	4.128	4.494	-98.8	-98.7	NS
	SD	7.867	0.620	0.578			
Chrysene, ng/g	Mean	492.676	10.482	11.355	-97.9	-97.7	NS
	SD	12.284	0.861	0.980			
Benzo(b)fluoranthene, ng/g	Mean	75.966	2.991	3.892	-96.1	-94.9	NS
	SD	1.222	0.266	0.343			
Benzo(k)fluoranthene, ng/g	Mean	28.940	1.276	1.761	-95.6	-93.9	NS
	SD	1.621	0.104	0.249			
Benzo(j)fluoranthene, ng/g	Mean	39.066	2.064	2.323	-94.7	-94.1	NS
	SD	1.959	0.129	0.204			
Benzo(e)pyrene, <sup>&amp;</sup> ng/g	Mean	67.956	2.183	2.837	-96.8	-95.8	NS
	SD	2.401	0.197	0.231			
Benzo(a)pyrene, ng/g	Mean	62.860	1.460	1.970	-97.7	-96.9	NS
	SD	1.934	0.218	0.216			
Perylene, <sup>&amp;</sup> ng/g	Mean	8.080	* 0.227	0.416	-97.2	-94.9	83.0*
	SD	0.191	0.061	0.054			
Indeno(1,2,3-cd)pyrene, ng/g	Mean	24.244	1.215	1.825	-95.0	-92.5	NS**

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Analyte	Mean SD	Test Articles			Comparisons (% Difference)		
		2S3	Non-Ground	Ground	Non-Ground vs. 2S3	Ground vs. 2S3	Non-Ground vs. Ground
	SD	1.381	0.158	0.309			
Dibenz(a,h)anthracene, ng/g	Mean	5.472	* 0.210	* 0.297	-96.2	-94.6	NA
	SD	1.306	0.056	0.136			
Benzo(g,h,i)perylene,* ng/g	Mean	25.327	1.447	2.009	-94.3	-92.1	NS
	SD	1.799	0.147	0.208			
Dry Matter, %	Mean	45.475	89.659	89.371	97.2	96.5	-0.3
	SD	0.058	0.088	0.042			
Moisture, %	Mean	54.525	10.341	10.629	-81.0	-80.5	2.8
	SD	0.058	0.088	0.042			

<Indicates all LOD values, \*indicates some LOQ values, with midpoint value assigned

\*Not statistically significantly different on a dry weight basis

\*\*Statistically significantly different on a dry weight basis

&Indicates additional analytes not requested to be measured but measured and, therefore, reported

Results indicate that, although there were a few statistically significant differences between the ground and non-ground blends, these small statistically significant differences are not expected to translate into biological activity differences in the current set of assays. Therefore, the blends (ground and non-ground) are considered substantially equivalent.

For the available values, the analyte levels measured for the 2S3 reference indicated that the methods worked as expected.

## Conclusion

Taking all data into account, results to date 1) indicate that the test articles are appropriately controlled and 2) support the test articles use in the smokeless tobacco and extract rodent feeding toxicology studies.

**APPENDIX C: INDIVIDUAL ANIMAL DATA**

**Table C-1. Individual Animal Clinical Abnormalities – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Observation</b>	<b>Observed</b>			<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	<b>Interval</b>	
E0.2M	905	Abrasion, Body Lateral	8	15	8	2
	905	Abrasion, Neck	8	29	22	4
	905	Alopecia	22	29	8	2
	907	Abrasion, Body Lateral	8	29	22	4

**Table C-2. Individual Animal Clinical Abnormalities – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Observation</b>	<b>Observed</b>			<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	<b>Interval</b>	
E0.2F	955	Red Eye Discharge	1	30	30	5
	955	Alopecia	8	30	23	4
E8F	1152	Tremors	15	15	1	1
	1158	Tremors	22	22	1	1

**Table C-3. Paired and High Dose Individual Animal Clinical Abnormalities – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Observation</b>	<b>Observed</b>			<b>Total Number</b>
			<b>First Day</b>	<b>Last Day</b>	<b>Interval</b>	
B20M	710	Rough Coat	8	31	24	4
E20M	1202	Rough Coat	8	31	24	4
	1204	Rough Coat	8	31	24	4

**Table C-4. Pairfed and High Dose Individual Animal Clinical Abnormalities – Females**

Group	Animal ID	Observation	Observed			Total Number
			First Day	Last Day	Interval	
NT20F	258	Rough Coat	8	32	25	4
	258	Thin Appearance	15	32	18	3
PFCNTF	359	Rough Coat	8	32	25	4
B20F	753	Thin Appearance	32	32	1	1
	754	Thin Appearance	32	32	1	1
	756	Rough Coat	22	32	11	2
	756	Thin Appearance	15	32	18	3
	757	Red Eye Discharge	13	13	1	1
	757	Lethargic	13	13	1	1
	757	Thin Appearance	13	13	1	1
	1251	Thin Appearance	22	32	11	2
E20F	1252	Thin Appearance	22	32	11	2
	1252	Tremors	22	32	11	2
	1253	Thin Appearance	32	32	1	1

**Table C-5. Individual Animal Body Weight (g) – Males**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
CM	101	198.3	210.3	219.1	242.9	246.0	260.7	275.9	282.3
	102	199.3	215.3	244.4	256.6	265.5	287.1	310.8	317.8
	103	180.4	200.7	228.2	243.8	247.8	269.6	287.3	298.6
	104	181.7	196.3	213.7	227.9	238.4	251.5	266.3	276.8
	105	212.5	223.2	241.9	256.7	267.5	287.3	289.9	301.2
	106	199.3	211.5	215.7	243.6	254.3	260.2	268.2	276.2
	107	190.3	203.2	222.1	234.3	237.4	252.2	263.0	267.5
	108	208.4	217.8	243.2	258.2	261.0	273.2	286.6	298.9
	109	215.0	231.9	241.5	266.7	276.3	285.3	299.5	307.6
	110	217.4	235.5	258.0	270.6	285.0	294.5	310.2	321.5
B0.2M	401	173.3	181.4	199.3	209.5	209.9	216.4	222.5	229.8
	402	210.3	226.5	237.7	258.9	256.3	272.1	287.8	297.5
	403	203.0	214.8	237.0	246.4	247.7	264.7	274.8	283.7
	404	181.5	198.4	217.2	226.1	232.7	242.9	254.9	262.2
	405	208.3	224.9	229.1	252.4	264.7	277.6	286.9	291.4
	406	193.5	211.2	231.3	245.1	259.7	272.6	285.9	294.5
	407	189.1	197.9	218.4	235.3	246.2	253.3	260.7	263.2
	408	183.7	194.6	212.3	225.7	236.4	244.1	256.6	265.5
	409	202.8	217.4	234.4	249.2	251.4	270.0	280.1	290.5
	410	225.4	238.3	258.6	274.0	285.5	294.6	313.1	321.7
B2M	501	214.6	222.1	239.1	254.1	250.7	271.7	283.2	294.3
	502	216.1	224.8	248.7	263.6	266.2	284.6	298.9	305.5
	503	180.0	192.0	206.4	217.1	216.9	221.7	233.4	243.6
	504	205.1	211.3	226.5	241.4	248.4	267.1	278.6	285.6
	505	208.4	217.3	242.5	251.1	260.0	276.5	292.5	300.9
	506	189.9	203.5	223.4	236.8	247.0	254.8	262.3	269.9
	507	209.5	215.8	233.3	240.8	242.4	257.4	268.2	275.6

**Table C-5. Individual Animal Body Weight (g) – Males (Continued)**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
B2M	508	195.4	206.1	224.4	233.8	235.7	241.2	254.1	261.6
	509	192.0	202.9	225.0	238.4	248.8	252.8	264.3	270.9
	510	195.0	206.0	225.9	237.0	244.0	253.7	267.6	273.1
B8M	601	218.5	216.8	233.2	247.8	242.7	262.0	269.3	270.6
	602	178.9	177.3	199.8	206.0	198.1	207.9	207.2	213.1
	603	191.6	191.0	201.7	214.4	215.3	227.8	238.1	246.6
	604	203.4	203.2	212.7	227.2	220.8	231.6	244.2	249.7
	605	207.5	207.2	219.3	230.1	233.7	245.5	248.0	253.0
	606	198.7	194.9	207.8	218.4	232.9	239.5	241.2	247.6
	607	165.3	170.6	182.0	187.1	187.1	198.4	205.7	211.7
	608	207.1	203.3	208.1	226.2	224.1	231.9	247.4	251.2
	609	206.8	204.1	221.0	225.4	236.6	242.1	245.2	254.2
	610	195.6	187.1	203.6	212.2	215.5	222.9	232.8	244.0
E0.2M	901	194.6	207.2	229.2	245.9	263.8	283.1	289.3	301.9
	902	202.3	218.2	212.0	246.5	268.7	285.4	299.6	307.8
	903	216.4	229.7	228.4	267.0	283.6	294.4	310.4	320.4
	904	189.4	204.7	228.4	239.9	258.5	269.2	282.4	293.6
	905	203.3	215.9	219.4	248.2	263.5	267.1	284.4	285.8
	906	214.8	237.3	254.9	268.3	285.0	293.9	304.9	308.9
	907	224.1	239.3	253.4	277.0	296.3	302.3	316.2	320.2
	908	189.4	201.1	218.2	236.2	250.3	262.2	272.4	279.5
	909	189.2	199.1	225.1	244.4	260.4	269.1	281.1	290.6
	910	201.1	212.2	210.8	248.5	258.0	266.6	276.3	282.8
E2M	1001	212.4	218.3	235.5	246.0	257.3	267.7	273.1	282.0
	1002	188.1	198.5	220.1	232.5	251.0	262.2	274.7	280.3
	1003	215.0	229.6	255.8	268.6	289.5	302.0	318.5	329.0
	1004	182.2	191.8	212.0	227.2	238.6	245.0	253.3	260.2

**Table C-5. Individual Animal Body Weight (g) – Males (Continued)**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
E2M	1005	198.3	208.9	214.1	241.2	260.8	272.4	284.5	287.7
	1006	200.0	211.6	233.6	254.5	268.9	280.9	294.9	305.3
	1007	196.7	202.8	221.9	231.9	248.9	256.2	267.8	272.3
	1008	178.3	190.1	204.4	218.2	226.1	230.9	232.8	238.6
	1009	221.6	232.0	250.6	267.4	278.5	282.9	296.0	305.4
	1010	203.9	215.3	228.3	256.7	275.5	285.1	302.2	314.3
E8M	1101	217.8	220.1	223.4	232.7	244.0	255.0	262.5	271.0
	1102	206.5	206.3	219.8	234.8	240.5	251.0	257.9	266.6
	1103	210.9	206.4	224.8	233.0	247.5	259.9	265.8	273.5
	1104	195.3	202.7	216.2	222.5	233.9	244.6	250.3	250.8
	1105	181.7	186.0	201.6	211.9	222.6	230.0	232.1	235.8
	1106	204.9	198.8	214.0	227.8	231.4	238.5	246.2	247.3
	1107	180.2	181.6	193.2	208.0	218.6	227.5	233.9	237.9
	1108	205.6	202.6	217.1	229.4	234.9	244.3	245.6	250.6
	1109	179.6	181.6	194.4	203.7	212.1	216.5	225.5	225.5
	1110	193.9	194.8	209.7	225.1	235.1	240.8	246.2	248.7

**Table C-6. Individual Animal Body Weight (g) – Females**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
CF	151	140.8	144.3	154.5	160.2	162.4	174.1	180.5	183.9
	152	140.8	143.0	151.5	154.5	159.2	160.3	165.8	170.6
	153	145.3	152.1	161.5	165.6	171.2	173.1	181.8	181.9
	154	158.7	162.1	172.0	176.2	180.4	178.7	184.0	193.4
	155	146.7	148.6	148.8	151.7	152.8	165.4	167.2	170.8
	156	150.3	158.5	165.0	170.1	171.8	182.0	190.5	199.2
	157	151.8	152.0	156.3	166.2	173.1	178.4	187.9	187.7
	158	162.7	169.7	177.4	181.9	186.6	191.5	198.4	199.2
	159	148.3	149.5	151.7	147.3	146.1	152.9	161.6	165.4
	160	162.1	162.8	170.8	176.9	183.7	182.1	186.6	193.3
B0.2F	451	144.2	145.1	153.5	156.6	156.7	159.7	164.4	164.7
	452	153.0	156.6	162.8	165.9	170.1	171.6	177.6	178.6
	453	144.9	144.9	150.9	158.8	161.6	167.4	171.3	172.5
	454	144.3	150.5	158.2	163.5	168.1	165.6	175.2	180.0
	455	156.3	163.2	168.5	177.2	181.2	183.3	187.8	186.5
	456	143.5	146.1	152.3	157.3	162.0	166.5	175.5	177.9
	457	150.8	154.8	163.2	169.8	174.1	178.0	187.1	189.3
	458	157.7	161.5	171.5	175.4	182.0	182.5	193.0	193.8
	459	152.9	159.0	168.6	174.8	181.8	182.2	191.3	195.9
	460	138.3	148.8	151.0	155.7	154.4	162.3	169.5	171.8
B2F	551	143.5	144.4	149.6	151.5	153.5	154.4	159.0	168.9
	552	148.1	152.8	157.0	160.2	160.1	162.4	169.0	169.4
	553	148.1	152.0	154.5	159.1	163.4	165.7	176.4	181.4
	554	145.2	147.5	151.1	158.2	164.5	168.0	178.0	181.3
	555	155.2	153.0	157.2	164.9	171.2	174.8	181.1	180.5
	556	164.6	166.9	173.4	177.4	179.1	186.4	190.4	193.0
	557	154.6	156.7	159.7	167.5	170.3	172.3	179.3	177.6

**Table C-6. Individual Animal Body Weight (g) – Females (Continued)**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
B2F	558	130.9	137.3	143.0	148.1	150.0	152.0	160.4	163.7
	559	148.6	148.0	154.8	164.6	172.8	175.7	181.8	183.3
	560	146.8	149.4	156.9	159.6	166.6	164.2	171.9	180.6
B8F	651	154.7	140.9	146.8	150.8	157.9	155.5	158.7	164.2
	652	149.2	136.4	141.8	139.2	145.5	148.3	155.8	154.5
	653	160.6	149.4	150.0	155.2	160.8	164.1	168.7	169.5
	654	149.6	145.4	145.2	151.5	153.1	155.7	161.0	157.3
	655	158.0	145.2	150.8	154.7	151.4	165.8	168.3	165.0
	656	152.8	144.2	151.3	161.3	161.1	168.5	169.0	173.0
	657	154.0	147.8	152.0	159.7	164.3	166.7	173.8	175.0
	658	137.0	127.9	129.8	142.0	148.6	147.7	156.8	160.4
	659	138.1	127.7	134.1	142.8	142.5	145.5	150.3	150.1
	660	138.8	131.3	136.3	136.6	142.8	148.2	157.5	153.2
E0.2F	951	136.3	142.4	148.2	146.3	154.1	148.5	156.3	164.4
	952	150.6	154.5	163.8	166.1	169.8	178.5	182.0	186.4
	953	154.7	161.5	169.6	173.0	174.1	180.3	181.9	184.5
	954	147.3	151.1	156.9	160.2	165.2	172.3	179.9	179.8
	955	153.0	157.4	173.4	174.8	181.3	187.8	194.9	197.7
	956	138.6	143.9	152.1	157.7	169.8	170.6	177.8	179.1
	957	142.1	154.8	161.3	167.7	171.2	172.7	180.7	174.1
	958	158.4	164.4	174.5	180.4	184.6	186.0	194.5	201.1
	959	150.3	154.6	163.3	167.9	170.3	171.1	178.0	184.5
	960	159.1	166.7	177.6	183.7	188.0	189.9	196.5	191.5
E2F	1051	149.4	152.2	157.0	159.3	162.6	162.3	169.4	175.7
	1052	134.8	135.0	143.5	151.2	155.2	156.5	163.2	160.1
	1053	145.9	142.4	145.4	157.7	153.5	161.3	164.1	166.4
	1054	153.2	154.5	161.1	161.8	167.7	172.7	178.1	182.0

**Table C-6. Individual Animal Body Weight (g) – Females (Continued)**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
E2F	1055	153.7	158.0	166.3	171.9	177.3	173.4	184.1	188.1
	1056	148.3	147.0	148.1	155.2	152.0	159.0	165.9	163.0
	1057	145.7	149.0	158.9	162.8	168.2	168.1	176.6	179.8
	1058	144.5	151.2	155.1	157.9	160.7	156.9	159.2	164.1
	1059	158.6	161.8	169.3	173.3	174.3	174.1	181.3	186.2
	1060	135.2	138.0	146.2	149.8	152.5	155.2	160.7	164.2
E8F	1151	158.2	149.0	155.5	169.7	171.2	175.6	183.1	179.1
	1152	146.3	139.6	149.9	152.2	148.8	155.3	162.5	161.8
	1153	150.6	144.4	145.8	162.1	162.0	171.1	178.7	179.5
	1154	146.9	137.8	138.3	140.8	142.2	148.4	156.1	155.4
	1155	162.2	150.4	159.7	157.8	161.3	165.9	172.3	172.7
	1156	155.9	149.6	158.5	164.1	158.0	166.7	170.1	172.4
	1157	154.0	147.8	153.9	160.8	157.6	168.0	170.1	171.9
	1158	146.0	141.5	142.7	153.4	161.9	163.3	169.4	169.9
	1159	136.6	135.9	142.9	154.7	145.2	162.6	173.8	174.4
	1160	157.0	148.1	154.5	161.5	164.5	173.7	178.2	176.9

**Table C-7. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Males**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
NT20M	201	200.3	186.9	180.8	182.4	184.1	189.2	196.3	197.2
	202	210.3	194.7	180.9	190.9	198.6	207.2	217.8	218.0
	203	197.7	190.0	190.7	197.9	198.6	205.7	212.2	218.6
	204	216.2	195.6	194.6	196.4	195.4	201.0	208.3	212.4
	205	217.7	201.8	208.6	212.5	217.8	222.9	228.8	233.1
	206	197.3	177.4	177.0	181.3	185.7	189.8	200.1	208.5
	207	183.8	174.5	173.0	174.6	183.6	190.0	193.1	203.7
	208	191.4	179.5	189.1	190.0	193.2	193.3	200.5	201.4
	209	212.7	187.4	190.7	187.7	197.3	202.0	210.3	217.3
	210	207.8	194.2	195.3	202.5	203.6	206.6	221.1	226.9
PFCNTM	301	195.0	185.4	187.9	192.9	198.5	220.7	206.7	210.9
	302	207.1	198.4	201.1	203.8	210.5	234.4	223.8	228.4
	303	191.5	186.4	196.0	200.9	210.3	232.7	221.4	224.3
	304	211.5	207.3	207.4	209.7	216.9	239.3	223.8	224.2
	305	196.4	189.3	185.1	190.9	194.5	213.7	198.6	200.5
	306	215.1	209.2	204.8	207.3	208.2	229.6	212.2	217.7
	307	189.2	180.3	184.7	189.9	193.1	218.6	202.0	203.7
	308	201.7	196.5	194.4	198.0	200.6	220.4	208.1	210.1
	309	184.6	176.8	178.0	179.8	186.7	205.1	192.7	193.4
	310	215.9	210.4	214.6	215.7	218.1	244.4	225.3	225.5
B20M	701	196.1	176.3	185.2	189.9	193.5	201.8	202.1	211.3
	702	192.1	180.1	188.2	190.7	198.0	197.9	202.5	202.4
	703	195.8	176.8	174.8	176.6	183.4	184.9	188.6	193.7
	704	190.2	178.2	184.4	188.8	197.9	204.8	211.5	220.7
	705	225.5	202.4	187.6	179.6	178.6	180.3	186.7	191.5
	706	210.3	195.3	192.6	195.9	195.8	198.6	200.1	197.4
	707	177.0	162.0	165.1	173.4	178.3	180.6	191.9	197.3

**Table C-7. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Males**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
B20M	708	202.1	178.5	170.0	173.3	173.9	175.4	184.5	190.8
	709	229.7	202.9	206.4	217.9	217.4	218.9	228.2	233.4
	710	186.6	169.7	165.4	174.8	182.1	189.7	194.9	195.5
PFCBM	801	196.7	201.5	199.3	206.7	215.5	235.0	225.1	228.8
	802	203.9	208.0	205.5	213.6	221.4	239.5	231.1	233.1
	803	184.7	184.6	185.8	190.1	202.8	218.2	209.1	209.7
	804	220.9	223.8	209.0	212.7	217.2	242.9	225.4	225.5
	805	209.6	216.4	202.9	210.7	217.6	238.2	224.7	225.2
	806	182.5	189.9	179.3	189.4	194.9	211.7	201.0	203.2
	807	205.5	207.0	205.6	212.3	218.0	243.4	229.3	231.0
	808	181.1	188.6	180.8	189.1	196.4	217.1	214.2	216.6
	809	209.2	208.7	204.5	214.1	223.8	241.7	226.4	223.1
	810	207.8	216.8	204.8	208.4	215.3	232.4	227.2	230.7
E20M	1201	211.4	193.3	190.9	196.7	200.9	203.6	205.7	207.7
	1202	196.7	185.8	176.8	189.1	191.2	192.1	194.0	197.8
	1203	205.1	182.5	175.3	178.7	179.9	178.4	185.0	189.0
	1204	192.0	174.4	173.0	172.0	167.3	165.7	170.1	167.3
	1205	206.3	195.7	187.5	193.4	195.9	198.8	209.8	212.8
	1206	226.0	198.5	197.0	199.3	200.9	203.9	210.2	214.1
	1207	214.5	189.3	186.1	192.0	197.3	200.2	211.3	221.8
	1208	189.6	176.9	173.9	180.4	184.0	185.3	189.8	195.5
	1209	207.8	192.7	196.5	197.7	201.1	207.6	216.9	225.0
	1210	212.6	190.7	190.4	193.0	199.1	198.8	204.5	211.5
PFCBM	1301	202.6	217.1	205.4	208.7	219.0	226.4	224.5	223.7
	1302	182.9	199.2	186.3	190.7	202.9	211.4	215.7	216.7
	1303	191.2	208.7	197.6	199.9	211.1	223.8	223.1	227.1
	1304	191.9	211.5	197.8	201.5	207.0	217.6	216.3	220.7

**Table C-7. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>							
		<b>1</b>	<b>4</b>	<b>8</b>	<b>11</b>	<b>15</b>	<b>18</b>	<b>22</b>	<b>25</b>
PFCEM	1305	222.7	242.3	217.6	216.6	223.5	232.5	228.0	231.5
	1306	185.4	201.4	191.3	193.2	202.0	215.9	215.4	218.8
	1307	215.9	234.8	217.3	219.9	227.8	238.7	240.1	239.4
	1308	207.4	220.4	198.1	199.5	208.3	215.0	219.2	218.0
	1309	216.5	235.3	220.2	224.6	236.3	253.6	242.2	247.7
	1310	199.6	214.8	198.8	203.8	209.5	220.1	221.3	225.3

**Table C-8. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Females**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
NT20F	251	148.4	131.7	128.0	129.7	133.8	138.8	134.4	138.9
	252	159.7	140.7	142.6	141.4	145.9	145.5	148.7	154.3
	253	147.8	129.5	123.0	122.6	130.5	134.2	139.3	142.3
	254	144.9	136.3	132.1	141.0	143.5	141.6	142.7	144.3
	255	155.2	141.0	137.0	141.2	145.3	143.3	149.3	154.1
	256	150.7	144.3	140.9	146.5	148.7	147.5	156.3	161.4
	257	141.1	122.7	123.3	123.7	125.6	125.1	132.8	138.0
	258	150.9	128.0	121.0	119.9	121.8	116.5	124.6	127.1
	259	145.9	127.6	129.5	135.6	141.6	138.7	151.4	157.0
	260	140.6	127.1	120.9	125.3	129.5	127.7	131.7	137.0
PFCNTF	351	161.7	163.2	147.1	148.2	145.5	161.1	162.2	164.9
	352	132.2	137.6	123.0	124.9	123.9	141.2	144.8	144.7
	353	145.6	153.6	136.2	138.4	137.3	155.6	151.7	152.0
	354	165.0	164.9	150.0	150.4	146.8	164.4	161.9	161.2
	355	148.0	149.9	133.6	132.8	133.6	153.5	149.2	150.0
	356	154.9	156.0	138.5	139.7	139.1	150.5	152.9	152.7
	357	153.4	157.4	144.4	146.5	147.9	164.7	164.7	165.9
	358	150.1	154.9	135.4	134.0	133.4	151.4	152.7	153.0
	359	145.2	145.0	131.8	131.7	132.7	145.0	152.6	153.3
	360	154.3	160.5	141.9	139.9	139.9	160.5	158.0	157.1
B20F	751	144.3	131.1	120.9	123.4	126.2	132.7	130.2	133.0
	752	160.4	142.1	129.2	129.2	131.8	132.0	134.2	133.5
	753	156.3	140.6	134.1	134.6	132.9	136.3	134.5	138.3
	754	149.5	134.3	125.7	126.7	129.5	128.6	129.9	133.2
	755	140.8	123.0	117.2	119.3	118.8	118.0	125.4	130.2
	756	139.2	123.8	110.5	107.4	108.1	112.7	113.6	116.1
	757	143.6	122.5	109.7	104.4				

**Table C-8. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Females (Continued)**

Group	Animal ID	Day							
		1	4	8	11	15	18	22	25
B20F	758	148.9	131.8	128.4	130.5	130.0	128.7	133.2	138.4
	759	149.2	129.6	133.9	136.1	135.1	137.6	135.1	138.7
	760	140.4	122.0	120.6	131.2	141.9	139.7	146.9	146.4
PFCBF	851	145.0	152.5	145.9	147.7	146.2	159.8	165.5	161.2
	852	153.2	156.0	152.6	150.9	154.9	157.9	165.4	165.1
	853	145.1	152.1	147.3	147.8	149.3	155.5	164.0	161.0
	854	145.6	152.5	145.7	148.1	146.9	161.0	163.1	161.4
	855	141.6	144.6	141.4	140.1	143.6	153.0	164.3	159.2
	856	148.0	155.6	147.1	146.9	146.3	155.6	162.4	161.9
	857	160.7	168.0	160.9	162.2	158.8	171.9	180.6	177.4
	858	160.5	165.2	151.6	151.7	150.5	164.2	165.8	165.4
	859	156.8	160.3	155.1	155.0	153.6	162.9	169.7	166.0
	860	142.1	152.7	147.8	150.6	147.8	159.3	167.2	162.1
E20F	1251	153.5	135.7	129.6	126.6	125.5	125.6	126.6	129.4
	1252	162.5	141.8	136.4	134.9	129.1	129.5	124.7	126.5
	1253	137.1	123.6	120.6	124.6	127.7	133.1	134.2	134.0
	1254	141.1	122.6	113.3	121.6	123.7	122.2	126.8	130.9
	1255	159.7	143.4	138.6	142.6	147.3	147.7	147.7	152.0
	1256	157.9	139.8	134.1	138.1	134.8	135.3	141.2	146.6
	1257	154.1	136.5	130.4	129.2	124.8	122.4	121.9	123.4
	1258	153.3	137.2	133.0	128.2	126.4	129.5	129.9	133.1
	1259	146.4	132.1	128.7	126.5	139.2	144.5	148.2	148.7
	1260	145.7	129.9	125.9	128.8	130.1	129.0	128.3	135.6
PFCEF	1351	149.5	156.2	140.4	145.7	145.5	158.0	159.0	160.4
	1352	165.1	168.6	150.1	151.6	149.3	167.4	164.4	166.2
	1353	144.2	148.7	133.0	137.8	135.4	152.7	149.8	150.4
	1354	155.5	159.0	141.4	148.3	147.4	158.9	156.3	159.7

**Table C-8. Pairfed and High Dose Group Individual Animal Body Weight (g) Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>							
		<b>1</b>	<b>4</b>	<b>8</b>	<b>11</b>	<b>15</b>	<b>18</b>	<b>22</b>	<b>25</b>
PFCEF	1355	158.4	165.8	145.0	146.1	145.3	157.5	155.6	160.2
	1356	159.6	164.4	142.6	147.7	146.9	163.5	159.3	164.1
	1357	140.7	144.2	130.1	134.6	134.9	150.2	146.6	149.7
	1358	147.1	156.6	137.5	143.5	140.9	157.3	156.0	158.7
	1359	145.7	149.2	135.3	141.2	143.9	160.6	162.1	161.4
	1360	137.5	137.7	124.7	132.6	133.0	150.2	144.4	149.8

**Table C-9. TK Individual Animal Body Weight (g) Data – Males**

Group	Animal ID	Day				
		1	8	15	22	28
NT20M	211	165.5	160.4	166.2	174.8	188.3
	212	153.0	152.7	156.6	175.4	178.8
	213	161.9	155.7	157.7	170.8	180.2
	214	185.8	170.4	164.7	170.9	183.0
	215	171.0	162.1	171.2	180.4	198.8
	216	177.5	165.5	172.2	179.6	189.7
B0.2M	411	162.9	203.2	240.0	271.6	293.8
	412	175.5	213.7	246.4	277.4	289.9
	413	154.6	199.1	228.4	261.7	281.8
	414	188.6	223.4	243.0	263.7	283.5
	415	155.8	195.0	226.5	257.2	274.3
	416	184.4	217.9	243.5	267.7	282.7
B2M	511	180.6	220.0	252.3	277.0	297.9
	512	160.3	193.4	227.4	252.0	267.9
	513	182.5	217.4	240.1	268.3	286.6
	514	158.8	196.2	230.5	256.8	278.2
	515	149.5	184.7	209.5	241.1	256.8
	516	158.9	189.3	210.1	228.4	236.6
B8M	611	168.9	199.4	216.1	237.4	252.5
	612	164.1	180.5	191.0	210.1	219.9
	613	187.9	201.1	223.3	249.5	260.8
	614	168.2	183.1	203.5	222.3	244.8
	615	188.2	213.3	228.1	248.5	268.5
	616	163.1	180.4	193.3	229.6	245.2
B20M	711	166.0	139.4	135.9	141.6	142.9
	712	167.9	141.1	146.4	157.7	164.6
	713	185.7	180.8			

**Table C-9. TK Individual Animal Body Weight (g) Data – Males (Continued)**

Group	Animal ID	Day				
		1	8	15	22	28
B20M	714	178.3	174.9	191.4	208.9	222.0
	715	186.0	167.7	163.9	172.0	180.7
	716	173.8	161.0	166.0	174.8	188.8
E0.2M	911	182.0	221.4	251.1	287.5	302.8
	912	168.0	206.8	237.3	265.9	283.7
	913	189.6	224.5	247.3	272.6	283.1
	914	150.3	187.9	222.2	247.5	264.4
	915	173.3	217.0	244.8	277.8	297.6
	916	176.9	217.9	256.0	278.7	305.9
E2M	1011	157.5	187.5	211.0	236.9	256.3
	1012	187.2	221.0	252.9	276.8	296.7
	1013	177.9	218.6	222.1	272.0	294.5
	1014	187.7	219.0	249.9	269.9	289.0
	1015	170.5	203.7	236.4	265.6	283.8
	1016	165.6	202.3	234.3	264.7	289.2
E8M	1111	178.6	185.1	198.1	218.6	239.8
	1112	184.3	200.2	218.1	237.9	257.8
	1113	187.6	203.3			
	1114	167.6	191.3	205.8	238.0	257.7
	1115	154.8	175.2	189.6	217.3	230.1
	1116	163.8	188.9	204.4	227.2	250.7
E20M	1211	150.5	127.7	124.0	118.2	116.6
	1212	173.8	175.2	175.7	190.6	188.3
	1213	160.8	143.8	140.4	143.8	142.8
	1214	162.2	146.4	146.0	152.9	144.5
	1215	170.0	149.4	147.5	150.7	148.3
	1216	161.2	141.1	145.1	145.8	141.5

**Table C-10. TK Individual Animal Body Weight (g) Data – Females**

Group	Animal ID	Day				
		1	8	15	22	28
NT20F	261	143.2	121.6	125.2	133.8	140.3
	262	143.8	125.8	126.5	133.9	146.1
	263	150.7	127.5	132.8	136.4	148.6
	264	124.9	116.1	122.4	133.3	133.9
	265	140.0	124.5	124.9	135.3	144.2
	266	137.3	125.0	125.9	130.8	142.2
B0.2F	461	126.8	146.5	154.1	162.8	176.7
	462	141.7	160.3	168.9	176.9	198.5
	463	147.6	170.7	179.2	185.9	198.6
	464	144.7	157.3	162.0	170.9	182.3
	465	144.2	160.1	173.7	187.1	200.7
	466	139.8	158.7	166.2	182.3	182.7
B2F	561	138.6	144.7	162.0	171.5	178.2
	562	147.2	157.9	166.4	176.1	180.3
	563	144.5	150.3	168.8	181.6	193.9
	564	140.9	149.3	149.3	159.2	164.4
	565	140.6	149.3	156.4	171.8	174.2
	566	139.1	143.8	156.8	169.5	173.3
B8F	661	137.7	132.7	139.6	153.6	163.6
	662	150.5	141.2	159.9	170.9	177.1
	663	133.1	124.9	131.5	138.5	147.6
	664	148.3	135.9	145.6	165.0	174.2
	665	134.9	127.4	135.8	146.4	154.2
	666	130.8	135.2	137.3	154.9	158.3
B20F	761	154.0	124.3	123.3	127.0	132.9
	762	146.2	126.9	121.8	130.0	135.4
	763	134.5	114.1	113.5	121.5	127.1

**Table C-10. TK Individual Animal Body Weight (g) Data – Females (Continued)**

Group	Animal ID	Day				
		1	8	15	22	28
B20F	764	146.4	120.9	117.9	124.8	131.4
	765	152.9	125.9	124.4	129.1	132.0
	766	140.0	120.2	116.6	120.0	124.0
E0.2F	961	130.0	140.3	155.5	159.5	172.7
	962	137.2	146.7	159.7	166.6	183.6
	963	135.9	153.9	162.7	176.9	184.6
	964	147.0	162.3	169.8	182.8	191.6
	965	153.4	161.0	160.1	169.4	174.9
	966	147.0	162.7	171.4	184.5	191.2
E2F	1061	142.7	148.5	157.0	166.4	176.4
	1062	138.2	147.6	153.4	170.8	176.1
	1063	135.6	147.2	155.4	164.2	173.9
	1064	132.9	158.4	159.5	170.5	175.8
	1065	144.5	157.2	155.4	173.2	177.9
	1066	141.8	147.8	143.6	159.9	164.7
E8F	1161	143.7	136.6	145.7	164.7	162.9
	1162	140.4	140.9	146.7	156.6	161.4
	1163	123.7	125.6	139.1	151.1	162.1
	1164	135.0	131.8	143.7	153.2	161.5
	1165	135.2	130.0	135.8	160.9	163.6
	1166	133.5	128.4	137.2	142.5	151.2
E20F	1261	140.0	125.1	124.2	130.5	142.6
	1262	142.6	112.8	109.9	108.3	106.4
	1263	133.8	120.9	125.9	135.1	138.6
	1264	155.3	124.2	130.7	144.0	140.6
	1265	124.3	119.6	121.2	128.2	127.2
	1266	147.3	120.5	126.3	129.9	130.8

**Table C-11. Individual Animal Feed Consumed (g) per Day Data – Males**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
CM	101	25.1	22.6	25.5	14.8	26.5	27.6	22.7	27.3
	102	23.5	25.3	22.8	15.6	27.8	32.5	23.8	37.1
	103	22.3	23.8	25.1	15.0	29.0	26.8	26.1	26.9
	104	20.8	22.4	23.9	16.8	24.1	24.5	22.7	23.5
	105	24.7	25.9	25.7	22.9	29.4	28.2	25.7	26.6
	106	23.3	22.4	26.6	22.1	23.2	22.4	22.8	23.3
	107	20.3	20.3	20.2	13.9	23.4	21.9	18.8	18.4
	108	24.2	26.5	24.4	16.0	26.1	25.4	24.0	23.5
	109	24.2	23.1	28.2	18.7	23.1	24.4	22.0	25.1
	110	22.3	23.6	23.2	18.4	24.0	24.2	23.4	28.0
B0.2M	401	18.1	19.3	18.3	12.4	20.9	19.3	17.1	17.8
	402	24.0	22.3	27.5	14.8	28.8	25.4	24.5	24.6
	403	22.7	23.6	22.0	14.4	24.9	24.3	23.0	22.2
	404	21.3	21.7	21.3	31.7	23.2	33.2	21.4	25.8
	405	25.7	23.4	29.4	23.3	28.1	26.2	24.4	25.8
	406	26.1	25.3	26.8	26.8	28.9	29.0	26.9	28.5
	407	21.2	22.8	24.0	23.9	29.7	26.6	21.6	23.4
	408	18.7	19.6	19.2	15.0	24.2	23.2	20.3	20.4
	409	20.9	22.1	22.9	15.4	26.8	23.8	22.4	21.9
	410	24.5	24.8	25.2	20.0	27.0	26.5	25.1	24.8
B2M	501	19.2	20.1	21.0	13.0	25.0	24.6	21.8	22.8
	502	23.5	26.0	24.7	19.9	28.5	29.6	21.9	28.0
	503	18.6	18.7	18.8	12.7	20.5	17.7	18.3	16.9
	504	23.9	20.8	22.3	17.8	24.9	23.5	20.7	24.5
	505	21.4	23.4	22.9	21.0	27.4	26.1	24.4	26.0
	506	22.0	22.1	23.9	22.6	21.8	24.6	24.2	26.3
	507	18.2	20.8	19.8	12.7	21.8	22.0	19.6	21.1

**Table C-11. Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
B2M	508	20.3	20.7	18.9	15.1	24.6	23.0	19.3	20.1
	509	19.8	22.0	20.8	15.8	21.0	23.3	20.1	21.1
	510	21.1	23.1	21.1	15.9	23.2	24.7	20.7	22.8
B8M	601	22.6	20.2	19.7	15.1	22.5	19.8	17.3	18.5
	602	20.6	23.0	22.6	17.5	22.7	16.9	19.0	18.1
	603	18.2	16.1	19.7	14.0	20.9	18.4	19.8	19.7
	604	15.5	17.8	19.9	12.8	17.0	18.9	17.7	18.9
	605	19.7	17.6	18.4	15.6	18.5	16.8	15.9	16.6
	606	17.6	16.1	18.1	18.9	18.5	17.6	17.5	17.6
	607	28.3	15.1	12.4	9.7	17.1	15.4	14.5	14.6
	608	36.4	19.8	29.0	25.3	26.4	37.8	24.5	24.4
	609	21.3	18.4	19.9	21.7	19.7	18.4	19.7	18.5
	610	11.4	19.5	18.8	21.5	18.9	21.5	20.8	20.3
E0.2M	901	22.7	23.7	23.6	24.1	24.6	23.0	23.3	22.5
	902	26.4	20.8	29.9	27.1	25.5	26.6	24.5	24.5
	903	25.4	21.6	31.6	26.8	24.2	25.9	25.8	27.0
	904	24.6	24.2	24.1	24.1	23.1	24.7	25.1	26.4
	905	24.7	20.9	34.2	26.8	26.1	28.5	27.6	27.4
	906	28.6	26.7	33.4	31.7	28.0	30.5	30.8	28.3
	907	26.0	24.4	26.7	26.0	25.0	26.9	25.9	27.8
	908	23.3	23.6	24.5	23.7	22.5	24.3	25.0	26.3
	909	22.6	22.7	24.4	25.0	23.4	28.3	23.5	25.8
	910	25.3	19.2	27.8	25.3	22.9	25.6	21.3	20.6
E2M	1001	22.3	23.0	22.5	22.6	22.3	23.3	23.3	23.9
	1002	19.4	21.7	21.2	21.4	21.9	22.5	20.7	22.5
	1003	25.2	26.0	27.8	28.9	27.0	29.1	27.4	29.7
	1004	22.0	22.0	22.9	22.9	20.2	23.3	22.1	22.3

**Table C-11. Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
E2M	1005	24.2	21.4	27.7	25.6	25.3	25.7	25.7	25.2
	1006	24.7	25.1	25.0	25.6	24.2	27.1	24.2	24.7
	1007	22.3	22.6	21.8	24.3	21.2	25.8	22.0	26.7
	1008	17.1	17.5	19.2	18.6	18.0	18.0	17.3	17.6
	1009	22.8	23.0	24.9	23.1	20.2	22.9	23.4	22.7
	1010	23.3	22.2	26.8	25.0	24.3	26.4	25.6	26.4
E8M	1101	25.6	17.3	17.7	24.1	20.1	20.9	17.5	18.7
	1102	22.9	23.8	20.7	20.3	20.6	23.9	19.8	23.4
	1103	20.8	19.9	21.5	21.8	20.7	19.5	21.1	22.1
	1104	24.7	19.7	20.7	18.7	19.9	18.7	18.8	18.9
	1105	16.0	19.2	19.7	19.6	19.7	19.4	17.0	18.5
	1106	15.6	23.2	21.4	22.4	18.4	22.0	18.8	19.4
	1107	15.6	16.5	20.9	19.8	18.9	20.6	18.4	17.5
	1108	17.1	20.4	21.6	21.3	20.4	18.9	18.3	18.1
	1109	13.8	22.2	15.8	32.5	15.0	35.0	13.5	16.1
	1110	18.0	19.3	23.9	20.5	25.3	19.7	21.2	20.7

**Table C-12. Individual Animal Feed Consumed (g) per Day Data – Females**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
CF	151	15.5	15.8	16.2	16.0	16.3	16.1	14.7	16.8
	152	14.2	14.7	14.5	15.9	14.7	15.2	15.0	16.0
	153	19.5	17.2	16.2	16.3	16.5	17.9	15.6	17.2
	154	15.7	16.4	15.5	15.8	15.7	16.4	17.0	17.3
	155	15.1	14.9	16.1	15.8	15.9	16.8	14.0	16.4
	156	15.9	16.1	17.6	16.0	16.7	18.2	18.5	18.6
	157	14.9	15.0	16.0	17.3	14.2	17.4	15.7	18.0
	158	19.1	19.2	18.4	19.7	16.2	19.4	17.9	20.6
	159	14.2	14.2	17.0	12.4	12.4	16.2	13.8	14.6
	160	14.4	14.8	14.5	15.5	12.4	14.8	15.3	15.6
B0.2F	451	12.7	12.9	11.2	13.2	13.3	12.3	11.8	13.2
	452	15.5	16.0	15.5	16.1	17.4	17.1	15.5	16.8
	453	14.3	14.7	15.2	14.8	15.1	16.0	13.9	16.9
	454	14.4	14.4	14.4	15.1	14.4	16.5	15.2	15.0
	455	15.5	15.6	16.3	15.8	15.6	16.1	14.8	16.6
	456	13.7	14.1	14.1	15.1	14.6	16.6	14.4	15.6
	457	16.1	17.2	16.5	16.1	15.0	17.3	15.7	17.9
	458	16.4	16.5	16.2	16.3	15.1	17.4	17.6	
	459	16.2	17.4	17.2	17.4	16.1	18.5	19.0	20.1
	460	16.1	15.5	14.4	15.3	15.5	18.4	15.4	15.6
B2F	551	12.7	13.9	13.9	14.8	14.9	14.9	15.8	15.4
	552	23.3	14.8	14.0	14.4	13.5	17.2	15.1	18.1
	553	13.4	14.1	15.4	15.3	14.9	16.7	14.2	17.3
	554	13.7	13.8	14.2	14.4	13.8	16.0	14.8	15.4
	555	14.4	15.0	15.2	22.0	14.7	19.0	13.5	16.3
	556	13.9	16.0	15.5	15.6	14.8	15.7	14.8	15.9
	557	15.2	15.2	16.3	15.7	14.0	17.6	15.2	18.3

**Table C-12. Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
B2F	558	12.1	13.1	12.0	17.0	12.9	13.8	13.6	14.3
	559	13.8	16.0	16.7	16.6	14.5	17.2	14.6	15.7
	560	14.8	15.0	14.3	15.4	14.8	16.8	16.7	22.6
B8F	651	5.3	15.2	10.3	12.0	10.5	10.8	11.3	11.9
	652	40.2	10.4	12.9	23.0	11.5	12.5	10.6	11.9
	653	31.1	12.2	14.0	12.9	13.3	14.6	12.3	13.6
	654	47.1	12.2	13.3	18.7	12.9	13.2	12.4	13.9
	655	7.4	19.1	13.5	23.0	16.7	16.5	13.1	14.8
	656	18.4	12.9	15.6	17.0	13.9	17.4	14.1	14.7
	657	28.2	22.3	15.2	18.8	11.3	15.1	12.0	13.0
	658	8.7	13.5	14.5	13.1	11.1	12.8	12.1	13.3
	659	7.2	12.4	11.3	12.0	11.5	11.7	11.5	13.5
	660	6.9	10.8	12.2	13.1	12.2	13.2	12.2	14.9
E0.2F	951	15.4	16.3	13.9	17.5	14.5	16.4	14.8	16.7
	952	14.7	15.1	14.8	15.2	15.6	15.5	14.7	15.1
	953	16.0	15.4	14.8	15.1	17.2	17.3	14.0	18.1
	954	18.0	15.7	18.5	20.6	20.1	19.9	17.0	19.8
	955	18.4	18.5	17.5	18.8	18.0	19.3	17.9	18.5
	956	16.5	17.4	17.5	19.1	16.1	19.7	17.0	20.2
	957	16.6	16.4	16.9	17.6	16.5	18.4	17.2	19.7
	958	15.7	16.4	15.7	17.4	15.2	16.5	16.5	17.0
	959	20.4	17.8	18.1	30.5	18.3	17.6	27.8	16.7
	960	17.8	19.4	18.6	19.0	18.2	18.5	18.2	23.0
E2F	1051	14.5	13.7	13.0	15.8	14.3	15.4	14.2	15.5
	1052	12.7	13.9	14.1	14.5	13.8	15.4	14.0	16.8
	1053	12.7	13.7	16.1	13.4	15.2	14.8	13.5	14.4
	1054	13.7	14.4	15.1	15.4	14.9	14.8	15.2	15.7

**Table C-12. Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day							
		4	8	11	15	18	22	25	28
E2F	1055	15.9	18.0	18.5	18.8	17.8	19.1	19.4	20.7
	1056	13.4	14.3	15.9	13.3	14.1	15.5	14.1	16.3
	1057	15.6	16.3	15.2	16.0	15.5	16.2	15.1	16.2
	1058	12.9	13.2	13.1	13.5	12.3	12.7	13.8	14.2
	1059	17.9	16.8	16.5	17.1	14.7	16.5	16.6	16.4
	1060	13.6	14.8	14.5	15.1	14.8	16.3	15.0	17.1
E8F	1151	31.4	15.0	17.7	16.1	15.9	16.9	13.6	16.2
	1152	23.3	12.8	15.1	13.2	12.4	12.9	12.2	12.8
	1153	39.3	12.2	18.0	21.6	15.8	15.5	14.5	13.6
	1154	9.7	11.5	11.8	11.8	11.5	13.3	11.7	12.5
	1155	35.0	16.0	14.0	14.8	14.2	14.1	13.3	16.4
	1156	9.7	12.3	14.5	12.8	13.7	14.6	12.2	13.5
	1157	12.1	21.8	21.3	20.8	24.3	23.5	28.3	30.3
	1158	8.8	11.5	14.0	12.8	14.8	14.3	12.0	14.2
	1159	7.4	9.4	14.7	11.6	16.2	16.9	13.3	14.1
	1160	8.0	22.9	13.6	14.9	13.1	13.6	10.5	13.3

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males**

Group	Animal ID	Day								
		2	3	4	5	6	7	8	9	10
NT20M	201	14.0	31.9	20.5	19.9	15.9	14.3	12.8	9.3	11.2
	202	6.8	12.2	29.8	13.0	10.7	11.7	11.0	20.3	11.6
	203	9.2	11.1	14.8	12.1	13.2	18.6	13.7	9.8	11.4
	204	5.6	6.4	7.7	10.2	58.4	10.8	9.9	10.7	10.7
	205	12.6	7.0	11.2	11.6	14.6	19.7	16.7	12.0	14.0
	206	4.8	5.4	7.1	5.5	8.0	11.1	9.3	11.1	10.2
	207	4.8	7.5	9.8	10.0	10.1	10.9	8.5	9.7	9.8
	208	6.1	9.4	10.7	12.2	12.2	13.1	17.4	9.6	10.6
	209	4.0	1.9	4.9	4.6	8.8	27.0	41.1	9.8	8.8
	210	4.9	5.1	9.9	8.7	48.2	16.5	11.3	13.6	9.9
PFCNTM	301			7.4	10.8	12.7	10.4	20.1	16.1	15.9
	302			7.3	9.4	12.0	10.8	20.6	15.7	16.3
	303			7.5	9.9	13.0	11.5	21.0	15.8	16.3
	304			7.5	9.4	12.4	11.6	20.6	15.9	16.2
	305			7.3	10.6	11.8	10.3	20.5	16.3	16.2
	306			7.5	10.6	13.4	10.8	20.1	15.8	16.2
	307			7.5	9.2	12.3	11.3	20.0	15.7	15.9
	308			7.3	9.0	13.3	10.2	20.1	15.9	15.8
	309			7.4	9.3	13.3	10.8	20.3	15.5	16.3
	310			7.5	9.9	13.3	11.0	20.5	16.4	16.1
B20M	701	8.1	4.3	9.6	8.4	10.2	10.4	14.1	8.1	12.5
	702	6.9	35.7	11.8	11.4	10.3	15.4	12.8	12.7	12.0
	703	4.6	6.6	7.7	8.3	9.6	10.2	9.1	10.0	9.1
	704	7.3	9.2	10.3	22.6	57.4	16.3	14.2	12.1	13.3
	705	6.8	7.0	7.3	7.6	8.4	10.5	35.9	9.0	8.7
	706	4.7	11.0	12.4	14.6	26.6	18.5	28.4	32.1	26.2
	707	29.9	6.6	7.7	10.6	10.0	11.6	12.3	10.3	11.0

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day								
		2	3	4	5	6	7	8	9	10
B20M	708	63.9	29.9	10.9	10.2	8.4	10.0	9.2	10.9	9.1
	709	26.0	6.1	7.5	9.0	12.1	14.3	11.4	14.3	12.1
	710	13.2	34.3	28.2	13.8	11.6	11.0	12.1	14.3	11.5
PFCBM	801			17.1	14.2	11.9	11.1	16.5	13.5	17.0
	802			17.2	16.2	11.2	12.1	17.6	13.4	17.1
	803			17.3	16.1	11.6	11.6	17.4	12.9	17.0
	804			17.1	14.6	12.1	11.0	17.4	13.2	17.1
	805			17.2	15.4	11.2	11.0	16.9	13.6	17.1
	806			17.2	14.4	11.8	11.8	15.9	13.2	16.7
	807			17.1	15.4	11.9	11.6	16.6	13.2	17.1
	808			16.5	15.3	10.6	10.9	16.7	13.0	16.9
	809			17.1	15.7	12.1	11.6	16.3	13.8	17.4
	810			17.2	16.4	10.7	11.8	16.8	13.2	17.0
E20M	1201	93.6	24.8	7.6	10.4	9.7	12.3	10.8	9.0	10.1
	1202	29.5	35.0	25.9	47.9	25.9	18.5	10.4	17.9	11.1
	1203	5.1	6.2	7.5	6.9	10.5	8.1	9.1	9.9	7.5
	1204	5.7	9.0	5.1	9.6	8.1	8.7	9.8	8.3	7.2
	1205	66.5	38.2	13.5	14.0	10.6	12.6	10.1	12.4	12.0
	1206	47.8	6.3	7.5	13.8	24.9	14.8	13.4	14.8	12.8
	1207	6.3	35.6	12.5	12.7	11.4	15.2	12.3	11.1	10.9
	1208	11.0	10.5	9.8	10.3	37.2	21.8	10.9	14.5	13.5
	1209	7.7	6.6	10.4	11.1	13.4	16.6	13.1	11.6	10.6
	1210	23.4	4.9	5.4	8.5	10.2	10.3	12.0	8.7	11.2
PFCBM	1301			24.2	18.4	10.4	15.2	16.8	13.9	12.2
	1302			22.1	17.1	10.5	14.1	17.1	14.5	12.0
	1303			20.7	17.5	11.5	13.9	16.8	14.8	12.1
	1304			24.7	18.3	9.5	14.4	16.2	14.8	12.4

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>								
		<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
PFCEM	1305			29.7	17.3	10.6	14.2	16.3	14.0	12.2
	1306			25.3	18.2	10.4	15.2	16.0	14.5	12.1
	1307			23.8	18.1	11.4	14.0	16.3	14.0	12.5
	1308			28.1	17.2	10.7	14.8	16.4	14.2	12.1
	1309			23.6	17.4	10.2	14.0	16.6	14.2	12.1
	1310			21.9	18.7	10.2	15.2	16.3	14.9	12.2

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day								
		11	12	13	14	15	16	17	18	19
NT20M	201	9.6	10.3	11.0	31.9	19.4	11.2	10.6	11.6	11.4
	202	14.3	13.5	54.8	15.4	11.9	13.0	13.9	16.3	17.2
	203	14.6	11.5	13.8	14.7	17.4	11.3	11.8	14.8	16.0
	204	14.3	10.8	11.8	13.4	9.2	13.0	10.3	13.1	11.8
	205	12.8	15.6	19.8	16.0	16.2	14.1	10.2	13.5	13.8
	206	11.0	11.9	13.8	14.5	12.3	13.8	10.8	14.6	15.7
	207	11.1	11.1	13.8	11.4	13.2	14.1	8.5	15.2	10.9
	208	12.4	13.0	14.4	11.3	11.2	10.7	10.2	16.1	10.9
	209	9.8	11.4	13.1	13.7	10.4	11.0	8.7	13.4	13.2
	210	13.8	15.3	14.5	13.6	9.4	13.4	10.6	13.1	16.4
PFCNTM	301	12.4	11.6	10.9	12.7	18.6	15.9	13.7	13.3	11.2
	302	12.3	11.7	12.7	12.9	18.6	15.8	13.1	13.1	11.1
	303	12.4	11.1	12.5	12.9	18.7	16.0	13.7	13.0	11.2
	304	12.2	11.6	12.9	13.0	18.5	15.6	12.8	12.8	11.2
	305	12.1	11.4	12.5	12.7	18.5	15.8	13.0	12.9	11.1
	306	12.5	11.5	12.8	12.8	18.6	16.0	13.5	13.0	11.2
	307	12.4	11.4	12.5	12.6	18.2	16.3	13.2	13.6	11.5
	308	12.5	10.9	12.6	12.7	18.6	14.8	13.6	13.4	10.8
	309	12.7	10.8	12.9	12.7	18.3	15.6	14.0	12.7	11.5
	310	12.4	11.8	12.4	13.0	18.6	16.1	13.3	12.9	11.3
B20M	701	11.2	14.9	13.1	13.2	10.0	15.2	10.6	10.3	14.0
	702	11.7	14.6	15.6	36.3	11.3	13.9	13.5	11.8	17.3
	703	9.2	9.6	10.9	11.7	10.6	9.6	9.4	11.1	11.8
	704	14.4	14.6	19.1	13.7	13.6	14.2	11.0	16.8	14.1
	705	9.6	10.0	11.1	9.2	9.4	18.4	10.2	14.1	11.2
	706	20.5	22.1	71.0	38.4	14.1	45.1		31.2	16.1
	707	14.4	10.6	14.3	11.0	13.3	12.0	8.9	15.8	11.8

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day								
		11	12	13	14	15	16	17	18	19
B20M	708	10.0	10.0	10.7	10.5	9.2	12.1	10.2	12.9	12.1
	709	16.4	12.9	15.2	14.6	12.3	12.5	10.6	14.1	14.7
	710	12.4	12.9	14.8	15.8	12.3	12.0	12.0	13.7	13.3
PFCBM	801	14.1	13.4	13.0	13.6	19.8	17.7	12.5	17.1	11.4
	802	14.1	13.2	13.3	13.6	19.9	17.5	11.7	16.4	11.4
	803	14.2	13.3	13.3	13.7	19.8	18.3	11.0	17.0	11.7
	804	14.3	13.5	13.3	13.9	19.7	16.9	12.4	17.4	11.4
	805	14.4	13.1	13.1	13.5	19.6	17.9	11.7	17.3	11.5
	806	13.8	13.2	13.5	13.7	19.9	17.4	12.1	16.8	11.3
	807	14.2	13.5	13.2	13.6	20.2	17.2	12.4	16.7	11.4
	808	13.7	13.1	13.2	13.7	19.7	14.1	11.1	16.9	11.2
	809	13.7	13.3	13.1	13.7	19.9	17.9	11.3	17.2	11.4
	810	14.1	13.5	13.5	13.3	19.8	16.8	12.1	16.8	11.5
E20M	1201	11.4	10.9	11.8	12.1	12.6	11.4	12.4	12.1	10.8
	1202	11.8	14.7	11.5	15.1	12.6	13.0	11.0	13.6	11.2
	1203	9.6	11.0	9.4	9.7	9.8	9.9	9.1	9.6	9.5
	1204	8.5	7.6	13.0	12.5		12.5	12.0	13.0	19.9
	1205	11.5	16.0	15.7	13.8		13.6	12.7	15.8	15.4
	1206	11.6	13.7	12.9	11.8	14.6	12.1	11.9	14.4	14.0
	1207	11.8	12.3	105.5	30.3	12.3	10.5	9.6	17.8	13.6
	1208	11.4	10.9	12.8	12.4	11.4	10.3	10.1	11.9	12.6
	1209	13.8	13.3	12.0	12.6	13.4	12.2	12.1	14.8	14.6
	1210	11.5	13.8	13.7	12.8	12.6	10.7	7.5	13.2	13.5
PFCM	1301	12.4	11.2	11.3	13.0	22.2	14.8	13.1	12.1	11.7
	1302	12.7	11.8	11.6	12.8	22.1	14.2	12.3	12.1	11.7
	1303	12.3	11.2	11.7	12.8	21.9	14.4	11.7	12.1	11.7
	1304	12.3	11.3	11.6	13.0	22.3	14.1	12.8	12.2	11.6

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>								
		<b>11</b>	<b>12</b>	<b>13</b>	<b>14</b>	<b>15</b>	<b>16</b>	<b>17</b>	<b>18</b>	<b>19</b>
PFCM	1305	12.7	11.2	11.5	12.6	22.2	14.8	12.3	11.9	11.7
	1306	12.4	11.2	11.5	12.8	22.2	14.8	12.9	12.6	11.7
	1307	12.5	11.1	11.6	12.6	22.1	14.7	11.9	12.6	11.5
	1308	12.0	11.1	11.6	12.6	21.7	14.8	12.1	12.0	11.9
	1309	12.1	9.1	10.8	12.4	22.4	15.5	13.1	11.8	12.0
	1310	12.6	11.2	11.5	12.5	22.0	14.3	11.6	12.3	11.7

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day								
		20	21	22	23	24	25	26	27	28
NT20M	201	12.5	12.1	13.5	11.5	12.7	12.4	11.3	12.8	31.0
	202	25.1	13.5	20.1	13.5	16.4	20.3	12.3	18.5	17.3
	203	15.9	14.4	14.5	11.9	14.1	16.3	10.1	18.0	19.8
	204	12.0	14.3	11.1	10.4	13.0	13.1	11.4	11.3	10.2
	205	17.1	12.2	17.3	13.4	16.6	15.6	11.1	14.1	21.7
	206	14.2	13.5	15.3	14.4	15.5	16.9	16.8	15.9	21.4
	207	13.2	11.1	15.0	12.3	12.1	17.9	8.7	19.0	14.6
	208	14.3	11.1	13.3	11.1	13.7	13.4	10.8	13.5	16.0
	209	16.3	11.8	16.6	11.0	13.9	15.1	10.7	16.6	16.5
	210	13.5	15.0	14.1	12.5	15.0	15.4	10.8	16.6	13.7
PFCNTM	301	14.9	14.3	16.0	13.6	15.9	12.8	14.1	16.4	11.8
	302	15.1	14.4	16.0	13.0	15.9	12.6	14.5	15.7	12.4
	303	15.1	14.7	15.6	13.4	15.4	12.5	14.6	16.4	12.2
	304	14.9	14.3	16.0	13.7	15.5	13.0	14.2	16.1	12.3
	305	15.0	14.6	15.9	13.2	15.9	12.7	15.0	15.8	12.0
	306	14.9	14.4	16.1	13.8	15.9	13.1	13.6	16.6	11.8
	307	14.6	14.6	15.4	13.4	15.7	12.4	14.0	16.0	11.6
	308	14.8	14.6	16.1	13.6	15.4	11.1	15.2	16.2	11.9
	309	15.1	14.3	16.0	13.3	15.4	12.3	14.4	15.9	12.0
	310	14.8	14.3	15.8	13.4	15.9	12.9	15.1	16.0	11.7
B20M	701	18.4	10.6	18.2	10.8	18.9	14.1	16.0	17.7	15.7
	702	29.2	13.0	13.2	14.5	13.7	13.1	10.3	11.2	11.4
	703	12.9	9.6	12.1	12.1	11.5	14.5	10.3	11.7	13.5
	704	15.0	14.5	20.4	16.6	17.2	18.9	15.6	18.2	17.4
	705	12.7	10.9	11.9	11.5	13.2	14.6	11.3	13.1	12.7
	706	10.9	9.4	33.8			21.9	15.2	9.7	12.3
	707	12.3	10.5	15.5	11.5	13.7	13.7	10.7	14.2	15.1

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day								
		20	21	22	23	24	25	26	27	28
B20M	708	13.9	11.8	10.4	11.1	12.6	15.1	9.4	11.6	31.3
	709	15.9	11.2	14.2	11.8	17.5	13.3	13.1	14.6	14.0
	710	14.2	12.9	15.6	12.0	14.0	13.2	12.8	11.8	15.2
PFCBM	801	15.9	14.4	16.0	12.4	16.8	12.7	14.7	15.9	12.9
	802	15.8	14.6	15.9	12.3	17.1	12.9	15.0	15.7	13.5
	803	15.7	14.4	16.6	12.5	17.0	12.7	14.8	15.6	12.8
	804	15.8	14.6	15.8	12.3	17.0	12.8	15.1	15.8	13.0
	805	15.7	14.3	16.0	12.0	17.4	12.5	15.1	16.2	13.3
	806	15.8	14.4	15.9	12.4	17.0	13.0	14.8	15.9	12.7
	807	15.9	14.4	15.9	12.3	17.0	13.2	14.6	15.8	13.2
	808	16.1	12.8	15.6	11.9	17.1	12.4	15.4	15.5	13.1
	809	16.0	14.7	16.3	12.5	17.0	12.8	15.1	16.0	13.2
	810	15.9	14.4	16.1	14.6	17.3	13.4	14.2	15.8	13.4
E20M	1201	13.3	13.4	12.5	9.5	14.7	13.4	8.8	12.8	
	1202	14.1			11.7	13.3	14.2		49.3	22.2
	1203	12.5	10.5	13.6	8.7	12.9	10.9	9.1	12.0	12.4
	1204	11.9		28.7	12.1	13.0	32.5	45.9	14.1	13.0
	1205	23.6		30.2	18.4	18.1	17.7	23.1		20.7
	1206	15.5	12.7	15.3	11.7	17.1	14.4	11.2	14.3	14.0
	1207	87.0	13.8	18.9	13.7	19.9	20.5	13.4		18.3
	1208	32.6	27.3	26.9	13.6	13.8	12.9	11.8	12.4	15.2
	1209	17.4	10.9	15.9	12.3	17.3	13.6	13.8	13.0	14.2
	1210	12.8	12.7	12.8	13.2	14.3	14.3	10.3	13.5	13.8
PFCM	1301	14.2	14.6	24.4	15.4	20.2	13.3	15.3	16.7	17.3
	1302	14.2	14.3	24.6	15.2	20.2	12.6	15.6	17.2	17.1
	1303	14.5	14.4	24.8	15.2	19.7	13.2	15.7	17.0	17.1
	1304	14.4	14.3	24.9	15.3	19.7	13.0	15.4	16.8	16.8

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>								
		<b>20</b>	<b>21</b>	<b>22</b>	<b>23</b>	<b>24</b>	<b>25</b>	<b>26</b>	<b>27</b>	<b>28</b>
PFCEM	1305	14.1	14.2	25.0	15.1	19.9	12.7	15.7	17.1	17.0
	1306	14.4	14.3	24.9	15.4	20.1	13.2	16.4	17.2	16.8
	1307	14.4	14.5	24.6	15.4	19.9	12.7	15.5	16.5	17.1
	1308	14.6	14.5	24.7	15.0	19.7	13.2	15.6	17.2	17.1
	1309	14.4	14.0	24.0	15.4	20.1	12.6	16.2	16.7	17.1
	1310	14.3	14.6	24.6	15.1	20.1	12.6	15.1	16.4	16.6

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day	
		29	30
NT20M	201	13.6	16.1
	202	11.8	17.0
	203	11.2	16.7
	204	10.6	9.8
	205	9.4	15.0
	206	11.9	18.7
	207	8.0	14.7
	208	8.5	13.1
	209	12.7	13.5
	210	10.4	16.2
PFCNTM	301	15.9	18.3
	302	15.5	19.0
	303	15.7	19.1
	304	16.5	19.0
	305	15.4	18.9
	306	15.2	19.0
	307	16.5	18.8
	308	15.3	18.7
	309	15.2	18.6
	310	16.4	18.7
B20M	701	11.0	14.1
	702	12.2	12.5
	703	9.0	12.8
	704	14.7	19.4
	705	13.0	18.2
	706	9.4	69.3
	707	9.3	14.8

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

Group	Animal ID	Day	
		29	30
B20M	708	13.2	13.1
	709	9.6	14.6
	710	13.3	15.7
PFCBM	801	13.8	16.2
	802	14.4	16.1
	803	13.2	16.3
	804	14.0	15.9
	805	13.9	16.3
	806	13.6	16.7
	807	13.9	16.6
	808	13.0	16.6
	809	13.1	16.8
	810	13.0	17.1
E20M	1201	10.6	12.4
	1202	11.0	10.2
	1203	8.6	11.9
	1204	8.8	9.4
	1205	12.0	16.7
	1206	11.3	18.2
	1207	20.3	14.0
	1208	21.4	33.3
	1209	8.2	15.9
	1210	10.1	11.3
PFCM	1301	17.8	16.4
	1302	17.8	16.9
	1303	17.3	16.6
	1304	18.6	16.4

**Table C-13. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	
		<b>29</b>	<b>30</b>
PFCEM	1305	17.2	16.6
	1306	17.3	16.7
	1307	18.3	16.1
	1308	17.8	16.7
	1309	18.7	16.4
	1310	17.1	16.4

**Table C-14. Paired and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females**

Group	Animal ID	Day								
		2	3	4	5	6	7	8	9	10
NT20F	251	3.1	4.3	5.3	6.9	6.7	7.2	7.8	9.5	7.9
	252	96.4	8.1	8.7	12.0	9.4	10.0	10.8	7.7	9.6
	253	1.7	1.4	2.9	4.1	5.0	5.9	7.5	6.3	6.3
	254	73.8	7.3	26.5	8.3	8.0	9.7	10.0	11.6	9.2
	255	4.3	5.2	6.0	6.4	7.6	7.1	8.1	7.5	7.2
	256	5.7	8.1	9.6	26.2	18.3	10.7	9.4	14.9	9.4
	257	2.3	2.6	3.3	5.2	6.1	7.2	7.3	7.4	5.4
	258	2.6	2.1	3.6	4.7	41.5	13.1	6.4	8.7	6.4
	259	2.5	3.8	5.2	6.4	7.0	8.1	8.9	8.6	8.4
	260	3.8	5.4	6.4	6.2	6.6	8.1	7.4	7.6	7.7
PFCNTF	351			18.4	4.9	8.8	8.4	11.4	9.2	9.3
	352			13.1	5.0	7.2	8.2	12.2	8.9	9.5
	353			17.7	5.4	8.2	8.2	12.0	8.8	9.3
	354			17.7	5.8	8.6	9.5	12.0	9.6	9.7
	355			16.5	4.2	7.2	9.5	12.2	9.0	9.4
	356			16.3	5.2	8.5	8.2	12.6	9.3	9.3
	357			18.7	4.7	7.8	9.1	12.4	9.0	9.4
	358			17.1	4.0	7.4	7.9	11.6	9.8	9.3
	359			9.2	4.1	8.4	8.0	12.3	9.2	9.2
	360			14.6	4.6	8.5	8.3	11.7	8.9	9.4
B20F	751	57.6	23.7	12.4	8.4	7.4	7.3	7.7	9.3	6.6
	752	2.5	3.7	3.8	4.8	4.9	5.8	6.1	6.1	5.6
	753	3.8	4.6	5.4	6.0	7.0	6.7	6.1	7.2	6.2
	754	3.7	5.3	4.3	5.0	5.6	53.4	7.7	6.2	5.4
	755	2.8	3.4	5.5	8.9	30.7	47.6	10.7	7.5	6.1
	756	2.4	4.0	3.6	4.8	5.2	6.5	6.7	5.7	5.2
	757	6.8	31.6	36.0	15.0	13.5	9.1	7.1	5.4	5.1

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day								
		2	3	4	5	6	7	8	9	10
B20F	758	1.4	2.2	4.4	5.6	63.9	46.8	27.1	6.0	7.0
	759	77.1	5.6	6.8	7.8	7.7	8.7	8.7	8.9	8.6
	760	15.8	5.3	47.2	41.1	26.9	20.5	14.4	9.7	9.0
PFCBF	851			16.1	10.0	13.3	11.1	17.6	22.0	10.9
	852			16.6	8.2	12.8	10.6	17.7	18.6	10.9
	853			16.1	9.1	13.9	11.0	17.4	20.4	11.4
	854			14.2	8.2	12.0	10.2	17.8	21.9	11.3
	855			17.5	9.1	13.1	11.4	17.9	21.9	11.4
	856			17.6	9.9	12.5	10.6	17.8	20.5	11.5
	857			14.8	8.8	13.0	10.1	17.8	21.6	11.3
	858			17.4	8.2	12.2	10.8	18.2	22.1	11.2
	859			15.9	9.7	14.2	10.0	17.8	19.5	11.3
	860			17.4	8.2	13.2	11.1	17.4	21.9	11.3
E20F	1251	28.5	11.8	8.0	7.8	7.9	5.9	6.1	5.9	5.2
	1252	4.3	3.8	4.2	5.2	5.0	6.5	5.6	6.5	5.1
	1253	53.0	6.0	5.4	6.3	7.4	7.6	8.0	8.1	8.2
	1254	3.3	1.9	4.7	6.8	8.7	17.1	8.4	6.9	6.5
	1255	4.2	6.8	25.5	11.0	10.7	11.3	9.2	14.1	8.5
	1256	78.6	3.6	3.5	5.8	6.9	7.6	7.1	7.8	7.1
	1257	44.3	31.9	6.4	6.2	6.1	6.4	6.9	17.4	14.6
	1258	6.2	9.0	4.4	7.1	9.4	9.0	18.9	6.2	5.7
	1259	10.1	11.7	7.6	9.5	12.6	14.6	10.0	9.4	8.1
	1260	27.9	6.2	5.5	6.4	17.6	11.1	20.7	33.9	14.7
PFCEF	1351			18.7	9.9	7.5	8.1	9.8	10.0	11.2
	1352			18.8	9.4	6.9	8.0	9.4	10.5	11.4
	1353			19.3	9.6	7.5	7.8	9.8	10.1	11.2
	1354			17.2	10.1	8.5	7.7	9.3	10.5	11.0

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day								
		2	3	4	5	6	7	8	9	10
PFCEF	1355			16.7	10.2	6.9	7.8	9.6	10.4	11.2
	1356			20.4	8.8	7.2	7.3	10.0	10.2	11.0
	1357			16.7	10.1	7.0	6.7	9.6	10.1	11.2
	1358			17.8	9.8	7.1	6.4	10.3	10.1	11.4
	1359			15.9	8.9	7.8	7.1	9.2	10.1	11.2
	1360			15.8	9.2	6.8	7.7	9.3	10.7	11.1

**Table C-14. Paired and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day								
		11	12	13	14	15	16	17	18	19
NT20F	251	10.0	10.6	11.2	20.0	28.2	10.7	11.7	24.6	
	252	11.2	16.0	11.9	52.4	39.5	12.7	26.8	52.0	15.5
	253	7.1	9.3	9.0	8.8	9.4	14.7	9.1	12.5	12.0
	254	12.3		19.7	19.7	14.4	26.9	9.5	26.9	
	255	10.9	10.2	7.4	10.9	9.2	8.1	8.4	11.9	10.6
	256	10.4	12.3	10.0	11.8	8.7	22.6	9.0	8.0	15.1
	257	7.0	7.5	7.1	7.2	8.4	7.4	7.6	9.3	10.6
	258	5.9	15.5	9.3	8.6	9.6	7.5	8.4	6.7	10.9
	259	9.1	11.0	11.3	11.7	10.8	9.5	10.0	10.0	11.7
	260	8.1	10.7	8.5	9.3	10.0	8.7	9.6	7.8	9.6
PFCNTF	351	9.7	8.0	9.8	11.7	11.2	16.5	15.2	13.3	11.7
	352	9.9	8.8	9.6	12.0	10.8	16.7	15.4	13.5	11.8
	353	9.9	8.4	9.3	11.9	10.9	16.2	15.3	13.4	11.9
	354	9.7	8.7	9.2	11.7	11.2	16.2	15.3	14.0	11.5
	355	9.6	8.6	9.7	11.6	11.1	16.3	14.7	13.3	11.8
	356	9.8	8.1	9.6	12.0	10.7	16.9	15.3	13.4	11.8
	357	9.5	8.6	9.3	11.9	11.3	15.9	14.4	13.4	11.5
	358	9.6	8.7	9.6	11.8	11.0	16.6	14.2	13.1	11.5
	359	8.9	3.6	9.6	11.9	11.3	16.4	14.1	13.5	11.7
	360	10.0	6.8	9.4	11.7	11.2	16.9	14.7	13.7	11.7
B20F	751	7.2	8.9	10.5	8.7	8.7	7.2	8.4	12.0	8.3
	752	6.3	6.8	7.8	7.8	8.1	6.3	7.3	8.8	5.4
	753	7.9	8.8	7.9	8.5	6.8	8.2	7.0	7.6	7.1
	754	6.7	7.9	8.6	8.2	9.4	8.7	6.9	12.2	12.6
	755	7.8	8.5	8.4	7.9	8.3	7.4	8.7	8.7	10.6
	756	5.9	14.2	1.3	7.4	7.2	10.6	10.6	6.1	8.7
	757	4.8	36.1	5.5						

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day								
		11	12	13	14	15	16	17	18	19
B20F	758	9.0	29.2	39.4	72.4	14.8	11.5	9.3	13.9	13.0
	759	10.2	12.3	16.9	12.0	32.4	9.3	10.1	8.9	19.9
	760	10.8	9.5	22.0	11.1	12.8	10.2	15.6	9.8	11.2
PFCBF	851	7.8	7.1	8.0	14.6	13.5	15.7	11.5	9.3	9.9
	852	7.8	7.4	8.1	14.5	13.5	16.4	12.5	9.5	9.8
	853	8.1	7.1	8.1	14.7	13.8	16.8	12.7	9.1	9.9
	854	7.9	7.4	8.0	14.5	13.0	16.3	12.5	9.1	9.8
	855	7.9	7.4	8.0	14.7	13.3	16.2	11.9	9.4	9.9
	856	8.0	7.0	7.7	14.7	13.4	16.8	12.8	9.3	9.7
	857	7.9	7.4	8.0	14.3	12.9	15.9	12.1	9.2	10.1
	858	7.8	7.2	8.3	14.6	12.9	15.6	12.2	9.4	10.1
	859	7.7	7.2	8.1	12.8	13.5	15.7	12.9	9.8	9.8
	860	7.9	7.1	7.7	14.7	13.3	16.2	12.4	9.3	10.0
E20F	1251	6.9	7.5	7.6	7.8	8.5	7.1	7.4	7.8	7.9
	1252	6.5	7.7	7.5	8.2	7.8	9.0	6.6	8.0	6.5
	1253	9.4	10.5	8.2	10.2	9.2	9.1	10.8	10.2	8.6
	1254	7.5	9.1	7.5	9.1	8.7	8.2	7.4	8.7	10.8
	1255	11.8	12.2	9.0	15.2		36.1		27.9	16.8
	1256	8.1	8.9	9.9	8.0	9.2	10.5	12.6	9.5	10.9
	1257	15.8	22.1	19.3	10.0	10.4	34.1	20.7	12.5	12.9
	1258	7.1	8.4	9.0	8.7	13.1	9.0	11.6	8.5	9.3
	1259	9.1	9.4	9.4	9.3	25.1	12.0	10.7	15.9	41.8
	1260	8.2	10.8	37.9	31.1	32.5	23.9		29.9	27.1
PFCEF	1351	12.3	9.0	9.5	11.1	13.2	11.9	14.3	16.7	12.0
	1352	12.4	8.9	9.3	11.2	13.3	12.2	14.7	16.4	11.8
	1353	12.0	9.0	9.2	11.4	13.2	12.4	13.2	16.7	11.9
	1354	12.0	9.3	9.1	11.2	13.0	11.7	13.4	16.4	11.8

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>								
		<b>11</b>	<b>12</b>	<b>13</b>	<b>14</b>	<b>15</b>	<b>16</b>	<b>17</b>	<b>18</b>	<b>19</b>
PFCEF	1355	12.0	8.8	9.3	11.4	12.8	11.7	14.1	16.5	11.9
	1356	12.4	9.1	9.0	11.2	12.7	12.1	13.5	16.4	11.8
	1357	12.0	9.2	9.2	11.3	13.0	12.1	13.5	16.3	11.9
	1358	11.8	8.8	9.3	11.3	13.3	11.3	14.1	16.5	11.9
	1359	12.5	9.2	9.3	11.2	13.2	11.3	14.3	16.7	11.8
	1360	12.3	9.0	9.2	11.2	13.1	11.1	14.5	16.4	11.6



**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day								
		20	21	22	23	24	25	26	27	28
B20F	758	13.6	7.9	22.5	9.5	12.0	9.9	9.9	11.9	9.0
	759	36.6	47.9	13.5	10.4	17.4	13.9	42.3	31.0	12.9
	760	13.1	11.2		28.3	35.7		25.5	14.4	12.9
PFCBF	851	10.8	11.5	26.5	14.4	15.9	11.1	14.0	11.1	14.3
	852	10.6	11.7	22.9	13.6	16.0	11.2	14.5	11.0	14.5
	853	10.4	11.5	24.7	14.3	16.5	11.2	14.4	11.2	14.6
	854	10.8	11.7	26.4	14.1	15.6	11.5	13.4	11.1	14.4
	855	10.7	11.8	26.5	14.5	15.8	11.5	13.9	11.4	14.0
	856	10.7	11.8	23.6	13.5	15.1	11.8	13.1	11.1	14.4
	857	10.4	11.7	25.8	14.6	16.1	11.1	14.1	10.9	13.9
	858	10.7	11.6	26.5	14.7	15.8	11.6	12.7	10.9	14.0
	859	10.5	11.6	24.0	14.2	16.5	11.2	13.8	11.5	14.1
	860	10.6	11.8	26.9	14.7	15.9	11.2	13.3	11.5	14.1
E20F	1251	9.7	8.2	7.1	7.5	8.3	9.3	8.8	9.3	9.5
	1252	9.3	11.2	8.7	8.7	9.5	10.5	17.1	16.1	11.3
	1253	11.0	9.9	9.3	10.4	10.0	7.0	10.7	9.9	10.6
	1254	9.0	10.2	10.4	9.6	11.4	12.1	11.4	8.7	14.7
	1255	13.0	9.3	14.9	20.7	18.4		33.9	13.4	13.8
	1256	12.2	9.9	27.9	9.3	12.1	12.8	11.2	10.4	12.2
	1257	10.8	12.5	21.6	39.7	28.1	44.5	20.6	17.3	12.4
	1258	10.9	8.4	9.9	8.5	11.4	10.2	8.0	10.5	9.9
	1259	18.8	15.2	12.5	11.7	13.9	12.7	18.9	16.7	24.0
	1260	17.0	17.3	12.4		56.1	28.8	32.6	25.5	18.9
PFCEF	1351	14.7	16.1	12.9	11.3	14.5	14.4	18.7	17.3	18.2
	1352	14.9	16.0	13.0	11.8	14.4	14.6	18.4	17.3	17.7
	1353	14.6	16.1	12.7	12.0	13.8	14.7	18.5	17.3	18.2
	1354	14.6	16.1	12.4	12.2	14.2	14.5	18.1	17.1	18.4

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>								
		<b>20</b>	<b>21</b>	<b>22</b>	<b>23</b>	<b>24</b>	<b>25</b>	<b>26</b>	<b>27</b>	<b>28</b>
PFCEF	1355	14.6	16.1	12.8	11.7	13.8	14.9	18.6	17.1	17.7
	1356	14.6	16.1	12.9	11.7	13.8	14.7	18.1	16.7	17.8
	1357	14.6	15.9	12.3	12.3	13.8	14.8	18.6	16.6	18.0
	1358	14.4	16.0	12.8	11.6	13.7	14.2	17.8	17.0	17.6
	1359	14.6	16.0	13.0	12.1	13.9	14.5	18.8	16.7	16.6
	1360	14.6	16.2	12.6	12.0	14.0	14.1	18.4	17.2	17.8

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day		
		29	30	31
NT20F	251	9.6	11.7	8.7
	252	14.6	11.6	9.8
	253	7.9	9.5	10.1
	254		41.1	12.9
	255	11.3	10.4	10.8
	256	8.3	36.4	8.9
	257	8.1	10.7	9.1
	258	9.3	9.7	8.3
	259	7.3	11.3	8.1
	260	8.2	10.1	7.4
PFCNTF	351	12.6	13.7	9.8
	352	12.3	14.1	9.9
	353	12.7	13.3	9.7
	354	12.1	13.5	10.1
	355	12.9	13.3	9.7
	356	11.8	13.9	9.6
	357	12.2	13.7	9.7
	358	12.3	13.6	9.7
	359	13.0	13.7	10.0
	360	12.5	13.4	9.6
B20F	751	7.5	9.6	7.4
	752	7.1	9.4	6.3
	753	5.4	9.0	9.5
	754	8.7	10.7	10.3
	755	8.8	10.1	9.4
	756	7.1	9.9	8.2
	757			

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

Group	Animal ID	Day		
		29	30	31
B20F	758	9.5	10.1	16.5
	759	20.6	12.2	8.2
	760	8.5	11.2	9.3
PFCBF	851	13.6	12.7	10.1
	852	13.9	12.6	9.5
	853	14.0	12.7	10.0
	854	13.5	12.6	10.1
	855	13.7	12.7	9.4
	856	14.7	12.7	10.0
	857	14.9	12.5	9.6
	858	13.4	12.6	9.7
	859	13.5	12.7	9.5
	860	13.6	12.9	9.8
E20F	1251	7.4	9.0	8.9
	1252	8.6	10.2	9.5
	1253	8.3	9.4	8.0
	1254	8.3	8.3	11.1
	1255	8.5	9.4	9.4
	1256	9.4	8.7	15.6
	1257	10.5	10.5	7.1
	1258	7.5	10.5	7.8
	1259	40.9	12.0	10.8
	1260	9.2	7.5	6.5
PFCEF	1351	13.8	13.6	10.5
	1352	14.1	14.5	12.2
	1353	13.9	14.5	12.5
	1354	13.2	14.3	12.4

**Table C-14. Pairfed and High Dose Group Individual Animal Feed Consumed (g) per Day Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>		
		<b>29</b>	<b>30</b>	<b>31</b>
PFCEF	1355	13.5	14.4	12.5
	1356	13.1	14.5	12.2
	1357	14.0	14.4	12.3
	1358	13.2	14.2	12.4
	1359	13.9	14.3	12.8
	1360	13.6	14.4	12.2

**Table C-15. Individual Animal Hematology Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
CM	101	29	8.54	15.5	49.1
	102	29	8.71	15.4	49.7
	103	29	7.64	14.8	43.7
	104	29	8.23	14.8	47.7
	105	29	8.52	15.0	48.4
	106	29	8.76	16.2	51.3
	107	29	9.23	16.7	51.6
	108	29	9.66	17.8	55.6
	109	29	8.61	14.8	47.0
	110	29	8.77	15.5	48.5
B0.2M	401	29	8.72	15.9	48.2
	402	29	7.90	14.2	44.1
	403	29	8.84	15.4	49.0
	404	29	8.91	16.1	51.2
	405	29	9.63	17.4	55.3
	406	29	8.73	17.3	50.9
	407	29	8.94	15.5	49.3
	408	29	9.25	16.4	51.4
	409	29	8.29	14.8	47.0
	410	29	8.22	15.7	45.3
B2M	501	29	8.13	14.3	45.1
	502	29	8.60	16.4	49.2
	503	29	9.13	16.4	51.3
	504	29	8.77	16.0	48.4
	505	29	8.78	15.7	47.9
	506	29	8.49	15.8	49.6
	507	29	8.86	15.9	49.7

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
B2M	508	29	8.59	16.2	49.8
	509	29	9.18	16.4	51.4
	510	29	9.40	15.6	50.5
B8M	601	29	8.76	16.3	50.6
	602	29	8.85	16.3	49.5
	603	29	8.54	15.7	47.7
	604	29	8.62	14.9	47.8
	605	29	8.81	15.0	46.7
	606	29	9.34	16.3	51.7
	607	29	9.26	16.0	49.6
	608	29	9.18	16.9	51.3
	609	29	8.42	14.9	46.3
	610	29	8.87	15.5	49.2
E0.2M	901	29	8.68	15.5	47.9
	902	29	8.25	14.9	47.5
	903	29	8.06	14.7	46.0
	904	29	7.51	15.3	45.8
	905	29	8.48	15.6	49.4
	906	29	8.72	16.2	48.4
	907	29	8.34	14.7	46.8
	908	29	9.04	15.6	49.3
	909	29	8.41	15.3	47.2
	910	29	9.00	16.7	48.5
E2M	1001	29	8.30	15.8	48.0
	1002	29	8.83	15.6	50.3
	1003	29	8.55	14.8	47.3
	1004	29	8.61	15.8	50.3

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
E2M	1005	29	8.84	15.4	49.1
	1006	29	8.57	15.6	49.6
	1007	29	8.06	15.3	45.8
	1008	29	8.58	16.3	49.6
	1009	29	9.60	17.1	52.7
	1010	29	10.37	18.4	58.6
E8M	1101	29	9.08	16.3	51.4
	1102	29	8.93	15.8	48.9
	1103	29	8.39	15.4	45.5
	1104	29	8.91	17.0	52.3
	1105	29	10.32	17.5	54.7
	1106	29	8.92	16.3	50.9
	1107	29	9.63	16.4	50.6
	1108	29	9.07	16.6	51.5
	1109	29	9.06	15.3	48.1
	1110	29	9.56	17.1	52.5

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
CM	101	29	57.5	18.1	31.5
	102	29	57.1	17.7	31.0
	103	29	57.2	19.3	33.7
	104	29	58.0	18.0	31.0
	105	29	56.9	17.6	31.0
	106	29	58.6	18.5	31.5
	107	29	55.9	18.1	32.4
	108	29	57.6	18.4	32.0
	109	29	54.6	17.2	31.6
	110	29	55.3	17.6	31.9
B0.2M	401	29	55.3	18.2	32.9
	402	29	55.8	18.0	32.3
	403	29	55.4	17.5	31.5
	404	29	57.5	18.1	31.5
	405	29	57.4	18.1	31.4
	406	29	58.4	19.9	34.0
	407	29	55.1	17.4	31.5
	408	29	55.5	17.7	31.9
	409	29	56.7	17.9	31.6
	410	29	55.1	19.1	34.6
B2M	501	29	55.4	17.6	31.8
	502	29	57.3	19.1	33.3
	503	29	56.2	18.0	32.0
	504	29	55.2	18.3	33.1
	505	29	54.5	17.9	32.8

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
B2M	506	29	58.4	18.6	31.8
	507	29	56.1	18.0	32.0
	508	29	57.9	18.9	32.6
	509	29	56.0	17.9	31.9
	510	29	53.7	16.6	30.9
B8M	601	29	57.7	18.6	32.2
	602	29	56.0	18.5	33.0
	603	29	55.8	18.4	33.0
	604	29	55.5	17.3	31.2
	605	29	53.1	17.0	32.1
	606	29	55.3	17.5	31.6
	607	29	53.5	17.2	32.2
	608	29	55.9	18.4	32.8
	609	29	55.0	17.7	32.1
	610	29	55.5	17.4	31.4
E0.2M	901	29	55.2	17.9	32.4
	902	29	57.6	18.1	31.5
	903	29	57.1	18.3	32.0
	904	29	61.0	20.3	33.3
	905	29	58.3	18.4	31.5
	906	29	55.5	18.5	33.4
	907	29	56.1	17.6	31.4
	908	29	54.5	17.3	31.7
	909	29	56.1	18.1	32.3
	910	29	53.9	18.6	34.5

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
E2M	1001	29	57.8	19.0	32.9
	1002	29	57.0	17.7	31.0
	1003	29	55.3	17.3	31.4
	1004	29	58.4	18.3	31.4
	1005	29	55.6	17.4	31.4
	1006	29	57.9	18.2	31.4
	1007	29	56.8	19.0	33.4
	1008	29	57.8	19.0	32.8
	1009	29	54.9	17.8	32.4
	1010	29	56.5	17.7	31.4
E8M	1101	29	56.6	17.9	31.6
	1102	29	54.8	17.7	32.2
	1103	29	54.2	18.3	33.8
	1104	29	58.8	19.0	32.4
	1105	29	53.0	17.0	32.0
	1106	29	57.1	18.3	32.1
	1107	29	52.5	17.1	32.5
	1108	29	56.7	18.3	32.3
	1109	29	53.1	16.9	31.8
	1110	29	54.9	17.9	32.6

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
CM	101	29	936	205.0
	102	29	1015	167.0
	103	29	795	213.3
	104	29	781	213.5
	105	29	944	195.3
	106	29	912	244.7
	107	29	1027	217.4
	108	29	803	196.3
	109	29	959	180.3
	110	29	983	195.2
B0.2M	401	29	859	162.6
	402	29	813	171.1
	403	29	728	151.0
	404	29	714	187.3
	405	29	703	159.5
	406	29	763	196.6
	407	29	847	150.8
	408	29	829	242.5
	409	29	870	177.8
	410	29	926	184.9
B2M	501	29	1085	205.4
	502	29	879	186.3
	503	29	826	232.2
	504	29	1069	212.7
	505	29	816	190.1
	506	29	811	186.4
	507	29	681	160.9

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
B2M	508	29	715	166.8
	509	29	765	168.7
	510	29	991	209.5
B8M	601	29	949	182.0
	602	29	791	126.3
	603	29	836	180.7
	604	29	855	171.8
	605	29	922	186.7
	606	29	957	219.7
	607	29	831	192.6
	608	29	781	179.0
	609	29	904	186.2
	610	29	839	176.3
E0.2M	901	29	882	187.1
	902	29	725	218.2
	903	29	1127	177.9
	904	29	942	137.2
	905	29	1141	235.7
	906	29	964	184.4
	907	29	1203	213.8
	908	29	877	167.6
	909	29	985	189.6
	910	29	800	122.1
E2M	1001	29	819	196.9
	1002	29	763	186.4
	1003	29	780	253.8
	1004	29	806	187.0

**Table C-15. Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
E2M	1005	29	861	145.3
	1006	29	880	225.5
	1007	29	891	186.8
	1008	29	915	179.7
	1009	29	694	171.7
	1010	29	764	281.1
E8M	1101	29	756	141.6
	1102	29	988	195.5
	1103	29	839	165.9
	1104	29	788	150.4
	1105	29	752	228.0
	1106	29	900	177.2
	1107	29	838	154.4
	1108	29	906	143.4
	1109	29	862	114.2
	1110	29	772	180.7

**Table C-16. Individual Animal Hematology Data – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
CF	151	30	8.30	14.5	46.6
	152	30	8.49	15.5	47.1
	153	30	8.42	15.6	48.0
	154	30	8.46	15.1	46.1
	155	30	8.83	15.4	46.9
	156	30	8.34	15.4	47.5
	157	30	8.26	15.5	45.7
	158	30	7.74	13.8	41.9
	159	30	8.16	14.2	44.4
	160	30	8.36	15.0	45.9
B0.2F	451	30	8.23	14.7	45.7
	452	30	8.10	14.5	43.3
	453	30	8.86	15.0	46.7
	454	30	8.67	14.8	46.7
	455	30	8.27	15.0	45.7
	456	30	8.37	14.5	46.5
	457	30	9.69	16.8	50.0
	458	30	8.76	15.5	46.8
	459	30	7.69	14.7	43.5
	460	30	7.79	15.4	44.2
B2F	551	30	7.97	14.7	44.7
	552	30	7.95	15.0	45.6
	553	30	9.13	16.6	50.5
	554	30	7.97	14.4	44.7
	555	30	8.99	15.9	48.1
	556	30	8.63	14.9	47.1
	557	30	8.72	15.1	47.4

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
B2F	558	30	8.07	15.3	45.2
	559	30	9.63	16.8	51.1
	560	30	9.25	17.0	51.3
B8F	651	30	8.19	14.4	44.6
	652	30	8.50	15.1	47.2
	653	30	8.15	13.8	43.6
	654	30	8.21	14.5	44.7
	655	30	8.22	14.4	45.9
	656	30	8.29	15.0	45.4
	657	30	8.66	15.4	46.6
	658	30	9.08	15.7	48.1
	659	30	8.42	14.7	45.0
	660	30	7.96	14.4	44.2
E0.2F	951	30	8.95	15.0	47.0
	952	30	7.97	14.3	44.6
	953	30	8.18	14.8	44.7
	954	30	8.21	14.6	44.3
	955	30	8.56	15.5	46.6
	956	30	8.39	15.6	47.0
	957	30	8.41	16.3	47.6
	958	30	7.75	14.3	43.9
	959	30	8.81	16.0	48.7
	960	30	8.41	15.3	46.4
E2F	1051	30	8.08	14.4	46.0
	1052	30	7.85	15.2	45.0
	1053	30	8.52	14.9	46.4
	1054	30	8.33	15.6	46.8

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
E2F	1055	30	8.65	15.2	46.8
	1056	30	8.45	15.2	46.2
	1057	30	8.38	15.3	45.2
	1058	30	9.17	16.5	50.4
	1059	30	8.23	15.4	45.9
	1060	30	8.03	15.1	45.0
E8F	1151	30	7.86	13.9	43.4
	1152	30	8.46	15.3	47.8
	1153	30	8.25	14.4	45.6
	1154	30	8.49	14.7	45.7
	1155	30	8.19	15.4	43.5
	1156	30	9.68	16.4	50.3
	1157	30	8.62	15.3	47.4
	1158	30	9.26	16.0	49.8
	1159	30	10.23	17.5	54.4
	1160	30	9.52	16.5	51.3

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
CF	151	30	56.2	17.4	31.0
	152	30	55.5	18.2	32.9
	153	30	57.0	18.5	32.5
	154	30	54.5	17.8	32.7
	155	30	53.1	17.4	32.8
	156	30	56.9	18.4	32.3
	157	30	55.4	18.7	33.8
	158	30	54.1	17.8	33.0
	159	30	54.5	17.5	32.1
	160	30	54.9	17.9	32.6
B0.2F	451	30	55.5	17.8	32.1
	452	30	53.5	17.9	33.4
	453	30	52.7	16.9	32.1
	454	30	53.9	17.1	31.7
	455	30	55.3	18.1	32.8
	456	30	55.6	17.3	31.1
	457	30	51.7	17.3	33.5
	458	30	53.4	17.7	33.1
	459	30	56.5	19.1	33.8
	460	30	56.7	19.7	34.8
B2F	551	30	56.1	18.4	32.9
	552	30	57.3	18.9	33.0
	553	30	55.4	18.2	32.9
	554	30	56.1	18.0	32.1
	555	30	53.5	17.6	33.0

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
B2F	556	30	54.5	17.2	31.6
	557	30	54.4	17.3	31.9
	558	30	56.0	19.0	33.9
	559	30	53.0	17.5	32.9
	560	30	55.4	18.3	33.1
B8F	651	30	54.4	17.6	32.4
	652	30	55.5	17.8	32.1
	653	30	53.5	16.9	31.6
	654	30	54.4	17.7	32.5
	655	30	55.9	17.6	31.5
	656	30	54.7	18.1	33.1
	657	30	53.8	17.8	33.0
	658	30	52.9	17.2	32.6
	659	30	53.5	17.5	32.7
	660	30	55.6	18.1	32.5
E0.2F	951	30	52.6	16.8	31.9
	952	30	55.9	17.9	32.0
	953	30	54.6	18.1	33.2
	954	30	54.0	17.8	33.0
	955	30	54.5	18.1	33.2
	956	30	56.0	18.5	33.1
	957	30	56.5	19.4	34.4
	958	30	56.7	18.4	32.5
	959	30	55.3	18.1	32.8
	960	30	55.1	18.3	33.1

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
E2F	1051	30	56.9	17.9	31.4
	1052	30	57.4	19.4	33.8
	1053	30	54.5	17.4	32.0
	1054	30	56.1	18.7	33.4
	1055	30	54.1	17.6	32.5
	1056	30	54.7	18.0	33.0
	1057	30	54.0	18.3	33.9
	1058	30	54.9	18.0	32.7
	1059	30	55.8	18.7	33.6
	1060	30	56.1	18.8	33.5
E8F	1151	30	55.2	17.7	32.0
	1152	30	56.6	18.1	32.0
	1153	30	55.2	17.4	31.5
	1154	30	53.8	17.3	32.1
	1155	30	53.1	18.8	35.4
	1156	30	52.0	17.0	32.7
	1157	30	55.0	17.8	32.3
	1158	30	53.7	17.3	32.3
	1159	30	53.2	17.1	32.1
	1160	30	53.9	17.4	32.2

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
CF	151	30	924	252.9
	152	30	924	213.3
	153	30	804	180.7
	154	30	857	244.0
	155	30	851	157.8
	156	30	729	252.2
	157	30	924	197.0
	158	30	816	171.5
	159	30	1013	251.3
	160	30	1015	212.7
B0.2F	451	30	797	177.5
	452	30	783	178.5
	453	30	377	234.3
	454	30	785	221.6
	455	30	939	201.5
	456	30	883	224.1
	457	30	917	238.0
	458	30	777	200.4
	459	30	925	268.9
	460	30	888	246.2
B2F	551	30	976	246.0
	552	30	805	235.4
	553	30	727	244.1
	554	30	872	169.4
	555	30	826	203.2
	556	30	906	205.9
	557	30	716	192.7

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
B2F	558	30	922	233.2
	559	30	705	188.5
	560	30	817	266.6
B8F	651	30	724	167.0
	652	30	908	259.5
	653	30	699	162.0
	654	30	849	189.7
	655	30	966	277.6
	656	30	961	228.5
	657	30	787	226.4
	658	30	678	193.9
	659	30	795	229.9
	660	30	1219	325.8
E0.2F	951	30	865	229.8
	952	30	934	215.1
	953	30	830	139.7
	954	30	719	233.4
	955	30	969	175.0
	956	30	900	167.7
	957	30	557	276.5
	958	30	990	214.6
	959	30	912	224.6
	960	30	929	269.1
E2F	1051	30	663	210.1
	1052	30	973	188.9
	1053	30	773	206.4
	1054	30	613	156.1

**Table C-16. Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
E2F	1055	30	1093	261.6
	1056	30	853	253.0
	1057	30	980	184.4
	1058	30	595	288.6
	1059	30	960	247.9
	1060	30	727	272.0
E8F	1151	30	806	206.1
	1152	30	844	217.4
	1153	30	787	238.5
	1154	30	924	238.6
	1155	30	734	212.1
	1156	30	799	194.8
	1157	30	819	186.4
	1158	30	438	223.6
	1159	30	986	166.5
	1160	30	974	277.9

**Table C-17. Paired and High Dose Group Individual Animal Hematology Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
NT20M	201	31	9.42	16.6	51.4
	202	31	8.36	14.7	44.1
	203	31	7.89	14.7	42.4
	204	31	9.52	16.3	50.0
	205	31	8.47	14.7	43.7
	206	31	8.66	15.0	45.4
	207	31	8.01	14.4	41.9
	208	31	8.16	15.0	44.9
	209	31	8.40	14.0	43.8
	210	31	8.02	13.9	41.9
PFCNTM	301	31	9.37	17.3	51.4
	302	31	8.62	16.5	49.3
	303	31	8.76	15.6	47.5
	304	31	8.32	15.1	45.3
	305	31	8.92	16.4	50.2
	306	31	8.48	15.4	45.9
	307	31	8.85	15.8	47.6
	308	31	8.71	16.2	49.4
	309	31	8.88	15.4	48.4
	310	31	8.39	14.2	42.7
B20M	701	31	8.94	15.5	47.6
	702	31	8.24	14.5	43.5
	703	31	8.73	15.5	46.9
	704	31	9.48	17.1	50.6
	705	31	8.38	15.0	44.2
	706	31	8.96	15.6	46.4
	707	31	8.56	15.6	46.9

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
B20M	708	31	7.99	14.2	42.5
	709	31	8.67	15.6	46.6
	710	31	8.12	14.4	44.5
PFCBM	801	31	9.11	15.8	50.1
	802	31	9.17	16.5	48.3
	803	31	8.86	16.0	47.6
	804	31	8.93	15.4	47.9
	805	31	8.65	15.2	45.8
	806	31	9.05	15.2	47.8
	807	31	8.62	15.4	45.9
	808	31	9.84	17.1	54.1
	809	31	9.01	16.0	47.8
	810	31	8.23	15.0	43.5
E20M	1201	31	9.70	17.1	50.9
	1202	31	8.58	15.1	45.3
	1203	31	8.72	15.3	45.7
	1204	31	8.36	15.3	46.5
	1205	31	9.11	16.4	48.2
	1206	31	9.27	16.1	49.4
	1207	31	9.04	16.0	47.5
	1208	31	8.45	15.6	45.9
	1209	31	8.00	15.0	43.5
	1210	31	8.86	14.9	46.8
PFCM	1301	31	8.49	15.5	45.9
	1302	31	8.43	15.3	46.0
	1303	31	8.58	15.4	45.8
	1304	31	8.22	14.5	45.5

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
PFCEM	1305	31	8.54	15.1	46.1
	1306	31	8.49	15.0	45.6
	1307	31	8.87	15.9	48.7
	1308	31	9.21	16.3	50.7
	1309	31	8.89	15.8	49.1
	1310	31	8.06	14.9	44.3

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
NT20M	201	31	54.6	17.6	32.3
	202	31	52.8	17.6	33.3
	203	31	53.8	18.6	34.6
	204	31	52.5	17.1	32.5
	205	31	51.6	17.4	33.6
	206	31	52.4	17.3	33.1
	207	31	52.2	17.9	34.3
	208	31	55.0	18.4	33.5
	209	31	52.2	16.7	32.0
	210	31	52.2	17.3	33.2
PFCNTM	301	31	54.9	18.5	33.6
	302	31	57.2	19.1	33.4
	303	31	54.3	17.8	32.9
	304	31	54.5	18.2	33.4
	305	31	56.3	18.4	32.6
	306	31	54.1	18.1	33.5
	307	31	53.7	17.9	33.3
	308	31	56.7	18.6	32.8
	309	31	54.4	17.4	31.9
	310	31	50.9	16.9	33.2
B20M	701	31	53.2	17.3	32.5
	702	31	52.8	17.7	33.5
	703	31	53.7	17.7	32.9
	704	31	53.4	18.0	33.7
	705	31	52.7	18.0	34.1

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
B20M	706	31	51.8	17.4	33.5
	707	31	54.8	18.3	33.3
	708	31	53.2	17.7	33.3
	709	31	53.7	18.0	33.6
	710	31	54.8	17.7	32.3
PFCBM	801	31	55.0	17.3	31.5
	802	31	52.7	18.0	34.2
	803	31	53.8	18.0	33.6
	804	31	53.6	17.2	32.1
	805	31	52.9	17.6	33.3
	806	31	52.9	16.8	31.8
	807	31	53.2	17.9	33.7
	808	31	55.0	17.3	31.5
	809	31	53.1	17.8	33.5
	810	31	52.9	18.2	34.4
E20M	1201	31	52.5	17.6	33.5
	1202	31	52.8	17.6	33.3
	1203	31	52.4	17.5	33.4
	1204	31	55.6	18.4	33.0
	1205	31	52.9	18.0	34.1
	1206	31	53.3	17.4	32.7
	1207	31	52.5	17.6	33.6
	1208	31	54.3	18.5	34.0
	1209	31	54.4	18.8	34.5
	1210	31	52.9	16.8	31.9

**Table C-17. Paired and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
PFCM	1301	31	54.0	18.2	33.7
	1302	31	54.6	18.1	33.2
	1303	31	53.4	17.9	33.6
	1304	31	55.4	17.7	31.9
	1305	31	54.0	17.7	32.8
	1306	31	53.8	17.7	32.9
	1307	31	54.9	17.9	32.6
	1308	31	55.0	17.7	32.2
	1309	31	55.2	17.8	32.2
	1310	31	54.9	18.5	33.7

**Table C-17. Paired and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
NT20M	201	31	759	200.1
	202	31	859	175.4
	203	31	913	211.9
	204	31	766	132.3
	205	31	785	112.8
	206	31	942	226.5
	207	31	848	191.0
	208	31	921	129.3
	209	31	936	128.9
	210	31	922	183.9
PFCNTM	301	31	984	132.0
	302	31	890	123.7
	303	31	814	129.4
	304	31	972	184.9
	305	31	1002	129.2
	306	31	1071	98.9
	307	31	951	120.5
	308	31	990	116.3
	309	31	742	126.6
	310	31	953	157.3
B20M	701	31	910	181.2
	702	31	616	137.0
	703	31	909	170.0
	704	31	740	200.9
	705	31	593	138.7
	706	31	723	80.6
	707	31	732	170.9

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
B20M	708	31	706	187.4
	709	31	726	125.7
	710	31	904	123.4
PFCBM	801	31	856	107.1
	802	31	869	146.8
	803	31	752	138.0
	804	31	860	162.5
	805	31	712	145.9
	806	31	850	112.8
	807	31	814	128.1
	808	31	833	120.6
	809	31	911	132.2
	810	31	967	137.8
E20M	1201	31	921	160.7
	1202	31	882	124.4
	1203	31	888	91.2
	1204	31	875	56.6
	1205	31	754	174.4
	1206	31	756	112.3
	1207	31	893	200.0
	1208	31	935	175.6
	1209	31	751	108.7
	1210	31	878	133.7
PFCM	1301	31	751	122.0
	1302	31	985	222.3
	1303	31	859	145.0
	1304	31	866	137.0

**Table C-17. Pairfed and High Dose Group Individual Animal Hematology Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
PFCEM	1305	31	998	158.1
	1306	31	945	138.9
	1307	31	848	157.9
	1308	31	836	140.5
	1309	31	1020	132.1
	1310	31	763	149.4

**Table C-18. Paired and High Dose Group Individual Animal Hematology Data – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
NT20F	251	32	8.37	14.5	44.0
	252	32	8.41	15.3	44.5
	253	32	8.01	14.4	42.6
	254	32	8.24	15.2	45.3
	255	32	8.25	14.2	43.4
	256	32	8.28	14.4	44.6
	257	32	7.83	15.0	43.4
	258	32	8.70	15.2	45.6
	259	32	8.62	14.7	45.8
	260	32	8.80	14.8	46.0
PFCNTF	351	32	7.77	14.2	43.2
	352	32	8.76	15.9	47.7
	353	32	7.29	13.9	40.2
	354	32	8.46	15.2	46.9
	355	32	8.50	14.8	44.1
	356	32	8.04	15.5	45.5
	357	32	8.17	15.4	45.4
	358	32	8.32	14.9	44.1
	359	32	8.42	15.3	46.1
	360	32	8.10	14.6	45.3
B20F	751	32	8.09	15.0	44.3
	752	32	8.14	13.4	40.9
	753	32	9.29	16.2	48.8
	754	32	8.90	15.5	47.2
	755	32	8.80	15.8	47.9
	756	32	7.98	15.2	43.2
	758	32	7.89	14.4	42.1

**Table C-18. Pairfed and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
B20F	759	32	8.47	15.3	47.0
	760	32	8.51	14.9	44.6
PFCBF	851	32	7.99	15.4	45.0
	852	32	8.37	14.8	44.4
	853	32	8.89	15.5	47.5
	854	32	8.16	13.9	42.0
	855	32	8.53	15.2	45.7
	856	32	8.40	15.1	45.3
	857	32	7.79	14.3	43.2
	858	32	8.40	15.8	47.0
	859	32	8.25	15.1	44.8
	860	32	8.15	15.0	44.5
E20F	1251	32	8.52	15.1	44.8
	1252	32	8.55	16.0	48.0
	1253	32	8.45	14.7	43.2
	1254	32	8.98	17.3	49.4
	1255	32	8.12	15.1	43.7
	1256	32	8.05	14.2	42.3
	1257	32	8.21	14.4	42.7
	1258	32	9.22	15.7	46.1
	1259	32	8.23	14.6	43.4
	1260	32	8.38	15.6	43.9
PFCEF	1351	32	8.16	14.6	45.7
	1352	32	8.27	14.3	43.4
	1353	32	8.93	15.4	48.2
	1354	32	7.87	14.5	44.2
	1355	32	8.36	14.9	46.7

**Table C-18. Pairfed and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Red Blood Cell Count (10<sup>6</sup>/μL)</b>	<b>Hemoglobin (g/dL)</b>	<b>Hematocrit (%)</b>
PFCEF	1356	32	8.33	15.2	45.2
	1358	32	7.69	14.6	43.8
	1359	32	8.33	14.9	46.4
	1360	32	7.58	13.8	41.3

**Table C-18. Paired and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
NT20F	251	32	52.6	17.4	33.0
	252	32	52.9	18.2	34.4
	253	32	53.2	18.0	33.8
	254	32	55.0	18.5	33.5
	255	32	52.6	17.2	32.7
	256	32	53.9	17.3	32.2
	257	32	55.4	19.1	34.5
	258	32	52.5	17.5	33.3
	259	32	53.1	17.0	32.0
	260	32	52.3	16.9	32.3
PFCNTF	351	32	55.6	18.3	32.9
	352	32	54.4	18.1	33.3
	353	32	55.1	19.1	34.7
	354	32	55.5	18.0	32.4
	355	32	51.9	17.4	33.5
	356	32	56.5	19.2	34.0
	357	32	55.5	18.8	33.9
	358	32	53.0	17.9	33.8
	359	32	54.8	18.2	33.3
	360	32	55.9	18.0	32.3
B20F	751	32	54.8	18.5	33.8
	752	32	50.3	16.5	32.7
	753	32	52.5	17.5	33.3
	754	32	53.0	17.4	32.8
	755	32	54.5	17.9	32.9

**Table C-18. Pairfed and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
B20F	756	32	54.2	19.1	35.2
	758	32	53.4	18.3	34.3
	759	32	55.5	18.1	32.6
	760	32	52.4	17.5	33.4
PFCBF	851	32	56.4	19.3	34.2
	852	32	53.1	17.7	33.3
	853	32	53.5	17.5	32.6
	854	32	51.4	17.0	33.2
	855	32	53.6	17.9	33.3
	856	32	54.0	17.9	33.2
	857	32	55.5	18.4	33.2
	858	32	56.0	18.8	33.6
	859	32	54.3	18.3	33.6
	860	32	54.5	18.4	33.8
E20F	1251	32	52.6	17.7	33.6
	1252	32	56.1	18.7	33.4
	1253	32	51.0	17.4	34.0
	1254	32	55.0	19.2	34.9
	1255	32	53.7	18.6	34.7
	1256	32	52.5	17.6	33.6
	1257	32	52.0	17.5	33.7
	1258	32	50.0	17.0	34.0
	1259	32	52.7	17.8	33.7
	1260	32	52.3	18.6	35.5

**Table C-18. Paired and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Mean Corpuscular Volume (fL)</b>	<b>Mean Corpuscular Hemoglobin (pg)</b>	<b>Mean Corpuscular Hemoglobin Concentration (g/dL)</b>
PFCEF	1351	32	56.0	17.8	31.8
	1352	32	52.5	17.2	32.8
	1353	32	54.0	17.2	31.9
	1354	32	56.1	18.4	32.8
	1355	32	55.8	17.9	32.0
	1356	32	54.3	18.2	33.5
	1358	32	57.0	19.0	33.3
	1359	32	55.7	17.9	32.1
	1360	32	54.5	18.3	33.5

**Table C-18. Paired and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
NT20F	251	32	660	231.8
	252	32	817	192.8
	253	32	736	169.2
	254	32	842	239.6
	255	32	609	213.5
	256	32	825	151.8
	257	32	722	205.6
	258	32	837	179.5
	259	32	822	218.9
	260	32	678	151.3
PFCNTF	351	32	978	171.0
	352	32	814	221.0
	353	32	948	169.1
	354	32	782	141.5
	355	32	869	112.2
	356	32	612	173.5
	357	32	719	132.1
	358	32	888	157.0
	359	32	807	171.3
	360	32	948	185.0
B20F	751	32	714	140.6
	752	32	599	76.8
	753	32	739	132.6
	754	32	545	120.6
	755	32	832	229.9
	756	32	870	150.8
	758	32	778	156.8

**Table C-18. Paired and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
B20F	759	32	808	256.6
	760	32	692	121.6
PFCBF	851	32	699	137.8
	852	32	855	146.8
	853	32	767	194.4
	854	32	999	147.0
	855	32	857	244.8
	856	32	928	163.7
	857	32	818	209.8
	858	32	956	196.6
	859	32	955	268.3
	860	32	1060	187.1
E20F	1251	32	676	95.7
	1252	32	600	128.6
	1253	32	754	109.1
	1254	32	665	189.1
	1255	32	857	102.0
	1256	32	709	150.5
	1257	32	761	109.8
	1258	32	583	135.6
	1259	32	707	195.2
	1260	32	821	108.7
PFCEF	1351	32	1046	185.3
	1352	32	1015	208.8
	1353	32	836	215.4
	1354	32	1060	243.8
	1355	32	741	218.9

**Table C-18. Pairfed and High Dose Group Individual Animal Hematology Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Platelet Count (10<sup>3</sup>/μL)</b>	<b>Reticulocytes (10<sup>3</sup>/μL)</b>
PFCEF	1356	32	938	183.0
	1358	32	938	264.8
	1359	32	1106	180.5
	1360	32	881	174.2

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
CM	101	29	7.90		0.92	6.84
	102	29	6.79		0.76	5.85
	103	29	5.86		0.58	5.09
	104	29	6.44		1.20	5.14
	105	29	6.10		0.58	5.40
	106	29	8.63		0.83	7.59
	107	29	10.85		1.18	9.43
	108	29	8.61		0.82	7.59
	109	29	10.70		0.91	9.55
	110	29	7.45		0.92	6.21
B0.2M	401	29	7.10		0.85	6.07
	402	29	4.23		0.51	3.65
	403	29	4.35		0.79	3.46
	404	29	4.52		0.53	3.86
	405	29	5.54		0.48	4.94
	406	29	6.06		0.62	5.27
	407	29	4.53		0.75	3.69
	408	29	10.26		1.72	8.19
	409	29	7.81		0.76	6.90
	410	29	9.29		0.81	8.19
B2M	501	29	6.17		0.62	5.38
	502	29	8.79		1.06	7.48
	503	29	5.20		0.77	4.31
	504	29	5.93		0.74	5.02
	505	29	7.58		0.61	6.76
	506	29	7.61		1.09	6.38

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

Group	White Blood Cell				
	Animal ID	Day	Count (10 <sup>3</sup> /μL)	Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
B2M	507	29	7.94	0.61	7.18
	508	29	7.77	0.95	6.63
	509	29	5.09	0.56	4.42
	510	29	9.90	1.00	8.63
B8M	601	29	6.40	0.62	5.62
	602	29	1.84	1.11	0.62
	603	29	6.40	0.69	5.52
	604	29	2.54	1.20	1.21
	605	29	3.34	0.37	2.91
	606	29	6.23	0.76	5.36
	607	29	6.15	0.47	5.54
	608	29	4.16	0.42	3.66
	609	29	8.51	0.84	7.49
	610	29	11.30	1.08	10.01
E0.2M	901	29	9.15	1.53	7.38
	902	29	7.11	0.69	6.22
	903	29	4.44	0.63	3.71
	904	29	7.50	0.92	6.41
	905	29	8.22	1.99	5.98
	906	29	6.31	0.72	5.44
	907	29	9.64	2.20	7.19
	908	29	7.55	0.69	6.68
	909	29	6.71	1.11	5.44
	910	29	9.17	0.62	8.36
E2M	1001	29	6.43	1.07	5.16
	1002	29	6.33	0.96	5.22

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
				Count (10 <sup>3</sup> /μL)		
E2M	1003	29		4.72	0.46	4.16
	1004	29		7.90	0.87	6.69
	1005	29		7.78	1.14	6.39
	1006	29		6.02	0.54	5.37
	1007	29		7.42	0.77	6.51
	1008	29		5.75	0.62	5.02
	1009	29		6.05	0.85	5.08
	1010	29		11.12	0.76	10.05
E8M	1101	29		5.91	0.50	5.34
	1102	29		7.12	1.03	5.98
	1103	29		4.99	0.39	4.49
	1104	29		6.50	0.79	5.57
	1105	29		6.52	0.86	5.51
	1106	29		5.93	0.72	5.07
	1107	29		10.40	0.87	9.27
	1108	29		7.85	0.78	6.94
	1109	29		6.19	0.69	5.39
	1110	29		11.85	0.86	10.68

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
CM	101	29	0.06	0.05	0.03
	102	29	0.08	0.09	0.02
	103	29	0.09	0.07	0.02
	104	29	0.06	0.03	0.01
	105	29	0.06	0.04	0.03
	106	29	0.13	0.04	0.02
	107	29	0.14	0.04	0.05
	108	29	0.11	0.06	0.03
	109	29	0.12	0.09	0.03
	110	29	0.21	0.07	0.03
B0.2M	401	29	0.10	0.05	0.03
	402	29	0.03	0.02	0.01
	403	29	0.08	0.02	0.01
	404	29	0.10	0.02	0.01
	405	29	0.09	0.01	0.02
	406	29	0.05	0.08	0.03
	407	29	0.06	0.02	0.01
	408	29	0.16	0.15	0.03
	409	29	0.06	0.06	0.02
	410	29	0.18	0.07	0.04
B2M	501	29	0.08	0.07	0.01
	502	29	0.18	0.03	0.04
	503	29	0.09	0.02	0.02
	504	29	0.10	0.05	0.02
	505	29	0.10	0.09	0.02
	506	29	0.08	0.04	0.02
	507	29	0.07	0.06	0.02

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
B2M	508	29	0.14	0.02	0.02
	509	29	0.07	0.02	0.02
	510	29	0.14	0.09	0.04
B8M	601	29	0.10	0.05	0.02
	602	29	0.06	0.05	0.00
	603	29	0.10	0.06	0.02
	604	29	0.09	0.04	0.00
	605	29	0.03	0.03	0.00
	606	29	0.06	0.04	0.01
	607	29	0.10	0.03	0.02
	608	29	0.05	0.02	0.01
	609	29	0.11	0.05	0.02
	610	29	0.13	0.04	0.04
E0.2M	901	29	0.16	0.06	0.02
	902	29	0.14	0.04	0.02
	903	29	0.08	0.02	0.01
	904	29	0.11	0.05	0.01
	905	29	0.16	0.06	0.03
	906	29	0.09	0.04	0.02
	907	29	0.16	0.06	0.03
	908	29	0.12	0.05	0.02
	909	29	0.10	0.04	0.02
	910	29	0.11	0.06	0.02
E2M	1001	29	0.11	0.07	0.02
	1002	29	0.10	0.03	0.02
	1003	29	0.06	0.03	0.01
	1004	29	0.26	0.06	0.02

**Table C-19. Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
E2M	1005	29	0.14	0.07	0.03
	1006	29	0.06	0.03	0.01
	1007	29	0.10	0.03	0.01
	1008	29	0.05	0.04	0.01
	1009	29	0.07	0.03	0.01
	1010	29	0.17	0.06	0.07
E8M	1101	29	0.03	0.04	0.01
	1102	29	0.06	0.03	0.03
	1103	29	0.08	0.02	0.02
	1104	29	0.10	0.03	0.01
	1105	29	0.06	0.07	0.01
	1106	29	0.09	0.03	0.03
	1107	29	0.18	0.05	0.03
	1108	29	0.09	0.02	0.02
	1109	29	0.08	0.02	0.01
	1110	29	0.20	0.07	0.05

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
CF	151	30	6.04		0.81	5.08
	152	30	6.27		1.32	4.81
	153	30	3.72		0.48	3.14
	154	30	2.38		0.54	1.75
	155	30	4.97		1.00	3.78
	156	30	5.38		0.55	4.72
	157	30	5.22		0.88	4.14
	158	30	8.52		1.27	6.94
	159	30	5.00		0.56	4.20
	160	30	6.48		0.83	5.48
B0.2F	451	30	3.05		0.44	2.53
	452	30	4.49		0.56	3.79
	453	30	2.77		0.51	2.14
	454	30	5.74		1.65	3.87
	455	30	6.40		0.55	5.67
	456	30	3.73		0.57	3.05
	457	30	5.05		0.63	4.26
	458	30	5.60		0.85	4.49
	459	30	6.52		0.74	5.60
	460	30	4.81		0.47	4.13
B2F	551	30	5.02		1.01	3.84
	552	30	8.35		0.64	7.55
	553	30	5.37		0.47	4.76
	554	30	4.81		1.10	3.50
	555	30	6.16		0.69	5.32
	556	30	4.27		0.60	3.56

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
B2F	557	30	6.33		0.86	5.26
	558	30	5.73		0.64	4.97
	559	30	8.58		0.96	7.33
	560	30	6.42		0.80	5.45
B8F	651	30	5.61		0.90	4.53
	652	30	1.96		0.22	1.67
	653	30	4.25		0.67	3.43
	654	30	7.66		0.98	6.43
	655	30	6.77		0.49	6.09
	656	30	6.03		1.06	4.75
	657	30	9.33		0.81	8.25
	658	30	7.46		0.54	6.75
	659	30	5.15		1.45	3.57
	660	30	6.98		0.73	6.06
E0.2F	951	30	2.63		0.39	2.15
	952	30	2.94		0.40	2.46
	953	30	4.95		0.71	4.12
	954	30	4.02		0.95	2.92
	955	30	7.31		2.10	4.99
	956	30	5.09		0.89	4.03
	957	30	7.37		0.89	6.28
	958	30	5.38		1.47	3.79
	959	30	8.24		0.81	7.25
	960	30	3.95		0.48	3.36
E2F	1051	30	5.38		0.75	4.48
	1052	30	10.47		1.44	8.68

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
				Count (10 <sup>3</sup> /μL)		
E2F	1053	30		3.12	0.46	2.61
	1054	30		4.16	0.57	3.45
	1055	30		3.85	0.70	3.04
	1056	30		4.13	1.02	2.99
	1057	30		6.65	1.05	5.44
	1058	30		5.13	0.76	4.23
	1059	30		4.10	0.41	3.61
	1060	30		5.12	0.67	4.32
E8F	1151	30		4.91	0.55	4.25
	1152	30		3.46	0.27	3.13
	1153	30		4.89	0.62	4.15
	1154	30		4.69	0.67	3.89
	1155	30		7.59	0.74	6.66
	1156	30		6.42	0.98	5.25
	1157	30		5.03	0.61	4.26
	1158	30		3.27	0.33	2.84
	1159	30		9.05	0.50	8.33
	1160	30		5.19	0.68	4.40

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
CF	151	30	0.07	0.06	0.01
	152	30	0.08	0.05	0.02
	153	30	0.06	0.02	0.01
	154	30	0.03	0.05	0.01
	155	30	0.16	0.02	0.01
	156	30	0.06	0.03	0.01
	157	30	0.10	0.10	0.01
	158	30	0.19	0.08	0.04
	159	30	0.19	0.05	0.01
	160	30	0.07	0.08	0.01
B0.2F	451	30	0.06	0.02	0.01
	452	30	0.07	0.04	0.01
	453	30	0.05	0.06	0.01
	454	30	0.12	0.09	0.01
	455	30	0.11	0.05	0.02
	456	30	0.08	0.03	0.00
	457	30	0.08	0.06	0.01
	458	30	0.13	0.12	0.01
	459	30	0.10	0.06	0.02
	460	30	0.15	0.03	0.01
B2F	551	30	0.09	0.06	0.02
	552	30	0.08	0.04	0.03
	553	30	0.09	0.05	0.01
	554	30	0.11	0.09	0.01
	555	30	0.07	0.07	0.01
	556	30	0.07	0.05	0.00
	557	30	0.15	0.05	0.01

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
B2F	558	30	0.06	0.04	0.02
	559	30	0.17	0.09	0.03
	560	30	0.12	0.04	0.02
B8F	651	30	0.10	0.06	0.02
	652	30	0.04	0.02	0.00
	653	30	0.11	0.03	0.01
	654	30	0.16	0.06	0.02
	655	30	0.10	0.07	0.01
	656	30	0.14	0.06	0.02
	657	30	0.19	0.05	0.03
	658	30	0.11	0.03	0.03
	659	30	0.10	0.02	0.01
	660	30	0.12	0.05	0.02
E0.2F	951	30	0.07	0.02	0.00
	952	30	0.05	0.03	0.00
	953	30	0.05	0.05	0.01
	954	30	0.09	0.05	0.01
	955	30	0.15	0.04	0.02
	956	30	0.14	0.04	0.01
	957	30	0.13	0.05	0.03
	958	30	0.07	0.04	0.01
	959	30	0.10	0.06	0.02
	960	30	0.07	0.04	0.01
E2F	1051	30	0.11	0.04	0.01
	1052	30	0.20	0.11	0.03
	1053	30	0.04	0.02	0.00
	1054	30	0.07	0.05	0.02

**Table C-20. Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
E2F	1055	30	0.06	0.03	0.01
	1056	30	0.07	0.04	0.01
	1057	30	0.08	0.06	0.02
	1058	30	0.09	0.04	0.01
	1059	30	0.06	0.02	0.01
	1060	30	0.08	0.03	0.01
E8F	1151	30	0.08	0.03	0.01
	1152	30	0.05	0.01	0.00
	1153	30	0.06	0.04	0.00
	1154	30	0.07	0.04	0.01
	1155	30	0.14	0.04	0.02
	1156	30	0.14	0.03	0.01
	1157	30	0.10	0.04	0.02
	1158	30	0.07	0.03	0.00
	1159	30	0.11	0.07	0.04
	1160	30	0.08	0.01	0.01

**Table C-21. Pairfed and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
NT20M	201	31	8.18		0.86	7.12
	202	31	3.70		0.62	3.00
	203	31	11.16		1.52	9.18
	204	31	6.55		0.58	5.81
	205	31	5.44		0.81	4.52
	206	31	6.31		0.86	5.24
	207	31	7.57		0.66	6.70
	208	31	10.56		0.76	9.50
	209	31	7.85		0.83	6.76
	210	31	10.06		1.04	8.88
PFCNTM	301	31	7.08		0.98	5.85
	302	31	4.43		0.40	3.94
	303	31	2.00		0.62	1.30
	304	31	6.53		0.86	5.50
	305	31	4.07		0.37	3.63
	306	31	5.53		0.66	4.78
	307	31	6.56		0.66	5.80
	308	31	6.07		1.03	4.94
	309	31	6.42		0.56	5.75
	310	31	6.21		0.74	5.33
B20M	701	31	9.30		0.98	8.13
	702	31	6.33		1.15	5.03
	703	31	6.19		0.95	5.09
	704	31	6.63		0.72	5.75
	705	31	6.94		1.02	5.62
	706	31	4.64		0.54	4.00

**Table C-21. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
B20M	707	31	6.32		0.94	5.19
	708	31	6.61		1.16	5.24
	709	31	6.35		0.69	5.50
	710	31	6.11		0.60	5.39
PFCBM	801	31	5.35		0.75	4.50
	802	31	9.65		0.83	8.67
	803	31	5.10		0.86	4.07
	804	31	9.51		0.89	8.44
	805	31	6.27		1.07	5.06
	806	31	5.36		0.94	4.29
	807	31	6.62		1.00	5.38
	808	31	5.64		0.45	5.09
	809	31	5.17		0.33	4.76
	810	31	7.68		0.83	6.73
E20M	1201	31	5.59		1.12	4.26
	1202	31	6.85		0.77	5.94
	1203	31	6.32		1.07	5.03
	1204	31	5.88		1.40	4.14
	1205	31	7.33		0.92	6.21
	1206	31	9.61		0.97	8.39
	1207	31	7.54		0.92	6.36
	1208	31	6.83		0.47	6.25
	1209	31	4.88		0.72	4.02
	1210	31	5.51		0.79	4.61
PFCBM	1301	31	9.56		0.97	8.36
	1302	31	6.91		0.74	6.02

**Table C-21. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>White Blood Cell</b>		<b>Total Lymphocytes</b>
			<b>Count</b>	<b>Neutrophils</b>	
			<b>(10<sup>3</sup>/μL)</b>	<b>(10<sup>3</sup>/μL)</b>	<b>(10<sup>3</sup>/μL)</b>
PFCEM	1303	31	7.26	0.72	6.35
	1304	31	6.85	0.56	6.13
	1305	31	6.08	0.78	5.17
	1306	31	7.28	0.72	6.43
	1307	31	6.55	0.80	5.60
	1308	31	4.41	0.41	3.93
	1309	31	7.73	0.58	7.04
	1310	31	5.65	0.84	4.60

**Table C-21. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
NT20M	201	31	0.13	0.04	0.04
	202	31	0.07	0.01	0.00
	203	31	0.16	0.26	0.04
	204	31	0.08	0.05	0.03
	205	31	0.07	0.03	0.00
	206	31	0.13	0.06	0.02
	207	31	0.15	0.04	0.02
	208	31	0.23	0.04	0.02
	209	31	0.18	0.06	0.02
	210	31	0.10	0.02	0.02
PFCNTM	301	31	0.16	0.06	0.03
	302	31	0.05	0.03	0.01
	303	31	0.05	0.03	0.01
	304	31	0.11	0.05	0.01
	305	31	0.04	0.02	0.01
	306	31	0.06	0.02	0.01
	307	31	0.06	0.02	0.02
	308	31	0.06	0.03	0.01
	309	31	0.09	0.01	0.02
	310	31	0.09	0.04	0.02
B20M	701	31	0.13	0.04	0.02
	702	31	0.10	0.04	0.01
	703	31	0.10	0.04	0.02
	704	31	0.10	0.02	0.03
	705	31	0.17	0.12	0.02
	706	31	0.06	0.03	0.01
	707	31	0.13	0.03	0.02

**Table C-21. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
B20M	708	31	0.15	0.04	0.02
	709	31	0.11	0.02	0.02
	710	31	0.10	0.01	0.01
PFCBM	801	31	0.06	0.03	0.01
	802	31	0.08	0.03	0.04
	803	31	0.09	0.05	0.03
	804	31	0.08	0.07	0.03
	805	31	0.07	0.06	0.01
	806	31	0.07	0.05	0.02
	807	31	0.12	0.10	0.02
	808	31	0.06	0.02	0.02
	809	31	0.06	0.01	0.02
	810	31	0.08	0.03	0.01
E20M	1201	31	0.15	0.05	0.02
	1202	31	0.09	0.04	0.01
	1203	31	0.15	0.05	0.02
	1204	31	0.21	0.13	0.01
	1205	31	0.13	0.05	0.02
	1206	31	0.18	0.04	0.02
	1207	31	0.17	0.06	0.03
	1208	31	0.07	0.02	0.02
	1209	31	0.09	0.06	0.00
	1210	31	0.07	0.03	0.01
PFCM	1301	31	0.14	0.06	0.03
	1302	31	0.05	0.06	0.02
	1303	31	0.13	0.03	0.02
	1304	31	0.09	0.04	0.03

**Table C-21. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
PFCEM	1305	31	0.09	0.02	0.02
	1306	31	0.07	0.03	0.03
	1307	31	0.08	0.06	0.01
	1308	31	0.05	0.02	0.01
	1309	31	0.08	0.03	0.01
	1310	31	0.11	0.08	0.02

**Table C-22. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
NT20F	251	32	5.30		0.57	4.54
	252	32	6.97		1.00	5.72
	253	32	6.36		0.80	5.38
	254	32	6.79		0.96	5.64
	255	32	5.75		0.62	4.95
	256	32	5.02		0.75	4.12
	257	32	7.60		1.05	6.19
	258	32	5.13		0.93	4.00
	259	32	9.85		1.54	8.05
	260	32	5.48		0.62	4.64
PFCNTF	351	32	3.18		0.38	2.71
	352	32	4.53		1.15	3.24
	353	32	5.20		0.70	4.25
	354	32	4.76		0.58	4.00
	355	32	3.98		0.57	3.30
	356	32	11.00		1.59	9.04
	357	32	3.92		0.31	3.53
	358	32	6.69		0.78	5.78
	359	32	9.78		1.00	8.51
	360	32	4.40		0.69	3.60
B20F	751	32	7.62		0.96	6.39
	752	32	6.48		1.02	5.21
	753	32	6.75		0.74	5.78
	754	32	4.90		0.75	3.97
	755	32	3.89		2.39	1.29
	756	32	6.47		0.62	5.64

**Table C-22. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
B20F	758	32	5.81		0.74	4.83
	759	32	5.81		1.01	4.62
	760	32	6.51		0.91	5.43
PFCBF	851	32	8.86		0.71	7.93
	852	32	6.30		0.67	5.49
	853	32	6.41		0.92	5.30
	854	32	5.46		0.38	4.95
	855	32	4.05		0.79	3.16
	856	32	9.59		0.87	8.41
	857	32	3.61		0.60	2.93
	858	32	4.31		0.51	3.70
	859	32	2.36		0.36	1.94
	860	32	5.07		0.93	4.02
E20F	1251	32	9.03		1.19	7.55
	1252	32	4.26		0.64	3.48
	1253	32	8.49		1.19	7.07
	1254	32	8.07		1.11	6.79
	1255	32	5.96		0.78	5.06
	1256	32	3.04		0.48	2.47
	1257	32	8.20		1.08	6.76
	1258	32	4.22		0.69	3.37
	1259	32	3.24		0.42	2.73
	1260	32	7.97		0.56	7.24
PFCEF	1351	32	5.00		0.84	4.01
	1352	32	6.29		0.65	5.47
	1353	32	5.21		0.58	4.51

**Table C-22. Pairfed and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

Group	Animal ID	Day	White Blood Cell		Neutrophils (10 <sup>3</sup> /μL)	Total Lymphocytes (10 <sup>3</sup> /μL)
			Count (10 <sup>3</sup> /μL)			
PFCEF	1354	32	3.83		0.65	3.10
	1355	32	4.24		0.34	3.76
	1356	32	8.38		0.85	7.34
	1358	32	5.18		0.62	4.44
	1359	32	6.39		0.90	5.26
	1360	32	3.65		0.33	3.21

**Table C-22. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
NT20F	251	32	0.13	0.06	0.02
	252	32	0.17	0.04	0.04
	253	32	0.12	0.04	0.02
	254	32	0.12	0.05	0.02
	255	32	0.12	0.04	0.01
	256	32	0.09	0.05	0.01
	257	32	0.29	0.05	0.02
	258	32	0.14	0.05	0.01
	259	32	0.19	0.06	0.02
	260	32	0.14	0.07	0.01
PFCNTF	351	32	0.05	0.02	0.01
	352	32	0.07	0.07	0.01
	353	32	0.17	0.06	0.03
	354	32	0.08	0.08	0.01
	355	32	0.07	0.04	0.00
	356	32	0.19	0.14	0.05
	357	32	0.04	0.03	0.01
	358	32	0.06	0.06	0.02
	359	32	0.12	0.12	0.03
	360	32	0.05	0.05	0.01
B20F	751	32	0.19	0.05	0.02
	752	32	0.21	0.03	0.01
	753	32	0.20	0.03	0.01
	754	32	0.13	0.03	0.01
	755	32	0.13	0.06	0.00
	756	32	0.17	0.03	0.02
	758	32	0.20	0.03	0.02

**Table C-22. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
B20F	759	32	0.13	0.04	0.01
	760	32	0.15	0.01	0.00
PFCBF	851	32	0.10	0.11	0.01
	852	32	0.08	0.04	0.01
	853	32	0.10	0.08	0.02
	854	32	0.09	0.04	0.01
	855	32	0.03	0.06	0.01
	856	32	0.10	0.17	0.04
	857	32	0.04	0.02	0.01
	858	32	0.05	0.04	0.01
	859	32	0.03	0.02	0.00
	860	32	0.05	0.05	0.02
E20F	1251	32	0.23	0.04	0.02
	1252	32	0.08	0.05	0.01
	1253	32	0.20	0.01	0.02
	1254	32	0.11	0.04	0.03
	1255	32	0.07	0.03	0.01
	1256	32	0.08	0.02	0.00
	1257	32	0.27	0.05	0.03
	1258	32	0.13	0.01	0.01
	1259	32	0.06	0.03	0.01
	1260	32	0.11	0.04	0.03
PFCEF	1351	32	0.07	0.08	0.01
	1352	32	0.09	0.07	0.02
	1353	32	0.07	0.04	0.02
	1354	32	0.05	0.03	0.01
	1355	32	0.05	0.08	0.01

**Table C-22. Paired and High Dose Group Individual Animal Absolute WBC Differential Count Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Monocytes (10<sup>3</sup>/μL)</b>	<b>Eosinophils (10<sup>3</sup>/μL)</b>	<b>Basophils (10<sup>3</sup>/μL)</b>
PFCEF	1356	32	0.09	0.08	0.02
	1358	32	0.06	0.04	0.02
	1359	32	0.12	0.09	0.01
	1360	32	0.07	0.04	0.01

**Table C-23. Individual Animal Coagulation Data – Males**

<b>Group</b>	<b>Animal</b>		<b>Prothrombin Time (Seconds)</b>
	<b>ID</b>	<b>Day</b>	
CM	101	29	14.5
	102	29	15.0
	103	29	15.1
	104	29	15.6
	105	29	15.8
	106	29	14.3
	107	29	15.6
	108	29	15.0
	109	29	15.1
	110	29	15.0
B0.2M	401	29	15.0
	402	29	15.3
	404	29	15.2
	406	29	14.7
	407	29	15.3
	408	29	16.4
	409	29	16.3
	410	29	16.1
B2M	501	29	15.2
	502	29	15.3
	503	29	15.6
	505	29	14.8
	506	29	15.6
	507	29	16.3
	508	29	16.3
	509	29	15.8
	510	29	16.2

**Table C-23. Individual Animal Coagulation Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
B8M	601	29	14.7
	603	29	16.1
	605	29	16.1
	607	29	15.9
	609	29	16.1
	610	29	15.5
E0.2M	901	29	15.2
	902	29	15.5
	903	29	15.2
	904	29	16.5
	905	29	14.5
	906	29	14.8
	907	29	15.9
	908	29	16.7
	909	29	16.2
	910	29	16.5
E2M	1001	29	15.9
	1002	29	15.2
	1003	29	15.4
	1004	29	16.3
	1006	29	15.3
	1007	29	16.3
	1008	29	17.6
	1009	29	17.2
	1010	29	15.4
E8M	1101	29	14.9
	1102	29	15.3

**Table C-23. Individual Animal Coagulation Data – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Prothrombin Time (Seconds)</b>
	<b>ID</b>	<b>Day</b>	
E8M	1103	29	16.2
	1104	29	16.2
	1106	29	14.6
	1107	29	16.1
	1109	29	15.4
	1110	29	16.0

**Table C-24. Individual Animal Coagulation Data – Females**

<b>Group</b>	<b>Animal</b>		<b>Prothrombin Time (Seconds)</b>
	<b>ID</b>	<b>Day</b>	
CF	151	30	15.3
	152	30	15.3
	153	30	14.6
	154	30	14.7
	155	30	16.2
	156	30	16.1
	157	30	15.7
	158	30	15.9
	159	30	14.8
	160	30	14.8
B0.2F	451	30	15.0
	452	30	16.2
	453	30	14.8
	454	30	15.3
	455	30	15.7
	456	30	15.3
	457	30	15.2
	458	30	14.3
	459	30	15.7
	460	30	14.5
B2F	551	30	14.8
	553	30	15.6
	554	30	15.0
	555	30	16.6
	556	30	15.4
	558	30	15.6
	559	30	15.7

**Table C-24. Individual Animal Coagulation Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
B8F	651	30	15.0
	653	30	15.4
	654	30	14.9
	655	30	16.3
	656	30	15.4
	657	30	14.8
	658	30	14.2
	659	30	14.3
	660	30	14.9
E0.2F	951	30	15.5
	953	30	16.1
	954	30	15.6
	955	30	15.3
	956	30	16.5
	957	30	15.8
	958	30	14.7
	959	30	14.7
	960	30	15.1
E2F	1051	30	15.6
	1052	30	15.1
	1054	30	15.5
	1056	30	15.9
	1057	30	15.5
	1058	30	14.0
	1059	30	15.8
	1060	30	15.7

**Table C-24. Individual Animal Coagulation Data – Females (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Prothrombin Time (Seconds)</b>
	<b>ID</b>	<b>Day</b>	
E8F	1152	30	16.3
	1153	30	15.2
	1154	30	15.1
	1155	30	16.4
	1156	30	14.8
	1158	30	14.5
	1159	30	15.1

**Table C-25. Pairfed and High Dose Group Individual Animal Coagulation Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
NT20M	201	31	15.4
	202	31	14.5
	203	31	15.2
	204	31	16.1
	205	31	16.0
	206	31	14.2
	207	31	15.4
	208	31	15.9
	209	31	15.3
	210	31	15.9
PFCNTM	301	31	15.2
	302	31	16.2
	303	31	16.4
	304	31	16.4
	305	31	15.8
	306	31	15.9
	307	31	15.5
	308	31	16.6
	309	31	16.2
	310	31	17.2
B20M	701	31	14.7
	702	31	16.1
	703	31	16.4
	704	31	14.7
	705	31	15.9
	706	31	16.1
	707	31	15.2

**Table C-25. Paired and High Dose Group Individual Animal Coagulation Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
B20M	708	31	16.6
	709	31	15.0
	710	31	15.7
PFCBM	801	31	15.1
	802	31	15.5
	803	31	16.3
	804	31	16.7
	805	31	16.7
	806	31	15.7
	807	31	16.3
	808	31	16.4
	809	31	15.6
	810	31	18.0
E20M	1201	31	16.1
	1202	31	16.3
	1203	31	16.6
	1204	31	16.2
	1205	31	16.9
	1206	31	16.2
	1207	31	15.3
	1208	31	15.4
	1209	31	15.5
	1210	31	16.9
PFCM	1301	31	15.6
	1302	31	16.3
	1303	31	15.7
	1304	31	15.7

**Table C-25. Pairfed and High Dose Group Individual Animal Coagulation Data – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Prothrombin Time (Seconds)</b>
	<b>ID</b>	<b>Day</b>	
PFCEM	1305	31	17.0
	1306	31	15.9
	1307	31	16.7
	1308	31	15.4
	1309	31	16.3
	1310	31	16.0

**Table C-26. Paired and High Dose Group Individual Animal Coagulation Data – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
NT20F	252	32	15.6
	253	32	15.8
	255	32	15.3
	256	32	15.4
	258	32	15.2
	260	32	16.8
PFCNTF	351	32	15.6
	352	32	15.8
	353	32	15.6
	355	32	16.0
	356	32	16.2
	357	32	16.5
	358	32	15.2
	359	32	16.7
	360	32	16.7
B20F	751	32	15.5
	752	32	15.5
	753	32	16.0
	754	32	17.1
	755	32	15.8
	759	32	15.4
	760	32	16.2
PFCBF	851	32	15.4
	852	32	15.6
	853	32	15.6
	854	32	16.8
	855	32	16.2

**Table C-26. Paired and High Dose Group Individual Animal Coagulation Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Prothrombin Time (Seconds)</b>
PFCBF	856	32	16.9
	857	32	16.9
	859	32	16.1
	860	32	16.2
E20F	1251	32	15.7
	1254	32	15.3
	1255	32	16.5
	1259	32	15.7
	1260	32	18.3
PFCEF	1351	32	15.4
	1352	32	15.7
	1354	32	15.8
	1355	32	16.9
	1356	32	16.1
	1357	32	15.2
	1358	32	16.1
	1359	32	15.9

**Table C-27. Individual Animal Serum Chemistry Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
CM	101	29	119	56	1
	102	29	149	58	1
	103	29	141	58	1
	104	29	139	63	1
	105	29	139	68	1
	106	29	117	68	1
	107	29	93	57	1
	108	29	102	58	1
	109	29	144	60	1
	110	29	152	62	1
B0.2M	401	29	114	62	1
	402	29	177	58	1
	403	29	93	64	1
	404	29	138	64	1
	405	29	136	68	1
	406	29	108	99	1
	407	29	117	75	1
	408	29	117	61	1
	409	29	138	59	1
	410	29	132	58	1
B2M	501	29	111	58	1
	502	29	126	69	1
	503	29	114	59	1
	504	29	133	59	1
	505	29	143	62	1
	506	29	154	68	1

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
B2M	507	29	139	63	1
	508	29	174	78	1
	509	29	174	72	1
	510	29	182	92	1
B8M	601	29	96	60	1
	602	29	135	66	0
	603	29	119	59	1
	604	29	102	57	1
	605	29	115	58	1
	606	29	102	67	1
	607	29	120	62	1
	608	29	162	70	1
	609	29	113	57	1
	610	29	185	105	1
E0.2M	901	29	112	53	1
	902	29	102	56	1
	903	29	141	61	1
	904	29	109	57	1
	905	29	96	67	1
	906	29	109	64	1
	907	29	89	67	1
	908	29	97	58	1
	909	29	145	73	1
	910	29	85	52	1
E2M	1001	29	88	76	1
	1002	29	127	65	1

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
E2M	1003	29	98	63	1
	1004	29	162	73	0
	1005	29	151	59	1
	1006	29	108	64	1
	1007	29	128	64	1
	1008	29	105	74	1
	1009	29	140	63	1
	1010	29	155	83	1
E8M	1101	29	119	61	1
	1102	29	160	69	1
	1103	29	116	67	1
	1104	29	169	68	1
	1105	29	157	72	1
	1106	29	117	67	1
	1107	29	118	57	1
	1108	29	99	61	1
	1109	29	117	60	1
	1110	29	92	69	1

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
CM	101	29	0.10	0.04	6.2
	102	29	0.12	0.03	6.4
	103	29	0.10	0.03	6.1
	104	29	0.10	0.03	6.4
	105	29	0.11	0.04	6.3
	106	29	0.12	0.04	6.2
	107	29	0.13	0.05	6.8
	108	29	0.10	0.03	6.4
	109	29	0.13	0.04	6.2
	110	29	0.11	0.04	6.3
B0.2M	401	29	0.11	0.04	6.3
	402	29	0.08	0.03	6.1
	403	29	0.14	0.05	6.1
	404	29	0.13	0.03	6.7
	405	29	0.10	0.03	6.9
	406	29	0.13	0.05	6.3
	407	29	0.11	0.05	6.7
	408	29	0.08	0.04	6.1
	409	29	0.12	0.04	6.2
	410	29	0.12	0.03	6.2
B2M	501	29	0.10	0.03	5.8
	502	29	0.13	0.04	6.4
	503	29	0.13	0.05	6.3
	504	29	0.10	0.04	6.7
	505	29	0.12	0.04	6.5
	506	29	0.10	0.03	6.1
	507	29	0.13	0.04	6.1

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
B2M	508	29	0.11	0.05	6.1
	509	29	0.14	0.06	6.2
	510	29	0.10	0.04	6.4
B8M	601	29	0.10	0.04	6.5
	602	29	0.15	0.06	6.0
	603	29	0.13	0.06	6.4
	604	29	0.12	0.04	6.0
	605	29	0.11	0.04	6.0
	606	29	0.13	0.03	6.4
	607	29	0.10	0.05	6.2
	608	29	0.07	0.03	7.0
	609	29	0.10	0.03	5.9
	610	29	0.10	0.04	6.1
E0.2M	901	29	0.12	0.03	6.1
	902	29	0.14	0.04	6.4
	903	29	0.08	0.02	6.1
	904	29	0.09	0.04	6.1
	905	29	0.13	0.04	6.6
	906	29	0.11	0.03	6.5
	907	29	0.09	0.03	6.1
	908	29	0.11	0.04	6.1
	909	29	0.09	0.04	6.5
	910	29	0.12	0.04	6.3
E2M	1001	29	0.10	0.03	6.4
	1002	29	0.11	0.04	6.3
	1003	29	0.11	0.04	6.4
	1004	29	0.13	0.05	6.5

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
E2M	1005	29	0.12	0.04	6.0
	1006	29	0.11	0.04	6.5
	1007	29	0.10	0.03	6.3
	1008	29	0.14	0.03	6.1
	1009	29	0.14	0.05	6.1
	1010	29	0.09	0.04	7.4
E8M	1101	29	0.12	0.04	6.2
	1102	29	0.12	0.05	6.4
	1103	29	0.10	0.05	6.4
	1104	29	0.10	0.03	6.3
	1105	29	0.13	0.06	6.7
	1106	29	0.06	0.03	6.4
	1107	29	0.11	0.04	6.3
	1108	29	0.14	0.05	6.4
	1109	29	0.10	0.03	6.4
	1110	29	0.09	0.03	6.8

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
CM	101	29	97	4.0	2.2
	102	29	94	4.2	2.2
	103	29	82	3.9	2.2
	104	29	107	4.1	2.3
	105	29	80	4.2	2.1
	106	29	150	4.2	2.0
	107	29	71	4.5	2.3
	108	29	147	4.3	2.1
	109	29	94	4.2	2.0
	110	29	80	4.1	2.2
B0.2M	401	29	91	4.3	2.0
	402	29	98	3.9	2.2
	403	29	86	4.3	1.8
	404	29	93	4.4	2.3
	405	29	115	4.3	2.6
	406	29	82	4.3	2.0
	407	29	72	4.7	2.0
	408	29	74	4.1	2.0
	409	29	90	4.2	2.0
	410	29	68	4.0	2.2
B2M	501	29	93	3.8	2.0
	502	29	83	4.0	2.4
	503	29	72	4.5	1.8
	504	29	92	4.4	2.3
	505	29	86	4.1	2.4
	506	29	110	4.3	1.8
	507	29	90	4.1	2.0

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
B2M	508	29	101	4.2	1.9
	509	29	80	4.4	1.8
	510	29	80	4.3	2.1
B8M	601	29	75	4.3	2.2
	602	29	70	4.3	1.7
	603	29	80	4.5	1.9
	604	29	67	4.0	2.0
	605	29	57	4.3	1.7
	606	29	62	4.3	2.1
	607	29	57	4.4	1.8
	608	29	79	4.6	2.4
	609	29	83	4.1	1.8
	610	29	104	4.1	2.0
E0.2M	901	29	102	4.2	1.9
	902	29	91	4.2	2.2
	903	29	84	3.9	2.2
	904	29	87	4.1	2.0
	905	29	73	4.2	2.4
	906	29	89	4.2	2.3
	907	29	81	3.8	2.3
	908	29	69	4.2	1.9
	909	29	65	4.3	2.2
	910	29	79	4.1	2.2
E2M	1001	29	103	4.3	2.1
	1002	29	87	4.1	2.2
	1003	29	100	4.1	2.3
	1004	29	93	4.5	2.0

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
E2M	1005	29	76	4.1	1.9
	1006	29	76	4.4	2.1
	1007	29	70	4.2	2.1
	1008	29	70	4.2	1.9
	1009	29	62	4.2	1.9
	1010	29	60	4.7	2.7
E8M	1101	29	82	4.2	2.0
	1102	29	78	4.3	2.1
	1103	29	75	4.3	2.1
	1104	29	106	4.2	2.1
	1105	29	65	4.7	2.0
	1106	29	71	4.2	2.2
	1107	29	85	4.2	2.1
	1108	29	70	4.5	1.9
	1109	29	73	4.2	2.2
	1110	29	69	4.5	2.3

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
CM	101	29	1.82	17	0.7
	102	29	1.91	17	0.7
	103	29	1.77	14	0.6
	104	29	1.78	15	0.7
	105	29	2.00	9	0.6
	106	29	2.10	14	0.7
	107	29	1.96	10	0.6
	108	29	2.05	14	0.6
	109	29	2.10	10	0.6
	110	29	1.86	16	0.7
B0.2M	401	29	2.15	16	0.7
	402	29	1.77	12	0.6
	403	29	2.39	18	0.7
	404	29	1.91	17	0.7
	405	29	1.65	13	0.7
	406	29	2.15	13	0.6
	407	29	2.35	16	0.6
	408	29	2.05	11	0.6
	409	29	2.10	10	0.6
	410	29	1.82	16	0.7
B2M	501	29	1.90	14	0.7
	502	29	1.67	18	0.6
	503	29	2.50	13	0.7
	504	29	1.91	18	0.7
	505	29	1.71	15	0.7
	506	29	2.39	16	0.6
	507	29	2.05	13	0.6

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
B2M	508	29	2.21	12	0.6
	509	29	2.44	16	0.6
	510	29	2.05	18	0.6
B8M	601	29	1.95	13	0.6
	602	29	2.53	18	0.7
	603	29	2.37	14	0.7
	604	29	2.00	20	0.6
	605	29	2.53	21	0.7
	606	29	2.05	20	0.7
	607	29	2.44	16	0.6
	608	29	1.92	20	0.7
	609	29	2.28	14	0.6
	610	29	2.05	15	0.6
E0.2M	901	29	2.21	14	0.7
	902	29	1.91	12	0.7
	903	29	1.77	22	0.7
	904	29	2.05	15	0.6
	905	29	1.75	14	0.6
	906	29	1.83	15	0.7
	907	29	1.65	15	0.6
	908	29	2.21	12	0.6
	909	29	1.95	10	0.6
	910	29	1.86	12	0.6
E2M	1001	29	2.05	17	0.7
	1002	29	1.86	22	0.7
	1003	29	1.78	17	0.7
	1004	29	2.25	19	0.7

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
E2M	1005	29	2.16	17	0.7
	1006	29	2.10	15	0.7
	1007	29	2.00	18	0.6
	1008	29	2.21	15	0.6
	1009	29	2.21	14	0.7
	1010	29	1.74	12	0.6
E8M	1101	29	2.10	19	0.7
	1102	29	2.05	14	0.7
	1103	29	2.05	16	0.7
	1104	29	2.00	17	0.6
	1105	29	2.35	21	0.7
	1106	29	1.91	17	0.7
	1107	29	2.00	20	0.6
	1108	29	2.37	14	0.6
	1109	29	1.91	16	0.6
	1110	29	1.96	18	0.6

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
CM	101	29	27	75	11.3
	102	29	56	97	11.2
	103	29	33	71	11.1
	104	29	37	65	11.1
	105	29	22	50	11.2
	106	29	34	88	11.7
	107	29	26	68	11.4
	108	29	54	78	11.4
	109	29	36	95	11.0
	110	29	35	72	11.4
B0.2M	401	29	52	65	11.2
	402	29	31	80	10.9
	403	29	51	54	11.2
	404	29	26	86	11.6
	405	29	30	79	11.7
	406	29	39	77	11.6
	407	29	48	60	11.1
	408	29	36	71	11.1
	409	29	24	76	11.0
	410	29	60	71	10.8
B2M	501	29	44	48	11.3
	502	29	34	86	11.2
	503	29	24	66	10.8
	504	29	27	83	11.4
	505	29	22	78	11.4
	506	29	33	95	11.5
	507	29	31	77	11.5

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
B2M	508	29	35	78	11.6
	509	29	30	77	11.4
	510	29	38	77	12.1
B8M	601	29	42	75	11.4
	602	29	28	81	11.1
	603	29	30	83	11.2
	604	29	33	72	10.9
	605	29	39	70	11.2
	606	29	48	66	11.4
	607	29	70	111	11.4
	608	29	49	74	11.5
	609	29	66	64	11.0
	610	29	43	84	11.0
E0.2M	901	29	33	61	11.1
	902	29	63	69	11.4
	903	29	52	81	11.0
	904	29	51	83	11.2
	905	29	52	93	11.5
	906	29	35	81	10.8
	907	29	36	69	11.0
	908	29	59	71	11.7
	909	29	75	77	10.9
	910	29	70	76	11.4
E2M	1001	29	55	56	11.3
	1002	29	35	64	11.0
	1003	29	60	73	11.7
	1004	29	37	79	12.0

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
E2M	1005	29	61	83	11.8
	1006	29	26	69	11.6
	1007	29	44	69	11.5
	1008	29	43	91	11.2
	1009	29	54	62	11.2
	1010	29	64	86	11.9
E8M	1101	29	36	102	11.2
	1102	29	29	80	11.5
	1103	29	37	92	11.1
	1104	29	38	107	11.8
	1105	29	67	88	11.4
	1106	29	72	90	11.0
	1107	29	33	63	11.4
	1108	29	100	84	11.9
	1109	29	87	98	11.3
	1110	29	97	93	11.7

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
CM	101	29	9.9	146	4.7
	102	29	10.0	145	6.1
	103	29	11.4	145	5.3
	104	29	9.9	147	6.2
	105	29	10.8	147	6.1
	106	29	10.6	147	5.0
	107	29	12.2	146	6.6
	108	29	10.3	146	4.0
	109	29	10.9	146	5.7
	110	29	12.0	147	5.5
B0.2M	401	29	10.0	148	5.6
	402	29	10.6	146	5.6
	403	29	10.2	145	6.4
	404	29	11.0	148	6.1
	405	29	10.5	147	5.5
	406	29	11.6	145	6.4
	407	29	9.9	148	5.8
	408	29	10.9	146	5.2
	409	29	10.2	145	6.4
	410	29	12.0	146	5.6
B2M	501	29	11.2	146	6.2
	502	29	9.9	147	5.8
	503	29	11.4	147	6.7
	504	29	11.5	147	5.2
	505	29	12.7	145	5.5
	506	29	10.3	147	5.6
	507	29	9.3	146	6.0

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
B2M	508	29	11.9	148	6.2
	509	29	12.7	147	6.1
	510	29	13.1	147	5.5
B8M	601	29	9.1	148	6.1
	602	29	9.0	148	6.1
	603	29	10.2	147	5.9
	604	29	10.2	147	6.1
	605	29	14.5	148	6.3
	606	29	15.3	147	4.9
	607	29	12.9	145	6.7
	608	29	11.5	146	5.6
	609	29	10.2	147	5.6
	610	29	8.5	146	6.5
E0.2M	901	29	9.6	146	6.0
	902	29	9.5	146	6.0
	903	29	9.7	146	6.2
	904	29	10.3	147	5.3
	905	29	10.9	148	6.3
	906	29	10.6	146	5.6
	907	29	10.3	146	6.0
	908	29	11.3	147	6.0
	909	29	9.9	146	5.6
	910	29	10.9	147	5.8
E2M	1001	29	9.3	146	5.9
	1002	29	10.4	146	6.0
	1003	29	10.8	146	6.1
	1004	29	13.6	146	5.7

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
E2M	1005	29	11.4	147	6.0
	1006	29	11.3	147	4.8
	1007	29	12.8	147	6.5
	1008	29	10.9	148	5.0
	1009	29	12.7	148	6.3
	1010	29	11.1	147	6.5
E8M	1101	29	9.5	147	6.1
	1102	29	9.4	147	6.3
	1103	29	10.4	147	6.2
	1104	29	11.8	147	5.2
	1105	29	9.8	146	6.5
	1106	29	9.4	146	6.0
	1107	29	11.7	147	5.8
	1108	29	11.4	146	6.7
	1109	29	12.0	145	5.9
	1110	29	10.7	146	5.8

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
CM	101	29	100
	102	29	98
	103	29	98
	104	29	102
	105	29	100
	106	29	103
	107	29	98
	108	29	100
	109	29	99
	110	29	100
B0.2M	401	29	99
	402	29	99
	403	29	99
	404	29	100
	405	29	101
	406	29	99
	407	29	100
	408	29	100
	409	29	100
	410	29	99
B2M	501	29	101
	502	29	99
	503	29	100
	504	29	102
	505	29	101
	506	29	102
	507	29	102

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
B2M	508	29	100
	509	29	100
	510	29	100
B8M	601	29	102
	602	29	101
	603	29	100
	604	29	101
	605	29	101
	606	29	101
	607	29	98
	608	29	99
	609	29	102
	610	29	101
E0.2M	901	29	100
	902	29	101
	903	29	100
	904	29	101
	905	29	100
	906	29	101
	907	29	100
	908	29	99
	909	29	98
	910	29	98
E2M	1001	29	99
	1002	29	100
	1003	29	100
	1004	29	100

**Table C-27. Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
E2M	1005	29	99
	1006	29	100
	1007	29	100
	1008	29	102
	1009	29	99
	1010	29	98
E8M	1101	29	100
	1102	29	99
	1103	29	100
	1104	29	101
	1105	29	99
	1106	29	100
	1107	29	99
	1108	29	98
	1109	29	99
	1110	29	98

**Table C-28. Individual Animal Serum Chemistry Data – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
CF	151	30	72	64	1
	152	30	84	64	1
	153	30	51	54	1
	154	30	44	64	1
	155	30	81	85	1
	156	30	64	80	1
	157	30	78	64	1
	158	30	61	66	1
	159	30	39	63	1
	160	30	76	63	1
B0.2F	451	30	41	57	1
	452	30	73	62	1
	453	30	32	79	1
	454	30	73	71	1
	455	30	68	69	1
	456	30	42	69	1
	457	30	44	72	1
	458	30	56	66	1
	459	30	56	68	1
	460	30	46	69	2
B2F	551	30	54	68	1
	552	30	54	62	1
	553	30	85	65	1
	554	30	63	70	1
	555	30	33	66	1
	556	30	55	76	1

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
B2F	557	30	71	68	1
	558	30	82	89	1
	559	30	63	63	1
	560	30	72	98	1
B8F	651	30	48	61	1
	652	30	62	69	2
	653	30	50	82	1
	654	30	41	57	1
	655	30	50	73	1
	656	30	60	68	1
	657	30	137	70	2
	658	30	57	65	2
	659	30	96	100	2
	660	30	42	79	2
E0.2F	951	30	59	69	1
	952	30	69	65	1
	953	30	58	89	1
	954	30	49	62	1
	955	30	48	66	1
	956	30	70	65	1
	957	30	73	71	1
	958	30	66	73	1
	959	30	49	57	1
	960	30	80	85	1
E2F	1051	30	65	75	1
	1052	30	53	72	1

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
E2F	1053	30	56	65	1
	1054	30	73	64	1
	1055	30	76	75	2
	1056	30	40	60	1
	1057	30	65	62	1
	1058	30	37	70	1
	1059	30	61	61	1
	1060	30	77	65	1
E8F	1151	30	69	61	1
	1152	30	75	71	1
	1153	30	72	76	1
	1154	30	47	80	1
	1155	30	50	67	1
	1156	30	54	61	2
	1157	30	78	72	1
	1158	30	72	92	1
	1159	30	65	82	2
	1160	30	59	59	1

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
CF	151	30	0.09	0.01	6.3
	152	30	0.14	0.05	6.5
	153	30	0.10	0.04	6.5
	154	30	0.11	0.03	6.8
	155	30	0.11	0.03	6.3
	156	30	0.07	0.02	6.6
	157	30	0.09	0.03	6.1
	158	30	0.09	0.02	6.2
	159	30	0.10	0.03	6.9
	160	30	0.12	0.04	7.2
B0.2F	451	30	0.13	0.04	7.0
	452	30	0.09	0.03	6.7
	453	30	0.08	0.02	7.3
	454	30	0.13	0.04	6.4
	455	30	0.15	0.04	7.2
	456	30	0.11	0.03	7.1
	457	30	0.11	0.04	6.6
	458	30	0.11	0.04	7.2
	459	30	0.11	0.05	7.2
	460	30	0.14	0.04	7.1
B2F	551	30	0.09	0.02	6.0
	552	30	0.14	0.05	6.9
	553	30	0.10	0.04	6.8
	554	30	0.09	0.03	6.3
	555	30	0.11	0.03	6.9
	556	30	0.15	0.05	6.9
	557	30	0.10	0.02	6.0

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
B2F	558	30	0.12	0.05	6.5
	559	30	0.08	0.03	6.4
	560	30	0.10	0.04	7.1
B8F	651	30	0.11	0.06	6.1
	652	30	0.09	0.03	6.4
	653	30	0.07	0.03	6.2
	654	30	0.11	0.03	6.4
	655	30	0.09	0.04	6.1
	656	30	0.13	0.04	6.4
	657	30	0.11	0.04	6.1
	658	30	0.08	0.03	6.3
	659	30	0.09	0.04	6.1
	660	30	0.13	0.06	6.4
E0.2F	951	30	0.12	0.05	6.8
	952	30	0.10	0.03	6.5
	953	30	0.11	0.03	6.8
	954	30	0.08	0.03	6.5
	955	30	0.07	0.02	6.5
	956	30	0.14	0.06	6.9
	957	30	0.11	0.02	6.9
	958	30	0.12	0.03	7.6
	959	30	0.17	0.05	6.4
	960	30	0.10	0.04	6.6
E2F	1051	30	0.11	0.04	6.2
	1052	30	0.11	0.04	6.6
	1053	30	0.11	0.04	6.3
	1054	30	0.07	0.03	6.4

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
E2F	1055	30	0.09	0.03	7.0
	1056	30	0.08	0.03	6.8
	1057	30	0.09	0.03	6.3
	1058	30	0.11	0.06	7.1
	1059	30	0.11	0.03	6.1
	1060	30	0.12	0.04	6.3
E8F	1151	30	0.09	0.04	6.1
	1152	30	0.12	0.03	6.4
	1153	30	0.08	0.02	5.9
	1154	30	0.12	0.04	6.1
	1155	30	0.15	0.03	6.3
	1156	30	0.12	0.04	6.2
	1157	30	0.10	0.03	6.4
	1158	30	0.10	0.04	6.1
	1159	30	0.04	0.01	6.1
	1160	30	0.14	0.06	6.4

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
CF	151	30	99	4.7	1.6
	152	30	84	4.9	1.6
	153	30	104	4.8	1.7
	154	30	79	4.8	2.0
	155	30	72	4.6	1.7
	156	30	74	4.7	1.9
	157	30	70	4.2	1.9
	158	30	72	4.5	1.7
	159	30	67	5.0	1.9
	160	30	66	5.0	2.2
B0.2F	451	30	75	5.2	1.8
	452	30	85	4.8	1.9
	453	30	76	5.2	2.1
	454	30	77	4.5	1.9
	455	30	72	5.2	2.0
	456	30	74	5.0	2.1
	457	30	70	4.8	1.8
	458	30	62	5.2	2.0
	459	30	75	5.3	1.9
	460	30	59	5.4	1.7
B2F	551	30	80	4.2	1.8
	552	30	64	5.2	1.7
	553	30	74	4.7	2.1
	554	30	70	4.6	1.7
	555	30	61	5.0	1.9
	556	30	68	5.0	1.9
	557	30	66	4.2	1.8

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
B2F	558	30	69	4.8	1.7
	559	30	67	4.2	2.2
	560	30	76	4.9	2.2
B8F	651	30	72	4.2	1.9
	652	30	87	4.5	1.9
	653	30	71	4.3	1.9
	654	30	63	4.4	2.0
	655	30	67	4.3	1.8
	656	30	63	4.4	2.0
	657	30	70	4.2	1.9
	658	30	60	4.4	1.9
	659	30	62	4.2	1.9
	660	30	62	4.7	1.7
E0.2F	951	30	74	5.1	1.7
	952	30	90	4.6	1.9
	953	30	94	4.9	1.9
	954	30	86	4.4	2.1
	955	30	76	4.2	2.3
	956	30	74	5.1	1.8
	957	30	62	4.8	2.1
	958	30	68	5.2	2.4
	959	30	69	4.6	1.8
	960	30	66	4.4	2.2
E2F	1051	30	89	4.3	1.9
	1052	30	76	4.8	1.8
	1053	30	74	4.4	1.9
	1054	30	71	4.5	1.9

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
E2F	1055	30	81	5.0	2.0
	1056	30	75	4.8	2.0
	1057	30	65	4.4	1.9
	1058	30	84	5.2	1.9
	1059	30	72	4.3	1.8
	1060	30	66	4.6	1.7
E8F	1151	30	86	4.3	1.8
	1152	30	73	4.6	1.8
	1153	30	74	4.2	1.7
	1154	30	72	4.3	1.8
	1155	30	71	4.4	1.9
	1156	30	77	4.3	1.9
	1157	30	67	4.6	1.8
	1158	30	70	4.4	1.7
	1159	30	46	4.2	1.9
	1160	30	91	4.6	1.8

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
CF	151	30	2.94	14	0.7
	152	30	3.06	17	0.7
	153	30	2.82	12	0.6
	154	30	2.40	19	0.7
	155	30	2.71	14	0.7
	156	30	2.47	16	0.7
	157	30	2.21	16	0.7
	158	30	2.65	18	0.7
	159	30	2.63	18	0.7
	160	30	2.27	16	0.8
B0.2F	451	30	2.89	18	0.8
	452	30	2.53	15	0.7
	453	30	2.48	16	0.8
	454	30	2.37	22	0.8
	455	30	2.60	15	0.7
	456	30	2.38	15	0.7
	457	30	2.67	15	0.7
	458	30	2.60	18	0.7
	459	30	2.79	16	0.7
	460	30	3.18	13	0.7
B2F	551	30	2.33	21	0.7
	552	30	3.06	14	0.7
	553	30	2.24	19	0.8
	554	30	2.71	21	0.7
	555	30	2.63	16	0.7
	556	30	2.63	17	0.8
	557	30	2.33	17	0.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
B2F	558	30	2.82	17	0.8
	559	30	1.91	15	0.7
	560	30	2.23	19	0.7
B8F	651	30	2.21	25	0.7
	652	30	2.37	25	0.7
	653	30	2.26	22	0.6
	654	30	2.20	19	0.6
	655	30	2.39	18	0.7
	656	30	2.20	16	0.7
	657	30	2.21	23	0.6
	658	30	2.32	18	0.6
	659	30	2.21	19	0.6
	660	30	2.76	26	0.7
E0.2F	951	30	3.00	14	0.7
	952	30	2.42	19	0.7
	953	30	2.58	15	0.7
	954	30	2.10	13	0.7
	955	30	1.83	15	0.6
	956	30	2.83	21	0.7
	957	30	2.29	13	0.7
	958	30	2.17	15	0.8
	959	30	2.56	17	0.7
	960	30	2.00	16	0.7
E2F	1051	30	2.26	15	0.7
	1052	30	2.67	16	0.7
	1053	30	2.32	17	0.7
	1054	30	2.37	16	0.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
E2F	1055	30	2.50	21	0.8
	1056	30	2.40	18	0.7
	1057	30	2.32	17	0.6
	1058	30	2.74	17	0.7
	1059	30	2.39	19	0.7
	1060	30	2.71	18	0.7
E8F	1151	30	2.39	24	0.7
	1152	30	2.56	26	0.8
	1153	30	2.47	21	0.7
	1154	30	2.39	23	0.6
	1155	30	2.32	18	0.6
	1156	30	2.26	20	0.6
	1157	30	2.56	19	0.7
	1158	30	2.59	16	0.7
	1159	30	2.21	19	0.6
	1160	30	2.56	19	0.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
CF	151	30	23	55	10.6
	152	30	36	56	11.2
	153	30	33	82	11.5
	154	30	32	42	10.7
	155	30	28	25	11.0
	156	30	20	46	11.4
	157	30	32	48	10.9
	158	30	21	63	10.9
	159	30	38	59	11.6
	160	30	33	57	11.2
B0.2F	451	30	56	46	11.6
	452	30	30	57	10.8
	453	30	30	53	11.2
	454	30	33	41	10.4
	455	30	27	69	11.5
	456	30	32	51	11.2
	457	30	21	57	11.0
	458	30	34	59	11.1
	459	30	27	44	11.2
	460	30	48	75	11.4
B2F	551	30	28	44	10.9
	552	30	25	63	11.5
	553	30	25	64	10.9
	554	30	22	38	11.0
	555	30	26	37	11.4
	556	30	22	36	11.2
	557	30	34	28	10.3

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
B2F	558	30	35	43	10.7
	559	30	28	32	10.8
	560	30	25	48	11.7
B8F	651	30	58	43	11.3
	652	30	30	98	11.0
	653	30	21	58	11.1
	654	30	23	70	10.9
	655	30	30	52	11.3
	656	30	45	74	11.2
	657	30	120	81	11.4
	658	30	34	74	11.5
	659	30	35	74	10.5
	660	30	43	59	11.4
E0.2F	951	30	35	53	11.2
	952	30	40	58	11.1
	953	30	23	50	11.1
	954	30	20	49	10.6
	955	30	24	40	11.1
	956	30	32	48	10.8
	957	30	26	42	10.6
	958	30	38	61	11.2
	959	30	30	65	11.5
	960	30	29	50	11.1
E2F	1051	30	23	39	11.2
	1052	30	34	45	11.0
	1053	30	20	41	10.8
	1054	30	31	51	11.1

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
E2F	1055	30	25	53	11.1
	1056	30	26	46	11.2
	1057	30	38	55	11.4
	1058	30	23	49	10.9
	1059	30	40	71	11.4
	1060	30	27	53	11.4
E8F	1151	30	30	61	11.0
	1152	30	34	54	11.2
	1153	30	30	56	11.0
	1154	30	45	63	11.1
	1155	30	44	72	10.9
	1156	30	66	77	11.2
	1157	30	28	40	11.1
	1158	30	28	92	10.9
	1159	30	37	79	11.0
	1160	30	103	65	11.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
CF	151	30	9.2	145	4.8
	152	30	10.3	147	5.6
	153	30	8.7	147	5.3
	154	30	7.9	146	5.4
	155	30	10.1	146	5.3
	156	30	11.7	147	5.4
	157	30	10.7	146	5.7
	158	30	8.9	147	5.4
	159	30	10.5	146	5.2
	160	30	10.0	147	5.4
B0.2F	451	30	9.0	146	6.0
	452	30	7.7	146	5.7
	453	30	7.8	146	5.5
	454	30	8.8	145	5.5
	455	30	9.6	147	6.1
	456	30	7.5	146	5.6
	457	30	9.9	147	5.4
	458	30	8.2	144	5.2
	459	30	8.5	143	5.7
	460	30	9.5	150	5.5
B2F	551	30	8.5	146	6.1
	552	30	8.8	148	5.7
	553	30	10.3	146	5.7
	554	30	9.5	146	6.0
	555	30	10.4	147	6.4
	556	30	9.0	146	5.5
	557	30	8.9	145	5.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
B2F	558	30	9.5	147	5.5
	559	30	10.3	146	6.2
	560	30	12.5	146	6.0
B8F	651	30	8.6	146	6.3
	652	30	8.7	145	6.1
	653	30	9.5	145	5.9
	654	30	9.5	147	6.0
	655	30	11.2	145	5.8
	656	30	7.9	146	6.0
	657	30	11.0	146	5.8
	658	30	10.3	147	6.2
	659	30	9.4	148	5.7
	660	30	9.7	146	6.2
E0.2F	951	30	8.6	147	5.4
	952	30	10.4	147	6.4
	953	30	7.9	149	4.8
	954	30	9.1	149	5.5
	955	30	10.4	147	5.7
	956	30	8.8	146	5.3
	957	30	8.3	147	5.3
	958	30	8.2	149	4.9
	959	30	11.5	145	5.9
	960	30	10.4	148	5.5
E2F	1051	30	8.4	146	6.3
	1052	30	7.8	147	5.9
	1053	30	8.6	146	5.9
	1054	30	9.1	147	5.7

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
E2F	1055	30	9.6	147	5.8
	1056	30	10.0	146	5.7
	1057	30	11.9	146	5.6
	1058	30	8.2	147	5.9
	1059	30	10.8	149	6.0
	1060	30	11.3	148	4.7
E8F	1151	30	9.5	146	5.6
	1152	30	9.0	145	5.4
	1153	30	9.8	145	5.2
	1154	30	9.0	147	6.3
	1155	30	9.2	146	5.6
	1156	30	10.8	147	5.5
	1157	30	9.2	148	6.4
	1158	30	11.0	147	6.0
	1159	30	8.1	148	6.0
	1160	30	9.6	147	6.4

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
CF	151	30	106
	152	30	101
	153	30	101
	154	30	105
	155	30	102
	156	30	100
	157	30	102
	158	30	102
	159	30	99
	160	30	99
B0.2F	451	30	101
	452	30	104
	453	30	104
	454	30	100
	455	30	101
	456	30	102
	457	30	102
	458	30	98
	459	30	98
	460	30	101
B2F	551	30	103
	552	30	102
	553	30	101
	554	30	102
	555	30	101
	556	30	101
	557	30	100

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
B2F	558	30	100
	559	30	100
	560	30	97
B8F	651	30	101
	652	30	101
	653	30	101
	654	30	103
	655	30	102
	656	30	102
	657	30	99
	658	30	101
	659	30	103
	660	30	100
E0.2F	951	30	102
	952	30	102
	953	30	104
	954	30	104
	955	30	100
	956	30	98
	957	30	101
	958	30	102
	959	30	99
	960	30	99
E2F	1051	30	103
	1052	30	101
	1053	30	102
	1054	30	103

**Table C-28. Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
E2F	1055	30	103
	1056	30	101
	1057	30	99
	1058	30	102
	1059	30	101
	1060	30	103
E8F	1151	30	102
	1152	30	103
	1153	30	103
	1154	30	101
	1155	30	101
	1156	30	100
	1157	30	102
	1158	30	101
	1159	30	100
	1160	30	99

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
NT20M	201	31	155	50	2
	202	31	89	57	1
	203	31	111	83	1
	204	31	118	66	2
	205	31	114	66	1
	206	31	117	61	1
	207	31	166	55	1
	208	31	126	48	1
	209	31	123	53	1
	210	31	137	61	1
PFCNTM	301	31	107	67	1
	302	31	164	54	1
	303	31	144	67	1
	304	31	122	61	1
	305	31	106	72	1
	306	31	140	58	1
	307	31	167	47	1
	308	31	145	56	1
	309	31	121	70	1
	310	31	161	49	1
B20M	701	31	131	70	1
	702	31	182	69	2
	703	31	274	64	2
	704	31	150	68	1
	705	31	139	61	2
	706	31	75	73	1

**Table C-29. Paired and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
B20M	707	31	87	56	1
	708	31	131	55	1
	709	31	94	48	1
	710	31	173	57	1
PFCBM	801	31	110	96	1
	802	31	144	55	1
	803	31	90	69	1
	804	31	160	54	1
	805	31	119	68	1
	806	31	186	63	1
	807	31	122	81	1
	808	31	126	64	1
	809	31	116	48	1
	810	31	123	59	1
E20M	1201	31	154	85	1
	1202	31	152	70	2
	1203	31	162	52	2
	1204	31	282	87	2
	1205	31	149	68	1
	1206	31	153	57	2
	1207	31	103	60	1
	1208	31	202	61	1
	1209	31	175	62	1
	1210	31	119	53	1
PFCM	1301	31	147	51	1
	1302	31	147	64	1

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate</b>	<b>Gamma</b>
				<b>Aminotransferase (U/L)</b>	<b>Glutamyltransferase (U/L)</b>
PFCEM	1303	31	147	57	1
	1304	31	108	52	1
	1305	31	160	62	1
	1306	31	186	59	1
	1307	31	102	48	1
	1308	31	121	62	1
	1309	31	118	49	1
	1310	31	131	59	1

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
NT20M	201	31	0.11	0.05	5.8
	202	31	0.08	0.04	5.8
	203	31	0.10	0.04	5.7
	204	31	0.17	0.09	6.0
	205	31	0.07	0.01	5.7
	206	31	0.09	0.03	5.7
	207	31	0.17	0.10	5.5
	208	31	0.14	0.05	5.5
	209	31	0.08	0.05	5.7
	210	31	0.16	0.09	5.7
PFCNTM	301	31	0.11	0.04	6.3
	302	31	0.10	0.03	6.4
	303	31	0.05	0.02	5.8
	304	31	0.10	0.02	6.3
	305	31	0.12	0.04	6.1
	306	31	0.13	0.05	6.4
	307	31	0.11	0.03	6.4
	308	31	0.08	0.02	6.0
	309	31	0.11	0.03	5.8
	310	31	0.11	0.04	6.2
B20M	701	31	0.07	0.04	5.9
	702	31	0.28	0.18	5.8
	703	31	0.20	0.10	5.6
	704	31	0.09	0.03	6.2
	705	31	0.23	0.17	5.0
	706	31	0.14	0.09	5.3
	707	31	0.05	0.03	5.9

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
B20M	708	31	0.13	0.11	5.4
	709	31	0.13	0.09	5.6
	710	31	0.20	0.12	5.9
PFCBM	801	31	0.06	0.03	6.3
	802	31	0.07	0.02	6.4
	803	31	0.11	0.04	6.0
	804	31	0.10	0.03	5.9
	805	31	0.08	0.02	5.9
	806	31	0.08	0.02	5.9
	807	31	0.08	0.02	5.8
	808	31	0.09	0.03	6.4
	809	31	0.07	0.02	6.1
	810	31	0.06	0.03	5.8
E20M	1201	31	0.06	0.02	6.6
	1202	31	0.41	0.30	5.5
	1203	31	0.15	0.08	5.6
	1204	31	0.17	0.09	5.3
	1205	31	0.04	0.03	6.1
	1206	31	0.08	0.04	6.4
	1207	31	0.09	0.05	5.9
	1208	31	0.23	0.15	6.0
	1209	31	0.14	0.07	6.1
	1210	31	0.13	0.08	5.8
PFCM	1301	31	0.06	0.02	6.4
	1302	31	0.09	0.04	6.3
	1303	31	0.09	0.01	5.9
	1304	31	0.07	0.02	5.9

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
PFCEM	1305	31	0.08	0.02	6.3
	1306	31	0.08	0.02	5.7
	1307	31	0.10	0.03	6.0
	1308	31	0.09	0.03	6.4
	1309	31	0.10	0.03	5.9
	1310	31	0.06	0.02	6.1

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
NT20M	201	31	71	4.2	1.6
	202	31	72	4.1	1.7
	203	31	75	4.0	1.7
	204	31	71	4.3	1.7
	205	31	71	3.9	1.8
	206	31	69	3.7	2.0
	207	31	69	3.9	1.6
	208	31	74	3.9	1.6
	209	31	61	3.9	1.8
	210	31	80	4.1	1.6
PFCNTM	301	31	99	4.4	1.9
	302	31	116	4.3	2.1
	303	31	116	4.0	1.8
	304	31	112	4.1	2.2
	305	31	191	4.4	1.7
	306	31	113	4.4	2.0
	307	31	112	4.4	2.0
	308	31	178	4.1	1.9
	309	31	100	4.1	1.7
	310	31	108	4.2	2.0
B20M	701	31	75	4.0	1.9
	702	31	86	4.2	1.6
	703	31	77	4.1	1.5
	704	31	69	4.1	2.1
	705	31	82	3.6	1.4
	706	31	84	4.0	1.3
	707	31	70	4.1	1.8

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
B20M	708	31	64	4.0	1.4
	709	31	73	4.1	1.5
	710	31	81	4.3	1.6
PFCBM	801	31	118	4.3	2.0
	802	31	113	4.2	2.2
	803	31	88	4.4	1.6
	804	31	124	3.9	2.0
	805	31	110	4.0	1.9
	806	31	119	4.2	1.7
	807	31	117	3.9	1.9
	808	31	128	4.5	1.9
	809	31	129	4.2	1.9
	810	31	110	4.1	1.7
E20M	1201	31	108	4.3	2.3
	1202	31	70	4.2	1.3
	1203	31	66	4.0	1.6
	1204	31	78	4.0	1.3
	1205	31	68	4.0	2.1
	1206	31	66	4.4	2.0
	1207	31	64	3.9	2.0
	1208	31	60	4.3	1.7
	1209	31	79	4.3	1.8
	1210	31	72	4.3	1.5
PFCM	1301	31	107	4.5	1.9
	1302	31	108	4.5	1.8
	1303	31	121	3.9	2.0
	1304	31	124	4.0	1.9

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
PFCEM	1305	31	129	4.4	1.9
	1306	31	131	4.0	1.7
	1307	31	123	4.2	1.8
	1308	31	105	4.3	2.1
	1309	31	119	4.3	1.6
	1310	31	96	4.1	2.0

**Table C-29. Paired and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
NT20M	201	31	2.63	24	0.6
	202	31	2.41	22	0.6
	203	31	2.35	19	0.6
	204	31	2.53	21	0.6
	205	31	2.17	20	0.6
	206	31	1.85	21	0.5
	207	31	2.44	24	0.6
	208	31	2.44	22	0.5
	209	31	2.17	19	0.5
	210	31	2.56	20	0.5
PFCNTM	301	31	2.32	14	0.7
	302	31	2.05	13	0.7
	303	31	2.22	12	0.6
	304	31	1.86	12	0.7
	305	31	2.59	17	0.7
	306	31	2.20	14	0.7
	307	31	2.20	10	0.6
	308	31	2.16	8	0.6
	309	31	2.41	7	0.6
	310	31	2.10	12	0.6
B20M	701	31	2.11	19	0.6
	702	31	2.63	26	0.7
	703	31	2.73	19	0.6
	704	31	1.95	23	0.6
	705	31	2.57	32	0.5
	706	31	3.08	24	0.6
	707	31	2.28	19	0.6

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
B20M	708	31	2.86	29	0.6
	709	31	2.73	22	0.6
	710	31	2.69	23	0.6
PFCBM	801	31	2.15	10	0.7
	802	31	1.91	10	0.6
	803	31	2.75	13	0.6
	804	31	1.95	9	0.6
	805	31	2.11	10	0.6
	806	31	2.47	10	0.6
	807	31	2.05	9	0.6
	808	31	2.37	9	0.6
	809	31	2.21	7	0.6
	810	31	2.41	9	0.6
E20M	1201	31	1.87	22	0.7
	1202	31	3.23	31	0.6
	1203	31	2.50	29	0.6
	1204	31	3.08	25	0.6
	1205	31	1.90	17	0.6
	1206	31	2.20	23	0.6
	1207	31	1.95	20	0.6
	1208	31	2.53	22	0.6
	1209	31	2.39	20	0.6
	1210	31	2.87	23	0.6
PFCBM	1301	31	2.37	11	0.6
	1302	31	2.50	8	0.7
	1303	31	1.95	8	0.6
	1304	31	2.11	11	0.6

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
PFCEM	1305	31	2.32	11	0.6
	1306	31	2.35	10	0.6
	1307	31	2.33	7	0.6
	1308	31	2.05	9	0.6
	1309	31	2.69	10	0.6
	1310	31	2.05	7	0.6

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
NT20M	201	31	50	80	11.4
	202	31	43	82	11.4
	203	31	53	85	11.1
	204	31	40	85	10.7
	205	31	44	64	10.7
	206	31	58	110	11.7
	207	31	52	90	11.0
	208	31	76	86	11.0
	209	31	55	100	11.2
	210	31	48	77	11.0
PFCNTM	301	31	74	100	11.2
	302	31	62	107	11.6
	303	31	45	65	11.0
	304	31	52	83	10.9
	305	31	32	79	11.2
	306	31	53	80	11.3
	307	31	35	98	11.2
	308	31	45	95	11.2
	309	31	22	79	10.6
	310	31	34	84	10.8
B20M	701	31	75	101	11.5
	702	31	65	65	11.4
	703	31	48	88	11.5
	704	31	76	79	11.4
	705	31	38	100	10.9
	706	31	63	67	10.6
	707	31	96	73	10.9

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
B20M	708	31	173	103	10.7
	709	31	33	84	10.9
	710	31	132	66	11.6
PFCBM	801	31	66	74	11.6
	802	31	32	88	11.3
	803	31	44	83	10.7
	804	31	86	70	11.0
	805	31	49	75	10.5
	806	31	57	69	10.8
	807	31	41	81	10.8
	808	31	72	88	11.5
	809	31	33	60	10.8
	810	31	24	74	10.8
E20M	1201	31	186	77	11.9
	1202	31	49	67	11.0
	1203	31	72	121	11.1
	1204	31	32	77	10.8
	1205	31	77	89	11.4
	1206	31	92	110	11.7
	1207	31	71	74	11.0
	1208	31	77	93	11.6
	1209	31	76	95	11.4
	1210	31	47	69	10.9
PFCM	1301	31	72	74	11.2
	1302	31	35	69	11.0
	1303	31	41	87	11.2
	1304	31	25	98	11.0

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
PFCEM	1305	31	69	78	11.7
	1306	31	40	69	11.1
	1307	31	36	77	10.7
	1308	31	32	109	11.1
	1309	31	33	78	11.1
	1310	31	19	90	10.7

**Table C-29. Paired and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
NT20M	201	31	12.3	146	5.7
	202	31	10.8	145	6.2
	203	31	9.1	144	6.4
	204	31	9.9	143	6.1
	205	31	9.9	147	5.0
	206	31	13.8	144	6.7
	207	31	10.8	143	5.6
	208	31	11.0	143	5.9
	209	31	11.9	146	5.6
	210	31	10.1	143	5.5
PFCNTM	301	31	8.3	147	5.8
	302	31	9.0	146	6.1
	303	31	9.6	146	6.2
	304	31	7.8	145	5.7
	305	31	10.0	145	5.0
	306	31	8.9	146	6.0
	307	31	9.0	145	6.0
	308	31	10.2	145	4.7
	309	31	9.6	146	5.5
	310	31	8.1	145	5.7
B20M	701	31	9.3	144	6.4
	702	31	7.5	143	5.8
	703	31	9.0	145	6.0
	704	31	11.8	141	6.2
	705	31	12.5	142	5.9
	706	31	9.7	146	4.9
	707	31	9.5	145	6.0

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
B20M	708	31	11.9	145	5.8
	709	31	10.3	143	5.6
	710	31	9.5	145	6.2
PFCBM	801	31	9.1	146	6.4
	802	31	8.7	146	5.8
	803	31	9.1	146	6.1
	804	31	9.6	143	5.9
	805	31	9.1	144	6.2
	806	31	10.6	145	6.6
	807	31	8.3	145	5.6
	808	31	9.4	144	5.9
	809	31	9.3	144	5.3
	810	31	9.8	144	6.4
E20M	1201	31	5.8	149	6.2
	1202	31	10.2	145	5.8
	1203	31	10.8	146	5.7
	1204	31	8.4	149	5.6
	1205	31	11.2	144	6.2
	1206	31	10.3	145	5.7
	1207	31	10.8	143	6.3
	1208	31	12.4	144	5.7
	1209	31	8.7	142	5.5
	1210	31	10.2	143	6.0
PFCM	1301	31	8.2	146	5.9
	1302	31	9.7	145	6.5
	1303	31	9.0	145	6.3
	1304	31	10.0	144	6.0

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
PFCEM	1305	31	10.1	145	5.6
	1306	31	11.4	146	5.9
	1307	31	10.0	144	5.8
	1308	31	8.8	148	5.9
	1309	31	9.8	145	5.9
	1310	31	9.4	144	6.2

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
NT20M	201	31	99
	202	31	100
	203	31	100
	204	31	98
	205	31	100
	206	31	98
	207	31	98
	208	31	100
	209	31	99
	210	31	98
PFCNTM	301	31	102
	302	31	104
	303	31	103
	304	31	101
	305	31	103
	306	31	101
	307	31	101
	308	31	102
	309	31	102
	310	31	102
B20M	701	31	99
	702	31	99
	703	31	102
	704	31	97
	705	31	97
	706	31	100
	707	31	101

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
B20M	708	31	100
	709	31	98
	710	31	99
PFCBM	801	31	101
	802	31	102
	803	31	102
	804	31	103
	805	31	105
	806	31	104
	807	31	104
	808	31	102
	809	31	102
	810	31	102
E20M	1201	31	104
	1202	31	102
	1203	31	100
	1204	31	107
	1205	31	100
	1206	31	101
	1207	31	97
	1208	31	97
	1209	31	101
	1210	31	98
PFCM	1301	31	102
	1302	31	103
	1303	31	103
	1304	31	102

**Table C-29. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
PFCEM	1305	31	103
	1306	31	102
	1307	31	102
	1308	31	104
	1309	31	102
	1310	31	105

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
NT20F	251	32	131	64	2
	252	32	112	65	2
	253	32	142	59	3
	254	32	97	68	2
	255	32	144	84	3
	256	32	59	77	2
	257	32	90	92	3
	258	32	138	83	2
	259	32	159	77	3
	260	32	159	72	3
PFCNTF	351	32	157	55	1
	352	32	70	73	1
	353	32	111	53	1
	354	32	95	62	1
	355	32	71	63	1
	356	32	54	61	1
	357	32	131	70	2
	358	32	107	56	1
	359	32	77	72	1
	360	32	143	57	1
B20F	751	32	112	72	3
	752	32	116	56	3
	753	32	163	69	4
	754	32	95	73	4
	755	32	126	74	3
	756	32	93	86	2

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate Aminotransferase (U/L)</b>	<b>Gamma Glutamyltransferase (U/L)</b>
B20F	758	32	171	63	4
	759	32	107	65	3
	760	32	194	63	3
PFCBF	851	32	66	59	2
	852	32	46	60	1
	853	32	65	61	1
	854	32	88	107	1
	855	32	66	55	1
	856	32	47	66	1
	857	32	56	69	1
	858	32	56	65	1
	859	32	103	55	1
	860	32	69	58	1
E20F	1251	32	106	72	3
	1252	32	73	77	3
	1253	32	168	96	3
	1254	32	134	71	5
	1255	32	94	66	2
	1256	32	157	65	3
	1257	32	89	59	3
	1258	32	102	67	3
	1259	32	128	62	2
	1260	32	120	73	2
PFCEF	1351	32	45	53	1
	1352	32	70	61	1
	1353	32	48	64	1

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Alkaline Phosphatase (U/L)</b>	<b>Aspartate</b>	<b>Gamma</b>
				<b>Aminotransferase (U/L)</b>	<b>Glutamyltransferase (U/L)</b>
PFCEF	1354	32	53	57	1
	1355	32	44	55	1
	1356	32	127	57	1
	1357	32	44	52	1
	1358	32	48	46	1
	1359	32	34	56	1
	1360	32	52	48	1

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
NT20F	251	32	0.17	0.09	5.8
	252	32	0.10	0.06	5.7
	253	32	0.31	0.25	5.6
	254	32	0.23	0.14	5.7
	255	32	0.15	0.08	5.8
	256	32	0.18	0.14	5.1
	257	32	0.25	0.15	6.1
	258	32	0.24	0.23	5.5
	259	32	0.15	0.08	5.8
	260	32	0.17	0.10	6.3
PFCNTF	351	32	0.08	0.03	7.1
	352	32	0.12	0.05	6.4
	353	32	0.08	0.04	6.6
	354	32	0.14	0.04	6.9
	355	32	0.10	0.04	6.9
	356	32	0.10	0.04	6.6
	357	32	0.10	0.03	6.2
	358	32	0.10	0.04	6.5
	359	32	0.12	0.05	6.5
	360	32	0.13	0.03	6.4
B20F	751	32	0.20	0.13	5.6
	752	32	0.27	0.21	5.7
	753	32	0.35	0.29	6.2
	754	32	0.28	0.20	5.7
	755	32	0.15	0.07	5.8
	756	32	0.16	0.11	5.8
	758	32	0.62	0.54	5.9

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
B20F	759	32	0.24	0.15	6.6
	760	32	0.28	0.20	5.6
PFCBF	851	32	0.06	0.04	6.2
	852	32	0.11	0.03	6.2
	853	32	0.14	0.04	6.8
	854	32	0.14	0.07	6.3
	855	32	0.10	0.03	6.5
	856	32	0.08	0.04	6.3
	857	32	0.09	0.04	6.7
	858	32	0.07	0.03	6.4
	859	32	0.09	0.03	7.0
	860	32	0.08	0.03	7.0
E20F	1251	32	0.38	0.30	5.7
	1252	32	0.15	0.06	5.9
	1253	32	0.32	0.27	5.5
	1254	32	0.16	0.10	6.3
	1255	32	0.16	0.07	5.5
	1256	32	0.21	0.14	5.1
	1257	32	0.28	0.19	5.5
	1258	32	0.26	0.17	6.0
	1259	32	0.16	0.10	5.9
	1260	32	0.22	0.15	5.5
PFCEF	1351	32	0.12	0.04	6.9
	1352	32	0.12	0.03	6.7
	1353	32	0.10	0.03	7.1
	1354	32	0.14	0.05	6.9
	1355	32	0.10	0.03	6.6

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Total Bilirubin (mg/dL)</b>	<b>Direct Bilirubin (mg/dL)</b>	<b>Total Protein (g/dL)</b>
PFCEF	1356	32	0.10	0.04	6.5
	1357	32	0.09	0.03	6.5
	1358	32	0.07	0.01	6.4
	1359	32	0.11	0.04	7.2
	1360	32	0.10	0.04	6.4

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
NT20F	251	32	74	4.0	1.8
	252	32	73	4.2	1.5
	253	32	74	4.2	1.4
	254	32	72	4.1	1.6
	255	32	78	4.1	1.7
	256	32	72	3.7	1.4
	257	32	67	4.5	1.6
	258	32	64	4.1	1.4
	259	32	66	4.4	1.4
	260	32	61	4.6	1.7
PFCNTF	351	32	118	5.1	2.0
	352	32	86	4.6	1.8
	353	32	132	4.8	1.8
	354	32	107	4.7	2.2
	355	32	86	4.9	2.0
	356	32	102	5.1	1.5
	357	32	100	4.4	1.8
	358	32	100	4.6	1.9
	359	32	66	4.8	1.7
	360	32	97	4.7	1.7
B20F	751	32	61	4.0	1.6
	752	32	69	4.0	1.7
	753	32	61	4.6	1.6
	754	32	71	4.4	1.3
	755	32	68	4.3	1.5
	756	32	59	4.2	1.6
	758	32	64	4.5	1.4

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
B20F	759	32	76	4.8	1.8
	760	32	62	4.2	1.4
PFCBF	851	32	103	4.5	1.7
	852	32	78	4.6	1.6
	853	32	84	4.8	2.0
	854	32	104	4.6	1.7
	855	32	98	4.7	1.8
	856	32	74	4.5	1.8
	857	32	92	4.9	1.8
	858	32	108	4.7	1.7
	859	32	85	5.0	2.0
	860	32	86	5.1	1.9
E20F	1251	32	75	4.1	1.6
	1252	32	77	4.2	1.7
	1253	32	74	4.1	1.4
	1254	32	57	4.5	1.8
	1255	32	73	4.0	1.5
	1256	32	65	3.9	1.2
	1257	32	66	4.3	1.2
	1258	32	72	4.4	1.6
	1259	32	68	4.1	1.8
	1260	32	59	4.0	1.5
PFCEF	1351	32	90	5.0	1.9
	1352	32	96	4.7	2.0
	1353	32	86	4.8	2.3
	1354	32	98	5.0	1.9
	1355	32	83	4.6	2.0

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Glucose (mg/dL)</b>	<b>Albumin (g/dL)</b>	<b>Globulin (g/dL)</b>
PFCEF	1356	32	89	4.7	1.8
	1357	32	81	4.6	1.9
	1358	32	79	4.5	1.9
	1359	32	64	5.3	1.9
	1360	32	83	4.9	1.5

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
NT20F	251	32	2.22	25	0.6
	252	32	2.80	24	0.6
	253	32	3.00	23	0.6
	254	32	2.56	28	0.6
	255	32	2.41	23	0.6
	256	32	2.64	25	0.6
	257	32	2.81	21	0.6
	258	32	2.93	25	0.6
	259	32	3.14	20	0.6
	260	32	2.71	26	0.7
PFCNTF	351	32	2.55	11	0.7
	352	32	2.56	17	0.7
	353	32	2.67	10	0.6
	354	32	2.14	9	0.7
	355	32	2.45	13	0.7
	356	32	3.40	13	0.7
	357	32	2.44	13	0.6
	358	32	2.42	9	0.7
	359	32	2.82	14	0.6
	360	32	2.76	14	0.7
B20F	751	32	2.50	28	0.6
	752	32	2.35	32	0.6
	753	32	2.88	32	0.6
	754	32	3.38	42	0.6
	755	32	2.87	24	0.6
	756	32	2.63	27	0.6
	758	32	3.21	33	0.7

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
B20F	759	32	2.67	27	0.7
	760	32	3.00	29	0.6
PFCBF	851	32	2.65	11	0.7
	852	32	2.88	14	0.7
	853	32	2.40	17	0.8
	854	32	2.71	8	0.6
	855	32	2.61	12	0.7
	856	32	2.50	11	0.7
	857	32	2.72	11	0.7
	858	32	2.76	12	0.7
	859	32	2.50	12	0.7
	860	32	2.68	12	0.7
E20F	1251	32	2.56	33	0.6
	1252	32	2.47	33	0.7
	1253	32	2.93	38	0.6
	1254	32	2.50	25	0.6
	1255	32	2.67	25	0.6
	1256	32	3.25	24	0.5
	1257	32	3.58	32	0.6
	1258	32	2.75	30	0.6
	1259	32	2.28	28	0.7
	1260	32	2.67	29	0.6
PFCEF	1351	32	2.63	15	0.7
	1352	32	2.35	12	0.7
	1353	32	2.09	9	0.7
	1354	32	2.63	11	0.7
	1355	32	2.30	16	0.6

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Albumin/Globulin Ratio</b>	<b>Blood Urea Nitrogen (mg/dL)</b>	<b>Creatinine (mg/dL)</b>
PFCEF	1356	32	2.61	9	0.7
	1357	32	2.42	11	0.6
	1358	32	2.37	9	0.6
	1359	32	2.79	16	0.6
	1360	32	3.27	10	0.6

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
NT20F	251	32	96	89	11.4
	252	32	70	109	11.5
	253	32	51	100	11.7
	254	32	51	104	11.7
	255	32	103	101	11.2
	256	32	50	76	11.5
	257	32	121	78	11.5
	258	32	293	89	11.4
	259	32	86	94	11.5
	260	32	65	97	10.9
PFCNTF	351	32	71	55	11.9
	352	32	34	61	10.6
	353	32	38	61	10.9
	354	32	32	56	11.0
	355	32	36	60	11.0
	356	32	41	50	11.0
	357	32	51	65	10.9
	358	32	54	73	11.3
	359	32	75	51	10.9
	360	32	49	67	11.0
B20F	751	32	121	105	11.7
	752	32	95	103	12.0
	753	32	107	84	12.1
	754	32	47	79	11.7
	755	32	85	82	11.6
	756	32	76	89	11.5
	758	32	118	70	11.7

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
B20F	759	32	53	95	11.9
	760	32	70	82	10.8
PFCBF	851	32	25	78	11.3
	852	32	22	42	11.0
	853	32	31	55	10.7
	854	32	38	62	10.6
	855	32	22	57	10.5
	856	32	24	59	11.1
	857	32	25	38	10.5
	858	32	42	82	10.8
	859	32	41	69	10.8
	860	32	39	68	10.6
E20F	1251	32	77	94	11.7
	1252	32	50	74	12.1
	1253	32	67	80	11.4
	1254	32	203	121	11.4
	1255	32	26	77	10.8
	1256	32	144	68	11.0
	1257	32	80	88	10.8
	1258	32	56	106	11.8
	1259	32	44	79	11.2
	1260	32	79	75	10.6
PFCEF	1351	32	31	68	11.5
	1352	32	41	71	11.5
	1353	32	35	56	11.2
	1354	32	24	66	11.0
	1355	32	19	64	10.6

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Triglycerides (mg/dL)</b>	<b>Cholesterol (mg/dL)</b>	<b>Calcium (mg/dL)</b>
PFCEF	1356	32	30	91	10.9
	1357	32	35	63	11.1
	1358	32	25	66	10.6
	1359	32	24	49	11.3
	1360	32	42	57	10.7

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
NT20F	251	32	8.5	144	5.6
	252	32	6.8	146	5.8
	253	32	8.1	144	6.0
	254	32	9.4	146	5.8
	255	32	7.6	146	5.8
	256	32	11.3	144	6.2
	257	32	10.0	146	5.9
	258	32	9.1	146	5.5
	259	32	8.4	145	6.0
	260	32	8.3	148	5.3
PFCNTF	351	32	7.5	147	5.7
	352	32	7.9	146	6.4
	353	32	7.9	147	5.7
	354	32	7.7	146	6.2
	355	32	7.1	144	5.3
	356	32	8.0	146	5.9
	357	32	8.3	145	5.9
	358	32	8.6	145	6.7
	359	32	8.5	146	5.9
	360	32	8.7	147	5.5
B20F	751	32	10.3	150	6.1
	752	32	8.4	147	4.8
	753	32	8.6	145	6.0
	754	32	10.7	146	4.7
	755	32	8.9	148	6.3
	756	32	12.1	145	5.9
	758	32	11.0	145	5.6

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
B20F	759	32	11.0	147	5.9
	760	32	9.8	148	5.2
PFCBF	851	32	9.4	145	6.3
	852	32	7.9	146	6.2
	853	32	7.6	145	5.5
	854	32	8.1	146	5.5
	855	32	7.0	146	5.8
	856	32	8.9	144	6.9
	857	32	7.6	145	5.6
	858	32	6.8	144	5.8
	859	32	6.8	146	5.3
	860	32	6.5	144	5.4
E20F	1251	32	7.7	144	6.0
	1252	32	8.2	143	6.7
	1253	32	10.7	144	5.8
	1254	32	9.0	145	6.2
	1255	32	9.4	146	5.8
	1256	32	8.4	144	5.6
	1257	32	12.4	148	5.7
	1258	32	9.5	147	5.5
	1259	32	10.9	144	6.0
	1260	32	10.3	147	5.6
PFCEF	1351	32	7.2	146	5.8
	1352	32	8.0	145	6.5
	1353	32	6.3	146	5.9
	1354	32	7.7	146	5.7
	1355	32	7.9	146	5.7

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Phosphorus (mg/dL)</b>	<b>Sodium (mmol/L)</b>	<b>Potassium (mmol/L)</b>
PFCEF	1356	32	8.1	147	5.9
	1357	32	9.3	144	5.9
	1358	32	6.4	145	5.6
	1359	32	9.0	144	6.3
	1360	32	8.6	146	5.8

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
NT20F	251	32	101
	252	32	101
	253	32	97
	254	32	100
	255	32	102
	256	32	100
	257	32	101
	258	32	99
	259	32	104
	260	32	103
PFCNTF	351	32	103
	352	32	104
	353	32	104
	354	32	104
	355	32	102
	356	32	101
	357	32	102
	358	32	102
	359	32	99
	360	32	103
B20F	751	32	101
	752	32	98
	753	32	97
	754	32	101
	755	32	105
	756	32	97
	758	32	98

**Table C-30. Paired and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
B20F	759	32	98
	760	32	100
PFCBF	851	32	103
	852	32	103
	853	32	102
	854	32	102
	855	32	104
	856	32	104
	857	32	105
	858	32	104
	859	32	104
	860	32	103
E20F	1251	32	97
	1252	32	101
	1253	32	95
	1254	32	100
	1255	32	101
	1256	32	104
	1257	32	98
	1258	32	98
	1259	32	98
	1260	32	102
PFCEF	1351	32	101
	1352	32	101
	1353	32	103
	1354	32	103
	1355	32	104

**Table C-30. Pairfed and High Dose Group Individual Animal Serum Chemistry Data – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Chloride (mmol/L)</b>
PFCEF	1356	32	104
	1357	32	103
	1358	32	103
	1359	32	99
	1360	32	103

**APPENDIX D: PATHOLOGY INDIVIDUAL ANIMAL DATA**

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
CM	101	29	0.062	1.974	1.0600	0.885
	102	29	0.072	1.933	1.0738	1.081
	103	29	0.067	1.995	0.8469	1.077
	104	29	0.057	1.782	0.8560	0.851
	105	29	0.067	2.032	1.0758	1.071
	106	29	0.076	1.862	0.8852	0.990
	107	29	0.063	1.954	0.9175	0.849
	108	29	0.064	1.942	1.1682	1.031
	109	29	0.067	1.943	0.9341	1.000
	110	29	0.075	1.961	1.1279	0.938
B0.2M	401	29	0.049	1.865	0.8997	0.733
	402	29	0.064	1.917	1.0301	0.944
	403	29	0.064	2.004	1.0395	1.046
	404	29	0.067	1.876	0.8529	0.738
	405	29	0.050	1.966	0.9528	0.987
	406	29	0.064	1.817	0.8767	0.999
	407	29	0.055	1.959	0.9374	0.902
	408	29	0.059	1.922	0.9614	0.886
	409	29	0.065	1.879	1.0899	0.894
	410	29	0.070	2.065	1.0294	0.888
B2M	501	29	0.072	1.881	1.0327	0.923
	502	29	0.064	1.966	0.9984	0.987
	503	29	0.055	1.810	0.9857	0.797
	504	29	0.070	1.955	0.9708	0.969
	505	29	0.088	2.101	1.0028	1.002
	506	29	0.060	1.842	0.9176	0.849
	507	29	0.058	1.967	0.9592	0.815
	508	29	0.058	1.969	0.9811	0.763

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
B2M	509	29	0.064	1.943	0.8361	0.826
	510	29	0.062	1.891	0.8694	0.843
B8M	601	29	0.058	1.995	0.8796	0.794
	602	29	0.046	1.741	0.9102	0.721
	603	29	0.044	1.863	0.8811	0.858
	604	29	0.048	1.845	0.8984	0.800
	605	29	0.039	1.781	0.9521	0.719
	606	29	0.047	1.781	0.8841	0.710
	607	29	0.039	1.918	0.7351	0.635
	608	29	0.053	1.932	0.8256	0.888
	609	29	0.053	1.798	0.9692	0.777
	610	29	0.065	1.779	0.9925	0.729
E0.2M	901	29	0.042	1.836	0.7876	0.856
	902	29	0.069	1.872	0.8802	0.978
	903	29	0.063	1.906	1.0794	0.941
	904	29	0.060	2.019	0.9183	0.964
	905	29	0.049	2.001	0.7655	0.898
	906	29	0.080	1.926	1.0747	1.145
	907	29	0.076	1.985	1.0150	1.065
	908	29	0.057	1.895	0.8835	0.916
	909	29	0.053	1.840	0.8943	0.870
	910	29	0.057	1.950	1.0385	0.848
E2M	1001	29	0.066	2.009	0.9026	0.867
	1002	29	0.076	1.896	0.8800	0.902
	1003	29	0.054	1.960	0.9496	1.164
	1004	29	0.055	1.799	0.9153	0.871
	1005	29	0.056	1.920	0.8418	1.019

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
E2M	1006	29	0.068	1.888	0.8197	0.832
	1007	29	0.045	1.883	0.7783	0.880
	1008	29	0.044	1.918	0.9602	0.716
	1009	29	0.072	2.017	1.1469	0.925
	1010	29	0.069	2.027	0.9418	1.032
E8M	1101	29	0.057	1.858	1.1057	0.819
	1102	29	0.049	1.829	0.8675	0.861
	1103	29	0.061	1.844	0.8306	0.894
	1104	29	0.065	1.773	0.9480	0.851
	1105	29	0.053	1.872	0.8081	0.819
	1106	29	0.057	1.880	0.9715	0.774
	1107	29	0.048	1.933	0.8723	0.708
	1108	29	0.062	1.891	1.1157	0.811
	1109	29	0.057	1.915	0.8682	0.724
	1110	29	0.049	1.896	0.8186	0.835

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Kidneys</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>
	<b>ID</b>	<b>Day</b>				
CM	101	29	1.955	7.095	0.590	0.552
	102	29	2.072	8.666	0.624	0.519
	103	29	1.874	8.087	0.626	0.651
	104	29	1.746	7.477	0.585	0.437
	105	29	2.067	7.604	0.607	0.614
	106	29	1.859	8.459	0.601	0.467
	107	29	1.831	6.237	0.596	0.486
	108	29	2.157	8.147	0.656	0.583
	109	29	2.069	9.107	0.722	0.508
	110	29	1.930	7.947	0.582	0.524
B0.2M	401	29	1.736	6.066	0.469	0.474
	402	29	1.964	7.082	0.543	0.726
	403	29	2.016	7.278	0.642	0.577
	404	29	1.635	6.388	0.516	0.422
	405	29	1.908	7.581	0.626	0.492
	406	29	2.109	7.860	0.573	0.503
	407	29	1.878	6.469	0.568	0.551
	408	29	1.910	6.556	0.521	0.588
	409	29	1.833	7.643	0.641	0.543
	410	29	2.173	7.139	0.594	0.630
B2M	501	29	1.982	6.682	0.665	0.574
	502	29	2.143	7.600	0.779	0.572
	503	29	1.451	4.960	0.556	0.408
	504	29	2.063	8.024	0.647	0.639
	505	29	2.069	7.597	0.662	0.499
	506	29	1.860	7.205	0.561	0.638
	507	29	1.869	6.295	0.513	0.518
	508	29	1.772	6.724	0.637	0.452

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>
B2M	509	29	1.769	6.013	0.576	0.465
	510	29	1.603	6.134	0.533	0.470
B8M	601	29	1.945	6.995	0.596	0.557
	602	29	1.348	4.958	0.498	0.266
	603	29	1.956	6.561	0.538	0.458
	604	29	1.665	6.912	0.586	0.288
	605	29	1.647	5.618	0.587	0.411
	606	29	1.552	5.861	0.563	0.399
	607	29	1.380	4.916	0.477	0.387
	608	29	1.729	6.437	0.535	0.386
	609	29	1.795	6.673	0.593	0.532
	610	29	1.765	7.704	0.517	0.439
E0.2M	901	29	1.829	7.229	0.583	0.620
	902	29	2.042	8.173	0.622	0.571
	903	29	2.111	7.999	0.515	0.459
	904	29	2.173	7.283	0.635	0.537
	905	29	2.013	7.524	0.519	0.568
	906	29	1.937	8.069	0.706	0.507
	907	29	2.041	8.248	0.732	0.667
	908	29	1.859	6.513	0.554	0.496
	909	29	1.935	7.282	0.505	0.495
	910	29	2.068	6.658	0.590	0.443
E2M	1001	29	1.788	6.813	0.603	0.562
	1002	29	1.858	7.577	0.675	0.566
	1003	29	2.122	8.788	0.634	0.576
	1004	29	1.652	5.887	0.588	0.452
	1005	29	1.784	7.158	0.688	0.492
	1006	29	2.088	7.303	0.600	0.583

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Kidneys</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>
E2M	1007	29	1.978	6.533	0.620	0.504
	1008	29	1.540	5.476	0.484	0.345
	1009	29	2.035	7.295	0.643	0.559
	1010	29	2.198	7.737	0.734	0.540
E8M	1101	29	1.633	6.863	0.606	0.533
	1102	29	1.711	6.672	0.627	0.413
	1103	29	1.717	7.269	0.635	0.584
	1104	29	1.642	7.093	0.548	0.524
	1105	29	1.536	5.917	0.575	0.450
	1106	29	1.739	6.107	0.634	0.445
	1107	29	1.752	5.786	0.560	0.457
	1108	29	1.771	6.104	0.560	0.486
	1109	29	1.446	5.494	0.498	0.384
	1110	29	1.656	6.261	0.525	0.413

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

Group	Animal		Testes	Thymus
	ID	Day		
CM	101	29	3.751	0.646
	102	29	3.361	0.784
	103	29	3.518	0.580
	104	29	2.855	0.561
	105	29	3.526	0.559
	106	29	2.778	0.519
	107	29	3.261	0.628
	108	29	3.371	0.636
	109	29	3.328	0.743
	110	29	3.872	0.617
B0.2M	401	29	2.855	0.533
	402	29	3.246	0.524
	403	29	3.467	0.492
	404	29	3.187	0.571
	405	29	3.437	0.584
	406	29	3.211	0.734
	407	29	3.288	0.529
	408	29	3.333	0.420
	409	29	3.307	0.561
	410	29	3.328	0.715
B2M	501	29	3.521	0.471
	502	29	3.385	0.499
	503	29	3.046	0.347
	504	29	3.488	0.456
	505	29	3.386	0.661
	506	29	3.159	0.481
	507	29	3.206	0.482
	508	29	3.345	0.415

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Testes</b>	<b>Thymus</b>
B2M	509	29	3.302	0.429
	510	29	3.296	0.493
B8M	601	29	3.156	0.601
	602	29	3.031	0.290
	603	29	2.922	0.484
	604	29	3.038	0.384
	605	29	3.241	0.354
	606	29	3.104	0.427
	607	29	3.248	0.411
	608	29	3.292	0.349
	609	29	3.360	0.508
	610	29	2.994	0.461
E0.2M	901	29	2.937	0.475
	902	29	2.831	0.710
	903	29	3.340	0.605
	904	29	3.240	0.525
	905	29	2.820	0.486
	906	29	3.484	0.437
	907	29	3.640	0.725
	908	29	3.233	0.453
	909	29	3.180	0.706
	910	29	3.508	0.527
E2M	1001	29	2.935	0.539
	1002	29	3.308	0.533
	1003	29	3.177	0.524
	1004	29	3.174	0.619
	1005	29	3.184	0.517
	1006	29	3.031	0.584

**Table D-1. Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Testes</b>	<b>Thymus</b>
E2M	1007	29	2.806	0.438
	1008	29	3.094	0.275
	1009	29	3.984	0.529
	1010	29	3.318	0.651
E8M	1101	29	3.790	0.590
	1102	29	3.224	0.624
	1103	29	3.007	0.604
	1104	29	3.319	0.451
	1105	29	2.978	0.406
	1106	29	3.136	0.435
	1107	29	3.271	0.394
	1108	29	3.516	0.462
	1109	29	3.088	0.476
	1110	29	3.345	0.625

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>
CF	151	30	0.077	1.715	0.627	1.265
	152	30	0.069	1.758	0.612	1.155
	153	30	0.075	1.775	0.656	1.296
	154	30	0.066	1.835	0.690	1.265
	155	30	0.075	1.862	0.613	1.382
	156	30	0.086	1.863	0.654	1.395
	157	30	0.069	1.759	0.649	1.374
	158	30	0.078	1.820	0.660	1.209
	159	30	0.065	1.752	0.545	1.090
	160	30	0.064	1.823	0.542	1.201
B0.2F	451	30	0.063	1.794	0.511	1.201
	452	30	0.057	1.729	0.634	1.274
	453	30	0.066	1.724	0.610	1.197
	454	30	0.062	1.816	0.561	1.183
	455	30	0.070	1.869	0.615	1.242
	456	30	0.061	1.717	0.682	1.151
	457	30	0.070	1.786	0.655	1.389
	458	30	0.077	1.754	0.734	1.387
	459	30	0.075	1.777	0.615	1.283
	460	30	0.065	1.698	0.662	1.194
B2F	551	30	0.065	1.765	0.624	1.201
	552	30	0.079	1.795	0.562	1.154
	553	30	0.084	1.819	0.626	1.119
	554	30	0.069	1.883	0.581	1.154
	555	30	0.055	1.921	0.603	1.220
	556	30	0.082	1.858	0.598	1.219
	557	30	0.063	1.771	0.608	1.229
	558	30	0.067	1.711	0.571	1.064

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>
B2F	559	30	0.080	1.785	0.718	1.305
	560	30	0.076	1.876	0.649	1.288
B8F	651	30	0.052	1.790	0.485	1.184
	652	30	0.052	1.621	0.498	1.076
	653	30	0.062	1.847	0.546	1.181
	654	30	0.060	1.607	0.517	1.054
	655	30	0.070	1.798	0.533	1.092
	656	30	0.077	1.752	0.562	1.243
	657	30	0.061	1.742	0.521	1.116
	658	30	0.045	1.717	0.463	1.229
	659	30	0.057	1.832	0.478	0.994
	660	30	0.059	1.713	0.546	1.081
E0.2F	951	30	0.071	1.804	0.599	1.192
	952	30	0.078	1.764	0.677	1.212
	953	30	0.079	1.731	0.659	1.268
	954	30	0.077	1.728	0.662	1.287
	955	30	0.075	1.742	0.692	1.397
	956	30	0.076	1.803	0.717	1.334
	957	30	0.087	1.811	0.707	1.268
	958	30	0.066	1.709	0.602	1.205
	959	30	0.089	1.670	0.651	1.262
	960	30	0.082	1.841	0.687	1.360
E2F	1051	30	0.066	1.814	0.605	1.232
	1052	30	0.075	1.809	0.637	1.176
	1053	30	0.103	1.787	0.546	1.246
	1054	30	0.084	1.761	0.617	1.241
	1055	30	0.116	1.820	0.665	1.431
	1056	30	0.070	1.720	0.582	1.126

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>
E2F	1057	30	0.065	1.760	0.567	1.196
	1058	30	0.082	1.748	0.563	1.230
	1059	30	0.052	1.820	0.510	1.152
	1060	30	0.071	1.738	0.643	1.240
E8F	1151	30	0.068	1.797	0.597	1.218
	1152	30	0.055	1.671	0.483	0.949
	1153	30	0.057	1.884	0.634	1.176
	1154	30	0.049	1.716	0.486	1.250
	1155	30	0.036	1.763	0.577	1.236
	1156	30	0.059	1.705	0.586	1.192
	1157	30	0.069	1.722	0.564	1.130
	1158	30	0.071	1.797	0.492	1.122
	1159	30	0.065	1.708	0.585	1.248
	1160	30	0.053	1.730	0.573	1.234

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Liver</b>	<b>Ovaries</b>	<b>Salivary Gland</b>	<b>Spleen</b>
CF	151	30	4.707	0.081	0.424	0.418
	152	30	4.573	0.123	0.424	0.342
	153	30	4.873	0.111	0.437	0.368
	154	30	4.460	0.100	0.416	0.402
	155	30	4.272	0.104	0.456	0.382
	156	30	5.187	0.159	0.454	0.496
	157	30	4.729	0.094	0.386	0.384
	158	30	4.914	0.135	0.524	0.415
	159	30	4.328	0.089	0.344	0.457
	160	30	4.678	0.082	0.392	0.400
B0.2F	451	30	4.181	0.127	0.357	0.293
	452	30	4.623	0.090	0.392	0.376
	453	30	4.603	0.096	0.370	0.290
	454	30	4.157	0.169	0.394	0.391
	455	30	4.775	0.083	0.422	0.458
	456	30	4.302	0.068	0.384	0.335
	457	30	4.658	0.084	0.457	0.379
	458	30	5.158	0.094	0.449	0.438
	459	30	4.435	0.112	0.446	0.439
	460	30	4.510	0.109	0.391	0.392
B2F	551	30	4.353	0.099	0.494	0.398
	552	30	4.354	0.086	0.423	0.414
	553	30	4.281	0.098	0.533	0.371
	554	30	4.271	0.102	0.424	0.380
	555	30	4.115	0.078	0.447	0.331
	556	30	4.663	0.090	0.521	0.465
	557	30	4.208	0.087	0.502	0.421
	558	30	3.867	0.143	0.378	0.338
	559	30	4.933	0.099	0.409	0.452

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

Group	Animal		Liver	Ovaries	Salivary Gland	Spleen
	ID	Day				
B2F	560	30	4.651	0.127	0.436	0.377
	651	30	4.336	0.084	0.468	0.377
B8F	652	30	4.063	0.068	0.399	0.299
	653	30	4.224	0.101	0.428	0.367
	654	30	4.248	0.079	0.467	0.401
	655	30	3.953	0.086	0.463	0.392
	656	30	4.546	0.149	0.496	0.370
	657	30	4.691	0.055	0.451	0.348
	658	30	4.501	0.070	0.419	0.311
	659	30	3.991	0.128	0.445	0.307
	660	30	4.366	0.089	0.463	0.306
E0.2F	951	30	4.218	0.076	0.385	0.330
	952	30	4.425	0.076	0.437	0.366
	953	30	4.344	0.099	0.449	0.384
	954	30	4.546	0.102	0.443	0.517
	955	30	5.170	0.103	0.513	0.489
	956	30	4.729	0.111	0.469	0.403
	957	30	4.558	0.087	0.537	0.493
	958	30	5.092	0.093	0.360	0.416
	959	30	4.406	0.087	0.402	0.415
	960	30	4.999	0.152	0.375	0.394
E2F	1051	30	4.054	0.094	0.465	0.406
	1052	30	4.387	0.106	0.448	0.417
	1053	30	4.254	0.138	0.450	0.380
	1054	30	4.373	0.088	0.475	0.380
	1055	30	5.103	0.094	0.567	0.399
	1056	30	3.843	0.089	0.389	0.382
	1057	30	4.342	0.098	0.439	0.364
	1058	30	4.464	0.119	0.391	0.448

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Liver</b>	<b>Ovaries</b>	<b>Salivary Gland</b>	<b>Spleen</b>
E2F	1059	30	3.813	0.074	0.353	0.344
	1060	30	4.448	0.112	0.479	0.409
E8F	1151	30	4.680	0.104	0.471	0.399
	1152	30	3.878	0.063	0.387	0.324
	1153	30	4.601	0.082	0.455	0.476
	1154	30	3.964	0.050	0.419	0.341
	1155	30	4.656	0.083	0.439	0.428
	1156	30	4.437	0.086	0.423	0.382
	1157	30	4.105	0.098	0.464	0.397
	1158	30	4.441	0.084	0.446	0.340
	1159	30	4.346	0.083	0.420	0.490
	1160	30	4.993	0.089	0.513	0.392

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

Group	Animal		Thymus	Uterus
	ID	Day		
CF	151	30	0.531	0.694
	152	30	0.481	0.709
	153	30	0.356	0.643
	154	30	0.537	0.600
	155	30	0.373	0.387
	156	30	0.487	1.006
	157	30	0.439	0.539
	158	30	0.481	0.420
	159	30	0.363	0.876
	160	30	0.354	0.439
B0.2F	451	30	0.331	0.424
	452	30	0.329	0.758
	453	30	0.358	0.373
	454	30	0.420	0.511
	455	30	0.458	0.422
	456	30	0.409	0.775
	457	30	0.527	0.399
	458	30	0.501	0.436
	459	30	0.444	0.400
	460	30	0.471	0.729
B2F	551	30	0.382	0.566
	552	30	0.381	0.345
	553	30	0.277	0.448
	554	30	0.489	0.441
	555	30	0.393	0.437
	556	30	0.375	0.416
	557	30	0.404	0.399
	558	30	0.447	0.593
	559	30	0.468	0.654

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Thymus</b>	<b>Uterus</b>
B2F	560	30	0.494	0.539
	651	30	0.396	0.389
B8F	652	30	0.375	0.845
	653	30	0.364	0.371
	654	30	0.444	0.388
	655	30	0.440	0.368
	656	30	0.378	0.855
	657	30	0.345	0.640
	658	30	0.310	0.254
	659	30	0.361	0.514
	660	30	0.356	0.332
E0.2F	951	30	0.368	0.779
	952	30	0.504	0.695
	953	30	0.472	0.487
	954	30	0.376	0.870
	955	30	0.420	0.667
	956	30	0.424	0.433
	957	30	0.326	0.458
	958	30	0.390	0.767
	959	30	0.524	0.823
	960	30	0.360	0.435
E2F	1051	30	0.391	0.510
	1052	30	0.446	0.387
	1053	30	0.383	0.378
	1054	30	0.453	0.785
	1055	30	0.543	0.587
	1056	30	0.377	0.749
	1057	30	0.484	0.956
	1058	30	0.294	0.490

**Table D-2. Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Thymus</b>	<b>Uterus</b>
E2F	1059	30	0.339	0.261
	1060	30	0.368	0.568
E8F	1151	30	0.366	0.392
	1152	30	0.435	0.331
	1153	30	0.414	0.461
	1154	30	0.311	0.973
	1155	30	0.304	0.825
	1156	30	0.479	0.330
	1157	30	0.315	0.311
	1158	30	0.410	0.320
	1159	30	0.407	0.666
	1160	30	0.317	0.636

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
NT20M	201	31	0.048	1.747	0.8830	0.646
	202	31	0.046	1.901	0.9747	0.731
	203	31	0.035	1.840	0.7741	0.643
	204	31	0.049	1.794	0.8963	0.619
	205	31	0.053	1.957	0.9593	0.740
	206	31	0.049	1.909	0.8068	0.809
	207	31	0.036	1.801	0.8210	0.717
	208	31	0.040	1.803	0.7688	0.802
	209	31	0.044	1.782	0.9181	0.692
	210	31	0.048	1.852	0.8964	0.703
PFCNTM	301	31	0.052	1.814	0.9066	0.695
	302	31	0.046	1.973	0.9949	0.772
	303	31	0.049	2.009	1.0372	0.760
	304	31	0.057	1.876	0.9817	0.747
	305	31	0.053	1.794	0.9527	0.679
	306	31	0.055	1.878	0.8560	0.721
	307	31	0.049	1.825	0.8891	0.751
	308	31	0.057	1.784	1.0849	0.751
	309	31	0.039	1.823	1.0725	0.701
	310	31	0.049	1.924	0.9486	0.821
B20M	701	31	0.050	1.730	0.8472	0.683
	702	31	0.053	1.737	0.8640	0.636
	703	31	0.046	1.785	0.7715	0.569
	704	31	0.042	1.772	0.8276	0.676
	705	31	0.051	1.774	0.7506	0.672
	706	31	0.043	1.759	0.8330	0.583
	707	31	0.042	1.773	0.7772	0.640
	708	31	0.048	1.826	0.8527	0.594

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
B20M	709	31	0.051	1.788	0.9233	0.789
	710	31	0.040	1.638	0.8353	0.689
PFCBM	801	31	0.055	1.958	1.0708	0.719
	802	31	0.056	1.899	0.9648	0.715
	803	31	0.049	1.762	0.9309	0.684
	804	31	0.046	1.912	0.9036	0.833
	805	31	0.040	1.826	0.8709	0.789
	806	31	0.047	1.793	0.9187	0.714
	807	31	0.058	1.875	0.9369	0.821
	808	31	0.050	1.678	0.8251	0.742
	809	31	0.043	2.014	0.9219	0.867
	810	31	0.059	2.050	0.9212	0.755
E20M	1201	31	0.043	1.789	0.8858	0.634
	1202	31	0.042	1.800	0.7391	0.712
	1203	31	0.037	1.776	0.7590	0.626
	1204	31	0.046	1.700	0.6780	0.500
	1205	31	0.036	1.862	0.9223	0.637
	1206	31	0.049	1.885	0.8374	0.693
	1207	31	0.057	1.892	0.8420	0.703
	1208	31	0.037	1.680	0.7100	0.638
	1209	31	0.040	1.773	0.8222	0.685
	1210	31	0.048	1.775	0.7665	0.657
PFCM	1301	31	0.066	1.701	0.7852	0.753
	1302	31	0.064	1.735	0.9715	0.796
	1303	31	0.042	1.917	0.9851	0.780
	1304	31	0.048	1.874	0.9850	0.820
	1305	31	0.052	1.869	0.8899	0.834
	1306	31	0.039	1.740	0.9570	0.701

**Table D-3. Pairfed and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
PFCM	1307	31	0.056	1.899	1.0384	0.767
	1308	31	0.044	1.881	0.9568	0.766
	1309	31	0.058	1.941	1.0131	0.804
	1310	31	0.056	1.880	0.9251	0.796

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

Group	Animal		Kidneys	Liver	Salivary Gland	Spleen
	ID	Day				
NT20M	201	31	1.524	5.567	0.421	0.373
	202	31	1.686	5.779	0.629	0.365
	203	31	1.525	6.263	0.520	0.512
	204	31	1.443	5.763	0.509	0.454
	205	31	1.664	6.312	0.605	0.432
	206	31	1.689	6.238	0.555	0.347
	207	31	1.471	6.467	0.502	0.442
	208	31	1.558	6.315	0.563	0.433
	209	31	1.750	6.328	0.543	0.429
	210	31	1.819	6.725	0.594	0.399
PFCNTM	301	31	1.524	6.088	0.666	0.398
	302	31	1.548	6.867	0.630	0.402
	303	31	1.522	6.440	0.600	0.354
	304	31	1.766	6.682	0.588	0.457
	305	31	1.557	5.623	0.542	0.422
	306	31	1.520	6.498	0.643	0.422
	307	31	1.593	6.616	0.574	0.338
	308	31	1.716	6.529	0.583	0.394
	309	31	1.403	5.249	0.592	0.413
	310	31	1.644	6.389	0.568	0.399
B20M	701	31	1.566	5.887	0.624	0.387
	702	31	1.415	6.354	0.385	0.408
	703	31	1.408	5.730	0.561	0.358
	704	31	1.651	6.489	0.556	0.429
	705	31	1.621	5.748	0.480	0.327
	706	31	1.354	4.935	0.537	0.353
	707	31	1.416	5.024	0.463	0.333
	708	31	1.369	5.430	0.638	0.376

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

Group	Animal		Kidneys	Liver	Salivary Gland	Spleen
	ID	Day				
B20M	709	31	1.646	6.699	0.556	0.400
	710	31	1.752	6.656	0.414	0.431
PFCBM	801	31	1.526	6.452	0.572	0.345
	802	31	1.711	6.630	0.628	0.519
	803	31	1.428	5.282	0.437	0.366
	804	31	1.738	6.880	0.667	0.460
	805	31	1.475	5.888	0.605	0.373
	806	31	1.386	6.366	0.575	0.401
	807	31	1.749	6.918	0.665	0.539
	808	31	1.728	7.223	0.612	0.448
	809	31	1.799	6.729	0.642	0.428
	810	31	1.657	5.723	0.551	0.416
E20M	1201	31	1.482	7.059	0.550	0.403
	1202	31	1.484	6.300	0.465	0.401
	1203	31	1.235	5.357	0.437	0.338
	1204	31	1.297	4.746	0.383	0.232
	1205	31	1.577	6.038	0.562	0.470
	1206	31	1.497	6.104	0.470	0.384
	1207	31	1.709	6.347	0.584	0.407
	1208	31	1.325	6.112	0.472	0.393
	1209	31	1.590	6.371	0.555	0.362
	1210	31	1.434	5.933	0.517	0.332
PFCM	1301	31	1.758	6.433	0.539	0.457
	1302	31	1.458	6.583	0.626	0.571
	1303	31	1.549	6.720	0.598	0.526
	1304	31	1.711	6.523	0.590	0.452
	1305	31	1.793	7.440	0.639	0.449
	1306	31	1.635	6.500	0.655	0.510

**Table D-3. Pairfed and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Kidneys</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>
	<b>ID</b>	<b>Day</b>				
PFCM	1307	31	1.622	7.536	0.524	0.556
	1308	31	1.612	6.779	0.647	0.390
	1309	31	1.659	7.441	0.695	0.551
	1310	31	1.647	5.984	0.546	0.433

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

Group	Animal		Testes	Thymus
	ID	Day		
NT20M	201	31	3.596	0.380
	202	31	3.526	0.320
	203	31	3.075	0.468
	204	31	3.108	0.337
	205	31	3.704	0.332
	206	31	3.005	0.308
	207	31	2.899	0.228
	208	31	2.931	0.326
	209	31	3.181	0.394
	210	31	3.255	0.398
PFCNTM	301	31	3.005	0.369
	302	31	3.225	0.422
	303	31	3.412	0.389
	304	31	3.253	0.497
	305	31	3.124	0.394
	306	31	3.168	0.396
	307	31	3.055	0.349
	308	31	3.534	0.447
	309	31	3.473	0.421
	310	31	3.423	0.282
B20M	701	31	3.058	0.430
	702	31	3.143	0.316
	703	31	2.967	0.226
	704	31	2.987	0.413
	705	31	3.136	0.249
	706	31	3.167	0.230
	707	31	3.017	0.303
	708	31	2.940	0.159

**Table D-3. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Testes</b>	<b>Thymus</b>
	<b>ID</b>	<b>Day</b>		
B20M	709	31	3.594	0.318
	710	31	3.064	0.321
PFCBM	801	31	3.206	0.366
	802	31	2.931	0.588
	803	31	3.395	0.314
	804	31	3.658	0.475
	805	31	2.946	0.344
	806	31	3.323	0.358
	807	31	3.389	0.525
	808	31	3.098	0.523
	809	31	3.302	0.354
	810	31	3.286	0.475
E20M	1201	31	3.284	0.220
	1202	31	2.997	0.228
	1203	31	2.969	0.149
	1204	31	2.394	0.114
	1205	31	3.400	0.288
	1206	31	3.168	0.241
	1207	31	2.917	0.331
	1208	31	2.958	0.315
	1209	31	2.792	0.301
	1210	31	3.071	0.301
PFCM	1301	31	2.704	0.351
	1302	31	3.057	0.448
	1303	31	3.395	0.435
	1304	31	3.289	0.463
	1305	31	3.072	0.371
	1306	31	3.368	0.503

**Table D-3. Pairfed and High Dose Group Individual Animal Absolute Organ Weights (g) – Males (Continued)**

<b>Group</b>	<b>Animal</b>		<b>Testes</b>	<b>Thymus</b>
	<b>ID</b>	<b>Day</b>		
PFCM	1307	31	3.639	0.431
	1308	31	3.382	0.295
	1309	31	3.401	0.652
	1310	31	3.162	0.364

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>
NT20F	251	32	0.044	1.623	0.543	0.967
	252	32	0.048	1.679	0.458	0.961
	253	32	0.039	1.722	0.527	1.029
	254	32	0.038	1.744	0.468	0.921
	255	32	0.050	1.763	0.499	1.069
	256	32	0.047	1.589	0.497	1.034
	257	32	0.042	1.584	0.464	0.992
	258	32	0.038	1.645	0.416	0.974
	259	32	0.044	1.658	0.469	0.965
	260	32	0.037	1.640	0.469	0.940
PFCNTF	351	32	0.062	1.778	0.629	1.267
	352	32	0.048	1.609	0.495	1.073
	353	32	0.060	1.760	0.623	1.115
	354	32	0.066	1.827	0.586	1.187
	355	32	0.071	1.722	0.548	1.119
	356	32	0.067	1.600	0.546	1.138
	357	32	0.046	1.715	0.637	1.217
	358	32	0.066	1.802	0.613	1.230
	359	32	0.076	1.699	0.598	1.034
	360	32	0.055	1.790	0.558	1.049
B20F	751	32	0.044	1.675	0.468	0.997
	752	32	0.051	1.641	0.454	1.024
	753	32	0.048	1.688	0.497	1.043
	754	32	0.035	1.764	0.435	0.938
	755	32	0.043	1.631	0.407	0.939
	756	32	0.051	1.637	0.488	0.924
	758	32	0.039	1.762	0.505	1.027
	759	32	0.050	1.775	0.429	1.020
	760	32	0.042	1.646	0.469	0.951

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Heart</b>	<b>Kidneys</b>
PFCBF	851	32	0.085	1.710	0.640	1.144
	852	32	0.055	1.816	0.568	1.121
	853	32	0.072	1.716	0.527	0.977
	854	32	0.052	1.743	0.576	1.097
	855	32	0.068	1.658	0.545	1.021
	856	32	0.050	1.726	0.642	1.127
	857	32	0.071	1.762	0.686	1.156
	858	32	0.065	1.833	0.650	1.243
	859	32	0.060	1.897	0.608	1.156
	860	32	0.068	1.607	0.563	1.031
E20F	1251	32	0.040	1.764	0.467	1.089
	1252	32	0.057	1.621	0.486	0.949
	1253	32	0.037	1.650	0.465	0.947
	1254	32	0.045	1.524	0.443	0.998
	1255	32	0.040	1.707	0.439	0.930
	1256	32	0.035	1.761	0.462	1.105
	1257	32	0.041	1.678	0.421	0.975
	1258	32	0.033	1.681	0.480	0.953
	1259	32	0.034	1.622	0.531	1.020
	1260	32	0.052	1.601	0.448	1.034
PFCEF	1351	32	0.054	1.677	0.677	1.131
	1352	32	0.065	1.716	0.582	1.170
	1353	32	0.048	1.734	0.559	1.143
	1354	32	0.063	1.713	0.608	1.255
	1355	32	0.068	1.825	0.621	1.180
	1356	32	0.063	1.752	0.594	1.132
	1357	32	0.047	1.627	0.570	1.021
	1358	32	0.059	1.649	0.577	1.183
	1359	32	0.056	1.829	0.566	1.170
	1360	32	0.057	1.758	0.603	1.131

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Liver</b>	<b>Ovaries</b>	<b>Salivary Gland</b>	<b>Spleen</b>
NT20F	251	32	4.264	0.059	0.405	0.328
	252	32	4.091	0.049	0.396	0.274
	253	32	4.764	0.041	0.386	0.272
	254	32	4.402	0.058	0.356	0.265
	255	32	4.610	0.058	0.416	0.358
	256	32	4.730	0.081	0.385	0.334
	257	32	4.666	0.068	0.298	0.306
	258	32	3.950	0.043	0.362	0.278
	259	32	4.788	0.048	0.367	0.283
	260	32	3.931	0.044	0.381	0.260
PFCNTF	351	32	5.002	0.090	0.460	0.385
	352	32	3.679	0.084	0.377	0.322
	353	32	4.870	0.090	0.489	0.426
	354	32	4.623	0.089	0.460	0.377
	355	32	4.135	0.072	0.373	0.318
	356	32	4.197	0.085	0.346	0.502
	357	32	4.257	0.083	0.426	0.284
	358	32	4.750	0.085	0.450	0.415
	359	32	4.097	0.100	0.383	0.522
	360	32	4.510	0.062	0.440	0.427
B20F	751	32	4.090	0.063	0.373	0.248
	752	32	4.166	0.039	0.348	0.258
	753	32	4.282	0.062	0.316	0.216
	754	32	3.798	0.044	0.350	0.219
	755	32	3.904	0.056	0.290	0.175
	756	32	3.641	0.066	0.322	0.163
	758	32	4.451	0.047	0.356	0.242
	759	32	4.086	0.060	0.385	0.259
	760	32	3.976	0.055	0.368	0.293

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Liver</b>	<b>Ovaries</b>	<b>Salivary Gland</b>	<b>Spleen</b>
PFCBF	851	32	4.573	0.090	0.398	0.442
	852	32	3.824	0.079	0.392	0.331
	853	32	4.015	0.079	0.413	0.377
	854	32	4.449	0.067	0.410	0.429
	855	32	4.260	0.105	0.419	0.398
	856	32	3.941	0.082	0.406	0.412
	857	32	4.957	0.129	0.429	0.395
	858	32	4.686	0.083	0.533	0.402
	859	32	4.055	0.085	0.427	0.353
	860	32	4.582	0.087	0.407	0.373
E20F	1251	32	4.159	0.057	0.373	0.230
	1252	32	4.388	0.079	0.293	0.381
	1253	32	3.931	0.052	0.327	0.215
	1254	32	4.068	0.043	0.354	0.285
	1255	32	3.884	0.043	0.374	0.218
	1256	32	4.278	0.057	0.357	0.189
	1257	32	3.753	0.052	0.345	0.250
	1258	32	3.766	0.058	0.399	0.179
	1259	32	4.234	0.065	0.406	0.286
	1260	32	3.751	0.063	0.361	0.223
PFCEF	1351	32	4.249	0.077	0.425	0.357
	1352	32	4.674	0.088	0.476	0.404
	1353	32	4.188	0.098	0.428	0.375
	1354	32	4.573	0.089	0.480	0.313
	1355	32	4.463	0.082	0.531	0.424
	1356	32	4.631	0.078	0.474	0.417
	1357	32	3.908	0.076	0.387	0.357
	1358	32	4.452	0.090	0.462	0.425
	1359	32	4.113	0.071	0.383	0.346
	1360	32	4.336	0.094	0.403	0.347

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Thymus</b>	<b>Uterus</b>
NT20F	251	32	0.218	0.131
	252	32	0.315	0.131
	253	32	0.171	0.147
	254	32	0.204	0.139
	255	32	0.337	0.261
	256	32	0.294	0.231
	257	32	0.280	0.104
	258	32	0.413	0.138
	259	32	0.294	0.198
	260	32	0.254	0.129
PFCNTF	351	32	0.390	1.368
	352	32	0.326	0.543
	353	32	0.321	0.672
	354	32	0.396	0.375
	355	32	0.306	0.375
	356	32	0.369	0.320
	357	32	0.530	0.298
	358	32	0.430	0.494
	359	32	0.411	0.211
	360	32	0.451	0.253
B20F	751	32	0.224	0.151
	752	32	0.129	0.117
	753	32	0.181	0.167
	754	32	0.132	0.132
	755	32	0.207	0.135
	756	32	0.222	0.184
	758	32	0.226	0.140
	759	32	0.260	0.148
	760	32	0.219	0.116

**Table D-4. Paired and High Dose Group Individual Animal Absolute Organ Weights (g) – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Thymus</b>	<b>Uterus</b>
PFCBF	851	32	0.447	0.293
	852	32	0.401	0.302
	853	32	0.445	0.518
	854	32	0.431	0.495
	855	32	0.311	0.400
	856	32	0.402	0.395
	857	32	0.435	0.509
	858	32	0.444	0.582
	859	32	0.736	1.573
	860	32	0.466	0.520
E20F	1251	32	0.221	0.138
	1252	32	0.163	0.146
	1253	32	0.179	0.113
	1254	32	0.195	0.096
	1255	32	0.251	0.108
	1256	32	0.202	0.106
	1257	32	0.186	0.130
	1258	32	0.195	0.105
	1259	32	0.352	0.104
	1260	32	0.156	0.152
PFCEF	1351	32	0.380	0.405
	1352	32	0.295	0.397
	1353	32	0.482	0.667
	1354	32	0.428	1.015
	1355	32	0.478	0.503
	1356	32	0.662	0.331
	1357	32	0.381	0.340
	1358	32	0.437	0.606
	1359	32	0.454	0.355
	1360	32	0.258	0.439

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males**

Group	Animal ID	Day	Terminal	Adrenal Glands	Brain	Epididymides	Heart
			Body Weight				
CM	101	29	278.8	0.022	0.708	0.3802	0.317
	102	29	317.4	0.023	0.609	0.3383	0.340
	103	29	298.9	0.022	0.667	0.2833	0.360
	104	29	272.6	0.021	0.654	0.3140	0.312
	105	29	293.5	0.023	0.692	0.3665	0.365
	106	29	279.3	0.027	0.667	0.3169	0.354
	107	29	256.3	0.025	0.762	0.3580	0.331
	108	29	288.6	0.022	0.673	0.4048	0.357
	109	29	316.1	0.021	0.615	0.2955	0.316
	110	29	314.5	0.024	0.623	0.3586	0.298
B0.2M	401	29	222.8	0.022	0.837	0.4038	0.329
	402	29	294.4	0.022	0.651	0.3499	0.321
	403	29	279.4	0.023	0.717	0.3720	0.374
	404	29	255.6	0.026	0.734	0.3337	0.289
	405	29	283.5	0.018	0.693	0.3361	0.348
	406	29	286.0	0.023	0.635	0.3065	0.349
	407	29	254.4	0.021	0.770	0.3685	0.354
	408	29	258.7	0.023	0.743	0.3716	0.342
	409	29	292.7	0.022	0.642	0.3724	0.306
	410	29	314.8	0.022	0.656	0.3270	0.282
B2M	501	29	289.9	0.025	0.649	0.3562	0.318
	502	29	297.4	0.022	0.661	0.3357	0.332
	503	29	232.3	0.024	0.779	0.4243	0.343
	504	29	276.3	0.025	0.707	0.3514	0.351
	505	29	295.9	0.030	0.710	0.3389	0.338
	506	29	273.8	0.022	0.673	0.3351	0.310
	507	29	278.5	0.021	0.706	0.3444	0.293
	508	29	259.7	0.022	0.758	0.3778	0.294
	509	29	266.6	0.024	0.729	0.3136	0.310

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal	Adrenal Glands	Brain	Epididymides	Heart
			Body Weight				
B2M	510	29	270.4	0.023	0.699	0.3215	0.312
B8M	601	29	267.1	0.022	0.747	0.3293	0.297
	602	29	202.1	0.023	0.861	0.4504	0.357
	603	29	241.0	0.018	0.773	0.3656	0.356
	604	29	242.8	0.020	0.760	0.3700	0.330
	605	29	239.3	0.016	0.744	0.3979	0.300
	606	29	239.6	0.020	0.743	0.3690	0.296
	607	29	207.4	0.019	0.925	0.3544	0.306
	608	29	241.0	0.022	0.802	0.3426	0.369
	609	29	244.2	0.022	0.736	0.3969	0.318
	610	29	247.5	0.026	0.719	0.4010	0.294
E0.2M	901	29	295.7	0.014	0.621	0.2664	0.289
	902	29	299.9	0.023	0.624	0.2935	0.326
	903	29	310.4	0.020	0.614	0.3477	0.303
	904	29	287.5	0.021	0.702	0.3194	0.335
	905	29	280.0	0.018	0.715	0.2734	0.321
	906	29	299.2	0.027	0.644	0.3592	0.383
	907	29	313.5	0.024	0.633	0.3238	0.340
	908	29	272.8	0.021	0.695	0.3239	0.336
	909	29	285.5	0.019	0.644	0.3132	0.305
	910	29	273.0	0.021	0.714	0.3804	0.311
E2M	1001	29	270.7	0.024	0.742	0.3334	0.320
	1002	29	274.1	0.028	0.692	0.3211	0.329
	1003	29	321.5	0.017	0.610	0.2954	0.362
	1004	29	255.6	0.022	0.704	0.3581	0.341
	1005	29	285.9	0.020	0.671	0.2944	0.356
	1006	29	295.9	0.023	0.638	0.2770	0.281
	1007	29	265.3	0.017	0.710	0.2934	0.332
	1008	29	234.6	0.019	0.817	0.4093	0.305

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Terminal Body Weight</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
E2M	1009	29	295.5	0.024	0.683	0.3881	0.313
	1010	29	304.9	0.023	0.665	0.3089	0.339
E8M	1101	29	266.9	0.022	0.696	0.4143	0.307
	1102	29	258.8	0.019	0.707	0.3352	0.333
	1103	29	265.3	0.023	0.695	0.3131	0.337
	1104	29	245.8	0.027	0.721	0.3857	0.346
	1105	29	225.4	0.024	0.830	0.3585	0.363
	1106	29	240.6	0.024	0.781	0.4038	0.322
	1107	29	228.1	0.021	0.847	0.3824	0.310
	1108	29	240.2	0.026	0.787	0.4645	0.338
	1109	29	223.1	0.025	0.858	0.3892	0.325
	1110	29	239.7	0.021	0.791	0.3415	0.349

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		Liver	Salivary Gland	Spleen
			Body Weight	Kidneys			
CM	101	29	278.8	0.701	2.545	0.212	0.198
	102	29	317.4	0.653	2.730	0.197	0.164
	103	29	298.9	0.627	2.706	0.210	0.218
	104	29	272.6	0.641	2.743	0.215	0.160
	105	29	293.5	0.704	2.591	0.207	0.209
	106	29	279.3	0.666	3.029	0.215	0.167
	107	29	256.3	0.715	2.433	0.233	0.190
	108	29	288.6	0.747	2.823	0.227	0.202
	109	29	316.1	0.655	2.881	0.228	0.161
	110	29	314.5	0.614	2.527	0.185	0.166
B0.2M	401	29	222.8	0.779	2.723	0.210	0.213
	402	29	294.4	0.667	2.406	0.184	0.246
	403	29	279.4	0.722	2.605	0.230	0.207
	404	29	255.6	0.640	2.499	0.202	0.165
	405	29	283.5	0.673	2.674	0.221	0.174
	406	29	286.0	0.737	2.748	0.200	0.176
	407	29	254.4	0.738	2.543	0.223	0.217
	408	29	258.7	0.738	2.534	0.202	0.227
	409	29	292.7	0.626	2.611	0.219	0.185
	410	29	314.8	0.690	2.268	0.189	0.200
B2M	501	29	289.9	0.684	2.305	0.229	0.198
	502	29	297.4	0.721	2.555	0.262	0.192
	503	29	232.3	0.625	2.135	0.239	0.176
	504	29	276.3	0.747	2.904	0.234	0.231
	505	29	295.9	0.699	2.567	0.224	0.169
	506	29	273.8	0.679	2.632	0.205	0.233
	507	29	278.5	0.671	2.260	0.184	0.186
	508	29	259.7	0.682	2.589	0.245	0.174
	509	29	266.6	0.664	2.256	0.216	0.174

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal Body Weight		Kidneys	Liver	Salivary Gland	Spleen
B2M	510	29	270.4		0.593	2.268	0.197	0.174
B8M	601	29	267.1		0.728	2.619	0.223	0.209
	602	29	202.1		0.667	2.453	0.246	0.132
	603	29	241.0		0.811	2.723	0.223	0.190
	604	29	242.8		0.686	2.847	0.241	0.118
	605	29	239.3		0.688	2.348	0.245	0.172
	606	29	239.6		0.648	2.446	0.235	0.167
	607	29	207.4		0.665	2.370	0.230	0.187
	608	29	241.0		0.717	2.671	0.222	0.160
	609	29	244.2		0.735	2.733	0.243	0.218
	610	29	247.5		0.713	3.113	0.209	0.177
E0.2M	901	29	295.7		0.618	2.445	0.197	0.210
	902	29	299.9		0.681	2.725	0.207	0.190
	903	29	310.4		0.680	2.577	0.166	0.148
	904	29	287.5		0.756	2.533	0.221	0.187
	905	29	280.0		0.719	2.687	0.185	0.203
	906	29	299.2		0.647	2.697	0.236	0.169
	907	29	313.5		0.651	2.631	0.234	0.213
	908	29	272.8		0.681	2.388	0.203	0.182
	909	29	285.5		0.678	2.551	0.177	0.173
	910	29	273.0		0.758	2.439	0.216	0.162
E2M	1001	29	270.7		0.661	2.517	0.223	0.208
	1002	29	274.1		0.678	2.764	0.246	0.206
	1003	29	321.5		0.660	2.733	0.197	0.179
	1004	29	255.6		0.646	2.303	0.230	0.177
	1005	29	285.9		0.624	2.504	0.241	0.172
	1006	29	295.9		0.706	2.468	0.203	0.197
	1007	29	265.3		0.745	2.463	0.234	0.190
	1008	29	234.6		0.656	2.334	0.206	0.147

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal	Kidneys	Liver	Salivary Gland	Spleen
			Body Weight				
E2M	1009	29	295.5	0.689	2.469	0.218	0.189
	1010	29	304.9	0.721	2.538	0.241	0.177
E8M	1101	29	266.9	0.612	2.571	0.227	0.200
	1102	29	258.8	0.661	2.578	0.242	0.159
	1103	29	265.3	0.647	2.740	0.239	0.220
	1104	29	245.8	0.668	2.885	0.223	0.213
	1105	29	225.4	0.682	2.625	0.255	0.200
	1106	29	240.6	0.723	2.538	0.264	0.185
	1107	29	228.1	0.768	2.537	0.246	0.200
	1108	29	240.2	0.737	2.541	0.233	0.202
	1109	29	223.1	0.648	2.463	0.223	0.172
	1110	29	239.7	0.691	2.612	0.219	0.172

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Testes	Thymus
CM	101	29	278.8	1.346	0.232
	102	29	317.4	1.059	0.247
	103	29	298.9	1.177	0.194
	104	29	272.6	1.047	0.206
	105	29	293.5	1.201	0.190
	106	29	279.3	0.995	0.186
	107	29	256.3	1.272	0.245
	108	29	288.6	1.168	0.220
	109	29	316.1	1.053	0.235
	110	29	314.5	1.231	0.196
B0.2M	401	29	222.8	1.281	0.239
	402	29	294.4	1.103	0.178
	403	29	279.4	1.241	0.176
	404	29	255.6	1.247	0.223
	405	29	283.5	1.212	0.206
	406	29	286.0	1.123	0.257
	407	29	254.4	1.292	0.208
	408	29	258.7	1.288	0.162
	409	29	292.7	1.130	0.192
	410	29	314.8	1.057	0.227
B2M	501	29	289.9	1.214	0.162
	502	29	297.4	1.138	0.168
	503	29	232.3	1.311	0.149
	504	29	276.3	1.262	0.165
	505	29	295.9	1.144	0.223
	506	29	273.8	1.154	0.176
	507	29	278.5	1.151	0.173
	508	29	259.7	1.288	0.160
	509	29	266.6	1.239	0.161

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		Thymus
			Body Weight	Testes	
B2M	510	29	270.4	1.219	0.182
B8M	601	29	267.1	1.182	0.225
	602	29	202.1	1.500	0.144
	603	29	241.0	1.212	0.201
	604	29	242.8	1.251	0.158
	605	29	239.3	1.354	0.148
	606	29	239.6	1.296	0.178
	607	29	207.4	1.566	0.198
	608	29	241.0	1.366	0.145
	609	29	244.2	1.376	0.208
	610	29	247.5	1.210	0.186
E0.2M	901	29	295.7	0.993	0.161
	902	29	299.9	0.944	0.237
	903	29	310.4	1.076	0.195
	904	29	287.5	1.127	0.183
	905	29	280.0	1.007	0.174
	906	29	299.2	1.164	0.146
	907	29	313.5	1.161	0.231
	908	29	272.8	1.185	0.166
	909	29	285.5	1.114	0.247
	910	29	273.0	1.285	0.193
E2M	1001	29	270.7	1.084	0.199
	1002	29	274.1	1.207	0.194
	1003	29	321.5	0.988	0.163
	1004	29	255.6	1.242	0.242
	1005	29	285.9	1.114	0.181
	1006	29	295.9	1.024	0.197
	1007	29	265.3	1.058	0.165
	1008	29	234.6	1.319	0.117

**Table D-5. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal	Testes	Thymus
			Body Weight		
E2M	1009	29	295.5	1.348	0.179
	1010	29	304.9	1.088	0.213
E8M	1101	29	266.9	1.420	0.221
	1102	29	258.8	1.246	0.241
	1103	29	265.3	1.133	0.228
	1104	29	245.8	1.350	0.183
	1105	29	225.4	1.321	0.180
	1106	29	240.6	1.303	0.181
	1107	29	228.1	1.434	0.173
	1108	29	240.2	1.464	0.192
	1109	29	223.1	1.384	0.213
	1110	29	239.7	1.395	0.261

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females**

Group	Animal ID	Day	Terminal	Adrenal Glands	Brain	Heart	Kidneys
			Body Weight				
CF	151	30	177.8	0.043	0.964	0.352	0.711
	152	30	163.0	0.042	1.078	0.376	0.708
	153	30	175.3	0.043	1.012	0.374	0.739
	154	30	183.6	0.036	1.000	0.376	0.689
	155	30	164.8	0.045	1.130	0.372	0.839
	156	30	189.3	0.046	0.984	0.345	0.737
	157	30	183.3	0.038	0.960	0.354	0.749
	158	30	190.5	0.041	0.955	0.346	0.635
	159	30	158.9	0.041	1.103	0.343	0.686
	160	30	184.2	0.035	0.990	0.294	0.652
B0.2F	451	30	159.1	0.039	1.128	0.321	0.755
	452	30	172.3	0.033	1.003	0.368	0.739
	453	30	167.8	0.039	1.027	0.363	0.714
	454	30	168.6	0.037	1.077	0.333	0.701
	455	30	180.9	0.039	1.033	0.340	0.687
	456	30	170.0	0.036	1.010	0.401	0.677
	457	30	181.3	0.038	0.985	0.361	0.766
	458	30	186.2	0.041	0.942	0.394	0.745
	459	30	189.6	0.039	0.937	0.324	0.676
	460	30	164.1	0.039	1.035	0.403	0.727
B2F	551	30	162.2	0.040	1.088	0.385	0.740
	552	30	157.9	0.050	1.137	0.356	0.731
	553	30	162.9	0.051	1.117	0.384	0.687
	554	30	175.2	0.039	1.075	0.332	0.659
	555	30	174.8	0.031	1.099	0.345	0.698
	556	30	185.2	0.044	1.003	0.323	0.658
	557	30	172.0	0.037	1.029	0.353	0.715
	558	30	157.6	0.042	1.086	0.362	0.675
	559	30	177.7	0.045	1.005	0.404	0.735

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal				
			Body Weight	Adrenal Glands	Brain	Heart	Kidneys
B2F	560	30	170.3	0.045	1.101	0.381	0.756
	651	30	161.2	0.032	1.110	0.301	0.734
B8F	652	30	146.1	0.035	1.110	0.341	0.736
	653	30	162.4	0.038	1.137	0.336	0.727
	654	30	153.5	0.039	1.047	0.337	0.687
	655	30	159.2	0.044	1.129	0.335	0.686
	656	30	166.6	0.046	1.051	0.338	0.746
	657	30	164.4	0.037	1.060	0.317	0.679
	658	30	151.7	0.030	1.132	0.305	0.810
	659	30	145.2	0.039	1.262	0.329	0.684
	660	30	148.7	0.040	1.152	0.367	0.727
E0.2F	951	30	157.0	0.045	1.149	0.381	0.759
	952	30	179.2	0.043	0.984	0.378	0.677
	953	30	177.1	0.045	0.978	0.372	0.716
	954	30	174.1	0.044	0.993	0.380	0.739
	955	30	188.9	0.040	0.922	0.366	0.740
	956	30	173.5	0.044	1.039	0.413	0.769
	957	30	170.8	0.051	1.060	0.414	0.742
	958	30	191.9	0.034	0.891	0.313	0.628
	959	30	171.9	0.052	0.971	0.379	0.734
	960	30	192.2	0.043	0.958	0.357	0.708
E2F	1051	30	169.4	0.039	1.071	0.357	0.727
	1052	30	158.5	0.047	1.141	0.402	0.742
	1053	30	157.5	0.065	1.135	0.346	0.791
	1054	30	173.2	0.048	1.017	0.356	0.716
	1055	30	175.0	0.066	1.040	0.380	0.818
	1056	30	159.3	0.044	1.080	0.365	0.707
	1057	30	173.5	0.037	1.015	0.327	0.689
	1058	30	153.8	0.053	1.137	0.366	0.800

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal	Adrenal Glands	Brain	Heart	Kidneys
			Body Weight				
E2F	1059	30	177.6	0.029	1.025	0.287	0.649
	1060	30	158.0	0.045	1.100	0.407	0.785
E8F	1151	30	171.6	0.039	1.047	0.348	0.710
	1152	30	149.7	0.037	1.116	0.323	0.634
	1153	30	169.4	0.033	1.112	0.374	0.694
	1154	30	145.4	0.034	1.180	0.334	0.860
	1155	30	168.8	0.021	1.044	0.342	0.732
	1156	30	163.6	0.036	1.042	0.358	0.729
	1157	30	159.3	0.043	1.081	0.354	0.709
	1158	30	163.5	0.043	1.099	0.301	0.686
	1159	30	151.3	0.043	1.129	0.387	0.825
	1160	30	165.4	0.032	1.046	0.347	0.746

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		Liver	Ovaries	Salivary Gland	Spleen
			Body Weight					
CF	151	30	177.8		2.648	0.046	0.238	0.235
	152	30	163.0		2.805	0.076	0.260	0.210
	153	30	175.3		2.780	0.063	0.249	0.210
	154	30	183.6		2.429	0.054	0.227	0.219
	155	30	164.8		2.592	0.063	0.276	0.232
	156	30	189.3		2.740	0.084	0.240	0.262
	157	30	183.3		2.580	0.051	0.210	0.209
	158	30	190.5		2.580	0.071	0.275	0.218
	159	30	158.9		2.724	0.056	0.217	0.287
	160	30	184.2		2.540	0.044	0.213	0.217
B0.2F	451	30	159.1		2.628	0.080	0.224	0.184
	452	30	172.3		2.683	0.052	0.228	0.218
	453	30	167.8		2.743	0.057	0.221	0.173
	454	30	168.6		2.466	0.100	0.234	0.232
	455	30	180.9		2.639	0.046	0.233	0.253
	456	30	170.0		2.531	0.040	0.226	0.197
	457	30	181.3		2.569	0.046	0.252	0.209
	458	30	186.2		2.770	0.051	0.241	0.235
	459	30	189.6		2.339	0.059	0.235	0.231
	460	30	164.1		2.749	0.066	0.238	0.239
B2F	551	30	162.2		2.684	0.061	0.304	0.245
	552	30	157.9		2.757	0.054	0.268	0.262
	553	30	162.9		2.628	0.060	0.327	0.228
	554	30	175.2		2.438	0.058	0.242	0.217
	555	30	174.8		2.354	0.045	0.256	0.189
	556	30	185.2		2.518	0.049	0.281	0.251
	557	30	172.0		2.446	0.050	0.292	0.245
	558	30	157.6		2.453	0.091	0.240	0.214
	559	30	177.7		2.776	0.056	0.230	0.254

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		Liver	Ovaries	Salivary Gland	Spleen
			Body Weight					
B2F	560	30	170.3		2.731	0.074	0.256	0.221
	651	30	161.2		2.690	0.052	0.290	0.234
B8F	652	30	146.1		2.781	0.046	0.273	0.204
	653	30	162.4		2.601	0.062	0.263	0.226
	654	30	153.5		2.767	0.051	0.304	0.261
	655	30	159.2		2.483	0.054	0.291	0.246
	656	30	166.6		2.729	0.089	0.298	0.222
	657	30	164.4		2.853	0.034	0.274	0.212
	658	30	151.7		2.967	0.046	0.276	0.205
	659	30	145.2		2.749	0.088	0.306	0.212
	660	30	148.7		2.936	0.060	0.311	0.206
E0.2F	951	30	157.0		2.687	0.048	0.245	0.210
	952	30	179.2		2.469	0.042	0.244	0.204
	953	30	177.1		2.453	0.056	0.254	0.217
	954	30	174.1		2.611	0.058	0.255	0.297
	955	30	188.9		2.737	0.055	0.271	0.259
	956	30	173.5		2.725	0.064	0.270	0.232
	957	30	170.8		2.669	0.051	0.314	0.289
	958	30	191.9		2.653	0.049	0.188	0.217
	959	30	171.9		2.563	0.051	0.234	0.241
	960	30	192.2		2.601	0.079	0.195	0.205
E2F	1051	30	169.4		2.393	0.055	0.274	0.240
	1052	30	158.5		2.768	0.067	0.283	0.263
	1053	30	157.5		2.701	0.087	0.286	0.241
	1054	30	173.2		2.525	0.051	0.274	0.219
	1055	30	175.0		2.916	0.054	0.324	0.228
	1056	30	159.3		2.412	0.056	0.244	0.240
	1057	30	173.5		2.503	0.056	0.253	0.210
	1058	30	153.8		2.903	0.077	0.254	0.291

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal Body Weight		Liver	Ovaries	Salivary Gland	Spleen
E2F	1059	30	177.6		2.147	0.041	0.199	0.194
	1060	30	158.0		2.815	0.071	0.303	0.259
E8F	1151	30	171.6		2.727	0.060	0.274	0.232
	1152	30	149.7		2.590	0.042	0.259	0.216
	1153	30	169.4		2.716	0.048	0.269	0.281
	1154	30	145.4		2.726	0.034	0.288	0.235
	1155	30	168.8		2.758	0.049	0.260	0.253
	1156	30	163.6		2.712	0.053	0.258	0.233
	1157	30	159.3		2.577	0.061	0.291	0.249
	1158	30	163.5		2.716	0.051	0.273	0.208
	1159	30	151.3		2.872	0.055	0.278	0.324
	1160	30	165.4		3.019	0.054	0.310	0.237

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Thymus	Uterus
CF	151	30	177.8	0.299	0.390
	152	30	163.0	0.295	0.435
	153	30	175.3	0.203	0.367
	154	30	183.6	0.293	0.327
	155	30	164.8	0.226	0.235
	156	30	189.3	0.257	0.532
	157	30	183.3	0.240	0.294
	158	30	190.5	0.252	0.220
	159	30	158.9	0.229	0.551
	160	30	184.2	0.192	0.239
B0.2F	451	30	159.1	0.208	0.266
	452	30	172.3	0.191	0.440
	453	30	167.8	0.214	0.222
	454	30	168.6	0.249	0.303
	455	30	180.9	0.253	0.233
	456	30	170.0	0.240	0.456
	457	30	181.3	0.290	0.220
	458	30	186.2	0.269	0.234
	459	30	189.6	0.234	0.211
	460	30	164.1	0.287	0.444
B2F	551	30	162.2	0.235	0.349
	552	30	157.9	0.242	0.218
	553	30	162.9	0.170	0.275
	554	30	175.2	0.279	0.251
	555	30	174.8	0.225	0.250
	556	30	185.2	0.203	0.225
	557	30	172.0	0.235	0.232
	558	30	157.6	0.284	0.376
	559	30	177.7	0.263	0.368

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Thymus	Uterus
B2F	560	30	170.3	0.290	0.316
	651	30	161.2	0.246	0.241
B8F	652	30	146.1	0.257	0.578
	653	30	162.4	0.224	0.228
	654	30	153.5	0.289	0.253
	655	30	159.2	0.276	0.231
	656	30	166.6	0.227	0.513
	657	30	164.4	0.210	0.389
	658	30	151.7	0.205	0.168
	659	30	145.2	0.249	0.354
	660	30	148.7	0.239	0.223
E0.2F	951	30	157.0	0.234	0.496
	952	30	179.2	0.281	0.388
	953	30	177.1	0.266	0.275
	954	30	174.1	0.216	0.500
	955	30	188.9	0.222	0.353
	956	30	173.5	0.244	0.250
	957	30	170.8	0.191	0.268
	958	30	191.9	0.203	0.400
	959	30	171.9	0.305	0.479
	960	30	192.2	0.187	0.226
E2F	1051	30	169.4	0.231	0.301
	1052	30	158.5	0.281	0.244
	1053	30	157.5	0.243	0.240
	1054	30	173.2	0.261	0.453
	1055	30	175.0	0.310	0.335
	1056	30	159.3	0.237	0.470
	1057	30	173.5	0.279	0.551
	1058	30	153.8	0.191	0.318

**Table D-6. Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Terminal Body Weight</b>		
				<b>Thymus</b>	<b>Uterus</b>
E2F	1059	30	177.6	0.191	0.147
	1060	30	158.0	0.233	0.359
E8F	1151	30	171.6	0.213	0.228
	1152	30	149.7	0.291	0.221
	1153	30	169.4	0.245	0.272
	1154	30	145.4	0.214	0.669
	1155	30	168.8	0.180	0.489
	1156	30	163.6	0.293	0.201
	1157	30	159.3	0.198	0.195
	1158	30	163.5	0.251	0.196
	1159	30	151.3	0.269	0.440
	1160	30	165.4	0.192	0.385

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males**

Group	Animal ID	Day	Terminal		Adrenal Glands	Brain	Epididymides	Heart
			Body Weight					
NT20M	201	31	196.0		0.024	0.891	0.4505	0.329
	202	31	212.2		0.022	0.896	0.4593	0.345
	203	31	218.8		0.016	0.841	0.3538	0.294
	204	31	205.5		0.024	0.873	0.4362	0.301
	205	31	227.9		0.023	0.859	0.4209	0.325
	206	31	211.6		0.023	0.902	0.3813	0.382
	207	31	198.9		0.018	0.905	0.4128	0.360
	208	31	204.0		0.020	0.884	0.3769	0.393
	209	31	214.3		0.020	0.832	0.4284	0.323
	210	31	219.7		0.022	0.843	0.4080	0.320
PFCNTM	301	31	224.2		0.023	0.809	0.4044	0.310
	302	31	245.0		0.019	0.805	0.4061	0.315
	303	31	246.8		0.020	0.814	0.4203	0.308
	304	31	246.2		0.023	0.762	0.3987	0.303
	305	31	212.1		0.025	0.846	0.4492	0.320
	306	31	239.8		0.023	0.783	0.3570	0.301
	307	31	229.1		0.021	0.797	0.3881	0.328
	308	31	230.1		0.025	0.775	0.4715	0.326
	309	31	216.2		0.018	0.843	0.4961	0.324
	310	31	254.4		0.019	0.756	0.3729	0.323
B20M	701	31	205.5		0.024	0.842	0.4123	0.332
	702	31	200.8		0.026	0.865	0.4303	0.317
	703	31	191.9		0.024	0.930	0.4020	0.296
	704	31	214.2		0.019	0.827	0.3864	0.316
	705	31	191.4		0.027	0.927	0.3922	0.351
	706	31	190.5		0.023	0.924	0.4373	0.306
	707	31	192.6		0.022	0.920	0.4035	0.332
	708	31	188.2		0.025	0.970	0.4531	0.315
	709	31	230.3		0.022	0.777	0.4009	0.343

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		Adrenal Glands	Brain	Epididymides	Heart
			Body Weight					
B20M	710	31	189.9		0.021	0.862	0.4399	0.363
PFCBM	801	31	243.0		0.023	0.806	0.4407	0.296
	802	31	254.7		0.022	0.745	0.3788	0.281
	803	31	221.9		0.022	0.794	0.4195	0.308
	804	31	248.2		0.019	0.770	0.3641	0.335
	805	31	240.8		0.017	0.758	0.3617	0.327
	806	31	223.6		0.021	0.802	0.4109	0.319
	807	31	252.5		0.023	0.742	0.3710	0.325
	808	31	233.5		0.021	0.718	0.3534	0.318
	809	31	243.6		0.018	0.827	0.3784	0.356
	810	31	244.5		0.024	0.839	0.3768	0.309
E20M	1201	31	209.7		0.021	0.853	0.4224	0.302
	1202	31	189.7		0.022	0.949	0.3896	0.375
	1203	31	182.0		0.020	0.976	0.4170	0.344
	1204	31	146.6		0.031	1.160	0.4625	0.341
	1205	31	215.1		0.017	0.865	0.4288	0.296
	1206	31	207.6		0.024	0.908	0.4034	0.334
	1207	31	214.8		0.027	0.881	0.3920	0.327
	1208	31	195.6		0.019	0.859	0.3630	0.326
	1209	31	222.7		0.018	0.796	0.3692	0.307
	1210	31	204.7		0.023	0.867	0.3745	0.321
PFCM	1301	31	241.5		0.027	0.704	0.3251	0.312
	1302	31	238.8		0.027	0.727	0.4068	0.333
	1303	31	246.6		0.017	0.777	0.3995	0.316
	1304	31	246.5		0.019	0.760	0.3996	0.332
	1305	31	252.2		0.021	0.741	0.3529	0.331
	1306	31	247.2		0.016	0.704	0.3871	0.284
	1307	31	263.9		0.021	0.719	0.3935	0.291
	1308	31	237.9		0.019	0.791	0.4022	0.322

**Table D-7. Pairfed and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Terminal Body Weight</b>	<b>Adrenal Glands</b>	<b>Brain</b>	<b>Epididymides</b>	<b>Heart</b>
PFCEM	1309	31	273.6	0.021	0.709	0.3703	0.294
	1310	31	250.2	0.023	0.751	0.3697	0.318

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal				Spleen
			Body Weight	Kidneys	Liver	Salivary Gland	
NT20M	201	31	196.0	0.778	2.840	0.215	0.190
	202	31	212.2	0.794	2.723	0.296	0.172
	203	31	218.8	0.697	2.863	0.238	0.234
	204	31	205.5	0.702	2.804	0.248	0.221
	205	31	227.9	0.730	2.770	0.265	0.190
	206	31	211.6	0.798	2.948	0.262	0.164
	207	31	198.9	0.739	3.251	0.252	0.222
	208	31	204.0	0.764	3.096	0.276	0.212
	209	31	214.3	0.817	2.953	0.254	0.200
	210	31	219.7	0.828	3.061	0.270	0.182
PFCNTM	301	31	224.2	0.680	2.715	0.297	0.177
	302	31	245.0	0.632	2.803	0.257	0.164
	303	31	246.8	0.617	2.609	0.243	0.143
	304	31	246.2	0.717	2.714	0.239	0.186
	305	31	212.1	0.734	2.651	0.256	0.199
	306	31	239.8	0.634	2.710	0.268	0.176
	307	31	229.1	0.695	2.888	0.251	0.147
	308	31	230.1	0.746	2.838	0.254	0.171
	309	31	216.2	0.649	2.428	0.274	0.191
	310	31	254.4	0.646	2.511	0.223	0.157
B20M	701	31	205.5	0.762	2.865	0.304	0.188
	702	31	200.8	0.705	3.164	0.192	0.203
	703	31	191.9	0.734	2.986	0.292	0.186
	704	31	214.2	0.771	3.029	0.260	0.200
	705	31	191.4	0.847	3.003	0.251	0.171
	706	31	190.5	0.711	2.590	0.282	0.185
	707	31	192.6	0.735	2.609	0.240	0.173
	708	31	188.2	0.728	2.885	0.339	0.200
	709	31	230.3	0.715	2.909	0.241	0.174

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		Liver	Salivary Gland	Spleen
			Body Weight	Kidneys			
B20M	710	31	189.9	0.923	3.505	0.218	0.227
PFCBM	801	31	243.0	0.628	2.655	0.235	0.142
	802	31	254.7	0.672	2.603	0.247	0.204
	803	31	221.9	0.644	2.380	0.197	0.165
	804	31	248.2	0.700	2.772	0.269	0.185
	805	31	240.8	0.612	2.445	0.251	0.155
	806	31	223.6	0.620	2.847	0.257	0.179
	807	31	252.5	0.693	2.740	0.263	0.214
	808	31	233.5	0.740	3.093	0.262	0.192
	809	31	243.6	0.738	2.762	0.264	0.176
	810	31	244.5	0.678	2.340	0.225	0.170
E20M	1201	31	209.7	0.707	3.366	0.262	0.192
	1202	31	189.7	0.782	3.321	0.245	0.211
	1203	31	182.0	0.679	2.943	0.240	0.186
	1204	31	146.6	0.885	3.237	0.261	0.158
	1205	31	215.1	0.733	2.807	0.261	0.219
	1206	31	207.6	0.721	2.940	0.227	0.185
	1207	31	214.8	0.796	2.955	0.272	0.190
	1208	31	195.6	0.677	3.125	0.241	0.201
	1209	31	222.7	0.714	2.861	0.249	0.163
	1210	31	204.7	0.700	2.899	0.253	0.162
PFCM	1301	31	241.5	0.728	2.664	0.223	0.189
	1302	31	238.8	0.610	2.757	0.262	0.239
	1303	31	246.6	0.628	2.725	0.242	0.213
	1304	31	246.5	0.694	2.646	0.239	0.183
	1305	31	252.2	0.711	2.950	0.253	0.178
	1306	31	247.2	0.661	2.629	0.265	0.206
	1307	31	263.9	0.615	2.856	0.198	0.210
	1308	31	237.9	0.678	2.850	0.272	0.164

**Table D-7. Pairfed and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Terminal Body Weight</b>		<b>Kidneys</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>
PFCEM	1309	31	273.6		0.606	2.720	0.254	0.201
	1310	31	250.2		0.658	2.392	0.218	0.173

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Testes	Thymus
NT20M	201	31	196.0	1.835	0.194
	202	31	212.2	1.661	0.151
	203	31	218.8	1.405	0.214
	204	31	205.5	1.513	0.164
	205	31	227.9	1.625	0.146
	206	31	211.6	1.420	0.145
	207	31	198.9	1.457	0.115
	208	31	204.0	1.437	0.160
	209	31	214.3	1.484	0.184
	210	31	219.7	1.481	0.181
PFCNTM	301	31	224.2	1.340	0.165
	302	31	245.0	1.316	0.172
	303	31	246.8	1.382	0.157
	304	31	246.2	1.321	0.202
	305	31	212.1	1.473	0.186
	306	31	239.8	1.321	0.165
	307	31	229.1	1.334	0.152
	308	31	230.1	1.536	0.194
	309	31	216.2	1.606	0.195
	310	31	254.4	1.345	0.111
B20M	701	31	205.5	1.488	0.209
	702	31	200.8	1.565	0.157
	703	31	191.9	1.546	0.118
	704	31	214.2	1.394	0.193
	705	31	191.4	1.638	0.130
	706	31	190.5	1.662	0.121
	707	31	192.6	1.566	0.157
	708	31	188.2	1.562	0.085
	709	31	230.3	1.561	0.138

**Table D-7. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Testes	Thymus
B20M	710	31	189.9	1.614	0.169
	801	31	243.0	1.319	0.151
PFCBM	802	31	254.7	1.151	0.231
	803	31	221.9	1.530	0.142
	804	31	248.2	1.474	0.191
	805	31	240.8	1.223	0.143
	806	31	223.6	1.486	0.160
	807	31	252.5	1.342	0.208
	808	31	233.5	1.327	0.224
	809	31	243.6	1.356	0.145
	810	31	244.5	1.344	0.194
E20M	1201	31	209.7	1.566	0.105
	1202	31	189.7	1.580	0.120
	1203	31	182.0	1.631	0.082
	1204	31	146.6	1.633	0.078
	1205	31	215.1	1.581	0.134
	1206	31	207.6	1.526	0.116
	1207	31	214.8	1.358	0.154
	1208	31	195.6	1.512	0.161
	1209	31	222.7	1.254	0.135
	1210	31	204.7	1.500	0.147
PFCM	1301	31	241.5	1.120	0.145
	1302	31	238.8	1.280	0.187
	1303	31	246.6	1.377	0.176
	1304	31	246.5	1.334	0.188
	1305	31	252.2	1.218	0.147
	1306	31	247.2	1.362	0.204
	1307	31	263.9	1.379	0.163
	1308	31	237.9	1.422	0.124

**Table D-7. Pairfed and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Terminal</b>		
			<b>Body Weight</b>	<b>Testes</b>	<b>Thymus</b>
PFCEM	1309	31	273.6	1.243	0.238
	1310	31	250.2	1.264	0.145

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females**

Group	Animal ID	Day	Terminal	Adrenal Glands	Brain	Heart	Kidneys
			Body Weight				
NT20F	251	32	138.3	0.032	1.173	0.393	0.699
	252	32	151.4	0.032	1.109	0.302	0.635
	253	32	141.8	0.027	1.214	0.372	0.726
	254	32	138.6	0.027	1.258	0.337	0.664
	255	32	149.5	0.033	1.179	0.334	0.715
	256	32	151.6	0.031	1.048	0.328	0.682
	257	32	137.5	0.031	1.152	0.338	0.722
	258	32	123.5	0.031	1.332	0.336	0.789
	259	32	154.7	0.028	1.072	0.303	0.624
	260	32	129.3	0.028	1.269	0.363	0.727
PFCNTF	351	32	175.4	0.035	1.014	0.359	0.722
	352	32	148.2	0.033	1.086	0.334	0.724
	353	32	166.3	0.036	1.058	0.375	0.670
	354	32	172.9	0.038	1.056	0.339	0.686
	355	32	154.0	0.046	1.118	0.356	0.727
	356	32	160.3	0.042	0.998	0.341	0.710
	357	32	177.6	0.026	0.966	0.358	0.685
	358	32	171.5	0.038	1.051	0.357	0.717
	359	32	164.6	0.046	1.032	0.364	0.628
	360	32	176.5	0.031	1.014	0.316	0.594
B20F	751	32	128.9	0.034	1.300	0.363	0.773
	752	32	125.9	0.041	1.303	0.360	0.813
	753	32	137.3	0.035	1.230	0.362	0.760
	754	32	122.5	0.029	1.440	0.355	0.766
	755	32	122.8	0.035	1.328	0.332	0.765
	756	32	117.7	0.044	1.391	0.415	0.785
	758	32	137.2	0.029	1.285	0.368	0.749
	759	32	132.4	0.038	1.340	0.324	0.770
	760	32	129.4	0.033	1.272	0.362	0.735

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal				
			Body Weight	Adrenal Glands	Brain	Heart	Kidneys
PFCBF	851	32	171.5	0.049	0.997	0.373	0.667
	852	32	165.5	0.033	1.097	0.343	0.677
	853	32	162.1	0.045	1.059	0.325	0.603
	854	32	169.5	0.031	1.028	0.340	0.647
	855	32	164.4	0.042	1.009	0.331	0.621
	856	32	167.0	0.030	1.034	0.384	0.675
	857	32	179.7	0.040	0.981	0.382	0.643
	858	32	174.1	0.037	1.053	0.373	0.714
	859	32	170.4	0.035	1.113	0.357	0.678
	860	32	166.1	0.041	0.968	0.339	0.620
E20F	1251	32	132.3	0.030	1.333	0.353	0.823
	1252	32	128.6	0.045	1.260	0.378	0.738
	1253	32	127.1	0.029	1.298	0.365	0.745
	1254	32	131.3	0.034	1.160	0.338	0.760
	1255	32	143.5	0.028	1.190	0.306	0.648
	1256	32	142.9	0.024	1.232	0.323	0.773
	1257	32	118.6	0.035	1.415	0.355	0.822
	1258	32	126.9	0.026	1.324	0.378	0.751
	1259	32	146.0	0.023	1.111	0.363	0.698
	1260	32	128.6	0.040	1.245	0.348	0.804
PFCEF	1351	32	172.0	0.032	0.975	0.393	0.657
	1352	32	182.2	0.036	0.942	0.320	0.642
	1353	32	168.0	0.028	1.032	0.333	0.680
	1354	32	166.6	0.038	1.028	0.365	0.753
	1355	32	171.0	0.040	1.067	0.363	0.690
	1356	32	176.9	0.035	0.990	0.336	0.640
	1357	32	161.4	0.029	1.008	0.353	0.633
	1358	32	173.8	0.034	0.949	0.332	0.681
	1359	32	168.8	0.033	1.084	0.335	0.693
	1360	32	162.6	0.035	1.081	0.371	0.696

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		Liver	Ovaries	Salivary Gland	Spleen
			Body Weight					
NT20F	251	32	138.3		3.083	0.043	0.293	0.237
	252	32	151.4		2.702	0.033	0.261	0.181
	253	32	141.8		3.360	0.029	0.272	0.192
	254	32	138.6		3.176	0.042	0.257	0.191
	255	32	149.5		3.083	0.039	0.278	0.239
	256	32	151.6		3.120	0.054	0.254	0.221
	257	32	137.5		3.393	0.050	0.217	0.223
	258	32	123.5		3.198	0.035	0.293	0.225
	259	32	154.7		3.095	0.031	0.237	0.183
	260	32	129.3		3.041	0.034	0.295	0.201
PFCNTF	351	32	175.4		2.852	0.051	0.262	0.219
	352	32	148.2		2.482	0.057	0.254	0.217
	353	32	166.3		2.928	0.054	0.294	0.256
	354	32	172.9		2.674	0.051	0.266	0.218
	355	32	154.0		2.685	0.047	0.242	0.206
	356	32	160.3		2.618	0.053	0.216	0.313
	357	32	177.6		2.397	0.047	0.240	0.160
	358	32	171.5		2.770	0.049	0.263	0.242
	359	32	164.6		2.489	0.061	0.233	0.317
	360	32	176.5		2.555	0.035	0.249	0.242
B20F	751	32	128.9		3.173	0.049	0.289	0.192
	752	32	125.9		3.309	0.031	0.277	0.205
	753	32	137.3		3.119	0.045	0.230	0.157
	754	32	122.5		3.100	0.036	0.285	0.179
	755	32	122.8		3.179	0.046	0.236	0.143
	756	32	117.7		3.093	0.056	0.273	0.138
	758	32	137.2		3.244	0.034	0.259	0.176
	759	32	132.4		3.086	0.045	0.291	0.195
	760	32	129.4		3.073	0.042	0.284	0.227

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		Liver	Ovaries	Salivary Gland	Spleen
			Body Weight					
PFCBF	851	32	171.5		2.666	0.052	0.232	0.258
	852	32	165.5		2.311	0.048	0.237	0.200
	853	32	162.1		2.477	0.049	0.255	0.233
	854	32	169.5		2.625	0.039	0.242	0.253
	855	32	164.4		2.591	0.064	0.255	0.242
	856	32	167.0		2.360	0.049	0.243	0.247
	857	32	179.7		2.758	0.072	0.239	0.220
	858	32	174.1		2.691	0.048	0.306	0.231
	859	32	170.4		2.380	0.050	0.251	0.207
	860	32	166.1		2.759	0.052	0.245	0.225
E20F	1251	32	132.3		3.144	0.043	0.282	0.174
	1252	32	128.6		3.412	0.061	0.228	0.297
	1253	32	127.1		3.093	0.041	0.258	0.169
	1254	32	131.3		3.098	0.033	0.269	0.217
	1255	32	143.5		2.706	0.030	0.261	0.152
	1256	32	142.9		2.994	0.040	0.250	0.132
	1257	32	118.6		3.164	0.044	0.291	0.210
	1258	32	126.9		2.968	0.045	0.314	0.141
	1259	32	146.0		2.900	0.045	0.278	0.196
	1260	32	128.6		2.917	0.049	0.281	0.174
PFCEF	1351	32	172.0		2.470	0.044	0.247	0.208
	1352	32	182.2		2.565	0.048	0.261	0.221
	1353	32	168.0		2.493	0.059	0.255	0.223
	1354	32	166.6		2.745	0.053	0.288	0.188
	1355	32	171.0		2.610	0.048	0.311	0.248
	1356	32	176.9		2.618	0.044	0.268	0.236
	1357	32	161.4		2.421	0.047	0.240	0.221
	1358	32	173.8		2.561	0.052	0.266	0.244
	1359	32	168.8		2.436	0.042	0.227	0.205
	1360	32	162.6		2.667	0.058	0.248	0.214

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Thymus	Uterus
NT20F	251	32	138.3	0.158	0.095
	252	32	151.4	0.208	0.086
	253	32	141.8	0.121	0.104
	254	32	138.6	0.147	0.100
	255	32	149.5	0.225	0.174
	256	32	151.6	0.194	0.152
	257	32	137.5	0.203	0.076
	258	32	123.5	0.334	0.112
	259	32	154.7	0.190	0.128
	260	32	129.3	0.196	0.100
PFCNTF	351	32	175.4	0.223	0.780
	352	32	148.2	0.220	0.366
	353	32	166.3	0.193	0.404
	354	32	172.9	0.229	0.217
	355	32	154.0	0.199	0.244
	356	32	160.3	0.230	0.200
	357	32	177.6	0.298	0.168
	358	32	171.5	0.251	0.288
	359	32	164.6	0.250	0.128
	360	32	176.5	0.256	0.143
B20F	751	32	128.9	0.173	0.117
	752	32	125.9	0.103	0.093
	753	32	137.3	0.131	0.122
	754	32	122.5	0.108	0.108
	755	32	122.8	0.168	0.110
	756	32	117.7	0.188	0.156
	758	32	137.2	0.165	0.102
	759	32	132.4	0.196	0.111
	760	32	129.4	0.170	0.090

**Table D-8. Paired and High Dose Group Individual Animal Terminal Body Weights (g) and Percent Organ-to-Body Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Terminal		
			Body Weight	Thymus	Uterus
PFCBF	851	32	171.5	0.261	0.171
	852	32	165.5	0.242	0.183
	853	32	162.1	0.275	0.320
	854	32	169.5	0.254	0.292
	855	32	164.4	0.189	0.243
	856	32	167.0	0.241	0.237
	857	32	179.7	0.242	0.283
	858	32	174.1	0.255	0.334
	859	32	170.4	0.432	0.923
	860	32	166.1	0.281	0.313
E20F	1251	32	132.3	0.167	0.104
	1252	32	128.6	0.127	0.114
	1253	32	127.1	0.141	0.089
	1254	32	131.3	0.148	0.073
	1255	32	143.5	0.175	0.075
	1256	32	142.9	0.141	0.074
	1257	32	118.6	0.157	0.110
	1258	32	126.9	0.154	0.083
	1259	32	146.0	0.241	0.071
	1260	32	128.6	0.121	0.118
PFCEF	1351	32	172.0	0.221	0.235
	1352	32	182.2	0.162	0.218
	1353	32	168.0	0.287	0.397
	1354	32	166.6	0.257	0.609
	1355	32	171.0	0.280	0.294
	1356	32	176.9	0.374	0.187
	1357	32	161.4	0.236	0.211
	1358	32	173.8	0.251	0.348
	1359	32	168.8	0.269	0.211
	1360	32	162.6	0.159	0.270

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males**

Group	Animal ID	Day	Absolute Brain Weight	Adrenal Glands	Epididymides	Heart	Kidneys
CM	101	29	1.974	3.12	53.690	44.80	99.02
	102	29	1.933	3.70	55.554	55.91	107.20
	103	29	1.995	3.36	42.462	54.01	93.98
	104	29	1.782	3.17	48.049	47.76	98.01
	105	29	2.032	3.29	52.935	52.68	101.73
	106	29	1.862	4.08	47.545	53.16	99.87
	107	29	1.954	3.24	46.957	43.47	93.73
	108	29	1.942	3.31	60.154	53.08	111.08
	109	29	1.943	3.42	48.083	51.45	106.52
	110	29	1.961	3.84	57.525	47.86	98.44
B0.2M	401	29	1.865	2.60	48.236	39.30	93.09
	402	29	1.917	3.33	53.727	49.22	102.43
	403	29	2.004	3.21	51.882	52.22	100.64
	404	29	1.876	3.59	45.473	39.35	87.19
	405	29	1.966	2.54	48.476	50.22	97.08
	406	29	1.817	3.54	48.247	54.97	116.08
	407	29	1.959	2.78	47.856	46.03	95.90
	408	29	1.922	3.09	50.021	46.07	99.39
	409	29	1.879	3.45	58.010	47.59	97.56
	410	29	2.065	3.41	49.862	42.99	105.26
B2M	501	29	1.881	3.82	54.890	49.05	105.33
	502	29	1.966	3.27	50.778	50.21	108.99
	503	29	1.810	3.03	54.450	44.00	80.17
	504	29	1.955	3.59	49.667	49.59	105.54
	505	29	2.101	4.17	47.725	47.66	98.46
	506	29	1.842	3.24	49.824	46.10	100.97
	507	29	1.967	2.97	48.775	41.44	95.06
	508	29	1.969	2.96	49.827	38.75	90.01
	509	29	1.943	3.31	43.036	42.49	91.06
	510	29	1.891	3.26	45.981	44.56	84.78

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Adrenal Glands	Epididymides	Heart	Kidneys
B8M	601	29	1.995	2.92	44.092	39.78	97.50
	602	29	1.741	2.65	52.289	41.41	77.42
	603	29	1.863	2.36	47.285	46.02	104.95
	604	29	1.845	2.57	48.691	43.37	90.24
	605	29	1.781	2.17	53.474	40.37	92.50
	606	29	1.781	2.64	49.641	39.89	87.13
	607	29	1.918	2.04	38.328	33.11	71.95
	608	29	1.932	2.76	42.726	45.97	89.45
	609	29	1.798	2.95	53.901	43.21	99.84
	610	29	1.779	3.66	55.799	40.97	99.21
E0.2M	901	29	1.836	2.31	42.900	46.61	99.60
	902	29	1.872	3.67	47.029	52.25	109.11
	903	29	1.906	3.30	56.644	49.35	110.75
	904	29	2.019	2.95	45.481	47.73	107.61
	905	29	2.001	2.45	38.258	44.87	100.58
	906	29	1.926	4.13	55.808	59.44	100.59
	907	29	1.985	3.84	51.128	53.65	102.83
	908	29	1.895	3.03	46.623	48.35	98.08
	909	29	1.840	2.90	48.614	47.30	105.19
	910	29	1.950	2.94	53.267	43.50	106.08
E2M	1001	29	2.009	3.29	44.937	43.18	89.03
	1002	29	1.896	4.03	46.404	47.55	97.98
	1003	29	1.960	2.75	48.449	59.38	108.26
	1004	29	1.799	3.06	50.890	48.40	91.85
	1005	29	1.920	2.91	43.853	53.08	92.95
	1006	29	1.888	3.60	43.421	44.06	110.61
	1007	29	1.883	2.40	41.342	46.74	105.05
	1008	29	1.918	2.28	50.073	37.34	80.30
	1009	29	2.017	3.57	56.850	45.83	100.85
	1010	29	2.027	3.41	46.456	50.92	108.43

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Adrenal Glands</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>
E8M	1101	29	1.858	3.09	59.504	44.07	87.90
	1102	29	1.829	2.66	47.435	47.10	93.54
	1103	29	1.844	3.32	45.036	48.49	93.08
	1104	29	1.773	3.68	53.475	48.03	92.62
	1105	29	1.872	2.84	43.172	43.76	82.08
	1106	29	1.880	3.03	51.689	41.19	92.51
	1107	29	1.933	2.49	45.136	36.61	90.68
	1108	29	1.891	3.26	59.007	42.91	93.69
	1109	29	1.915	2.95	45.342	37.82	75.54
	1110	29	1.896	2.60	43.184	44.07	87.33

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Liver	Salivary Gland	Spleen	Testes
CM	101	29	1.974	359.34	29.88	27.94	190.01
	102	29	1.933	448.35	32.30	26.86	173.88
	103	29	1.995	405.47	31.40	32.63	176.40
	104	29	1.782	419.69	32.83	24.52	160.25
	105	29	2.032	374.16	29.89	30.23	173.47
	106	29	1.862	454.35	32.27	25.06	149.22
	107	29	1.954	319.20	30.50	24.86	166.87
	108	29	1.942	419.50	33.76	30.03	173.60
	109	29	1.943	468.77	37.17	26.15	171.32
	110	29	1.961	405.29	29.69	26.70	197.46
B0.2M	401	29	1.865	325.22	25.13	25.41	153.06
	402	29	1.917	369.38	28.32	37.84	169.30
	403	29	2.004	363.26	32.04	28.80	173.02
	404	29	1.876	340.60	27.50	22.47	169.90
	405	29	1.966	385.71	31.84	25.04	174.85
	406	29	1.817	432.57	31.55	27.70	176.69
	407	29	1.959	330.25	29.01	28.13	167.85
	408	29	1.922	341.11	27.12	30.60	173.40
	409	29	1.879	406.82	34.13	28.88	176.02
	410	29	2.065	345.82	28.75	30.52	161.21
B2M	501	29	1.881	355.18	35.33	30.50	187.13
	502	29	1.966	386.53	39.64	29.09	172.17
	503	29	1.810	273.96	30.72	22.54	168.25
	504	29	1.955	410.52	33.09	32.67	178.44
	505	29	2.101	361.56	31.49	23.73	161.14
	506	29	1.842	391.24	30.44	34.62	171.53
	507	29	1.967	320.09	26.08	26.32	163.02
	508	29	1.969	341.50	32.35	22.94	169.90
	509	29	1.943	309.51	29.66	23.93	169.96
	510	29	1.891	324.41	28.18	24.86	174.34

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>
B8M	601	29	1.995	350.66	29.89	27.92	158.22
	602	29	1.741	284.83	28.58	15.28	174.13
	603	29	1.863	352.11	28.88	24.57	156.78
	604	29	1.845	374.64	31.77	15.59	164.64
	605	29	1.781	315.55	32.95	23.07	182.02
	606	29	1.781	329.09	31.60	22.43	174.30
	607	29	1.918	256.33	24.88	20.19	169.33
	608	29	1.932	333.10	27.69	19.97	170.35
	609	29	1.798	371.14	32.96	29.60	186.88
	610	29	1.779	433.12	29.08	24.66	168.32
E0.2M	901	29	1.836	393.76	31.76	33.75	159.95
	902	29	1.872	436.66	33.23	30.49	151.27
	903	29	1.906	419.78	27.01	24.07	175.27
	904	29	2.019	360.73	31.45	26.62	160.48
	905	29	2.001	376.05	25.92	28.39	140.95
	906	29	1.926	419.01	36.68	26.33	180.92
	907	29	1.985	415.46	36.88	33.62	183.34
	908	29	1.895	343.70	29.22	26.17	170.60
	909	29	1.840	395.87	27.47	26.90	172.85
	910	29	1.950	341.52	30.24	22.72	179.92
E2M	1001	29	2.009	339.17	30.02	27.99	146.13
	1002	29	1.896	399.57	35.58	29.82	174.41
	1003	29	1.960	448.36	32.34	29.37	162.09
	1004	29	1.799	327.33	32.66	25.15	176.45
	1005	29	1.920	372.90	35.84	25.61	165.84
	1006	29	1.888	386.86	31.80	30.87	160.54
	1007	29	1.883	347.04	32.94	26.79	149.05
	1008	29	1.918	285.57	25.23	17.98	161.33
	1009	29	2.017	361.58	31.86	27.71	197.46
	1010	29	2.027	381.64	36.22	26.61	163.68

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute Brain Weight		Salivary Gland	Spleen	Testes
				Liver			
E8M	1101	29	1.858	369.33	32.60	28.68	203.96
	1102	29	1.829	364.80	34.29	22.56	176.29
	1103	29	1.844	394.13	34.44	31.64	163.04
	1104	29	1.773	400.07	30.92	29.56	187.21
	1105	29	1.872	316.12	30.70	24.05	159.11
	1106	29	1.880	324.94	33.75	23.67	166.86
	1107	29	1.933	299.39	28.98	23.64	169.24
	1108	29	1.891	322.81	29.64	25.71	185.94
	1109	29	1.915	286.92	26.00	20.04	161.26
	1110	29	1.896	330.30	27.71	21.77	176.45

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute	
			Brain Weight	Thymus
CM	101	29	1.974	32.73
	102	29	1.933	40.58
	103	29	1.995	29.09
	104	29	1.782	31.46
	105	29	2.032	27.51
	106	29	1.862	27.86
	107	29	1.954	32.16
	108	29	1.942	32.75
	109	29	1.943	38.23
	110	29	1.961	31.45
B0.2M	401	29	1.865	28.55
	402	29	1.917	27.35
	403	29	2.004	24.54
	404	29	1.876	30.45
	405	29	1.966	29.72
	406	29	1.817	40.38
	407	29	1.959	26.99
	408	29	1.922	21.83
	409	29	1.879	29.86
	410	29	2.065	34.65
B2M	501	29	1.881	25.02
	502	29	1.966	25.37
	503	29	1.810	19.16
	504	29	1.955	23.34
	505	29	2.101	31.44
	506	29	1.842	26.11
	507	29	1.967	24.51
	508	29	1.969	21.09
	509	29	1.943	22.07
	510	29	1.891	26.09

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute	
			Brain Weight	Thymus
B8M	601	29	1.995	30.13
	602	29	1.741	16.68
	603	29	1.863	25.98
	604	29	1.845	20.83
	605	29	1.781	19.85
	606	29	1.781	24.00
	607	29	1.918	21.43
	608	29	1.932	18.06
	609	29	1.798	28.27
	610	29	1.779	25.94
E0.2M	901	29	1.836	25.88
	902	29	1.872	37.95
	903	29	1.906	31.76
	904	29	2.019	26.02
	905	29	2.001	24.28
	906	29	1.926	22.69
	907	29	1.985	36.53
	908	29	1.895	23.90
	909	29	1.840	38.40
	910	29	1.950	27.03
E2M	1001	29	2.009	26.83
	1002	29	1.896	28.08
	1003	29	1.960	26.75
	1004	29	1.799	34.44
	1005	29	1.920	26.94
	1006	29	1.888	30.95
	1007	29	1.883	23.27
	1008	29	1.918	14.36
	1009	29	2.017	26.20
	1010	29	2.027	32.11

**Table D-9. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

Group	Animal ID	Day	Absolute	
			Brain Weight	Thymus
E8M	1101	29	1.858	31.74
	1102	29	1.829	34.14
	1103	29	1.844	32.76
	1104	29	1.773	25.43
	1105	29	1.872	21.69
	1106	29	1.880	23.16
	1107	29	1.933	20.40
	1108	29	1.891	24.44
	1109	29	1.915	24.83
	1110	29	1.896	32.99

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females**

Group	Animal ID	Day	Absolute Brain Weight	Adrenal Glands	Heart	Kidneys	Liver
CF	151	30	1.715	4.49	36.55	73.75	274.54
	152	30	1.758	3.93	34.84	65.70	260.16
	153	30	1.775	4.23	36.94	73.03	274.58
	154	30	1.835	3.61	37.57	68.93	243.00
	155	30	1.862	4.02	32.91	74.21	229.40
	156	30	1.863	4.63	35.08	74.88	278.46
	157	30	1.759	3.93	36.88	78.10	268.85
	158	30	1.820	4.26	36.25	66.42	270.00
	159	30	1.752	3.73	31.12	62.21	247.05
	160	30	1.823	3.52	29.72	65.87	256.57
B0.2F	451	30	1.794	3.50	28.47	66.90	233.00
	452	30	1.729	3.27	36.70	73.68	267.42
	453	30	1.724	3.83	35.36	69.45	266.99
	454	30	1.816	3.40	30.91	65.11	228.87
	455	30	1.869	3.73	32.87	66.45	255.41
	456	30	1.717	3.52	39.73	67.08	250.63
	457	30	1.786	3.89	36.65	77.78	260.80
	458	30	1.754	4.39	41.85	79.08	294.02
	459	30	1.777	4.21	34.58	72.17	249.56
	460	30	1.698	3.80	38.97	70.29	265.57
B2F	551	30	1.765	3.67	35.35	68.04	246.68
	552	30	1.795	4.41	31.32	64.26	242.52
	553	30	1.819	4.59	34.40	61.51	235.33
	554	30	1.883	3.64	30.87	61.30	226.82
	555	30	1.921	2.86	31.38	63.50	214.22
	556	30	1.858	4.44	32.19	65.60	251.02
	557	30	1.771	3.55	34.34	69.43	237.66
	558	30	1.711	3.90	33.36	62.21	225.97
	559	30	1.785	4.48	40.22	73.12	276.30
	560	30	1.876	4.05	34.61	68.68	247.93

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Adrenal Glands	Heart	Kidneys	Liver
B8F	651	30	1.790	2.92	27.07	66.12	242.25
	652	30	1.621	3.19	30.69	66.35	250.61
	653	30	1.847	3.35	29.59	63.98	228.73
	654	30	1.607	3.74	32.18	65.57	264.25
	655	30	1.798	3.87	29.67	60.75	219.88
	656	30	1.752	4.40	32.11	70.96	259.53
	657	30	1.742	3.49	29.90	64.02	269.20
	658	30	1.717	2.63	26.97	71.58	262.11
	659	30	1.832	3.09	26.09	54.24	217.87
	660	30	1.713	3.46	31.86	63.13	254.87
E0.2F	951	30	1.804	3.95	33.18	66.07	233.79
	952	30	1.764	4.41	38.36	68.73	250.81
	953	30	1.731	4.56	38.04	73.25	250.90
	954	30	1.728	4.45	38.31	74.45	263.07
	955	30	1.742	4.32	39.72	80.18	296.72
	956	30	1.803	4.21	39.78	73.97	262.27
	957	30	1.811	4.79	39.06	70.02	251.70
	958	30	1.709	3.86	35.20	70.51	297.95
	959	30	1.670	5.31	38.97	75.61	263.85
	960	30	1.841	4.46	37.30	73.88	271.54
E2F	1051	30	1.814	3.63	33.34	67.92	223.51
	1052	30	1.809	4.12	35.20	65.03	242.56
	1053	30	1.787	5.77	30.53	69.75	238.08
	1054	30	1.761	4.74	35.07	70.46	248.39
	1055	30	1.820	6.38	36.55	78.64	280.33
	1056	30	1.720	4.05	33.84	65.46	223.47
	1057	30	1.760	3.69	32.18	67.92	246.70
	1058	30	1.748	4.67	32.21	70.35	255.36
	1059	30	1.820	2.87	28.00	63.29	209.49
	1060	30	1.738	4.07	37.01	71.36	255.95

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Adrenal Glands</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
E8F	1151	30	1.797	3.77	33.23	67.79	260.45
	1152	30	1.671	3.27	28.89	56.79	232.00
	1153	30	1.884	3.00	33.65	62.43	244.21
	1154	30	1.716	2.87	28.32	72.88	231.05
	1155	30	1.763	2.05	32.73	70.12	264.07
	1156	30	1.705	3.44	34.37	69.91	260.27
	1157	30	1.722	3.98	32.73	65.61	238.36
	1158	30	1.797	3.93	27.37	62.42	247.16
	1159	30	1.708	3.81	34.28	73.05	254.49
	1160	30	1.730	3.08	33.14	71.32	288.65

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Ovaries	Salivary Gland	Spleen	Thymus
CF	151	30	1.715	4.72	24.71	24.37	30.99
	152	30	1.758	7.00	24.14	19.48	27.36
	153	30	1.775	6.27	24.64	20.73	20.07
	154	30	1.835	5.43	22.69	21.91	29.28
	155	30	1.862	5.56	24.46	20.53	20.01
	156	30	1.863	8.51	24.36	26.64	26.14
	157	30	1.759	5.33	21.92	21.80	24.97
	158	30	1.820	7.43	28.78	22.80	26.41
	159	30	1.752	5.05	19.66	26.07	20.74
	160	30	1.823	4.48	21.49	21.91	19.39
B0.2F	451	30	1.794	7.06	19.87	16.32	18.47
	452	30	1.729	5.19	22.70	21.73	19.02
	453	30	1.724	5.55	21.48	16.82	20.79
	454	30	1.816	9.30	21.70	21.52	23.14
	455	30	1.869	4.45	22.60	24.52	24.52
	456	30	1.717	3.98	22.36	19.49	23.82
	457	30	1.786	4.68	25.61	21.19	29.49
	458	30	1.754	5.38	25.62	24.98	28.58
	459	30	1.777	6.32	25.10	24.68	24.98
	460	30	1.698	6.41	23.02	23.07	27.71
B2F	551	30	1.765	5.63	27.97	22.54	21.64
	552	30	1.795	4.76	23.59	23.04	21.25
	553	30	1.819	5.38	29.29	20.39	15.24
	554	30	1.883	5.42	22.52	20.18	25.96
	555	30	1.921	4.08	23.27	17.23	20.47
	556	30	1.858	4.86	28.06	25.04	20.21
	557	30	1.771	4.90	28.36	23.80	22.82
	558	30	1.711	8.36	22.06	19.75	26.15
	559	30	1.785	5.53	22.90	25.32	26.20
	560	30	1.876	6.75	23.23	20.10	26.36

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Ovaries	Salivary Gland	Spleen	Thymus
B8F	651	30	1.790	4.70	26.13	21.07	22.13
	652	30	1.621	4.18	24.60	18.42	23.12
	653	30	1.847	5.45	23.16	19.89	19.73
	654	30	1.607	4.91	29.05	24.96	27.64
	655	30	1.798	4.80	25.75	21.83	24.47
	656	30	1.752	8.51	28.34	21.10	21.56
	657	30	1.742	3.17	25.86	19.97	19.78
	658	30	1.717	4.05	24.39	18.13	18.08
	659	30	1.832	6.99	24.28	16.77	19.70
	660	30	1.713	5.18	27.03	17.85	20.77
E0.2F	951	30	1.804	4.18	21.31	18.30	20.37
	952	30	1.764	4.31	24.79	20.74	28.54
	953	30	1.731	5.69	25.95	22.20	27.23
	954	30	1.728	5.89	25.64	29.92	21.76
	955	30	1.742	5.92	29.43	28.09	24.09
	956	30	1.803	6.17	26.01	22.32	23.51
	957	30	1.811	4.81	29.63	27.25	18.02
	958	30	1.709	5.45	21.08	24.32	22.81
	959	30	1.670	5.21	24.08	24.83	31.38
	960	30	1.841	8.28	20.38	21.39	19.56
E2F	1051	30	1.814	5.18	25.64	22.39	21.58
	1052	30	1.809	5.84	24.78	23.03	24.63
	1053	30	1.787	7.69	25.18	21.24	21.44
	1054	30	1.761	4.97	26.96	21.58	25.71
	1055	30	1.820	5.18	31.13	21.94	29.80
	1056	30	1.720	5.16	22.60	22.23	21.94
	1057	30	1.760	5.54	24.92	20.69	27.47
	1058	30	1.748	6.78	22.36	25.63	16.81
	1059	30	1.820	4.04	19.40	18.88	18.60
	1060	30	1.738	6.43	27.58	23.53	21.18

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight		Salivary Gland	Spleen	Thymus
				Ovaries			
E8F	1151	30	1.797	5.77	26.19	22.20	20.35
	1152	30	1.671	3.78	23.15	19.36	26.04
	1153	30	1.884	4.35	24.17	25.27	22.00
	1154	30	1.716	2.90	24.44	19.88	18.15
	1155	30	1.763	4.71	24.88	24.25	17.25
	1156	30	1.705	5.06	24.78	22.38	28.09
	1157	30	1.722	5.68	26.93	23.06	18.30
	1158	30	1.797	4.66	24.80	18.92	22.82
	1159	30	1.708	4.88	24.61	28.71	23.83
	1160	30	1.730	5.15	29.65	22.66	18.34

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight		Uterus
CF	151	30	1.715		40.49
	152	30	1.758		40.32
	153	30	1.775		36.23
	154	30	1.835		32.67
	155	30	1.862		20.79
	156	30	1.863		54.03
	157	30	1.759		30.65
	158	30	1.820		23.05
	159	30	1.752		49.98
	160	30	1.823		24.10
B0.2F	451	30	1.794		23.62
	452	30	1.729		43.84
	453	30	1.724		21.64
	454	30	1.816		28.15
	455	30	1.869		22.58
	456	30	1.717		45.16
	457	30	1.786		22.33
	458	30	1.754		24.87
	459	30	1.777		22.49
	460	30	1.698		42.93
B2F	551	30	1.765		32.05
	552	30	1.795		19.20
	553	30	1.819		24.61
	554	30	1.883		23.40
	555	30	1.921		22.74
	556	30	1.858		22.40
	557	30	1.771		22.54
	558	30	1.711		34.67
	559	30	1.785		36.64
	560	30	1.876		28.71

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute	
			Brain Weight	Uterus
B8F	651	30	1.790	21.74
	652	30	1.621	52.12
	653	30	1.847	20.07
	654	30	1.607	24.13
	655	30	1.798	20.45
	656	30	1.752	48.81
	657	30	1.742	36.73
	658	30	1.717	14.81
	659	30	1.832	28.06
	660	30	1.713	19.38
E0.2F	951	30	1.804	43.18
	952	30	1.764	39.41
	953	30	1.731	28.12
	954	30	1.728	50.37
	955	30	1.742	38.26
	956	30	1.803	24.01
	957	30	1.811	25.31
	958	30	1.709	44.87
	959	30	1.670	49.31
	960	30	1.841	23.61
E2F	1051	30	1.814	28.13
	1052	30	1.809	21.39
	1053	30	1.787	21.16
	1054	30	1.761	44.59
	1055	30	1.820	32.24
	1056	30	1.720	43.56
	1057	30	1.760	54.31
	1058	30	1.748	28.00
	1059	30	1.820	14.32
	1060	30	1.738	32.69

**Table D-10. Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute	
			Brain Weight	Uterus
E8F	1151	30	1.797	21.82
	1152	30	1.671	19.82
	1153	30	1.884	24.47
	1154	30	1.716	56.74
	1155	30	1.763	46.77
	1156	30	1.705	19.33
	1157	30	1.722	18.05
	1158	30	1.797	17.81
	1159	30	1.708	38.98
	1160	30	1.730	36.79

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males**

Group	Animal ID	Day	Absolute				
			Brain Weight	Adrenal Glands	Epididymides	Heart	Kidneys
NT20M	201	31	1.747	2.73	50.555	36.96	87.27
	202	31	1.901	2.43	51.273	38.46	88.67
	203	31	1.840	1.92	42.064	34.91	82.86
	204	31	1.794	2.70	49.950	34.51	80.40
	205	31	1.957	2.72	49.009	37.80	85.01
	206	31	1.909	2.56	42.263	42.36	88.48
	207	31	1.801	1.97	45.596	39.81	81.68
	208	31	1.803	2.22	42.650	44.50	86.41
	209	31	1.782	2.44	51.521	38.82	98.20
	210	31	1.852	2.59	48.397	37.93	98.19
PFCNTM	301	31	1.814	2.84	49.986	38.30	84.01
	302	31	1.973	2.33	50.421	39.12	78.43
	303	31	2.009	2.45	51.620	37.83	75.74
	304	31	1.876	3.01	52.341	39.83	94.13
	305	31	1.794	2.97	53.099	37.84	86.77
	306	31	1.878	2.90	45.580	38.37	80.96
	307	31	1.825	2.69	48.723	41.16	87.31
	308	31	1.784	3.21	60.820	42.10	96.19
	309	31	1.823	2.12	58.822	38.47	76.95
	310	31	1.924	2.52	49.309	42.69	85.45
B20M	701	31	1.730	2.90	48.968	39.45	90.54
	702	31	1.737	3.04	49.752	36.60	81.47
	703	31	1.785	2.55	43.226	31.85	78.87
	704	31	1.772	2.34	46.699	38.15	93.16
	705	31	1.774	2.88	42.306	37.89	91.38
	706	31	1.759	2.47	47.346	33.11	76.97
	707	31	1.773	2.38	43.840	36.10	79.87
	708	31	1.826	2.61	46.705	32.52	75.00
	709	31	1.788	2.85	51.630	44.12	92.05
	710	31	1.638	2.43	51.008	42.04	106.98

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Adrenal Glands</b>	<b>Epididymides</b>	<b>Heart</b>	<b>Kidneys</b>
PFCBM	801	31	1.958	2.81	54.686	36.73	77.95
	802	31	1.899	2.94	50.814	37.66	90.11
	803	31	1.762	2.76	52.838	38.80	81.05
	804	31	1.912	2.42	47.252	43.54	90.86
	805	31	1.826	2.19	47.694	43.19	80.77
	806	31	1.793	2.62	51.244	39.80	77.33
	807	31	1.875	3.08	49.979	43.79	93.31
	808	31	1.678	2.97	49.186	44.22	102.99
	809	31	2.014	2.15	45.781	43.03	89.32
	810	31	2.050	2.89	44.928	36.82	80.82
E20M	1201	31	1.789	2.41	49.508	35.44	82.83
	1202	31	1.800	2.36	41.068	39.55	82.44
	1203	31	1.776	2.10	42.746	35.26	69.57
	1204	31	1.700	2.71	39.873	29.42	76.27
	1205	31	1.862	1.91	49.546	34.23	84.70
	1206	31	1.885	2.60	44.422	36.77	79.39
	1207	31	1.892	3.03	44.508	37.14	90.34
	1208	31	1.680	2.19	42.257	37.94	78.86
	1209	31	1.773	2.26	46.373	38.62	89.69
	1210	31	1.775	2.70	43.173	37.02	80.76
PFCM	1301	31	1.701	3.86	46.161	44.24	103.35
	1302	31	1.735	3.66	55.988	45.88	84.00
	1303	31	1.917	2.21	51.398	40.67	80.80
	1304	31	1.874	2.56	52.553	43.73	91.28
	1305	31	1.869	2.80	47.624	44.62	95.95
	1306	31	1.740	2.26	55.006	40.29	93.96
	1307	31	1.899	2.93	54.693	40.42	85.43
	1308	31	1.881	2.36	50.869	40.73	85.72
	1309	31	1.941	3.00	52.197	41.44	85.45
	1310	31	1.880	3.00	49.207	42.32	87.61

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>
NT20M	201	31	1.747	318.74	24.11	21.33	205.90
	202	31	1.901	304.00	33.09	19.21	185.46
	203	31	1.840	340.34	28.26	27.81	167.07
	204	31	1.794	321.17	28.37	25.28	173.22
	205	31	1.957	322.48	30.89	22.06	189.23
	206	31	1.909	326.74	29.08	18.16	157.39
	207	31	1.801	359.14	27.85	24.54	160.99
	208	31	1.803	350.35	31.23	24.03	162.58
	209	31	1.782	355.08	30.49	24.09	178.48
	210	31	1.852	363.06	32.07	21.53	175.73
PFCNTM	301	31	1.814	335.67	36.72	21.93	165.68
	302	31	1.973	348.01	31.92	20.38	163.45
	303	31	2.009	320.49	29.84	17.60	169.80
	304	31	1.876	356.26	31.33	24.35	173.44
	305	31	1.794	313.39	30.21	23.50	174.11
	306	31	1.878	345.98	34.23	22.44	168.70
	307	31	1.825	362.57	31.48	18.50	167.43
	308	31	1.784	366.03	32.71	22.08	198.13
	309	31	1.823	287.90	32.47	22.67	190.48
	310	31	1.924	332.08	29.54	20.72	177.91
B20M	701	31	1.730	340.29	36.09	22.39	176.74
	702	31	1.737	365.90	22.18	23.47	180.99
	703	31	1.785	321.07	31.45	20.04	166.24
	704	31	1.772	366.14	31.39	24.22	168.54
	705	31	1.774	323.97	27.04	18.44	176.76
	706	31	1.759	280.47	30.50	20.06	179.98
	707	31	1.773	283.42	26.12	18.76	170.17
	708	31	1.826	297.41	34.97	20.59	161.04
	709	31	1.788	374.62	31.07	22.37	200.98
	710	31	1.638	406.46	25.26	26.34	187.12

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Liver</b>	<b>Salivary Gland</b>	<b>Spleen</b>	<b>Testes</b>
PFCBM	801	31	1.958	329.50	29.20	17.61	163.74
	802	31	1.899	349.20	33.10	27.32	154.36
	803	31	1.762	299.80	24.80	20.80	192.69
	804	31	1.912	359.79	34.86	24.03	191.29
	805	31	1.826	322.44	33.13	20.41	161.34
	806	31	1.793	355.09	32.09	22.36	185.34
	807	31	1.875	369.04	35.48	28.76	180.80
	808	31	1.678	430.58	36.51	26.70	184.67
	809	31	2.014	334.18	31.89	21.24	164.00
	810	31	2.050	279.09	26.85	20.27	160.24
E20M	1201	31	1.789	394.51	30.72	22.54	183.56
	1202	31	1.800	350.04	25.82	22.26	166.54
	1203	31	1.776	301.68	24.60	19.06	167.18
	1204	31	1.700	279.09	22.54	13.64	140.77
	1205	31	1.862	324.35	30.19	25.26	182.66
	1206	31	1.885	323.78	24.95	20.38	168.07
	1207	31	1.892	335.48	30.85	21.53	154.20
	1208	31	1.680	363.75	28.11	23.40	176.04
	1209	31	1.773	359.35	31.30	20.43	157.45
	1210	31	1.775	334.20	29.14	18.69	172.96
PFCM	1301	31	1.701	378.18	31.69	26.85	158.97
	1302	31	1.735	379.40	36.05	32.89	176.19
	1303	31	1.917	350.61	31.18	27.43	177.12
	1304	31	1.874	348.04	31.49	24.09	175.47
	1305	31	1.869	398.14	34.19	24.05	164.42
	1306	31	1.740	373.61	37.62	29.29	193.57
	1307	31	1.899	396.91	27.58	29.26	191.68
	1308	31	1.881	360.41	34.39	20.75	179.80
	1309	31	1.941	383.39	35.83	28.38	175.25
	1310	31	1.880	318.28	29.04	23.03	168.19

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Thymus</b>
NT20M	201	31	1.747	21.74
	202	31	1.901	16.83
	203	31	1.840	25.41
	204	31	1.794	18.78
	205	31	1.957	16.96
	206	31	1.909	16.11
	207	31	1.801	12.66
	208	31	1.803	18.08
	209	31	1.782	22.10
	210	31	1.852	21.50
PFCNTM	301	31	1.814	20.36
	302	31	1.973	21.40
	303	31	2.009	19.34
	304	31	1.876	26.50
	305	31	1.794	21.98
	306	31	1.878	21.08
	307	31	1.825	19.14
	308	31	1.784	25.07
	309	31	1.823	23.09
	310	31	1.924	14.66
B20M	701	31	1.730	24.87
	702	31	1.737	18.18
	703	31	1.785	12.65
	704	31	1.772	23.29
	705	31	1.774	14.04
	706	31	1.759	13.06
	707	31	1.773	17.09
	708	31	1.826	8.72
	709	31	1.788	17.79
	710	31	1.638	19.63

**Table D-11. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Males (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Thymus</b>
PFCBM	801	31	1.958	18.69
	802	31	1.899	30.96
	803	31	1.762	17.82
	804	31	1.912	24.84
	805	31	1.826	18.84
	806	31	1.793	19.95
	807	31	1.875	28.01
	808	31	1.678	31.20
	809	31	2.014	17.57
	810	31	2.050	23.17
E20M	1201	31	1.789	12.29
	1202	31	1.800	12.69
	1203	31	1.776	8.39
	1204	31	1.700	6.72
	1205	31	1.862	15.48
	1206	31	1.885	12.77
	1207	31	1.892	17.49
	1208	31	1.680	18.72
	1209	31	1.773	16.99
	1210	31	1.775	16.93
PFCM	1301	31	1.701	20.61
	1302	31	1.735	25.80
	1303	31	1.917	22.68
	1304	31	1.874	24.72
	1305	31	1.869	19.88
	1306	31	1.740	28.93
	1307	31	1.899	22.72
	1308	31	1.881	15.68
	1309	31	1.941	33.58
	1310	31	1.880	19.36

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females**

Group	Animal ID	Day	Absolute Brain Weight	Adrenal Glands	Heart	Kidneys	Liver
NT20F	251	32	1.623	2.73	33.48	59.55	262.71
	252	32	1.679	2.85	27.24	57.24	243.62
	253	32	1.722	2.26	30.61	59.78	276.75
	254	32	1.744	2.17	26.83	52.82	252.49
	255	32	1.763	2.82	28.33	60.62	261.47
	256	32	1.589	2.98	31.27	65.09	297.63
	257	32	1.584	2.66	29.31	62.65	294.62
	258	32	1.645	2.29	25.26	59.24	240.16
	259	32	1.658	2.64	28.29	58.21	288.75
	260	32	1.640	2.24	28.59	57.27	239.66
PFCNTF	351	32	1.778	3.49	35.40	71.24	281.40
	352	32	1.609	3.00	30.79	66.66	228.62
	353	32	1.760	3.38	35.40	63.34	276.71
	354	32	1.827	3.59	32.06	64.98	253.10
	355	32	1.722	4.14	31.80	65.01	240.17
	356	32	1.600	4.19	34.13	71.14	262.39
	357	32	1.715	2.67	37.11	70.93	248.20
	358	32	1.802	3.66	33.99	68.24	263.61
	359	32	1.699	4.48	35.23	60.89	241.21
	360	32	1.790	3.06	31.17	58.58	251.94
B20F	751	32	1.675	2.65	27.93	59.50	244.13
	752	32	1.641	3.11	27.66	62.40	253.85
	753	32	1.688	2.83	29.41	61.79	253.67
	754	32	1.764	2.01	24.64	53.20	215.31
	755	32	1.631	2.66	24.97	57.57	239.35
	756	32	1.637	3.13	29.80	56.43	222.33
	758	32	1.762	2.22	28.67	58.29	252.52
	759	32	1.775	2.82	24.20	57.49	230.27
	760	32	1.646	2.56	28.50	57.78	241.65

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Adrenal Glands</b>	<b>Heart</b>	<b>Kidneys</b>	<b>Liver</b>
PFCBF	851	32	1.710	4.95	37.40	66.91	267.38
	852	32	1.816	3.02	31.30	61.74	210.61
	853	32	1.716	4.22	30.70	56.94	233.93
	854	32	1.743	3.00	33.05	62.93	255.23
	855	32	1.658	4.12	32.85	61.58	256.84
	856	32	1.726	2.91	37.19	65.30	228.34
	857	32	1.762	4.04	38.90	65.60	281.26
	858	32	1.833	3.55	35.46	67.80	255.56
	859	32	1.897	3.17	32.07	60.94	213.77
	860	32	1.607	4.21	34.99	64.11	285.07
E20F	1251	32	1.764	2.25	26.47	61.76	235.79
	1252	32	1.621	3.54	30.00	58.57	270.75
	1253	32	1.650	2.22	28.15	57.38	238.26
	1254	32	1.524	2.93	29.10	65.50	266.99
	1255	32	1.707	2.32	25.69	54.48	227.46
	1256	32	1.761	1.96	26.23	62.74	242.91
	1257	32	1.678	2.46	25.08	58.09	223.71
	1258	32	1.681	1.95	28.57	56.69	224.07
	1259	32	1.622	2.09	32.70	62.84	260.98
	1260	32	1.601	3.23	27.95	64.54	234.25
PFCEF	1351	32	1.677	3.24	40.35	67.42	253.37
	1352	32	1.716	3.81	33.93	68.17	272.37
	1353	32	1.734	2.76	32.24	65.94	241.56
	1354	32	1.713	3.69	35.52	73.30	267.02
	1355	32	1.825	3.72	34.01	64.67	244.53
	1356	32	1.752	3.57	33.91	64.61	264.38
	1357	32	1.627	2.91	35.01	62.75	240.23
	1358	32	1.649	3.56	35.00	71.76	269.92
	1359	32	1.829	3.08	30.93	63.96	224.82
	1360	32	1.758	3.24	34.33	64.35	246.69

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Ovaries	Salivary Gland	Spleen	Thymus
NT20F	251	32	1.623	3.62	24.93	20.20	13.45
	252	32	1.679	2.94	23.57	16.29	18.78
	253	32	1.722	2.40	22.40	15.82	9.96
	254	32	1.744	3.33	20.40	15.22	11.69
	255	32	1.763	3.31	23.57	20.29	19.11
	256	32	1.589	5.12	24.24	21.04	18.52
	257	32	1.584	4.31	18.80	19.32	17.65
	258	32	1.645	2.63	22.03	16.93	25.10
	259	32	1.658	2.92	22.15	17.09	17.74
	260	32	1.640	2.65	23.21	15.87	15.47
PFCNTF	351	32	1.778	5.04	25.85	21.65	21.96
	352	32	1.609	5.21	23.42	20.02	20.25
	353	32	1.760	5.11	27.80	24.19	18.24
	354	32	1.827	4.86	25.17	20.64	21.70
	355	32	1.722	4.19	21.66	18.46	17.77
	356	32	1.600	5.34	21.65	31.36	23.04
	357	32	1.715	4.85	24.86	16.58	30.90
	358	32	1.802	4.71	24.98	23.04	23.88
	359	32	1.699	5.89	22.57	30.71	24.19
	360	32	1.790	3.49	24.60	23.84	25.22
B20F	751	32	1.675	3.78	22.27	14.77	13.35
	752	32	1.641	2.36	21.22	15.71	7.87
	753	32	1.688	3.68	18.72	12.78	10.69
	754	32	1.764	2.47	19.82	12.41	7.49
	755	32	1.631	3.45	17.79	10.75	12.68
	756	32	1.637	4.01	19.65	9.93	13.53
	758	32	1.762	2.64	20.17	13.74	12.83
	759	32	1.775	3.36	21.69	14.58	14.63
	760	32	1.646	3.32	22.35	17.81	13.33

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

Group	Animal ID	Day	Absolute Brain Weight	Ovaries	Salivary Gland	Spleen	Thymus
PFCBF	851	32	1.710	5.26	23.26	25.86	26.14
	852	32	1.816	4.35	21.60	18.22	22.08
	853	32	1.716	4.61	24.08	21.97	25.95
	854	32	1.743	3.83	23.54	24.62	24.73
	855	32	1.658	6.35	25.29	24.01	18.76
	856	32	1.726	4.72	23.51	23.86	23.29
	857	32	1.762	7.32	24.33	22.41	24.71
	858	32	1.833	4.52	29.08	21.94	24.21
	859	32	1.897	4.46	22.53	18.63	38.81
	860	32	1.607	5.39	25.32	23.22	29.02
E20F	1251	32	1.764	3.21	21.15	13.02	12.53
	1252	32	1.621	4.85	18.09	23.53	10.04
	1253	32	1.650	3.12	19.84	13.02	10.84
	1254	32	1.524	2.80	23.20	18.71	12.79
	1255	32	1.707	2.51	21.92	12.76	14.68
	1256	32	1.761	3.22	20.26	10.72	11.46
	1257	32	1.678	3.08	20.55	14.88	11.08
	1258	32	1.681	3.42	23.73	10.62	11.63
	1259	32	1.622	4.02	25.02	17.62	21.69
	1260	32	1.601	3.94	22.56	13.95	9.75
PFCEF	1351	32	1.677	4.56	25.36	21.29	22.66
	1352	32	1.716	5.13	27.75	23.52	17.22
	1353	32	1.734	5.68	24.68	21.63	27.77
	1354	32	1.713	5.18	28.04	18.29	24.98
	1355	32	1.825	4.48	29.11	23.20	26.20
	1356	32	1.752	4.45	27.09	23.79	37.78
	1357	32	1.627	4.67	23.79	21.97	23.40
	1358	32	1.649	5.46	28.01	25.76	26.48
	1359	32	1.829	3.87	20.96	18.92	24.84
	1360	32	1.758	5.37	22.93	19.77	14.67

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Uterus</b>
NT20F	251	32	1.623	8.08
	252	32	1.679	7.77
	253	32	1.722	8.54
	254	32	1.744	7.97
	255	32	1.763	14.79
	256	32	1.589	14.52
	257	32	1.584	6.57
	258	32	1.645	8.40
	259	32	1.658	11.96
	260	32	1.640	7.85
PFCNTF	351	32	1.778	76.98
	352	32	1.609	33.74
	353	32	1.760	38.16
	354	32	1.827	20.55
	355	32	1.722	21.80
	356	32	1.600	19.99
	357	32	1.715	17.35
	358	32	1.802	27.44
	359	32	1.699	12.43
	360	32	1.790	14.14
B20F	751	32	1.675	9.02
	752	32	1.641	7.12
	753	32	1.688	9.90
	754	32	1.764	7.48
	755	32	1.631	8.26
	756	32	1.637	11.23
	758	32	1.762	7.96
	759	32	1.775	8.32
	760	32	1.646	7.07

**Table D-12. Paired and High Dose Group Individual Animal Brain Weights (g) and Percent Organ-to-Brain Weight Ratios – Females (Continued)**

<b>Group</b>	<b>Animal ID</b>	<b>Day</b>	<b>Absolute Brain Weight</b>	<b>Uterus</b>
PFCBF	851	32	1.710	17.15
	852	32	1.816	16.65
	853	32	1.716	30.20
	854	32	1.743	28.41
	855	32	1.658	24.10
	856	32	1.726	22.90
	857	32	1.762	28.85
	858	32	1.833	31.74
	859	32	1.897	82.92
	860	32	1.607	32.38
E20F	1251	32	1.764	7.80
	1252	32	1.621	9.02
	1253	32	1.650	6.85
	1254	32	1.524	6.32
	1255	32	1.707	6.34
	1256	32	1.761	6.02
	1257	32	1.678	7.76
	1258	32	1.681	6.25
	1259	32	1.622	6.39
	1260	32	1.601	9.49
PFCEF	1351	32	1.677	24.13
	1352	32	1.716	23.12
	1353	32	1.734	38.45
	1354	32	1.713	59.25
	1355	32	1.825	27.54
	1356	32	1.752	18.90
	1357	32	1.627	20.89
	1358	32	1.649	36.71
	1359	32	1.829	19.43
	1360	32	1.758	24.98

**APPENDIX E: CLINICAL PATHOLOGY AND ANATOMIC PATHOLOGY  
NARRATIVES**

3/10/09

CN49730C

## 28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS

### CLINICAL PATHOLOGY

Group mean hematology data are presented in Table 15 for core male rats, Table 16 for core female rats, Table 17 for the pair-fed male rats and Table 18 for the pair-fed female rats.

Although there were a few statistically significant differences as noted in these tables, there were no consistent dose-related trends that were indicative of any treatment-related effects. Group mean absolute white blood cell differential count data are included in Table 19 for core male rats, Table 20 for core female rats, Table 21 for pair-fed male rats, and Table 22 for pair-fed female rats. There were no dose- or treatment-related trends in the differential white blood count data. There were no treatment-related differences in coagulation as indicated in Table 23 for core male rats, Table 24 for core female rats, Table 25 for pair-fed male rats, and Table 26 for pair-fed female rats.

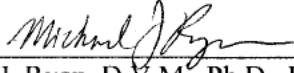
Group mean clinical chemistry data are presented for core male rats (Table 27), core female rats (Table 28), pair-fed male rats (Table 29), and pair-fed female rats (Table 30). A number of trends in the clinical chemistry results were noted in the groups given the three test articles at the highest dose (NT20M, NT20F, B20M, B20F, E20M and E20F group). These included: decreased total protein, albumin and globulin and decreased glucose with increased alkaline phosphatase, total and direct bilirubin, blood urea nitrogen, albumin/globulin ratio, triglycerides and cholesterol. The alterations in these parameters were modest in magnitude and were of similar magnitude in all of the cited groups and in both sexes. Analysis of results in pair-fed controls in comparison with the results of the NT20M, NT20F, B20M, B20F, E20M and E20F indicated that the alterations in cited parameters were not simply due to decreased food consumption. Other differences from control noted by the use of statistical methods were not interpreted to be related to test-article feeding, based on the small size of these differences in relation to variation that is found in untreated Wistar Han rats.

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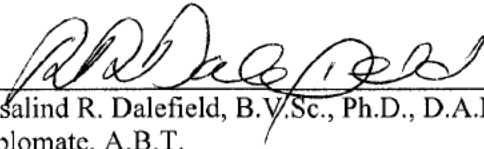
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Michael J. Ryan, D.V.M., Ph.D., D.A.B.T.  
Diplomate, A.C.V.P.  
Clinical Pathologist

Date



3/10/09

Rosalind R. Dalefield, B.V.Sc., Ph.D., D.A.B.V.T.  
Diplomate, A.B.T.  
Technical Review

Date

3/10/09

CN49730C

## 28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO BLEND AND AQUEOUS TOBACCO EXTRACT IN WISTER HAN RATS

### PATHOLOGY NARRATIVE

#### Organ Weight Changes

Group mean absolute organ weights are included in Table 31 for core male rats, Table 32 for core female rats, Table 33 for pair-fed male rats, and Table 34 for pair-fed female rats. Male rats in the higher dosage groups (NT20M, B8, B20M, E8M, and E20M) showed decreases in many absolute organ weights that were significantly different from the CM group. Female rats in the higher dosage groups (NT20F, B20F, and E20F) also showed a similar trend in decreased absolute organ weights. Group mean organ weight to body weight values are included in Table 35 for core male rats, Table 36 for core female rats, Table 37 for pair-fed male rats, and Table 38 for pair fed rats. Most of the male treatment groups which showed decreased absolute organ weights now show organ-to-body weights values which were either similar to or slightly increased relative to the CM group. Female treatment groups showed group mean organ weight values that were similar to that of the CF group (Table 36). Group mean organ-to-brain weight values are included in Table 39 for core male rats, Table 40 for core female rats, Table 41 for pair-fed male rats, and Table 42 for pair-fed female rats. The high-dose male (NT20M, B20M, and E20M) and female (NT20F, B20F, and E20F) groups showed a tendency for decreased organ-to-brain weight values when compared to those of their respective control group (CM or CF, respectively). These groups showed organ-to-brain weight values which were closer to that of their pair-fed male (Table 41) and female (Table 42) control groups suggesting reduced organ weight (size) was related to the rather large reduction in body weight.

#### Gross Findings

A few findings were noted at necropsy to include liver nodule (Group CM, animal 103), skin ulcer (Group E0.2M, animal 905), skin alopecia (Group E0.2M, animal 907), enlarged clitoral gland (Group E8F, animal 1160), renal pelvis dilatation and small thymus (Group E20M, animal

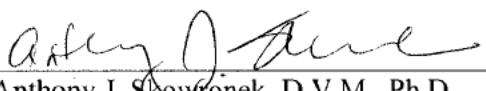
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1204), and kidney cyst (Group PFCNTF, animal 356). These findings were considered incidental and spontaneous in nature and unrelated to treatment.

### Conclusions

There were no treatment-related gross findings.

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\_\_\_\_\_  
Anthony J. Skowronek, D.V.M., Ph.D. Date  
Diplomate, A.C.V.P.  
Study Pathologist

 3/10/09  
\_\_\_\_\_  
Daphne Vasconcelos, D.V.M., Ph.D., D.A.B.T. Date  
Diplomate, A.C.V.P.  
Technical Review

**APPENDIX F: NICOTINE IN FEED FORMULATION ANALYSIS REPORT**

**28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO BLEND AND  
AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS**

**NICOTINE IN FEED**

**FORMULATION ANALYSIS REPORT**

Battelle Study Number: CN49730C

March 13, 2009

Prepared By:

Approved By:

End B 3/13/09  
Edward A. Purny, B.S./Date

Brian L. Burbach 3/13/09  
Brian L. Burbach, Ph.D./Date

### EXECUTIVE SUMMARY

Samples prepared for this study were submitted for analysis and successfully analyzed for nicotine concentrations. All pre-dose nicotine formulations that were analyzed for nicotine concentration met acceptance criteria (within 10% of the target concentrations; relative standard deviation [RSD] less than or equal to 10%). Post-dose (animal room) nicotine formulations were also analyzed for nicotine concentration and reported. Generally the post-dose concentrations agreed with the pre-dose values.

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## I. INTRODUCTION

This report contains a description of the analysis of submitted formulation samples from this study, the results of these analyses, and figures.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201.

## II. STANDARDS

Nicotine hydrogen tartrate, Lot No. 028K0705, obtained from Sigma-Aldrich Inc., was used as an analytical standard.

This standard was used to perform all work covered in this report.

## III. SAMPLES

The formulation samples submitted for analysis are shown in Table 1, (M=Male, F=Female).

**Table 1 – Samples Submitted for Formulation Analyses**

Type	Group	Formulation ID	Batch	Target Nicotine Concentration <sup>1</sup> (mg/kg)
Control	1 (CM/CF)	Control Formulation	1-Control-1	0
Tobacco Blend	B0.2F	114 mg/kg <sup>2</sup>	1-Blend-1	3.0
	B0.2M	137 mg/kg <sup>2</sup>	1-Blend-2	3.6
	B2F	1142 mg/kg <sup>2</sup>	1-Blend-3	30
	B2M	1370 mg/kg <sup>2</sup>	1-Blend-4	36
	B8F	4566 mg/kg <sup>2</sup>	1-Blend-5	120
	B8M	5479 mg/kg <sup>2</sup>	1-Blend-6	144
	B20F	11415 mg/kg <sup>2</sup>	1-Blend-7	300
	B20M	13698 mg/kg <sup>2</sup>	1-Blend-8	360
Nicotine Hydrogen Tartrate	NT20F	855 mg/kg <sup>2</sup>	1-NT-1	300
	NT20M	1026 mg/kg <sup>2</sup>	1-NT-2	360
Aqueous Tobacco Extract	E0.2F	130 mg/kg <sup>2</sup>	1-Extract-1	3.0
	E0.2M	157 mg/kg <sup>2</sup>	1-Extract-2	3.6
	E2F	1305 mg/kg <sup>2</sup>	1-Extract-3	30
	E2M	1566 mg/kg <sup>2</sup>	1-Extract-4	36
	E8F	5220 mg/kg <sup>2</sup>	1-Extract-5	120
	E8M	6264 mg/kg <sup>2</sup>	1-Extract-6	144
	E20F	13049 mg/kg <sup>2</sup>	1-Extract-7	300
	E20M	15659 mg/kg <sup>2</sup>	1-Extract-8	360

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of test article (mg) per kg of feed.

#### IV. FORMULATION ANALYSIS

##### A. METHOD

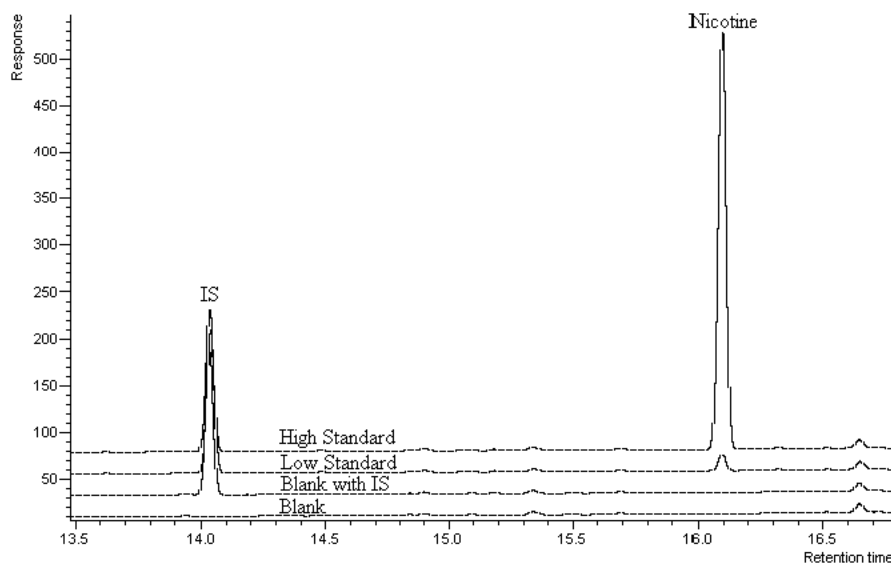
The samples were analyzed using the version of the standard operating procedure (SOP) current at the time of analysis. A copy is provided in Appendix A. The data acquisition system used was Atlas, Version 8.2, from Thermo Fisher Scientific.

##### B. RESULTS

The calibration standards met all acceptance criteria (the correlation coefficient [r] is greater than or equal to 0.99 and percent relative error [%RE] within 10% of nominal for all standards in all runs.

The asymmetry and percent relative standard deviation (RSD) for replicates of the system suitability acceptance criteria was met for each analysis. The efficiency for the system suitability acceptance criteria was met for each analysis. The drifts compared to the system suitability samples met acceptance criteria for each analysis.

Representative overlaid full scale chromatograms from high and low concentration standards, blank with internal standard (IS), and a blank are shown in Figure 1.



**Figure 1 – Representative Overlaid Chromatograms from High and Low Standards, Blank with IS, and a Blank – Full Scale**

The results from the formulation analysis for the pre-dose formulations are shown in Table 2 through Table 5. The concentration of all submitted formulations met acceptance criteria (within 10% of target; RSD less than or equal to 10%).

**Table 2 – Results for Pre-Dose Control Formulation**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
0 mg/kg <sup>2</sup> (CM/CF)	0	BLOQ	BLOQ	NA	NA	NA	NA
		BLOQ				NA	
		BLOQ				NA	

BLOQ = Below the limit of quantitation (not detected).

NA = Not applicable.

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of test article (mg) per kg of feed.

**Table 3 – Results for Pre-Dose Tobacco Blend Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
114 mg/kg <sup>2</sup> (B0.2F)	3.0	3.27E+00	3.22E+00	0.27	8.4	9.0	7.5
		2.83E+00				-5.7	
		3.29E+00				9.7	
		3.15E+00				5.0	
		3.58E+00				19.3	
137 mg/kg <sup>2</sup> (B0.2M)	3.6	3.40E+00	3.72E+00	0.33	8.9	-5.6	3.3
		4.05E+00				12.5	
		3.71E+00				3.1	
1142 mg/kg <sup>2</sup> (B2F)	30	3.18E+01	3.25E+01	1.3	4.0	6.0	8.4
		3.18E+01				6.0	
		3.40E+01				13.3	
1370 mg/kg <sup>2</sup> (B2M)	36	3.87E+01	3.85E+01	0.3	0.8	7.5	6.9
		3.82E+01				6.1	
		3.86E+01				7.2	
4566 mg/kg <sup>2</sup> (B8F)	120	1.23E+02	1.26E+02	3	2.0	2.5	5.0
		1.27E+02				5.8	
		1.28E+02				6.7	
5479 mg/kg <sup>2</sup> (B8M)	144	1.50E+02	1.55E+02	6	4.0	4.2	7.4
		1.61E+02				11.8	
		1.53E+02				6.3	

**Table 3 – Results for Pre-Dose Tobacco Blend Formulations (continued)**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
11415 mg/kg <sup>2</sup> (B20F)	300	3.14E+02	3.17E+02	3	0.9	4.7	5.6
		3.20E+02				6.7	
		3.16E+02				5.3	
13698 mg/kg <sup>2</sup> (B20M)	360	3.84E+02	3.76E+02	7	2.0	6.7	4.5
		3.73E+02				3.6	
		3.71E+02				3.1	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of tobacco blend (mg) per kg of feed.

**Table 4 – Results for Pre-Dose Nicotine Hydrogen Tartrate Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
855 mg/kg <sup>2</sup> (NT20F)	300	2.83E+02	2.88E+02	4	1.0	-5.7	-4.1
		2.91E+02				-3.0	
		2.89E+02				-3.7	
1026 mg/kg <sup>2</sup> (NT20M)	360	3.42E+02	3.40E+02	2	0.6	-5.0	-5.5
		3.40E+02				-5.6	
		3.39E+02				-5.8	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of nicotine hydrogen tartrate (mg) per kg of feed.

**Table 5 – Results for Pre-Dose Aqueous Tobacco Extract Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
130 mg/kg <sup>2</sup> (E0.2F)	3.0	3.05E+00	3.11E+00	0.07	2.0	1.7	3.6
		3.09E+00				3.0	
		3.18E+00				6.0	
157 mg/kg <sup>2</sup> (E0.2M)	3.6	3.84E+00	3.75E+00	0.08	2.0	6.7	4.1
		3.68E+00				2.2	
		3.72E+00				3.3	
1305 mg/kg <sup>2</sup> (E2F)	30	2.95E+01	3.14E+01	1.6	5.1	-1.7	4.5
		3.22E+01				7.3	
		3.24E+01				8.0	
1566 mg/kg <sup>2</sup> (E2M)	36	3.73E+01	3.79E+01	1	2.6	3.6	5.3
		3.73E+01				3.6	
		3.91E+01				8.6	

**Table 5 – Results for Pre-Dose Aqueous Tobacco Extract Formulations (continued)**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
5220 mg/kg <sup>2</sup> (E8F)	120	1.21E+02	1.20E+02	1	0.8	0.8	-0.3
		1.19E+02				-0.8	
		1.19E+02				-0.8	
6264 mg/kg <sup>2</sup> (E8M)	144	1.34E+02	1.37E+02	5	4.0	-6.9	-4.6
		1.35E+02				-6.3	
		1.43E+02				-0.7	
13049 mg/kg <sup>2</sup> (E20F)	300	2.96E+02	2.92E+02	5	2.0	-1.3	-2.5
		2.87E+02				-4.3	
		2.94E+02				-2.0	
15659 mg/kg <sup>2</sup> (E20M)	360	3.74E+02	3.64E+02	9	2.0	3.9	1.0
		3.60E+02				0.0	
		3.57E+02				-0.8	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of aqueous tobacco extract (mg) per kg of feed.

The results from the formulation analysis for the post-dose formulations (animal room) are shown in Table 6 through Table 9. The concentration of all submitted formulations met the following criteria for concentration (%RE within 10% of target; RSD less than or equal to 10%), except for the following:

- The 114 mg/kg tobacco blend formulation had an RSD of 12.5%.
- The 137 mg/kg tobacco blend formulation had a RE of 12.6%.
- The 1142 mg/kg tobacco blend formulation had a RE of 14.5 %.
- The 1370 mg/kg tobacco blend formulation had a RE of 12.8%.

There was no impact of these failures of the post-dose samples to meet acceptance criteria on the study. Post-dose samples are taken from the animal room feeders. They have been exposed to the animal and are subject to the impact from this exposure on concentration. This may include selective eating of the feed or analyte from the formulation by the animal, contamination of the formulation by urine, feces, bedding, or other materials, and exposure of the formulation to the animal room environment. For these reasons, animal samples should only be used to determine any general trends that may result from exposure of the formulation to the animal room environment.

**Table 6 – Results for Post-Dose Control Formulation**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
0 mg/kg <sup>2</sup> (CM/CF)	0	BLOQ	BLOQ	NA	NA	NA	NA
		BLOQ				NA	
		BLOQ				NA	

BLOQ = Below the limit of quantitation (not detected).

NA = Not applicable.

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of test article (mg) per kg of feed.

**Table 7– Results for Post-Dose Tobacco Blend Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
114 mg/kg <sup>2</sup> (B0.2F)	3.0	2.89E+00	3.27E+00	0.41	12.5	-3.7	9.1
		3.71E+00				23.7	
		3.22E+00				7.3	
137 mg/kg <sup>2</sup> (B0.2M)	3.6	4.11E+00	4.05E+00	0.15	3.7	14.2	12.6
		4.17E+00				15.8	
		3.88E+00				7.8	
1142 mg/kg <sup>2</sup> (B2F)	30	3.43E+01	3.44E+01	0.8	2.0	14.3	14.5
		3.52E+01				17.3	
		3.36E+01				12.0	
1370 mg/kg <sup>2</sup> (B2M)	36	4.04E+01	4.06E+01	0.9	2.0	12.2	12.8
		3.98E+01				10.6	
		4.16E+01				15.6	
4566 mg/kg <sup>2</sup> (B8F)	120	1.29E+02	1.27E+02	5	4.0	7.5	5.8
		1.21E+02				0.8	
		1.31E+02				9.2	
5479 mg/kg <sup>2</sup> (B8M)	144	1.50E+02	1.51E+02	2	1.0	4.2	5.1
		1.51E+02				4.9	
		1.53E+02				6.3	
11415 mg/kg <sup>2</sup> (B20F)	300	3.07E+02	3.16E+02	10	3.0	2.3	5.4
		3.26E+02				8.7	
		3.16E+02				5.3	
13698 mg/kg <sup>2</sup> (B20M)	360	3.88E+02	3.83E+02	9	2.0	7.8	6.4
		3.73E+02				3.6	
		3.88E+02				7.8	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of tobacco blend (mg) per kg of feed.

**Table 8 – Results for Post-Dose Nicotine Hydrogen Tartrate Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
855 mg/kg <sup>2</sup> (NT20F)	300	2.87E+02	2.90E+02	3	1.0	-4.3	-3.3
		2.93E+02				-2.3	
		2.90E+02				-3.3	
1026 mg/kg <sup>2</sup> (NT20M)	360	3.45E+02	3.45E+02	2	0.6	-4.2	-4.2
		3.47E+02				-3.6	
		3.43E+02				-4.7	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of nicotine hydrogen tartrate (mg) per kg of feed.

**Table 9 – Results for Post-Dose Aqueous Tobacco Extract Formulations**

Formulation ID (Dose Group)	Target Concentration <sup>1</sup> (mg/kg)	Corrected Concentration <sup>1</sup> (mg/kg)	Average Corrected Concentration <sup>1</sup> (mg/kg)	s (mg/kg)	RSD	% RE	Average %RE
130 mg/kg <sup>2</sup> (E0.2F)	3.0	3.05E+00	3.02E+00	0.04	1.0	1.7	0.8
		2.98E+00				-0.7	
		3.04E+00				1.3	
157 mg/kg <sup>2</sup> (E0.2M)	3.6	3.71E+00	3.69E+00	0.02	0.5	3.1	2.4
		3.67E+00				1.9	
		3.68E+00				2.2	
1305 mg/kg <sup>2</sup> (E2F)	30	3.14E+01	3.16E+01	0.3	0.9	4.7	5.4
		3.16E+01				5.3	
		3.19E+01				6.3	
1566 mg/kg <sup>2</sup> (E2M)	36	3.79E+01	3.76E+01	0.3	0.8	5.3	4.4
		3.75E+01				4.2	
		3.73E+01				3.6	
5220 mg/kg <sup>2</sup> (E8F)	120	1.17E+02	1.16E+02	2	2.0	-2.5	-3.6
		1.17E+02				-2.5	
		1.13E+02				-5.8	
6264 mg/kg <sup>2</sup> (E8M)	144	1.40E+02	1.40E+02	1	0.7	-2.8	-2.8
		1.41E+02				-2.1	
		1.39E+02				-3.5	
13049 mg/kg <sup>2</sup> (E20F)	300	3.01E+02	2.98E+02	3	1.0	0.3	-0.8
		2.96E+02				-1.3	
		2.96E+02				-1.3	
15659 mg/kg <sup>2</sup> (E20M)	360	3.57E+02	3.58E+02	2	0.6	-0.8	-0.5
		3.58E+02				-0.6	
		3.60E+02				0.0	

1. Quantity of nicotine (mg) per kg of feed.

2. Quantity of aqueous tobacco extract (mg) per kg of feed.

**V. ACKNOWLEDGMENTS**

Hans Whittenburg and Dan Burnham performed the analytical work. Ed Psurny wrote this report. Maria Evascu reviewed the data and report for completeness and accuracy.

**APPENDIX A****STANDARD OPERATING PROCEDURE (SOP) FOR THE ANALYSIS OF  
NICOTINE IN NTP-2000 FEED**

**JUN 12 2008**

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Initials/Date: \_\_\_\_\_

**STANDARD OPERATING PROCEDURE (SOP) FOR THE ANALYSIS OF  
NICOTINE IN NTP-2000 FEED**

Originator: Ed B Date 6/12/08

Approved by: Brian Buhl Date 6/12/08  
Technical Reviewer

Approved by: Phil Hyatt Date 6/12/08  
Study Director

Approved by: Steven Hume Date 6/12/08  
Management

Reviewed and Registered by QAU: Nathan E. Reed Date 6-12-08

Battelle  
505 King Avenue  
Columbus, Ohio 43201

Manual Number: 4.7  
Battelle SOP Number: COMSPEC.II-055-00  
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**I. SCOPE**

This SOP describes the analytical method to determine the amount of nicotine in feed samples. Calibration standards are prepared from two independently prepared solutions. The calibration standards, blanks, and feed samples are extracted with methyl t-butyl ether and analyzed by gas chromatography (GC) with flame ionization detection (FID). Concentrations of nicotine are calculated using the peak response, dilution, and a regression line constructed from the concentrations and peak area responses of the calibration standards

**II. PURPOSE**

The purpose of this SOP is to provide instructions for conducting the analysis of nicotine in feed.

**III. REFERENCES**

Current SOP for Labeling Reagents, Solutions, Test and Control Articles, and Specimens  
Current SOP for Using Electronic Balances  
Current SOP for Recording, Reviewing, and Correcting Raw Data  
Current SOP for Operation, Calibration, and Maintenance of Fixed and Adjustable Volume Pipettors.  
Current SOP for Operation and Maintenance of Gas Chromatographs  
Current SOP for Numeric Data and Calculations  
Current SOP for Use and Training of the Atlas Chromatography Data System

**IV. DEFINITIONS**

None.

**V. GENERAL INSTRUCTIONS**

Calibrate all required balances according to the SOP on balance usage.

Make equivalent dilutions when the volume needed varies from the volume stated in the method.

Label all standard and reagent solutions as specified in the appropriate SOP.

Sign or initial on each page of this document to signify that you have followed the method as written, all materials and reagents are current, and all equipment has been properly calibrated.

Initial and date all data entries on the page on which they were made. If only one person enters all data on a page on a single day, then the documentation may be made in a single location on that page by that person. If multiple staff make entries or one

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person makes entries on different days, all must be initialed and dated by the person making the entry.

The method is written in general chronological order. However, it is not essential that all sections be performed sequentially. The analyst may determine the order for conducting the task in the most efficient manner, unless the order for certain activities is specified.

## **VI. PROCEDURE**

### **A. SAMPLES**

See Chain of Custody for samples.

### **B. MATERIALS**

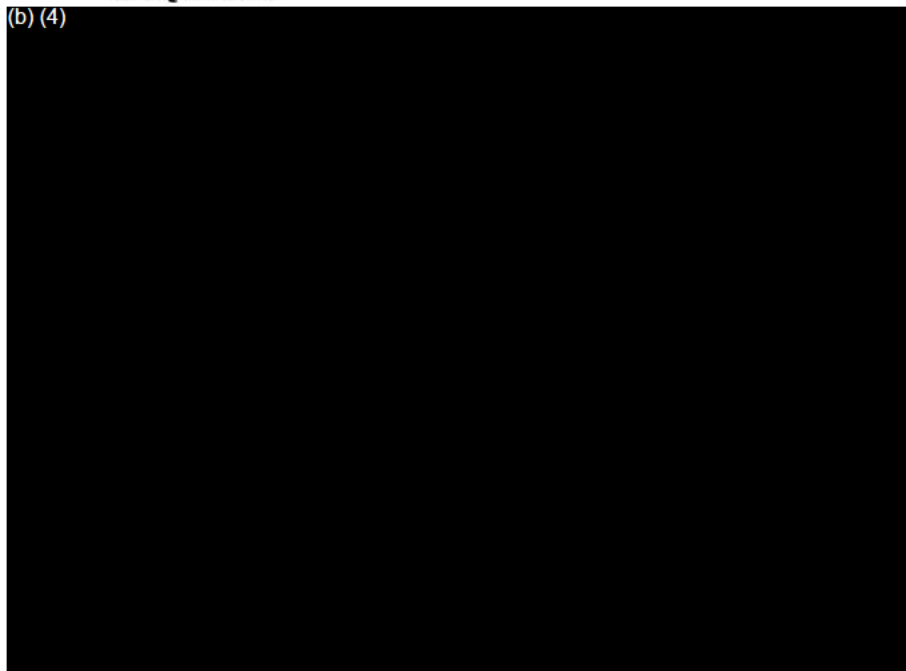
(b) (4)



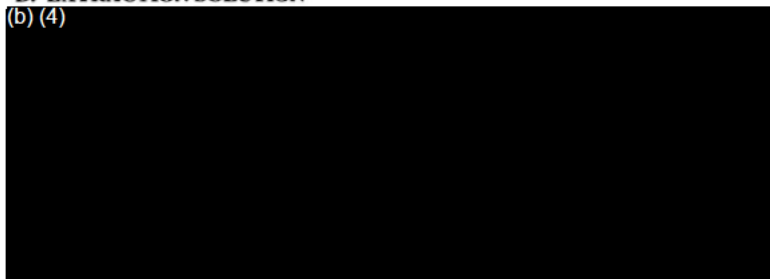
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**C. EQUIPMENT**

(b) (4)

**D. EXTRACTION SOLUTION**

(b) (4)



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**E. PREPARATION OF BLANK FEED EXTRACTED EXTRACTION SOLUTION**

(b) (4)

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**F. PREPARATION OF STANDARDS**

**1. Preparation of Solutions A and B**

(b) (4)

**Table 3 – Preparation of Solutions A and B**

ID	Target Concentration (µg/mL)	Target Weight (mg)	Actual Weight (mg)	Final Volume (mL)
A	116	33 ± 1		100
B	52.6	30 ± 1		200

Date Prepared: \_\_\_\_\_ Study Number: \_\_\_\_\_

**2. Preparation of Solutions C through F**

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Table 4 – Preparation of Solutions C - F

ID	Source	Source Volume (mL)	Final Volume (mL)	Target Concentration (µg/mL)
C	A	6.0	25	27.8
D	B	6.0	25	12.6
E	A	2.0	25	9.28
F	B	2.0	25	4.21

Date Prepared: \_\_\_\_\_ Study Number: \_\_\_\_\_

**3. Feed Standards**

Prepare single standards at each level. Into six 120 mL amber glass bottles, weigh  $10 \pm 1$  g of NTP 2000 feed. Add 5 mL of the appropriate solution as specified in Table 5. Cap each bottle and shake for approximately 15 seconds.

Table 5 – Preparation of Feed Standards

ID	Source	Source Volume (mL)	Target Concentration (mg/kg)
Std 1	A	5	58.0
Std 2	B	5	26.3
Std 3	C	5	13.9
Std 4	D	5	6.30
Std 5	E	5	4.64
Std 6	F	5	2.11

Add 20 mL of 2N sodium hydroxide to each standard, cap and mix well to wet all of feed, and let stand for ~15 minutes.

Add 15 mL of **extraction solution** to each standard, cap, and shake by hand for ~ 15 seconds. After shaking, break the feed by stirring it with a clean spatula until the clumping has been dissipated. Place the standards on the wrist action shaker for ~ 2 hours. During the ~2 hours of shaking, stop shaker and remove samples individually and shake by hand to make sure there is no feed sticking to the side of the bottle that is facing up.

Place samples in the centrifuge ~15 minutes at a setting of 2000 rpm.

Transfer an appropriate amount of the extraction solution portion of the extract into a GC vial. This solution may be stored protected from light at room temperature for 10 days.

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## G. PREPARATION OF BLANKS

### 1. Feed Blanks

To prepare each blank type (with and without IS) in singlet, weigh  $10 \pm 1$  g of NTP 2000 feed into two 120 mL amber glass bottles. Add 25 mL of 2N sodium hydroxide into each blank, cap and mix well to wet all of feed, and let stand for ~15 minutes.

**Feed Blank with IS** (single replicate): Add 15 mL of **extraction solution** to each sample, cap, and shake by hand for ~ 15 seconds. After shaking, break the feed by stirring it with a clean spatula until the clumping has been dissipated. Place the blank on the wrist action shaker for ~ 2 hours.

**Feed Blank without IS** (single replicate): Add 15 mL of **MTBE** to each sample, cap, and shake by hand for ~ 15 seconds. After shaking, break the feed by stirring it with a clean spatula until the clumping has been dissipated. Place the blank on the wrist action shaker for ~ 2 hours.

During the ~2 hours of shaking, stop shaker and remove samples individually and shake by hand to make sure there is no feed sticking to the side of the bottle that is facing up.

Place samples in the centrifuge ~15 minutes at a setting of 2000 rpm.

Transfer an appropriate amount of the extraction solution portion of the extract into a GC vial. This solution may be stored protected from light at room temperature for 10 days.

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## H. FEED SAMPLE ANALYSIS

To prepare each sample in triplicate, weigh triplicate  $10 \pm 1$  g of sample into individual 120 mL amber glass bottles and record the weight in Table 6, Table 7, Table 8, and Table 9. Add 25 mL of 2N sodium hydroxide into each sample, cap and mix well to wet all of feed, and let stand for ~15 minutes.

Table 6 –Control Sample Weights

Species	Target Formulation Concentration (mg/kg)	Nicotine Concentration (mg/kg)	Aliquot A (g)	Aliquot B (g)	Aliquot C (g)
Rat and/or Mouse	0	0			

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Table 7 – Tobacco Blend Sample Weights

Species	Target Formulation Concentration (mg/kg)	Nicotine Concentration (mg/kg)	Aliquot A (g)	Aliquot B (g)	Aliquot C (g)
Rat	114	3.0			
	137	3.6			
	1142	30			
	1370	36			
	4566	120			
	5479	144			
	11415	300			
	13698	360			
Mouse	571	15.0			
	666	17.5			
	5708	150			
	6659	175			
	22831	600			
	26636	700			
	57077	1500			
	66589	1750			

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Table 8– Nicotine Hydrogen Tartrate Sample Weights

Species	Target Formulation Concentration (mg/kg)	Nicotine Concentration (mg/kg)	Aliquot A (g)	Aliquot B (g)	Aliquot C (g)
Rat	855	300			
	1026	360			
Mouse	4275	1500			
	4988	1750			

Table 9– Tobacco Extract Sample Weights

Species	Target Formulation Concentration (mg/kg)	Nicotine Concentration (mg/kg)	Aliquot A (g)	Aliquot B (g)	Aliquot C (g)
Rat	130	3.0			
	157	3.6			
	1305	30			
	1566	36			
	5220	120			
	6264	144			
	13049	300			
	15659	360			
Mouse	653	15.0			
	761	17.5			
	6525	150			
	7612	175			
	26098	600			
	30448	700			
	65246	1500			
	76120	1750			

Add 15 mL of **extraction solution** to each standard, cap, and shake by hand for ~ 15 seconds. After shaking, break the feed by stirring it with a clean spatula until the clumping has been dissipated. Place the samples on the wrist action shaker for ~ 2 hours. During the ~2 hours of shaking, stop shaker and remove samples individually and shake by hand to make sure there is no feed sticking to the side of the bottle that is facing up.

Place samples in the centrifuge ~15 minutes at a setting of 2000 rpm.

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Follow Table 10 for the dilution of the feed samples with **blank feed extracted extraction solution** to dilute the samples into the standard curve.

**Table 10 –Dilution of Feed Samples**

Nicotine Concentration (mg/kg)	Volume of Extract (mL)	Final Dilution Volume (mL)
50-360	1	10
600-1200	1	25
1200-1750	0.5	25

Transfer an appropriate amount of the extraction solution portion of the extract into a GC vial.

#### I. ANALYSIS

Use the GC system conditions specified in Table 11. The designated conditions may be modified by the analyst to produce acceptable chromatography. Record the actual values inside the parentheses.

Inject system suitability samples at the beginning of the run. Use any mid-level standard as the system suitability. It is necessary that at least the 3 consecutive injections immediately preceding the run are acceptable for the run to be valid.

Make single injections of all standards, blanks, and samples.

**Table 11 – GC Conditions**

GC System No:	Agilent 6890 (Palo Alto, CA)
Analytical Column	Restek RTX-5 Amine (Bellefonte, PA), 30 m x 0.32 mm, 1.0 µm film thickness SN _____ or equivalent Column Length: _____ meters
Carrier Gas/Flow Rate	Hydrogen at 4.6 mL/min (or equivalent to 10.5 psi head pressure) _____ mL/min <b>Set to constant pressure.</b>
Oven Temperature Program*	60°C, hold for 3 minutes, increase at 8°C/minutes to 220°C, increase at 20°C/minute to 300°C/min hold for 5 minutes
Injection Volume*/Mode	2 µL/Splitless _____ µL
Inlet Liner	4 mm Base Deactivated Splitless Liner
Injector Temperature*	265°C
Detector Type	Flame Ionization Detector (FID)
Detector Flow Rates*	Hydrogen at ~ 30 mL/min; Air at ~ 280mL/min
Detector Temperature*	270°C
A/D Converter	Fisons Chrom Server _____

\*Parameters which may be modified by the analyst.

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\*Parameters which may be modified by the analyst.

- Use the Atlas automated chromatography data software (CDS) system to collect the electronic output.
- Set up the CDS to acquire the data and do appropriate calculations.

An additional GC system as shown in Table 12 may be used in order to analyze all of the samples in a shorter timeframe. The same standards and blanks will be used for both systems.

Make single injections of all standards, blanks, and samples.

**Table 12 – Additional GC Conditions**

<b>GC System No:</b>	Agilent 6890 (Palo Alto, CA)
<b>Analytical Column</b>	Restek RTX-5 Amine (Bellefonte, PA), 30 m x 0.32 mm, 1.0 µm film thickness SN _____ or equivalent Column Length: _____ meters
<b>Carrier Gas/Flow Rate</b>	Hydrogen at 4.6 mL/min (or equivalent to 10.5 psi head pressure) _____ mL/min <b>Set to constant pressure.</b>
<b>Oven Temperature Program*</b>	60°C, hold for 3 minutes, increase at 8°C/minutes to 220°C, increase at 20°C/minute to 300°C/min hold for 5 minutes
<b>Injection Volume*/Mode</b>	2 µL/Splitless _____ µL
<b>Inlet Liner</b>	4 mm Base Deactivated Splitless Liner
<b>Injector Temperature*</b>	265°C
<b>Detector Type</b>	Flame Ionization Detector (FID)
<b>Detector Flow Rates*</b>	Hydrogen at ~ 30 mL/min; Air at ~ 280mL/min
<b>Detector Temperature*</b>	270°C
<b>A/D Converter</b>	Fisons Chrom Server _____

\*Parameters which may be modified by the analyst.

- Use the Atlas automated chromatography data software (CDS) system to collect the electronic output.
- Set up the CDS to acquire the data and do appropriate calculations.

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## VII. CALCULATIONS

Examine the integration of the peaks. Modify, as necessary, to obtain consistent integration. Ensure that the response of the standards bracket the response for all filter samples.

Calculate the exact concentration of each standard and enter these into the chromatography data system.

Use the parameters in Table 13 to calculate the regression equation.

**Table 13 – Regression Parameters**

Model	Linear
Weighting	1/x
y-intercept	Calculate, Do Not Force through Origin
y-values	Nicotine/IS Peak Area Ratio
x-values	Nicotine Standard Concentrations

Calculate the % Relative Error (RE) for each standard. If the RE of any standard is not within 10% of the nominal concentration, evaluate the impact of omitting that calibration standard from the curve. One standard may be omitted from the curve, if deemed technically necessary.

Calculate the chromatography acceptance criteria parameters specified in Table 14 for the system suitabilities.

Calculate the concentration, the average concentration, the standard deviation (s), and the percent relative standard deviation (RSD) for the system suitabilities. Calculate the concentration for each "drift" and compare it to the average of the system suitabilities.

Calculate the amount of nicotine in each formulation sample using its peak ratio response, the regression equation, and dilution factor.

Calculate the average concentration, individual and average RE, s, and RSD for the triplicates. Examine any potential outliers using the Q-test with a 90% confidence interval.

The concentration units in Atlas are mg/kg.

## VIII. RESULTS

Place the spreadsheet in the data package. Report all values with concentrations below the specified limit of quantitation as "BLOQ". The Limit of Quantitation (LOQ) is 2.11 mg/kg.

Produce the Atlas Report "Run Reference" and include it the data package.

Include the chain of custody forms in the data package.

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**IX. ACCEPTANCE CRITERIA**

See Table 14 for acceptance criteria.

**Table 14- Acceptance Criteria**

(b) (4)



**X. TASK LEADER RESPONSE TO FAILURE TO MEET ACCEPTANCE CRITERIA**

**A. ASYMMETRY, EFFICIENCY, RESOLUTION**

Verify that the proper instrument system (column, gas, flow rates, etc.) was used for the analysis. If not, samples need to be re-injected using the correct instrument system.

If the correct instrument system was used, compare the current chromatograms to a past analysis. If the chromatography has changed substantially, determine and correct the problem with the instrument system and then re-inject the samples. If the chromatography has not changed substantially the run may be accepted.

**B. DRIFTS**

Verify that all calculations are correct.

Calculate the drift based on the standard that is used for the drift samples. If the drifts pass based on this calculation notify the CTC management.

If the drifts still do not pass, re-inject the entire analysis.

If the drifts fail after re-injection, repeat the entire analysis from the beginning on a new instrument system if possible.

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**C. RSD**

Verify that all calculations are correct.

**D. CORRELATION COEFFICIENT/RE OF STANDARDS**

Verify that all concentrations, the regression model, integration, and calculations are correct.

If the standards still fail after correcting any calculation errors, repeat the analysis from the beginning if possible. The Study Director may choose to accept data with standards outside the normal acceptance range.

**XI. COMMENTS/CONCLUSIONS**

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**XII. DATA REVIEW****A. TECHNICAL REVIEW**

Review at least the following to assure they are acceptable: rejection of calibration standards, integration of chromatograms, chromatography data processing and acquisition parameters, calibration standard concentrations, regression model, and compliance of data with acceptance criteria.

**B. DATA ACCURACY REVIEW**

Review at least the following: completeness and correctness of data entry, formulas used to calculate all values, and accuracy of calculations.

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### **XIII. SIGNATURES**

Technical Review Signature/Date:

\_\_\_\_\_  
\_\_\_\_\_

Signature of the technical reviewer will be considered documentation that all modifications and/or changes to this SOP (documented during the course of conducting this task) are technically acceptable and have no adverse technical impact unless otherwise noted. Changes or deviations to the acceptance criteria section require independent assessment by the technical reviewer.

Data Accuracy Review Signature/Date:

\_\_\_\_\_  
\_\_\_\_\_

**APPENDIX G: NEUROBEHAVIORAL TOXICOLOGY REPORT**

**Battelle Study Number CN49730C**

**28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO  
BLEND AND AQUEOUS TOBACCO EXTRACT IN WISTAR  
HAN RATS**

**Neurobehavioral Effects Report**

**Prepared For:  
R.J. Reynolds Tobacco Company**

**Battelle**  
*The Business of Innovation*

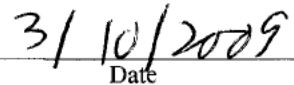
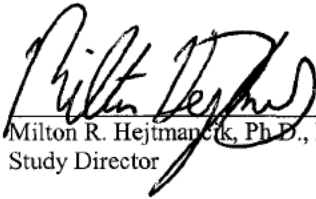
Battelle Study Number CN49730C

**28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO  
BLEND AND AQUEOUS TOBACCO EXTRACT IN WISTAR  
HAN RATS**

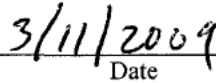
Approved, Battelle



Glenn D. Ritchie, Ph.D.  
Neurobehavioral Scientist

  
Date

Milton R. Hejtmancik, Ph.D., D.A.B.T.  
Study Director

  
Date

**Battelle Study Number CN49730C****INTRODUCTION AND STUDY DATA**

In this study, five Wistar Hanover rats of each sex were randomly selected from each core study group with the exception of pair fed control groups (see section 10.6 of the study protocol) for the functional observational battery (FOB). Vehicle control group animals (Group 1) were fed powdered NTP-2000 rodent diet without the test article. The nicotine tartrate high dose positive control group animals (Group 2) were fed powdered NTP-2000 rodent diet containing a target dosage of 20 mg/kg/day nicotine tartrate. Treated rats were fed the diet with the specified quantity of tobacco blend or (aqueous) tobacco extract with target dosages as follows:

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

To evaluate the toxicity of the tobacco blend and the (aqueous) tobacco extract on CNS/neurobehavioral activity in these animals, data were collected for the selected neurobehavioral parameters through use of a 40-test FOB as shown below.

Test	Parameter	Type of Measurement <sup>1</sup>
	<b>HOME CAGE</b>	
1	Posture	Score
2	Tremor Activity	Score
3	Convulsive Activity	Score
4	Lethargy/Arousal	Score
5	Eyelid Closure	Score
	<b>HANDLING RODENTS</b>	
6	Ease of Removing	Score
7	Ease of Handling	Score
8	Hand to Hand	Score
9	General Condition/Appearance	Score
10	Urine Stain	Score
11	Fecal Stain	Score
12	Salivation	Score
13	Piloerection	Score

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14	Fur Appearance	Score
15	Lacrimation	Score
16	Palpebral Reflex Responsivity	Score
17	Pupillary Diameter Test	Score
18	Pupil Response	Score
19	Vocalizations	Yes/No
	<b>OPEN FIELD</b>	
20	# Lines Crossed	Continuous
21	# Rearings	Continuous
22	# Urine Pools	Continuous
23	# Fecal Boluses	Continuous
24	Posture	Score
25	Tremor Activity	Score
26	Convulsive Activity	Score
27	Gait	Score
28	Gait Score	Score
29	Stereotypy	Score
30	Bizarre Behavior	Score
31	Vocalizations – Spontaneous	Yes/No
	<b>REFLEXES</b>	
32	Approach Response	Score
33	Touch Response	Score
34	Startle Response	Score
35	Tail Pinch Response	Score
36	Placing of Paws on Grid	Score
37	Righting Reflex Air	Score
38	Righting Reflex Surface	Score
39	Rectal Temperature (°F)	Continuous
46	Grip Strength	Score

<sup>1</sup> Score variables: response represented by a categorical score

Yes/No variables: response given by "Yes" or "No"

Continuous variables: response represents a numeric reading on a continuous scale.

Only data for the CM/CF group, NT20M/NT20F group, four tobacco blend dose groups, and four (aqueous) tobacco extract dose groups were considered in this data summary and statistical analysis.

This report describes the statistical methods applied to these FOB data, summarizes the statistical results, and interprets the neurobehavioral data. All statistical summaries and data analyses in this study were conducted using SAS 9.1.3 (SAS Institute, 2004).

**STATISTICAL METHODS**

(b) (4)

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**Battelle Study Number CN49730C****RESULTS**

Data summarization and statistical analyses were conducted independently for each parameter, and for males and females. Unless specified otherwise, the  $p \leq 0.05$  level was used to identify statistically significant dose effects.

**Categorical Variables (Score and Yes/No Variables)**

Significant differences among the dose groups were observed at the 0.05 level for the following FOB parameters:

**Male Rats**

- **Home cage Lethargy/Arousal** (FOB test 4), where the E20M group was significantly different from the B20M group. All five male rats in the B20M group received a zero score (alert), whereas 3 of the 5 rats in the E20M group received a score of -1 (slight lethargy). However, neither the B20M group nor the E20M group were significantly different from the CM group.
- **Home cage Eyelid Closure** (FOB test 5), where there was an overall statistically significant treatment effect, but none of the pairwise comparisons of interest were significantly different from each other. This overall statistical difference is not thought to be toxicologically meaningful, as there were no dramatic numerical differences among any of the test article or control groups.

**Female Rats**

- **Home cage Posture** (FOB test 1), where the B8F group, the B20F group, and the E2F group were all significantly different from the CF group. Rats in these three dose groups received either zero or negative scores (at least one animal with a negative score), while rats in the CF received zero or positive scores. These data suggested reduced arousal activity in the treated groups, as compared to the CF group.
- **Home cage Lethargy/Arousal** (FOB test 4), where there was an overall statistically significant treatment effect, but none of the pairwise comparisons of interest were significantly different from each other. It should be noted that at least one animal in each of the tobacco blend and tobacco extract groups exhibited negative scores, while all rats assigned to the CF group exhibited zero scores, suggested slightly reduced arousal in several of the treatment groups.
- **Ease of Removing** (FOB test 6), where there was an overall statistically significant treatment effect, but none of the pairwise comparisons of interest were significantly different from each other. This overall statistical difference is not thought to be toxicologically meaningful, as there were no dramatic numerical differences among any of the test article or control groups.
- **Ease of Handling** (FOB test 7), where there was an overall statistically significant treatment effect, but none of the pairwise comparisons of interest were significantly different from each other. This overall statistical difference is not thought to be toxicologically meaningful, as there were no dramatic numerical differences among any of the test article or control groups.

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- **Hand to Hand** (FOB test 8), where there was an overall statistically significant treatment effect, but none of the pairwise comparisons of interest were significantly different from each other. This overall statistical difference is not thought to be toxicologically meaningful, as there were no dramatic numerical differences among any of the test article or control groups.

**Continuous Variables**

Means and standard errors of the reported measurements for the continuous variables were calculated for each dose group. Based upon the outcome of the one-way ANOVA applied to these continuous measurements, significant differences were observed at the 0.05 level among the dose groups for the following variables:

**Male Rats**

- No significant differences were observed for the results of any of the FOB tests identified as continuous variables.

**Female Rats**

- **Rectal Temperature** (FOB test 39), where mean rectal temperatures of the NT20F group, the B20F group and the E20F group were significantly reduced as compared to the CF group.

**DISCUSSION AND CONCLUSIONS**

Male and female rats treated for a minimum of 28 days with feed containing the tobacco blend or tobacco extract test article generally exhibited a slightly reduced arousal level and emotionality, as compared to the CM/CF. In several cases, the NT20M/NT20F exhibited neurobehavioral effects similar to those seen in one or more tobacco blend or tobacco extract groups (as compared to the CM/CF group). In general, the effects of tobacco blend or tobacco extract treatment were slightly greater in female than in male rats, and the effects of the tobacco extract treatments were slightly greater than the effects of the tobacco blend treatments. For example, in female rats in the NT20F group, the B20F group or the E20F group, mean rectal temperature was significantly reduced as compared to the CF group. This effect can possibly be attributed to the hypothermic effect of nicotine ingestion in rodents (Ruskin et al., 2007).

The results of this study suggest that repeated oral ingestion of tobacco blend or tobacco extract, particularly at the high target dose (20 mg/kg/day) or ingestion of the nicotine tartrate high target dose positive control (20 mg/kg/day) resulted in slightly reduced arousal and emotionality, without significantly impacting other major neurobehavioral parameters including general physical appearance, postural integrity, spontaneous locomotor activity, muscular system integrity, equilibrium, sensory responsivity, pain thresholds or autonomic nervous system function. There was no evidence in male and female Wistar Hanover rats of the neurobehavioral effects (for example, increased spontaneous locomotor activity, tremor, stereotypy, etc.) that might be expected with treatments containing high levels of nicotine

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(Liang et al., 2008).

From the results of the FOB testing, it cannot be concluded that tobacco blend or tobacco extract had a significant effect on any specific CNS systems, although the reduced mean rectal temperature effects observed in several groups of female rats might suggest a slight modulation of one or more CNS neurotransmitter systems (e.g., serotonin) (Knapp et al., 2000).

**REFERENCES**

- Agresti A (ed.). 2002. *Categorical Data Analysis*, Second Edition, New York: Wiley.
- Ruskin DN, Anand R, LaHoste GJ. Menthol and nicotine oppositely modulate body temperature in the rat. *Eur J Pharmacol.* 2007;559:161-4.
- Knapp DJ, Sim-Selley LJ, Breese GR, Overstreet DH. Selective breeding of 5-HT(1A) receptor-mediated responses: application to emotion and receptor action. *Pharmacol Biochem Behav.* 2000;67:701-8.
- Liang Y, Boules M, Shaw AM, Williams K, Fredrickson P, Richelson E. Effect of a novel neurotensin analog, NT69L, on nicotine-induced alterations in monoamine levels in rat brain. *Brain Res.* 2008 Jul 19. [Epub ahead of print]
- Miller, R.G., Jr. (ed.). 1981. *Simultaneous Statistical Inference*, Springer Verlag, NY.
- Neter, J., Kutner, M., Nachtsheim, C. and Wasserman, W. (eds.). 1996. *Applied Linear Statistical Models*, Fourth Edition, Chicago: Irwin.
- SAS Institute, Inc. (2004). *SAS/STAT 9.1 User's Guide*. Cary, N.C.: SAS Institute, Inc.

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**Battelle Study Number CN49730C****STATISTICAL METHODS AND RESULTS****INTRODUCTION AND STUDY DATA**

In this study, five Wistar Hanover rats of each sex were randomly assigned to 10 dose groups (see section 10.6 of the study protocol). To evaluate the toxicity of tobacco blend and aqueous tobacco extract on CNS/neurobehavioral activity in these animals, data were collected for the selected parameters through a functional observational battery (FOB).

Test	Parameter	Type of Measurement <sup>1</sup>
	<b>HOME CAGE</b>	
1	Posture	Score
2	Tremor Activity	Score
3	Convulsive Activity	Score
4	Lethargy/Arousal	Score
5	Eyelid Closure	Score
	<b>HANDLING RODENTS</b>	
6	Ease of Removing	Score
7	Ease of Handling	Score
8	Hand to Hand	Score
9	General Condition/Appearance	Score
10	Urine Stain	Score
11	Fecal Stain	Score
12	Salivation	Score
13	Piloerection	Score
14	Fur Appearance	Score
15	Lacrimation	Score
16	Palpebral Reflex Responsivity	Score
17	Pupillary Diameter Test	Score
18	Pupil Response	Score
19	Vocalizations	Yes/No
	<b>OPEN FIELD</b>	
20	# Lines Crossed	Continuous
21	# Rearings	Continuous
22	# Urine Pools	Continuous
23	# Fecal Boluses	Continuous
24	Posture	Score
25	Tremor Activity	Score
26	Convulsive Activity	Score
27	Gait	Score
28	Gait Score	Score
29	Stereotypy	Score
30	Bizarre Behavior	Score
31	Vocalizations – Spontaneous	Yes/No
	<b>REFLEXES</b>	
32	Approach Response	Score
33	Touch Response	Score

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34	Startle Response	Score
35	Tail Pinch Response	Score
36	Placing of Paws on Grid	Score
37	Righting Reflex Air	Score
38	Righting Reflex Surface	Score
39	Rectal Temperature (°F)	Continuous
46	Grip Strength	Score

<sup>1</sup> Score variables: response represented by a categorical score

Yes/No variables: response given by "Yes" or "No"

Continuous variables: response represents a numeric reading on a continuous scale.

Only data for the following groups were considered in this data summary and statistical analysis:

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

This report describes the statistical methods applied to these FOB data and summarizes the statistical analysis results. All statistical summaries and analyses of data in this study were conducted using SAS 9.1.3 (SAS Institute, 2004).

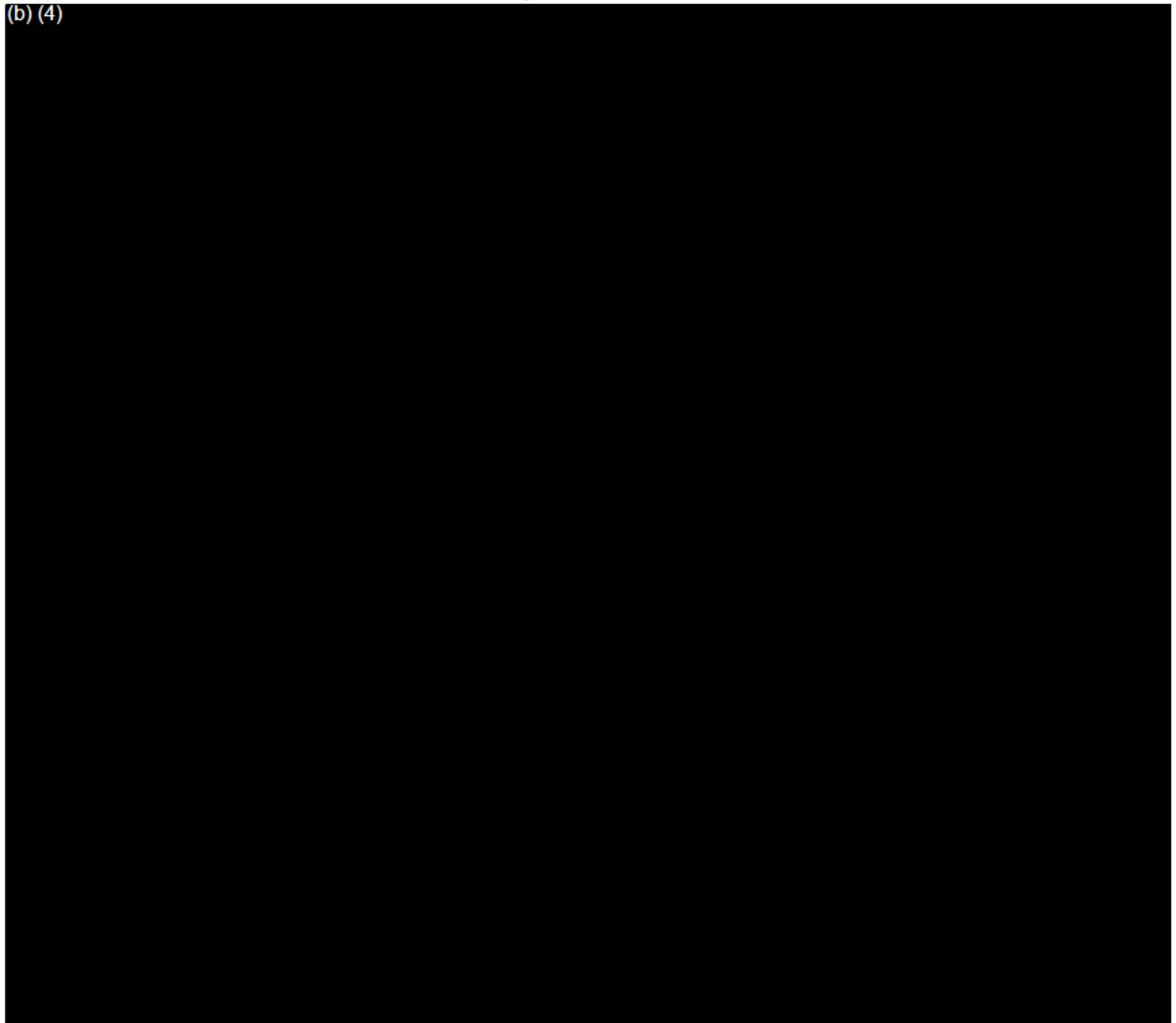
**STATISTICAL METHODS**

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**RESULTS**

Data summarization and statistical analyses were conducted independently for each parameter and for males and females. Unless specified otherwise, the significance level is at the 0.05 level for the dose effect.

**Categorical Variables (Score and Yes/No Variables)**

Table 1A (for males) and Table 1B (for females) present frequency tables that represent the number of animals with responses within each response category, presented by dose group. The results of statistical analyses performed on these variables are summarized in Table 2A (for males) and Table 2B (for females). These tables show that significant differences among the dose groups were observed at the 0.05

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**Battelle Study Number CN49730C**

level in the following parameters:

Male Rats (Tables 1A and 2A)

- Lethargy/Arousal, where the E20M dose was significantly different from the B20M dose. All five male rats in the B20M group received a zero score (alert), and three rats in the E20M group received a score of -1 (slightly lethargic).
- Eyelid Closure, where none of the pairwise comparisons of interest were significantly different from each other.

Female Rats (Tables 1B and 2B)

- Posture in home cage, the B8F, B20F, and the E2F groups were significantly different from the CF group. Animals in these dose groups received either zero or negative scores (at least one animal with a negative score), while animals in CF group and the other dose groups received non negative positive scores (at least one animal with a positive score).
- Lethargy/Arousal, where none of the pairwise comparisons of interest were significantly different from each other.
- Ease of removing, where none of the pairwise comparisons of interest were significantly different from each other.
- Ease of handling, where none of the pairwise comparisons of interest were significantly different from each other.
- Hand to hand, where none of the pairwise comparisons were significantly different from each other.

**Continuous Variables**

Means and standard errors of the reported measurements for the continuous variables were calculated for each dose group and are presented in Table 3A (for males) and Table 3B (for females). Based upon the outcome of the one-way ANOVA applied to these continuous measurements, significant differences were observed at the 0.05 level among the dose groups for the following variables:

Male Rats (Table 3A)

- No significant difference among dose groups was observed for any continuous variables.

Female Rats (Table 3B)

- Rectal temperature, where NT20F, B20F, and E20F groups were significantly different (and lower than) the CF group.

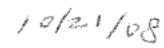
**REFERENCES**


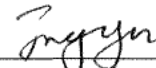
- Agresti A. (2002). *Categorical Data Analysis*, Second Edition, New York: Wiley.
- Miller, R.G., Jr. (1981). *Simultaneous Statistical Inference*, Springer Verlag, NY.
- Neter, J., Kutner, M., Nachtsheim, C. and Wasserman, W. (1996). *Applied Linear Statistical Models*. Fourth Edition, Chicago: Irwin.
- SAS Institute, Inc. (2004). *SAS/STAT 9.1 User's Guide*. Cary, N.C.: SAS Institute, Inc.

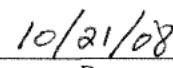
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**Battelle Study Number CN49730C****SIGNATURES**

  
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James Ma, Ph.D.  
Study Statistician

  
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Date

   
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Jinyu Feng, M.S.  
Study Statistician

  
\_\_\_\_\_  
Date

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Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)  
Male Animals, Test=T1, HomeCage Parameter=posture

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-5	Animal found dead	0	0	0	0	0	0	0	0	0	0
-4	Lying flat limbs splayed out	0	0	0	0	0	0	0	0	0	0
-3	Lying on side limbs in the air	0	0	0	0	0	0	0	0	0	0
-2	Hunched posture (crouching over)	0	0	0	0	0	0	0	0	0	0
-1	Sleeping, resting, recumbent	1	1	0	2	1	0	2	1	1	3
0	Awake, alert, without rearing	4	4	4	2	3	4	1	1	3	2
1	Rearing, ambulating	0	0	1	1	1	1	2	3	1	0
2	Jumping, running	0	0	0	0	0	0	0	0	0	0
Mean Score		-0.20	-0.20	0.20	-0.20	0.00	0.20	0.00	0.40	0.00	-0.60

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T3, HomeCage Parameter=convulsive activity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	5	5	5	5	5
1	Excessive stereotype behavior (grooming, fixed staring, etc.)	0	0	0	0	0	0	0	0	0	0
2	Forebody myoclonus (clonic chewing)	0	0	0	0	0	0	0	0	0	0
3	Popcorn seizures (bouncing or popping behavior)	0	0	0	0	0	0	0	0	0	0
4	Clonic seizures (slight/mild tremors or jerkings, contractions followed by relaxations)	0	0	0	0	0	0	0	0	0	0
5	Tonic seizures (repetitive moderate/severe whole body tremors, body is rigid and arched)	0	0	0	0	0	0	0	0	0	0
6	Tonic/clonic seizures (loss of righting)	0	0	0	0	0	0	0	0	0	0
7	Post-ictal depression	0	0	0	0	0	0	0	0	0	0
8	Seizures followed by death	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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1  
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4  
5  
6  
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9

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-4	Completely unresponsive/unconscious	0	0	0	0	0	0	0	0	0	0
-3	Severe lethargy, lying on side, immobile but conscious	0	0	0	0	0	0	0	0	0	0
-2	Moderate lethargy, immobile, may be prostrate	0	0	0	0	0	0	0	0	0	0
-1	Slight lethargy, little exploration, but not prostrate	1	1	0	2	1	0	2	1	1	3
0	Alert, responsive, exploratory movements	4	4	5	3	4	5	2	4	4	2
1	Slight arousal, slight excitement, tense	0	0	0	0	0	1	0	0	0	0
2	Moderate arousal, moderate excitement, sudden darting and freezing	0	0	0	0	0	0	0	0	0	0
3	Severe arousal, severe excitement, hyperalert, overaggressive	0	0	0	0	0	0	0	0	0	0
Mean Score		-0.20	-0.20	0.00	-0.40	-0.20	0.00	-0.20	-0.20	-0.20	-0.60

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
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7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	4	4	5	3	4	4	3	4	4	2
1	Slightly drooping	1	0	0	0	1	1	0	1	0	2
2	Drooping approximately half-way	0	1	0	1	0	0	1	0	1	1
3	Completely shut	0	0	0	1	0	0	1	0	0	0
Mean Score		0.20	0.40	0.00	1.00	0.20	0.20	1.00	0.20	0.40	0.80

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T6, HomeCage**      **Parameter=ease of removing**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No resistance, body limp	0	0	0	0	0	0	0	0	0	0
-1	Very little resistance, body relaxed	0	0	0	0	0	0	0	1	0	0
0	Little resistance, but body tense, may rear slightly, with/without vocalization	5	5	5	4	5	4	5	4	5	4
1	Slight resistance, rodent runs around cage, is difficult to grab, with/without vocalization	0	0	0	1	0	1	0	0	0	1
2	Moderate resistance, rodent may jump from cage, may attempt to bite defensively or initially, with/without vocalization	0	0	0	0	0	0	0	0	0	0
3	Extreme resistance, rodent makes repetitive attempts to bite/attack technician's hand and to escape, with/without vocalizations	0	0	0	0	0	0	0	0	0	0
4	Rodent freezes (with/without vocalizations)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.20	0.00	0.20	0.00	-0.20	0.00	0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T7, HomeCage Parameter=ease of handling**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	Rodent is limp, lethargic, or even unresponsive	0	0	0	0	0	0	0	0	0	0
-1	Rodent is relaxed and may have limbs pulled up against body	0	0	0	0	0	0	0	0	0	0
0	Rodent is alert, but with little or no resistance	5	5	4	4	5	5	5	5	5	4
1	Moderate resistance, rodent is tense (may squirm, twist, with or without vocalization)	0	0	1	1	0	0	0	0	0	1
2	Extreme resistance, animal attempts to bite, escape	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T8, HomeCage Parameter=hand to hand**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	Rodent is limp, lethargic, or even unresponsive	0	0	0	0	0	0	0	0	0	0
-1	Rodent is relaxed and may have limbs pulled up against body	1	1	0	1	0	0	0	0	0	0
0	Rodent is alert, but with little or no resistance	2	4	4	3	4	5	5	4	4	4
1	Moderate resistance, rodent is tense (may squirm, twist, with or without vocalization)	2	0	1	1	1	0	0	1	1	1
2	Extreme resistance, animal attempts to bite, escape	0	0	0	0	0	0	0	0	0	0
3	Convulsing	0	0	0	0	0	0	0	0	0	0
Mean Score		0.20	-0.20	0.20	0.00	0.20	0.00	0.00	0.20	0.20	0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T9, HomeCage Parameter=general condition/appearance**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	4	5	5	5	5	5	5	5	5
1	Red or crusty deposits around eyes, nose, or mouth	0	1	0	0	0	0	0	0	0	0
2	Thin appearance	0	0	0	0	0	0	0	0	0	0
3	Dehydrated appearance (decreased skin elasticity, thin appearance, hunched posture)	0	0	0	0	0	0	0	0	0	0
4	Hunched posture (without signs of dehydrated appearance)	0	0	0	0	0	0	0	0	0	0
5	Diminished body tone (limp)	0	0	0	0	0	0	0	0	0	0
6	Excessive body tone (rigid)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T10, HomeCage Parameter=urine stain**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0 None		5	5	5	5	5	5	5	5	5	5
1 Slight		0	0	0	0	0	0	0	0	0	0
2 Moderate		0	0	0	0	0	0	0	0	0	0
3 Severe		0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**CONCLUSIONS**

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0 2M	B0 2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0 2M	E0 2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T14, HomeCage Parameter=fur appearance**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	5	5	5	5	5
1	Slightly rough coat	0	0	0	0	0	0	0	0	0	0
2	Moderately rough coat	0	0	0	0	0	0	0	0	0	0
3	Severely rough coat	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	4	5	5	4	5	5	5	4	5
1	Slight	0	1	0	0	1	0	0	0	1	0
2	Moderate	0	0	0	0	0	0	0	0	0	0
3	Severe	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.20	0.00	0.00	0.20	0.00	0.00	0.00	0.20	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

**CONCLUSIONS**

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Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-1	Pinpoint pupil (miosis)	0	0	0	0	0	0	0	0	0	0
0	Normal pupil, 1/4 -1/2 dilated	5	5	5	4	5	5	5	4	5	5
+1	Pupil fully dilated	0	0	0	1	0	0	0	1	0	0
Mean Score		0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.20	0.00	0.00

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T19, HomeCage Parameter=vocalizations (1=yes; 0=no)**

Score Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0 No	3	4	3	5	5	5	5	3	5	4
1 Yes	2	1	2	0	0	0	0	2	0	1

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T24, OpenField Parameter=posture**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-4	Lying flat limbs splayed out	0	0	0	0	0	0	0	0	0	0
-3	Lying on side limbs in the air	0	0	0	0	0	0	0	0	0	0
-2	Hunched posture (crouching over)	0	0	0	0	0	0	0	0	0	0
-1	Lying on side (curled up sleeping)	0	0	0	0	0	0	0	0	0	0
0	Normal (sitting or standing normally)	5	5	5	5	5	5	5	5	5	5
1	Rearing	0	0	0	0	0	0	0	0	0	0
2	Hyperactive (jumping, running, etc.)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)  
Male Animals, Test=T25, OpenField Parameter=tremor activity

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0None		5	5	5	5	5	5	5	5	5	5
1Slight		0	0	0	0	0	0	0	0	0	0
2Moderate		0	0	0	0	0	0	0	0	0	0
3Severe		0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T26, OpenField Parameter=convulsive activity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	5	5	5	5	5
1	Excessive stereotype behavior (grooming, fixed staring, etc.)	0	0	0	0	0	0	0	0	0	0
2	Forebody myoclonus (clonic chewing)	0	0	0	0	0	0	0	0	0	0
3	Popcorn seizures (bouncing or popping behavior)	0	0	0	0	0	0	0	0	0	0
4	Clonic seizures (slight/mild tremors or jerkings, contractions followed by relaxations)	0	0	0	0	0	0	0	0	0	0
5	Tonic seizures (repetitive moderate/severe whole body tremors, body is rigid and arched)	0	0	0	0	0	0	0	0	0	0
6	Tonic/clonic seizures (loss of righting)	0	0	0	0	0	0	0	0	0	0
7	Post-ictal depression	0	0	0	0	0	0	0	0	0	0
8	Seizures followed by death	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T27, OpenField Parameter=gait**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	5	5	5	5	5
1	Walking on tip toes	0	0	0	0	0	0	0	0	0	0
2	Ataxia (excessive swaying, rocking, or lurching during walk)	0	0	0	0	0	0	0	0	0	0
3	Feet pointing outward from body	0	0	0	0	0	0	0	0	0	0
4	Hindlimbs splayed	0	0	0	0	0	0	0	0	0	0
5	Front limbs dragging (unable to support weight)	0	0	0	0	0	0	0	0	0	0
6	Hindlimbs dragging	0	0	0	0	0	0	0	0	0	0
7	Inability to use all limbs	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T28, OpenField Parameter=gait score**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	5	5	5	5	5
1	Slightly abnormal	0	0	0	0	0	0	0	0	0	0
2	Moderately abnormal	0	0	0	0	0	0	0	0	0	0
3	Severely abnormal	0	0	0	0	0	0	0	0	0	0
4	No movement	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T29, OpenField Parameter=stereotype**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	5	5	5	5	5
1	Repetitive grooming	0	0	0	0	0	0	0	0	0	0
2	Pacing	0	0	0	0	0	0	0	0	0	0
3	Repetitive sniffing	0	0	0	0	0	0	0	0	0	0
4	Head weaving	0	0	0	0	0	0	0	0	0	0
5	Licking	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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[illegible]

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T31, OpenField Parameter=vocal.-spontaneous (1=yes; 0=no)**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	No	5	5	5	5	5	5	5	5	5	5
1	Yes	0	0	0	0	0	0	0	0	0	0

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T32, OpenField Parameter=approach response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
2	No reaction	0	0	0	0	0	0	0	0	0	0
1	Animal senses object but not interested and does not approach	0	1	0	0	0	0	0	0	0	0
0	Animal slowly approaches object, sniffs, and then turns away	5	4	5	5	5	5	5	5	5	5
1	Animal shows more energetic response with or without vocalization, rodent sways from side to side	0	0	0	0	0	0	0	0	0	0
2	Animal shows bizarre behavior, may include jumping, biting at object, attacking object with or without vocalization	0	0	0	0	0	0	0	0	0	0
3	Rodent freezes, animal may exhibit muscle contractions	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	-0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
Male Animals, Test=T33, OpenField Parameter=touch response

[illegible]

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**QUESTIONS**

[illegible]

**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
Male Animals, Test=T35, OpenField Parameter=tail pinch response

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
1	No reaction (i.e., due to stupor, coma, convulsions)	0	0	0	0	0	0	0	1	1	
0	Rodent may turn or walk forward	5	5	3	4	5	4	5	4	4	
1	More energetic response than 0, may include vocalizations	0	0	2	1	0	1	0	0	0	
2	Exaggerated reaction (e.g., jumps, bites, attacks with or without vocalizations)	0	0	0	0	0	0	0	0	0	
3	Rodent freezes, actual muscle contractions	0	0	0	0	0	0	0	0	0	
Mean Score		0.00	0.00	0.00	0.40	0.20	0.00	0.20	0.00	-0.20	-0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

[illegible]

**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
Male Animals, Test=T36, OpenField Parameter=placing of paws on grid

[illegible]

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

Figure 1. The effect of the concentration of the inhibitor on the rate of polymerization of  $\alpha$ -methylstyrene in the presence of  $\text{SnCl}_4$  at  $25^\circ\text{C}$ .

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T37, OpenField Parameter=righting reflex air**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
	-2 Rat does not right itself from 20 cm	0	0	0	0	0	0	0	0	0	0
	-1 Rat rights from 20 cm for 1 out of 2 trials	0	0	0	0	0	0	0	0	0	0
	0 Normal, rat rights from 20 cm for both trials	5	5	5	5	5	5	5	5	5	5
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Figure 1. The effect of the concentration of the *Agrobacterium* suspension on the transformation efficiency of *Agrobacterium* strains.

[illegible]

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**Table 1A. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Male Animals, Test=T46, OpenField Parameter=grip strength**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No gripping	0	0	0	0	0	0	0	0	0	0
-1	Weak gripping	0	0	0	0	0	0	0	0	0	0
0	Normal gripping	5	5	5	5	5	5	5	5	5	5
1	Excessive gripping	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 2A. Male Animals Test Result Summary for Categorical Variables (Score and Yes/No Variables)**

[illegible]

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+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.  
#: Comparisons to the control were performed if the overall dose effect was significant.  
++: Significantly different from the control at the 0.05/4=0.0125 level (two-sided) were marked with a 'yes'.  
\$: Significantly different from the control at the 0.05 level (two-sided) were marked with a 'yes'.  
NT: Not tested

Group #	Group Description	Group Coding		Target Dosage (mg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

Q. 10. What is the difference between a *trans* and a *cis* isomer?

**CONCLUSIONS**

Parameter	Dose Effect+ P-value (Chi-Square)	Group 9 vs 4 #++	Group 10 vs 5 #++	Group 11 vs 6 #++	Group 12 vs 7 #++
posture (Home Cage)	0.1427(13.46)	NT	NT	NT	NT
tremor activity	1.0000(0.00)	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT
lethargy/arousal	0.0423(17.44)*	No	No	No	Yes
eyelid closure	0.0216(19.45)*	No	No	No	No
ease of removing	0.8343(5.00)	NT	NT	NT	NT
ease of handling	0.9271(3.75)	NT	NT	NT	NT
hand to hand	0.5487(7.86)	NT	NT	NT	NT
general condition/appearance	0.9982(1.10)	NT	NT	NT	NT
urine stain	1.0000(0.00)	NT	NT	NT	NT
fecal stain	1.0000(0.00)	NT	NT	NT	NT
salivation	1.0000(0.00)	NT	NT	NT	NT
piloerection	1.0000(0.00)	NT	NT	NT	NT
fur appearance	1.0000(0.00)	NT	NT	NT	NT
lacrimation	0.9271(3.75)	NT	NT	NT	NT
palpebral reflex responsivity	1.0000(0.00)	NT	NT	NT	NT
pupillary diameter test	0.9809(2.50)	NT	NT	NT	NT
pupil response	1.0000(0.00)	NT	NT	NT	NT
vocalizations (1=yes; 0=no)	0.7695(5.70)	NT	NT	NT	NT
Posture (Open Field)	1.0000(0.00)	NT	NT	NT	NT
tremor activity	1.0000(0.00)	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT
gait	1.0000(0.00)	NT	NT	NT	NT
gait score	1.0000(0.00)	NT	NT	NT	NT
stereotype	1.0000(0.00)	NT	NT	NT	NT
bizarre behavior	1.0000(0.00)	NT	NT	NT	NT
vocal: spontaneous (1=yes; 0=no)	1.0000(0.00)	NT	NT	NT	NT
approach response	0.9986(1.25)	NT	NT	NT	NT
touch response	1.0000(0.00)	NT	NT	NT	NT
startle response	1.0000(0.00)	NT	NT	NT	NT
tail pinch response	0.5010(8.33)	NT	NT	NT	NT
placing of paws on grid	1.0000(0.00)	NT	NT	NT	NT
righting reflex air	1.0000(0.00)	NT	NT	NT	NT
righting reflex surface	1.0000(0.00)	NT	NT	NT	NT
grip strength	1.0000(0.00)	NT	NT	NT	NT

+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.  
#: Comparisons to the Blend were performed if the overall dose effect was significant.  
++: Significantly different from the corresponding Blend at the 0.05/4=0.0125 level (two-sided) were marked with a "yes".  
NT: Not tested

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

**DISCUSSION**

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Table 3A. Male Animals Test Result Summary --- Continuous Variables

Parameter	Dose Effect+ P-value	Gp 1 Mean (SE)	Gp 2 Mean (SE) #\$	Gp 4 Mean (SE) #++	Gp 5 Mean (SE) #++	Gp 6 Mean (SE) #++	Gp 7 Mean (SE) #++	Gp 9 Mean (SE) #++	Gp 10 Mean (SE) #++	Gp 11 Mean (SE) #++	Gp 12 Mean (SE) #++
lines crossed	0.3016	30.60(3.30)	41.00(2.14)	29.60(2.98)	35.40(2.73)	34.40(4.53)	30.20(2.78)	36.60(3.23)	30.00(4.56)	31.80(4.47)	30.60(1.44)
rearings	0.2446	15.60(2.62)	13.80(1.24)	14.80(2.56)	14.80(1.32)	11.80(0.97)	14.60(1.44)	17.20(1.62)	14.00(1.67)	15.60(1.03)	10.60(0.87)
urine pools	0.1720	1.40(0.40)	0.00(0.00)	1.00(0.45)	1.20(0.58)	1.20(0.37)	0.40(0.40)	0.40(0.24)	1.40(0.40)	0.60(0.40)	0.60(0.40)
fecal boluses	0.5190	2.00(0.71)	0.60(0.40)	0.80(0.58)	2.40(0.60)	1.80(0.66)	1.20(0.97)	0.60(0.40)	1.60(0.93)	1.80(0.37)	1.00(0.63)
rectal temperature	0.3718	101.00(0.26)	100.52(0.44)	100.96(0.30)	101.22(0.51)	100.92(0.22)	100.58(0.45)	101.32(0.26)	101.02(0.47)	101.44(0.65)	99.98(0.35)

+: Significant overall dose effects at the 0.05 level (two-sided) were marked by +.

#: Comparisons to the control were performed if the overall dose effect was significant.

++: Significantly different from the control at the 0.05/4=0.0125 level (two-sided) were marked by ++.

\$: Significantly different from the control at the 0.05 level (two-sided) were marked by \$.

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Table 3A. Male Animals Test Result Summary --- Continuous Variables

Parameter	Dose Effect* P-value	Gp 9 vs. Gp 4 #++	Gp 10 vs. Gp 5 #++	Gp 11 vs. Gp 6 #++	Gp 12 vs. Gp 7 #++
lines crossed	0.3016	NT	NT	NT	NT
rearings	0.2446	NT	NT	NT	NT
urine pools	0.1720	NT	NT	NT	NT
fecal boluses	0.5190	NT	NT	NT	NT
rectal temperature	0.3718	NT	NT	NT	NT

+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.

#: Comparisons to the blend were performed if the overall dose effect was significant.

++: Significantly different from the corresponding blend level at the 0.05/4=0.0125 level (two-sided) were marked by \*.

NT: Not tested.

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T1, HomeCage Parameter=posture**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-5	Animal found dead	0	0	0	0	0	0	0	0	0	0
-4	Lying flat limbs splayed out	0	0	0	0	0	0	0	0	0	0
-3	Lying on side limbs in the air	0	0	0	0	0	0	0	0	0	0
-2	Hunched posture (crouching over)	0	0	0	0	0	0	0	0	0	0
-1	Sleeping, resting, recumbent	0	1	2	1	2	2	2	1	0	1
0	Awake, alert, without rearing	2	2	1	3	3	2	2	4	4	3
1	Rearing, ambulating	3	2	2	1	0	0	1	0	1	1
2	Jumping, running	0	0	0	0	0	0	0	0	0	0
Mean Score		0.60	0.20	0.00	0.00	-0.40	-0.50	-0.20	-0.20	0.20	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T3, HomeCage Parameter=convulsive activity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	4	5	5	5	5
1	Excessive stereotype behavior (grooming, fixed staring, etc.)	0	0	0	0	0	0	0	0	0	0
2	Forebody myoclonus (clonic chewing)	0	0	0	0	0	0	0	0	0	0
3	Popcorn seizures (bouncing or popping behavior)	0	0	0	0	0	0	0	0	0	0
4	Clonic seizures (slight/mild tremors or jerkings, contractions followed by relaxations)	0	0	0	0	0	0	0	0	0	0
5	Tonic seizures (repetitive moderate/severe whole body tremors, body is rigid and arched)	0	0	0	0	0	0	0	0	0	0
6	Tonic/clonic seizures (loss of righting)	0	0	0	0	0	0	0	0	0	0
7	Post-ictal depression	0	0	0	0	0	0	0	0	0	0
8	Seizures followed by death	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T4, HomeCage Parameter=lethargy/arousal**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-4	Completely unresponsive/unconscious	0	0	0	0	0	0	0	0	0	0
-3	Severe lethargy, lying on side, immobile but conscious	0	0	0	0	0	0	0	0	0	0
-2	Moderate lethargy, immobile, may be prostrate	0	0	0	0	0	0	0	0	0	0
-1	Slight lethargy, little exploration, but not prostrate	0	1	2	1	2	2	2	1	1	1
0	Alert, responsive, exploratory movements	5	4	3	4	3	2	3	4	4	4
1	Slight arousal, slight excitement, tense	0	0	0	0	0	0	0	0	0	0
2	Moderate arousal, moderate excitement, sudden darting and freezing	0	0	0	0	0	0	0	0	0	0
3	Severe arousal, severe excitement, hyperalert, overaggressive	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	-0.20	-0.40	-0.20	-0.40	-0.50	-0.40	-0.20	-0.20	-0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T5, HomeCage Parameter=eyelid closure**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	4	4	4	4	2	5	4	5	4
1	Slightly drooping	0	1	0	1	0	1	0	1	0	0
2	Drooping approximately half-way	0	0	0	0	0	1	0	0	0	1
3	Completely shut	0	0	1	0	1	0	0	0	0	0
Mean Score		0.00	0.20	0.60	0.20	0.60	0.75	0.00	0.20	0.00	0.40

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T6, HomeCage Parameter=ease of removing**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No resistance, body limp	0	0	0	0	0	0	0	0	0	0
-1	Very little resistance, body relaxed	0	0	0	0	0	1	0	0	0	0
0	Little resistance, but body tense, may rear slightly, with or without vocalization	3	5	4	3	5	3	3	3	5	3
1	Slight resistance, rodent runs around cage, is difficult to grab, with or without vocalization	2	0	1	2	0	0	2	2	0	2
2	Moderate resistance, rodent may jump from cage, may attempt to bite defensively or initially, with or without vocalization	0	0	0	0	0	0	0	0	0	0
3	Extreme resistance, rodent makes repetitive attempts to bite/attack technician's hand and to escape, with or without vocalizations	0	0	0	0	0	0	0	0	0	0
4	Rodent freezes (with or without vocalizations)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.40	0.00	0.20	0.40	0.00	-0.25	0.40	0.40	0.00	0.40

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
Female Animals, Test=T7, HomeCage Parameter=ease of handling

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	Rodent is limp, lethargic, or even unresponsive	0	0	0	0	0	0	0	0	0	0
-1	Rodent is relaxed and may have limbs pulled up against body	0	0	0	0	0	0	0	0	0	0
0	Rodent is alert, but with little or no resistance	3	5	4	2	4	3	2	3	3	3
1	Moderate resistance, rodent is tense (may squirm, twist, with or without vocalization)	2	0	1	3	3	0	1	3	2	2
2	Extreme resistance, animal attempts to bite, escape	0	0	0	0	0	0	1	0	0	0
Mean Score		0.40	0.00	0.20	0.60	0.60	0.00	0.60	0.60	0.40	0.40

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

$\frac{d}{dt} \left( \frac{\partial L}{\partial \dot{x}} \right) = \frac{\partial L}{\partial x}$

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T8, HomeCage Parameter=hand to hand**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	Rodent is limp, lethargic, or even unresponsive	0	0	0	0	0	0	0	0	0	0
-1	Rodent is relaxed and may have limbs pulled up against body	0	0	0	0	0	1	0	0	0	0
0	Rodent is alert, but with little or no resistance	3	5	3	2	3	3	3	3	5	3
1	Moderate resistance, rodent is tense (may squirm, twist, with or without vocalization)	1	0	2	3	1	0	1	2	0	2
2	Extreme resistance, animal attempts to bite, escape	0	0	0	0	1	0	0	0	0	0
3	Convulsing	1	0	0	0	0	0	1	0	0	0
Mean Score		0.80	0.00	0.40	0.60	0.60	-0.25	0.80	0.40	0.00	0.40

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T9, HomeCage Parameter=general condition/appearance**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	4	5	5	5	4	5	5	5	5
1	Red or crusty deposits around eyes, nose, or mouth	0	1	0	0	0	0	0	0	0	0
2	Thin appearance	0	0	0	0	0	0	0	0	0	0
3	Dehydrated appearance (decreased skin elasticity, thin appearance, hunched posture)	0	0	0	0	0	0	0	0	0	0
4	Hunched posture (without signs of dehydrated appearance)	0	0	0	0	0	0	0	0	0	0
5	Diminished body tone (limp)	0	0	0	0	0	0	0	0	0	0
6	Excessive body tone (rigid)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Abstract**

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T11, HomeCage Parameter=fecal stain**

[illegible]

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T12, HomeCage Parameter=salivation**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0 None		5	5	5	5	5	4	5	5	5	5
1 Slight		0	0	0	0	0	0	0	0	0	0
2 Moderate		0	0	0	0	0	0	0	0	0	0
3 Severe		0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T14, HomeCage Parameter=fur appearance**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	4	5	5	5	5
1	Slightly rough coat	0	0	0	0	0	0	0	0	0	0
2	Moderately rough coat	0	0	0	0	0	0	0	0	0	0
3	Severely rough coat	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T15, HomeCage Parameter=lacrimation**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	4	5	2	4	4	5	4	5	5
1	Slight	0	1	0	3	1	0	0	1	0	0
2	Moderate	0	0	0	0	0	0	0	0	0	0
3	Severe	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.20	0.00	0.60	0.20	0.00	0.00	0.20	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T16, HomeCage Parameter=palpebral reflex responsivity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No response	0	0	0	0	0	0	0	0	0	0
-1	Sluggish closing of eyelid	0	0	0	0	0	0	0	0	0	0
0	Normal, immediate, brisk closing of eyelid	5	5	5	5	5	4	5	5	5	5
1	Escape or mild vocalization	0	0	0	0	0	0	0	0	0	0
2	Extreme response, vocalization, fleeing, attacking, and biting	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
Female Animals, Test=T17, HomeCage Parameter=pupillary diameter test

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-1	Pinpoint pupil (miosis)	0	0	0	0	0	0	0	1	0	0
0	Normal pupil, 1/4-1/2 dilated	5	5	5	5	5	4	5	4	5	5
1	Pupil fully dilated	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.20	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T18, HomeCage Parameter=pupil response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal reaction, constriction noted due to light	5	5	5	5	5	4	5	5	5	5
1	Pupils fully dilated	0	0	0	0	0	0	0	0	0	0
2	Pupils totally constricted	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T19, HomeCage Parameter=vocalizations (1=yes; 0=no)**

Score Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0 No	3	4	3	3	3	4	3	4	5	3
1 Yes	2	1	2	2	2	0	2	1	0	2

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T24, OpenField Parameter=posture**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-4	Lying flat limbs splayed out	0	0	0	0	0	0	0	0	0	0
-3	Lying on side limbs in the air	0	0	0	0	0	0	0	0	0	0
-2	Hunched posture (crouching over)	0	0	0	0	0	0	0	0	0	0
-1	Lying on side (curled up sleeping)	0	0	0	0	0	0	0	0	0	0
0	Normal (sitting or standing normally)	5	5	5	5	5	4	5	5	5	5
1	Rearing	0	0	0	0	0	0	0	0	0	0
2	Hyperactive (jumping, running, etc.)	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T25, OpenField Parameter=tremor activity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0None		4	5	5	5	5	4	4	5	5	3
1Slight		1	0	0	0	0	0	1	0	0	2
2Moderate		0	0	0	0	0	0	0	0	0	0
3Severe		0	0	0	0	0	0	0	0	0	0
Mean Score		0.20	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.40

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T26, OpenField Parameter=convulsive activity**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	4	5	5	5	5
1	Excessive stereotype behavior (grooming, fixed staring, etc.)	0	0	0	0	0	0	0	0	0	0
2	Forebody myoclonus (clonic chewing)	0	0	0	0	0	0	0	0	0	0
3	Popcorn seizures (bouncing or popping behavior)	0	0	0	0	0	0	0	0	0	0
4	Clonic seizures (slight/mild tremors or jerkings, contractions followed by relaxations)	0	0	0	0	0	0	0	0	0	0
5	Tonic seizures (repetitive moderate/severe whole body tremors, body is rigid and arched)	0	0	0	0	0	0	0	0	0	0
6	Tonic/clonic seizures (loss of righting)	0	0	0	0	0	0	0	0	0	0
7	Post-ictal depression	0	0	0	0	0	0	0	0	0	0
8	Seizures followed by death	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T27, OpenField Parameter=gait**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	4	5	5	5	5
1	Walking on tip toes	0	0	0	0	0	0	0	0	0	0
2	Ataxia (excessive swaying, rocking, or lurching during walk)	0	0	0	0	0	0	0	0	0	0
3	Feet pointing outward from body	0	0	0	0	0	0	0	0	0	0
4	Hindlimbs splayed	0	0	0	0	0	0	0	0	0	0
5	Front limbs dragging (unable to support weight)	0	0	0	0	0	0	0	0	0	0
6	Hindlimbs dragging	0	0	0	0	0	0	0	0	0	0
7	Inability to use all limbs	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T28, OpenField Parameter=gait score**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	Normal	5	5	5	5	5	4	5	5	5	5
1	Slightly abnormal	0	0	0	0	0	0	0	0	0	0
2	Moderately abnormal	0	0	0	0	0	0	0	0	0	0
3	Severely abnormal	0	0	0	0	0	0	0	0	0	0
4	No movement	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T29, OpenField Parameter=stereotype**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	5	5	5	4	5	5	5	5
1	Repetitive grooming	0	0	0	0	0	0	0	0	0	0
2	Pacing	0	0	0	0	0	0	0	0	0	0
3	Repetitive sniffing	0	0	0	0	0	0	0	0	0	0
4	Head weaving	0	0	0	0	0	0	0	0	0	0
5	Licking	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T30, OpenField Parameter=bizarre behavior**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0	None	5	5	4	5	5	4	5	5	5	5
1	Self-mutilation	0	0	1	0	0	0	0	0	0	0
2	Retropulsion	0	0	0	0	0	0	0	0	0	0
3	Writhing	0	0	0	0	0	0	0	0	0	0
4	Flopping	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T31, OpenField Parameter=vocal-spontaneous (1=yes; 0=no)**

Score Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
0 No	5	5	5	5	5	4	5	5	5	5
1 Yes	0	0	0	0	0	0	0	0	0	0

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

TABLE 1B  
 Female Animals  
 Test=T31, OpenField  
 Parameter=vocal-spontaneous  
 (1=yes; 0=no)

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T32, OpenField Parameter=approach response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No reaction	0	0	0	0	0	0	0	0	0	0
-1	Animal senses object but not interested and does not approach	0	0	0	0	0	0	0	0	0	0
0	Animal slowly approaches object, sniffs, and then turns away	5	5	5	5	5	4	5	5	5	5
1	Animal shows more energetic response with or without vocalization, rodent sways from side to side	0	0	0	0	0	0	0	0	0	0
2	Animal shows bizarre behavior, may include jumping, biting at object, attacking object with or without vocalization	0	0	0	0	0	0	0	0	0	0
3	Rodent freezes, animal may exhibit muscle contractions	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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 DATE: [illegible]

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T33, OpenField Parameter=touch response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-1	No reaction (i.e., due to stupor, coma, convulsions)	0	0	0	0	0	0	0	0	0	0
0	Rodent may slowly turn or walk away	4	5	5	5	3	4	5	5	5	5
1	More energetic response than 0, may include vocalizations	0	0	0	0	2	0	0	0	0	0
2	Exaggerated reaction (e.g., jumps, bites, attacks with or without vocalizations)	1	0	0	0	0	0	0	0	0	0
3	Rodent freezes, actual muscle contractions	0	0	0	0	0	0	0	0	0	0
Mean Score		0.40	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T34, OpenField Parameter=startle response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-1	No reaction (i.e., due to stupor, coma, convulsions)	0	0	0	0	0	0	0	0	0	0
0	Slight reaction, some evidence that noise was heard, normal flinching or flicking of ears	5	5	4	5	5	4	5	5	5	5
1	More energetic response than 0, may include vocalizations	0	0	1	0	0	0	1	0	0	0
2	Exaggerated reaction (e.g., jumps, bites, attacks with or without vocalizations)	0	0	0	0	0	0	0	0	0	0
3	Rodent freezes, actual muscle contractions	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.20	0.00	0.00	0.00	0.20	0.00	0.00	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

Figure 1. The structure of the proposed model.

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T35, OpenField Parameter=tail pinch response**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-1	No reaction (i.e., due to stupor, coma, convulsions)	0	0	0	0	0	0	0	0	0	0
0	Rodent may turn or walk forward	3	5	5	4	3	3	4	4	3	5
1	More energetic response than 0, may include vocalizations	1	0	0	1	2	1	1	1	2	0
2	Exaggerated reaction (e.g., jumps, bites, attacks with or without vocalizations)	1	0	0	0	0	0	0	0	0	0
3	Rodent freezes, actual muscle contractions	0	0	0	0	0	0	0	0	0	0
Mean Score		0.60	0.00	0.00	0.20	0.40	0.25	0.20	0.20	0.40	0.00

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T36, OpenField**    **Parameter=placing of paws on grid**

[illegible]

Group #	Group Description	Group Coding		Target Dosage (mg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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**Table 1B. Data Summary for Categorical Variables (Score and Yes/No Variables)**  
**Female Animals, Test=T46, OpenField Parameter=grip strength**

Score	Description	Gp 1	Gp 2	Gp 4	Gp 5	Gp 6	Gp 7	Gp 9	Gp 10	Gp 11	Gp 12
-2	No gripping	0	0	0	0	0	0	0	0	0	0
-1	Weak gripping	0	0	0	1	0	0	0	0	0	1
0	Normal gripping	5	5	5	4	5	4	5	5	5	4
1	Excessive gripping	0	0	0	0	0	0	0	0	0	0
Mean Score		0.00	0.00	0.00	-0.20	0.00	0.00	0.00	0.00	0.00	-0.20

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Table 2B. Female Animals Test Result Summary for Categorical Variables (Score and Yes/No Variables)

Parameter	Dose Effect+ P-value (Chi-Square)	Group 2 vs1 #S	Group 4 vs 1 #++	Group 5 vs 1 #++	Group 6 vs 1 #++	Group 7 vs 1 #++	Group 9 vs 1 #++	Group 10 vs 1 #++	Group 11 vs 1 #++	Group 12 vs 1 #++
Posture (home cage)	0.0356(17.96)*	No	No	No	Yes	Yes	No	Yes	No	No
tremor activity	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
lethargy/arousal	0.0164(20.25)*	No	No	No	No	No	No	No	No	No
eyelid closure	0.2918(10.77)	NT	NT	NT	NT	NT	NT	NT	NT	NT
ease of removing	0.0232(19.25)*	No	No	No	No	No	No	No	No	No
ease of handling	<0.0001(36.56)*	No	No	No	No	No	No	No	No	No
hand to hand	0.0018(26.34)*	No	No	No	No	No	No	No	No	No
general condition/appearance	0.9986(1.25)	NT	NT	NT	NT	NT	NT	NT	NT	NT
urine stain	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
fecal stain	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
Salivation	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
Piloerection	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
fur appearance	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
Lacrimation	0.2590(11.25)	NT	NT	NT	NT	NT	NT	NT	NT	NT
palpebral reflex responsivity	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
pupillary diameter test	0.9986(1.25)	NT	NT	NT	NT	NT	NT	NT	NT	NT
pupil response	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
vocalizations (1=yes; 0=no)	0.9071(4.06)	NT	NT	NT	NT	NT	NT	NT	NT	NT
Posture (open field)	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
tremor activity	0.7565(5.83)	NT	NT	NT	NT	NT	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
gait	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
gait score	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
stereotype	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
bizarre behavior	0.9986(1.25)	NT	NT	NT	NT	NT	NT	NT	NT	NT
vocal -spontaneous (1=yes; 0=no)	1.0000(0.22)	NT	NT	NT	NT	NT	NT	NT	NT	NT
approach response	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
touch response	0.8690(4.58)	NT	NT	NT	NT	NT	NT	NT	NT	NT
startle response	0.9809(2.50)	NT	NT	NT	NT	NT	NT	NT	NT	NT
tail pinch response	0.1037(14.56)	NT	NT	NT	NT	NT	NT	NT	NT	NT
placing of paws on grid	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
righting reflex air	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
righting reflex surface	1.0000(0.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
grip strength	0.9809(2.50)	NT	NT	NT	NT	NT	NT	NT	NT	NT

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+: Significant overall dose effects at the 0.05 level (two-sided) were marked by +.  
 #: Comparisons to the control were performed if the overall dose effect was significant.  
 ++: Significantly different from the control at the 0.05/4=0.0125 level (two-sided) were marked with a "yes".  
 \$: Significantly different from the control at the 0.05 level (two-sided) were marked with a "yes".  
 NT: Not tested

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Table 2B. Female Animals Test Result Summary for Categorical Variables (Score and Yes/No Variables)

Parameter	Dose Effect+ P-value (Chi-Square)	Group 9 vs 4 #++	Group 10 vs 5 #++	Group 11 vs 6 #++	Group 12 vs 7 #++
Posture (home cage)	0.0356(17.96)*	No	No	No	No
tremor activity	1.0000(0.00)	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT
lethargy/arousal	0.0164(20.25)*	No	No	No	No
eyelid closure	0.2918(10.77)	NT	NT	NT	NT
ease of removing	0.0232(19.25)*	No	No	No	No
ease of handling	<0.0001(36.56)*	No	No	No	No
hand to hand	0.0018(26.34)*	No	No	No	No
general condition/appearance	0.9986(1.25)	NT	NT	NT	NT
urine stain	1.0000(0.00)	NT	NT	NT	NT
fecal stain	1.0000(0.00)	NT	NT	NT	NT
salivation	1.0000(0.00)	NT	NT	NT	NT
pilorection	1.0000(0.00)	NT	NT	NT	NT
fur appearance	1.0000(0.00)	NT	NT	NT	NT
lacrimation	0.2590(11.25)	NT	NT	NT	NT
palpebral reflex responsivity	1.0000(0.00)	NT	NT	NT	NT
pupillary diameter test	0.9986(1.25)	NT	NT	NT	NT
pupil response	1.0000(0.00)	NT	NT	NT	NT
vocalizations (1=yes; 0=no)	0.9071(4.06)	NT	NT	NT	NT
Posture (open field)	1.0000(0.00)	NT	NT	NT	NT
tremor activity	0.7565(5.83)	NT	NT	NT	NT
convulsive activity	1.0000(0.00)	NT	NT	NT	NT
Gait	1.0000(0.00)	NT	NT	NT	NT
gait score	1.0000(0.00)	NT	NT	NT	NT
Stereotype	1.0000(0.00)	NT	NT	NT	NT
bizarre behavior	0.9986(1.25)	NT	NT	NT	NT
vocal -spontaneous (1=yes; 0=no)	1.0000(0.22)	NT	NT	NT	NT
approach response	1.0000(0.00)	NT	NT	NT	NT
touch response	0.8690(4.58)	NT	NT	NT	NT
startle response	0.9809(2.50)	NT	NT	NT	NT
tail pinch response	0.1037(14.56)	NT	NT	NT	NT
placing of paws on grid	1.0000(0.00)	NT	NT	NT	NT
righting reflex air	1.0000(0.00)	NT	NT	NT	NT
righting reflex surface	1.0000(0.00)	NT	NT	NT	NT
grip strength	0.9809(2.50)	NT	NT	NT	NT

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+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.

#: Comparisons to the blend were performed if the overall dose effect was significant.

++: Significantly different from the corresponding blend at the 0.05/4=0.0125 level (two-sided) and were marked with a "yes".

NT: Not tested

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

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Table 3B. Female Animals Test Result Summary — Continuous Variables

Parameter	Dose Effect+ P-value	Gp 1 Mean (SE)	Gp 2 Mean (SE) #S	Gp 4 Mean (SE) #++	Gp 5 Mean (SE) #++	Gp 6 Mean (SE) #++	Gp 7 Mean (SE) #++	Gp 9 Mean (SE) #++	Gp 10 Mean (SE) #++	Gp 11 Mean (SE) #++	Gp 12 Mean (SE) #++
lines crossed	0.4216	28.40(6.30)	27.80(5.26)	31.40(5.74)	41.80(5.05)	31.00(5.01)	28.50(2.22)	42.60(6.22)	36.80(2.24)	33.60(2.14)	31.40(7.92)
rearings	0.3124	17.40(2.36)	11.80(2.56)	17.20(3.38)	18.40(3.22)	17.60(2.54)	14.50(1.76)	21.40(2.56)	19.60(1.57)	17.20(2.35)	14.80(1.24)
urine pools	0.9292	0.60(0.40)	0.40(0.40)	1.00(1.00)	0.20(0.20)	0.00(0.00)	0.25(0.25)	1.40(1.40)	0.60(0.24)	1.20(0.97)	0.80(0.80)
fecal boluses	0.8812	1.60(0.68)	0.20(0.20)	1.40(0.75)	2.00(1.30)	0.80(0.58)	0.75(0.75)	1.40(1.17)	0.80(0.48)	1.80(0.92)	0.80(0.80)
rectal temperature	<0.0001*	102.24(0.24)	98.94(0.38)*	102.26(0.15)	101.72(0.45)	101.48(0.32)	97.10(2.53)*	102.04(0.55)	101.60(0.37)	101.06(0.31)	98.92(0.52)*

+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.

#: Comparisons to the control were performed if the overall dose effect was significant.

++: Significantly different from the control at the 0.05/4=0.0125 level (two-sided) were marked by \*.

\$: Significantly different from the control at the 0.05 level (two-sided) were marked by \*.

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

Table 3B. Female Animals Test Result Summary --- Continuous Variables

Parameter	Dose Effect+ P-value	Gp 9 vs. Gp 4 +++	Gp 10 vs. Gp 5 +++	Gp 11 vs. Gp 6 +++	Gp 12 vs. Gp 7 +++
lines crossed	0.4216	NT	NT	NT	NT
rearings	0.3124	NT	NT	NT	NT
urine pools	0.9292	NT	NT	NT	NT
focal boluses	0.8812	NT	NT	NT	NT
rectal temperature	<0.0001*	No	No	No	No

+: Significant overall dose effects at the 0.05 level (two-sided) were marked by \*.  
#: Comparisons to the blend were performed if the overall dose effect was significant.  
++: Significantly different from the corresponding blend level at the 0.05/4=0.0125 level (two-sided) were marked with a "yes".  
NT: Not tested

Group #	Group Description	Group Coding		Target Dosage (mg/kg/day)
		Males	Females	
1	Control	CM	CF	0
2	Nicotine Tartrate High Dose	NT20M	NT20F	20
4	Tobacco Blend Low Dose	B0.2M	B0.2F	0.2
5	Tobacco Blend Intermediate Dose 1	B2M	B2F	2
6	Tobacco Blend Intermediate Dose 2	B8M	B8F	8
7	Tobacco Blend High Dose	B20M	B20F	20
9	Tobacco Extract Low Dose	E0.2M	E0.2F	0.2
10	Tobacco Extract Intermediate Dose 1	E2M	E2F	2
11	Tobacco Extract Intermediate Dose 2	E8M	E8F	8
12	Tobacco Extract High Dose	E20M	E20F	20

**POLYMER LETTERS**

**APPENDIX H: TOXICOKINETIC REPORT**

**28-DAY REPEATED DOSE TOXICITY STUDY OF TOBACCO BLEND AND  
AQUEOUS TOBACCO EXTRACT IN WISTAR HAN RATS**

**SAMPLE ANALYSIS AND KINETICS REPORT**

**DETERMINATION OF NICOTINE AND COTININE IN RAT PLASMA BY LIQUID  
CHROMATOGRAPHY WITH MASS SPECTROMETRY (LC-MS)**

Battelle Study Number: CN49730C

March 11, 2009

Prepared By:

Ed A 3/11/09  
Edward A. Psurny, B.S./Date

Approved By:

Brian L. Burback 3-11-09  
Brian L. Burback, Ph.D./Date

Approved By:

Jerry D. Johnson 3-11-09  
Jerry Johnson, Ph.D./Date

**EXECUTIVE SUMMARY**

Rat plasma samples were received frozen from Battelle Memorial Institute's animal facility from the "28-Day Repeated Dose Toxicity Study of Tobacco Blend and Aqueous Tobacco Extract in Wistar Han Rats" study for analysis of nicotine and cotinine plasma concentration levels.

(b) (4)



The samples were successfully analyzed.

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**I. INTRODUCTION**

This report contains a description of the analysis of the rat plasma samples from this study, the results of these analyses, and figures.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201.

**II. STANDARDS**

Nicotine, Lot No. 127K4111, was obtained from Sigma-Aldrich, Inc., and was used to prepare the calibration standards and quality control (QC) samples for the analyses.

Nicotine-d<sub>3</sub> salicylate salt, Lot No. 037K4062, was obtained from Sigma-Aldrich, Inc., and used as the internal standard (IS) for nicotine.

Cotinine, Lot No. 048K4031, was obtained from Sigma Aldrich, Inc., and was used to prepare the calibration standards and QC samples for the analyses.

Cotinine-d<sub>3</sub>, Lot No. IS1107, was obtained from Sigma-Aldrich, Inc., and used as the IS for cotinine.

All four standards were used to perform the work covered in this report.

**III. MATRIX/SPECIES**

Plasma, Wistar Han rat with potassium ethylene diamine tetraacetic acid (EDTA), received from Bioreclamation.

**IV. PLASMA SAMPLE ANALYSIS****A. METHOD**

(b) (4)

**B. RESULTS**

A summary of each sample analysis, including any discrepancies, is shown in Table 1.

**Table 1 – Summary of Sample Analyses**(b) (4)  


Table 2 – Nicotine Low QC Level Results

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/08	Set 1	2.95E+00	2.77E+00	1.9	-6.1
7/10/08	Set 2	2.95E+00	3.19E+00	10.1	8.0
7/9/08	Set 3	2.95E+00	2.96E+00	14.0	0.3
7/10/08	Set 4	2.95E+00	2.76E+00	7.1	-6.4
7/11/08	Set 5	2.95E+00	3.06E+00	6.9	3.6
7/23/08	Set 6	2.95E+00	2.80E+00	11.5	-5.3
7/24/08	Set 7	2.95E+00	2.81E+00	4.2	-4.7

Table 3 – Nicotine Mid QC Level Results

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/2008	Set 1	2.95E+01	2.87E+01	5.6	-2.7
7/10/2008	Set 2	2.95E+01	3.02E+01	12.5	2.2
7/9/2008	Set 3	2.95E+01	2.93E+01	5.9	-0.8
7/10/2008	Set 4	2.95E+01	2.85E+01	7.5	-3.3
7/11/2008	Set 5	2.95E+01	3.02E+01	7.5	2.5
7/23/2008	Set 6	2.95E+01	2.74E+01	3.9	-7.3
7/24/2008	Set 7	2.95E+01	2.96E+01	4.3	0.2

Table 4 – Nicotine High QC Level Results

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/2008	Set 1	1.48E+02	1.51E+02	1.4	1.9
7/10/2008	Set 2	1.48E+02	1.44E+02	6.2	-2.2
7/9/2008	Set 3	1.48E+02	1.44E+02	6.5	-2.7
7/10/2008	Set 4	1.48E+02	1.44E+02	4.8	-2.9
7/11/2008	Set 5	1.48E+02	1.46E+02	3.8	-1.5
7/23/2008	Set 6	1.48E+02	1.38E+02	6.9	-6.8
7/24/2008	Set 7	1.48E+02	1.52E+02	4.0	2.4

**Table 5 – Cotinine Low QC Level Results**

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/2008	Set 1	2.96E+01	3.08E+01	3.7	4.1
7/10/2008	Set 2	2.96E+01	3.13E+01	9.1	5.4
7/9/2008	Set 3	2.96E+01	3.05E+01	7.0	2.9
7/10/2008	Set 4	2.96E+01	3.09E+01	5.8	4.5
7/11/2008	Set 5	2.96E+01	2.92E+01	7.7	-1.4
7/23/2008	Set 6	2.96E+01	2.71E+01	3.9	-8.4
7/24/2008	Set 7	2.96E+01	2.79E+01	5.9	-5.8

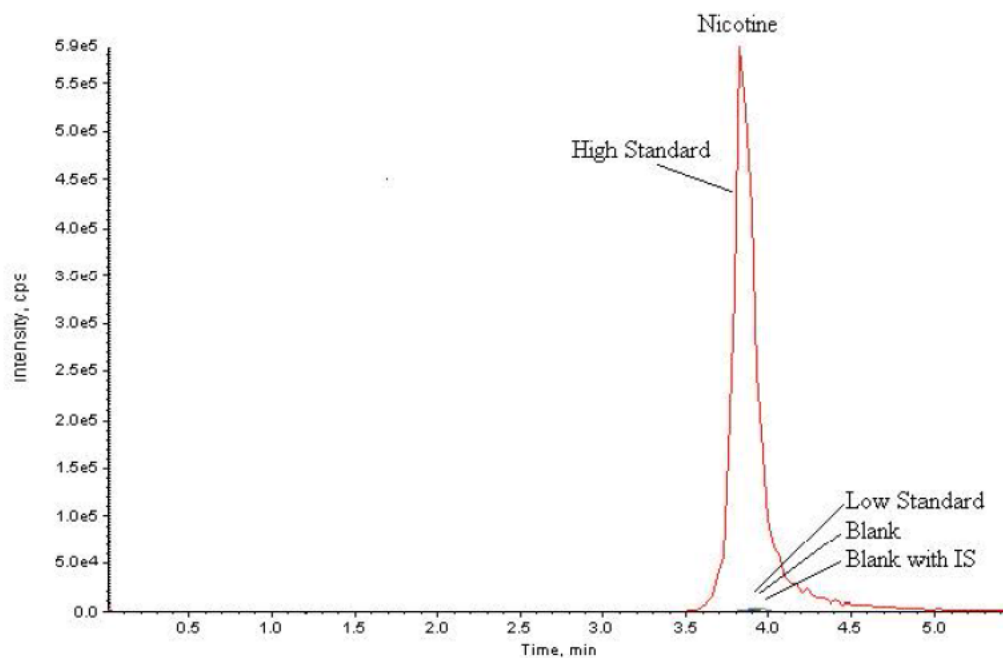
**Table 6 – Cotinine Mid QC Level Results**

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/2008	Set 1	2.96E+02	2.96E+02	3.8	0.1
7/10/2008	Set 2	2.96E+02	3.02E+02	4.2	1.9
7/9/2008	Set 3	2.96E+02	2.91E+02	5.6	-1.8
7/10/2008	Set 4	2.96E+02	2.94E+02	8.6	-0.7
7/11/2008	Set 5	2.96E+02	2.96E+02	13.2	-0.1
7/23/2008	Set 6	2.96E+02	2.86E+02	6.9	-3.3
7/24/2008	Set 7	2.96E+02	2.78E+02	3.4	-6.1

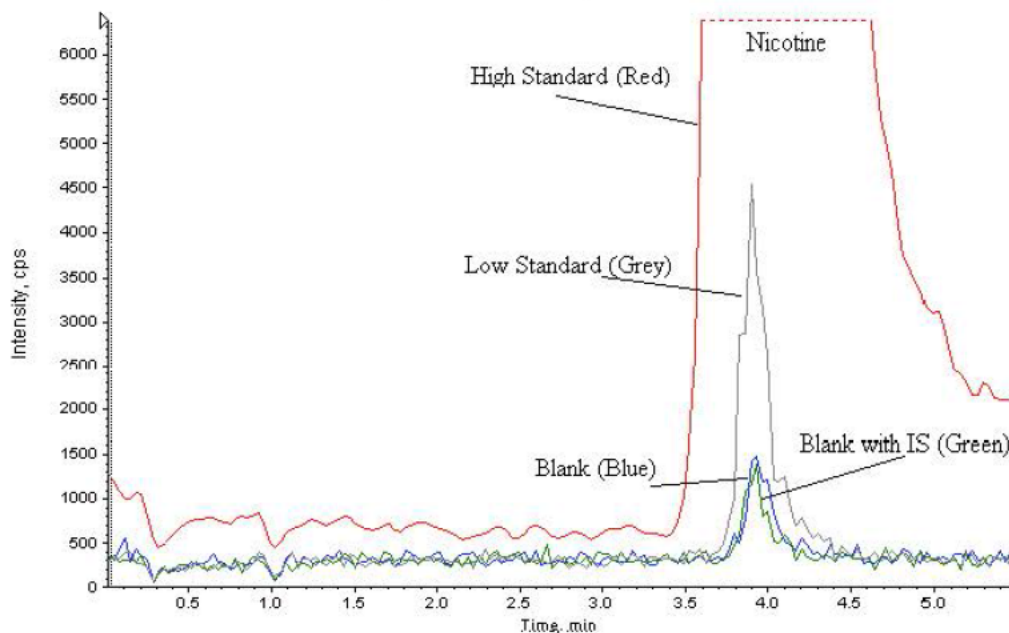
**Table 7 – Cotinine High QC Level Results**

Analysis Date	Analysis Set	Nominal Concentration (ng/mL)	Average Determined Concentration (ng/mL)	% RSD	Average % RE
7/7/2008	Set 1	1.48E+03	1.55E+03	2.0	4.4
7/10/2008	Set 2	1.48E+03	1.47E+03	6.8	-0.6
7/9/2008	Set 3	1.48E+03	1.60E+03	5.8	8.1
7/10/2008	Set 4	1.48E+03	1.37E+03	4.7	-7.4
7/11/2008	Set 5	1.48E+03	1.32E+03	6.2	-10.8
7/23/2008	Set 6	1.48E+03	1.51E+03	5.3	1.7
7/24/2008	Set 7	1.48E+03	1.50E+03	1.7	1.5

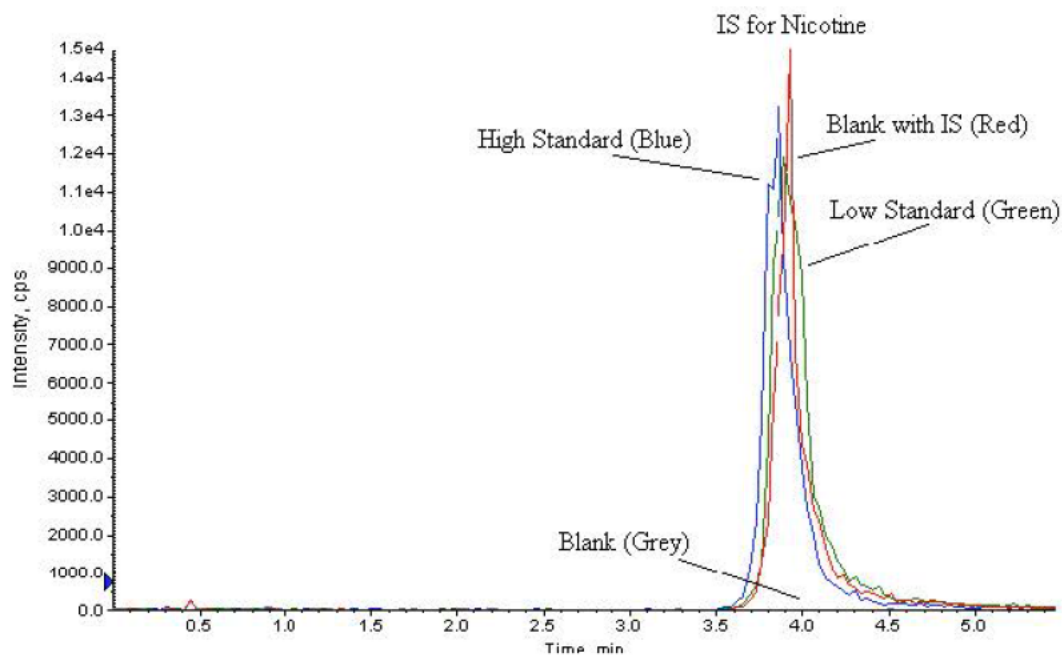
Representative overlaid nicotine full and reduced scale chromatograms of high and low concentration standards, a blank with IS, and a blank are shown in Figure 1 and Figure 2. Representative overlaid IS for nicotine full scale chromatograms of high and low concentration standards, a blank with IS, and a blank are shown in Figure 3. Representative overlaid cotinine full and reduced scale chromatograms of high and low concentration standards, a blank with IS, and a blank are shown in Figure 4 and Figure 5. Representative overlaid IS for cotinine full scale chromatograms of high and low concentration standards, a blank with IS, and a blank are shown in Figure 6.



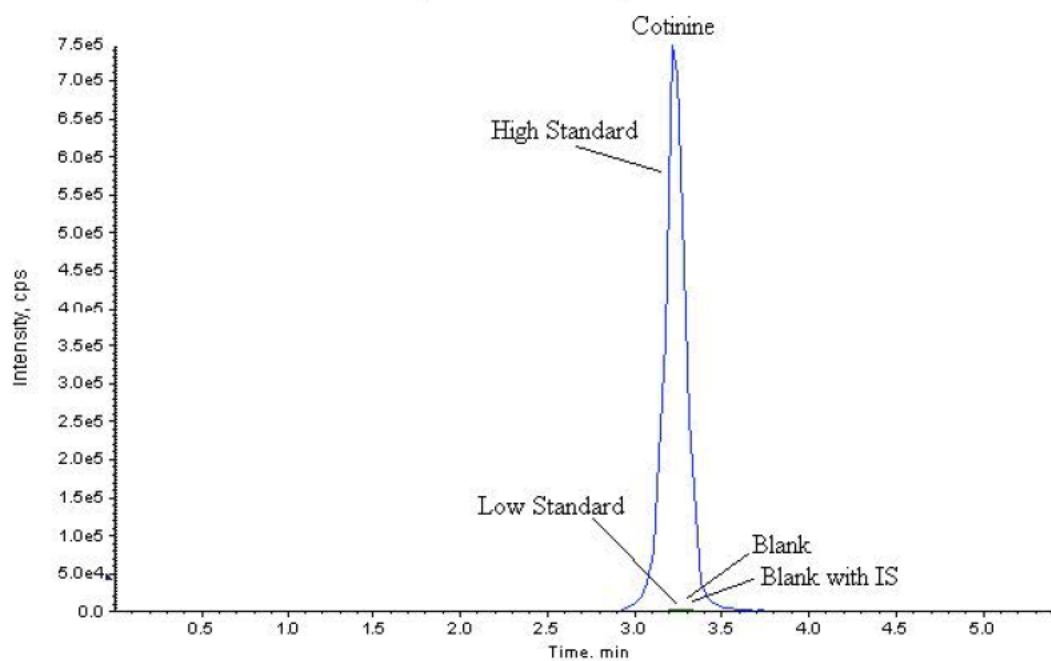
**Figure 1 – Representative Overlaid Nicotine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Full Scale**



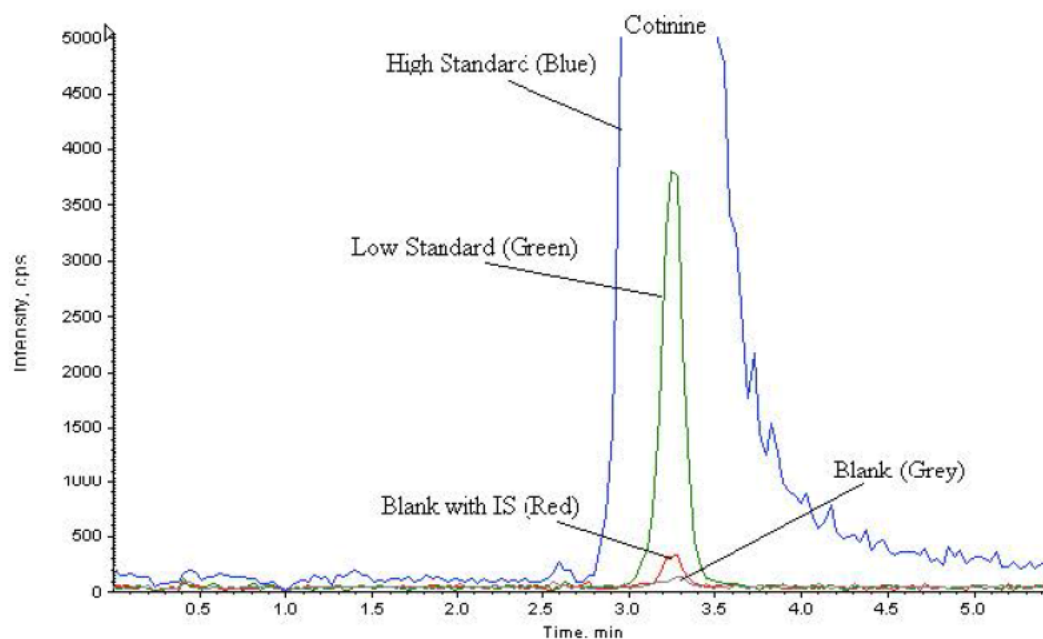
**Figure 2 – Representative Overlaid Nicotine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Reduced Scale**



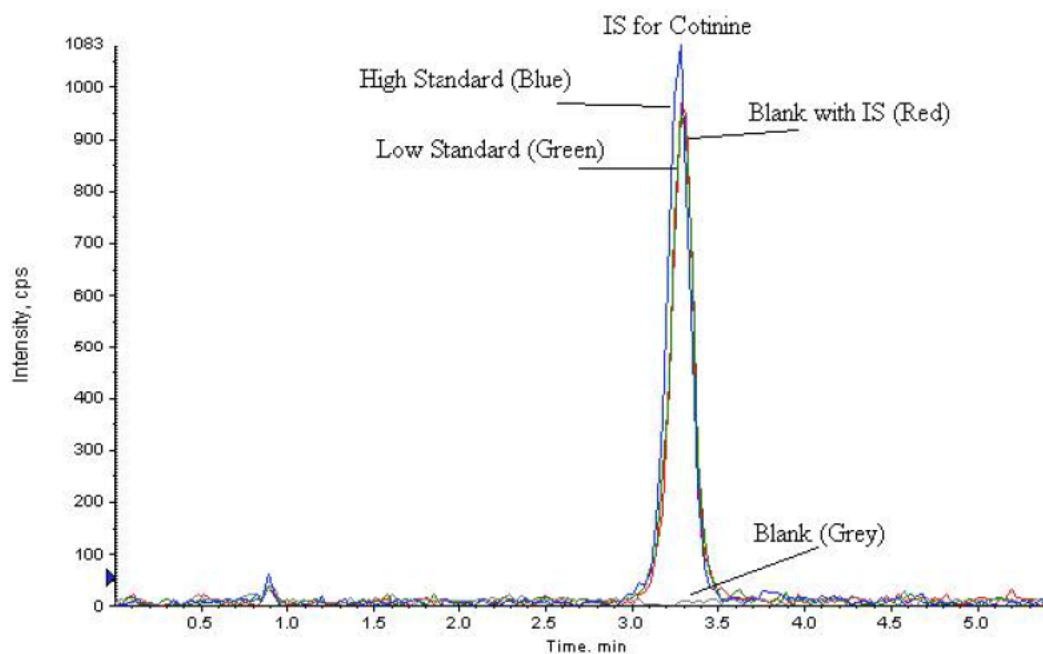
**Figure 3 – Representative Overlaid IS for Nicotine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Full Scale**



**Figure 4 – Representative Overlaid Cotinine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Full Scale**



**Figure 5 – Representative Overlaid Cotinine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Reduced Scale**



**Figure 6 – Representative Overlaid IS for Cotinine Chromatograms from High and Low Standards, a Blank with IS, and a Blank – Full Scale**

The results from the analyses for nicotine and cotinine for Days 13 and 14 are presented in Table 8 through Table 16. The results from the analyses for nicotine and cotinine for Day 28 are shown in Table 17 through Table 26. Any samples with calculated concentrations below the limit of quantitation are listed as BLOQ.

**Table 8 – NT20M and NT20F (20 mg/kg/day) Results**

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
211	Male	10:00 PM	1.76E+02	3.08E+03
212			2.67E+02	2.51E+03
213			3.41E+02	3.44E+03
214		12:00 AM	2.43E+02	2.87E+03
215			2.91E+02	3.53E+03
216			2.14E+02	2.57E+03
211		4:00 AM	3.03E+02	3.13E+03
212			2.04E+02	2.60E+03
213			2.11E+02	3.38E+03
214		6:00 AM	2.02E+02	2.55E+03
215			3.25E+02	3.52E+03
216			3.17E+02	3.13E+03
211		10:00 AM	1.99E+02	3.18E+03
212			1.82E+02	2.49E+03
213			2.15E+02	3.36E+03
214		12:00 PM	2.29E+02	2.36E+03
215			2.82E+02	3.76E+03
216			2.50E+02	3.03E+03
261	Female	10:00 PM	3.38E+02	3.98E+03
262			2.47E+02	2.56E+03
263			2.81E+02	2.85E+03
264		12:00 AM	3.87E+02	3.90E+03
265			3.76E+02	4.23E+03
266			4.01E+02	3.13E+03
261		4:00 AM	3.64E+02*	3.43E+03
262			2.01E+02	2.58E+03
263			2.86E+02	2.92E+03
264		6:00 AM	2.88E+02	3.67E+03
265			2.20E+02	3.69E+03
266			2.58E+02	2.85E+03
261		10:00 AM	2.95E+02	3.66E+03
262			3.02E+02	2.12E+03
263			2.38E+02	2.71E+03
264		12:00 PM	2.40E+02	3.42E+03
265			2.68E+02	3.14E+03
266			2.33E+02	2.96E+03

\* Average of two results.

Table 9 – B0.2M and B0.2F (0.2 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
411	Male	10:00 PM	5.89E+00	4.74E+01
412			3.51E+00	3.99E+01
413			3.64E+00	4.08E+01
414		12:00 AM	7.31E+00	3.89E+01
415			4.69E+00	4.64E+01
416			3.67E+00	4.02E+01
411		4:00 AM	6.22E+00	5.50E+01
412			5.31E+00	5.36E+01
413			2.12E+00	3.55E+01
414		6:00 AM	4.47E+00	4.70E+01
415			3.17E+00	4.88E+01
416			4.74E+00	4.74E+01
411		10:00 AM	2.08E+00	5.65E+01
412			3.31E+00	4.37E+01
413			BLOQ	2.30E+01
414		12:00 PM	2.07E+00	4.00E+01
415			1.02E+00	3.99E+01
416			1.75E+00	4.15E+01
461	Female	10:00 PM	6.00E+00	3.57E+01
462			7.23E+00	5.06E+01
463			5.32E+00	3.62E+01
464		12:00 AM	8.07E+00	5.18E+01
465			3.92E+00	3.87E+01
466			4.96E+00	5.56E+01
461		4:00 AM	6.03E+00	5.53E+01
462			7.96E+00	7.49E+01
463			3.19E+00	4.95E+01
464		6:00 AM	3.79E+00	6.44E+01
465			3.91E+00	4.80E+01
466			7.64E+00	9.14E+01
461		10:00 AM	2.85E+00	6.10E+01
462			3.06E+00	7.85E+01
463			2.25E+00	7.93E+01
464		12:00 PM	4.83E+00	6.81E+01
465			4.09E+00	6.32E+01
466			2.97E+00	7.66E+01

Table 10 – B2M and B2F (2 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
511	Male	10:00 PM	5.64E+01	4.67E+02
512			5.72E+01	3.71E+02
513			3.53E+01	3.44E+02
514		12:00 AM	5.16E+01	4.96E+02
515			6.08E+01	6.84E+02
516			4.66E+01	5.60E+02
511		4:00 AM	7.20E+01	6.16E+02
512			5.50E+01	5.59E+02
513			5.35E+01	4.30E+02
514		6:00 AM	4.21E+01	5.05E+02
515			2.16E+01	5.45E+02
516			3.00E+01	5.21E+02
511		10:00 AM	3.48E+01	6.13E+02
512			4.19E+01	6.34E+02
513			2.71E+01	5.15E+02
514		12:00 PM	1.86E+01	4.60E+02
515			1.50E+01	4.01E+02
516			2.19E+01	4.62E+02
561	Female	10:00 PM	8.44E+01	5.65E+02
562			3.73E+01	4.74E+02
563			6.81E+01	5.19E+02
564		12:00 AM	6.25E+01	4.03E+02
565			3.64E+01	3.70E+02
566			5.31E+01	5.31E+02
561		4:00 AM	5.06E+01	5.45E+02
562			7.20E+01	5.32E+02
563			5.72E+01	5.15E+02
564		6:00 AM	5.04E+01	4.40E+02
565			5.27E+01	4.38E+02
566			6.28E+01	5.56E+02
561		10:00 AM	3.48E+01	3.93E+02
562			4.03E+01	5.77E+02
563			4.65E+01	5.58E+02
564		12:00 PM	3.63E+01	3.40E+02
565			1.37E+01	3.68E+02
566			3.26E+01	5.76E+02

**Table 11 – B8M and B8F (8 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
611	Male	10:00 PM	1.59E+02	1.05E+03
612			1.47E+02	2.12E+03
613			6.12E+01	1.77E+03
614		12:00 AM	1.67E+02	1.98E+03
615			1.70E+02	1.80E+03
616			1.87E+02	2.00E+03
611		4:00 AM	1.63E+02	1.64E+03
612			2.01E+02	2.25E+03
613			1.24E+02	1.47E+03
614		6:00 AM	1.81E+02	2.21E+03
615			1.36E+02	2.23E+03
616			3.25E+01	1.04E+03
611		10:00 AM	6.66E+01	1.57E+03
612			1.00E+02	2.15E+03
613			3.09E+00	6.90E+02
614		12:00 PM	2.81E+01	1.54E+03
615			1.15E+02	2.14E+03
616			1.31E+01	5.55E+02
661	Female	10:00 PM	1.26E+02	2.33E+03
662			1.88E+02	2.14E+03
663			2.42E+02	2.44E+03
664		12:00 AM	1.27E+02	2.02E+03
665			2.15E+02	2.19E+03
666			1.67E+02	2.07E+03
661		4:00 AM	1.41E+02	2.43E+03
662			1.81E+02	2.33E+03
663			1.67E+02	2.34E+03
664		6:00 AM	3.41E+01	1.28E+03
665			1.13E+02	2.17E+03
666			1.50E+02	1.77E+03
661		10:00 AM	8.99E+01	1.74E+03
662			1.73E+02	2.03E+03
663			1.86E+02	2.55E+03
664		12:00 PM	1.25E+02	9.47E+02
665			1.69E+02	2.09E+03
666			1.70E+02	1.88E+03

Table 12 – B20M and B20F (20 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
711	Male	10:00 PM	1.76E+02	2.42E+03
712			2.99E+02	4.27E+03
713			2.81E+02	3.60E+03
714		12:00 AM	2.33E+02	4.12E+03
715			3.33E+02	2.85E+03
716			2.77E+02	3.69E+03
711		4:00 AM	2.44E+02	2.87E+03
712			2.60E+02	3.94E+03
713			Sample Not Received	
714		6:00 AM	2.95E+02*	4.15E+03
715			2.65E+02	2.97E+03
716			3.78E+02	3.88E+03
711		10:00 AM	1.76E+02	3.04E+03
712			3.06E+02	3.61E+03
713			Sample Not Received	
714		12:00 PM	2.15E+00*	4.33E+03
715			2.77E+02	2.85E+03
716			2.26E+02	3.70E+03
761	Female	10:00 PM	2.28E+02	2.57E+03
762			2.63E+02	4.09E+03
763			2.16E+02	3.88E+03
764		12:00 AM	4.05E+02	3.14E+03
765			2.58E+02	2.81E+03
766			3.72E+02	3.50E+03
761		4:00 AM	2.36E+02	2.02E+03
762			2.07E+02	2.83E+03
763			2.79E+02	3.20E+03
764		6:00 AM	3.25E+02	3.01E+03
765			2.81E+02	2.56E+03
766			3.24E+02	2.96E+03
761		10:00 AM	2.31E+02	2.07E+03
762			2.12E+02	2.37E+03
763			2.66E+02	3.22E+03
764		12:00 PM	2.90E+02	3.19E+03
765			3.24E+02	2.90E+03
766			3.27E+02	2.93E+03

\* Average of two results.

Table 13 – E0.2M and E0.2F (0.2 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
911	Male	10:00 PM	5.26E+00	4.86E+01
912			4.67E+00	3.73E+01
913			4.37E+00	3.69E+01
914		12:00 AM	4.67E+00	4.94E+01
915			5.82E+00	4.51E+01
916			6.46E+00	5.26E+01
911		4:00 AM	4.62E+00	4.61E+01
912			3.09E+00	3.48E+01
913			5.46E+00	4.76E+01
914		6:00 AM	3.96E+00	5.51E+01
915			4.93E+00	4.68E+01
916			5.84E+00	5.11E+01
911		10:00 AM	BLOQ	3.36E+01
912			1.48E+00	4.06E+01
913			2.68E+00	3.31E+01
914		12:00 PM	BLOQ	3.44E+01
915			3.38E+00	3.82E+01
916			1.96E+00	4.43E+01
961	Female	10:00 PM	4.99E+00	3.81E+01
962			3.92E+00	5.05E+01
963			5.34E+00	4.54E+01
964		12:00 AM	4.05E+00	3.74E+01
965			4.63E+00	4.63E+01
966			4.43E+00	5.32E+01
961		4:00 AM	4.27E+00	5.15E+01
962			4.05E+00	5.15E+01
963			4.89E+00	4.01E+01
964		6:00 AM	4.55E+00	6.06E+01
965			5.40E+00	7.51E+01
966			3.55E+00	4.89E+01
961		10:00 AM	2.16E+00	4.74E+01
962			2.67E+00	4.77E+01
963			2.48E+00	4.27E+01
964		12:00 PM	3.64E+00	5.63E+01
965			4.45E+00	5.41E+01
966			5.32E+00	5.36E+01

Table 14 – E2M and E2F (2 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
1011	Male	10:00 PM	4.06E+01	4.20E+02
1012			5.48E+01	4.65E+02
1013			5.62E+01	4.34E+02
1014		12:00 AM	5.32E+01	4.35E+02
1015			7.51E+01	5.11E+02
1016			8.29E+01	4.86E+02
1011		4:00 AM	5.16E+01	4.15E+02
1012			6.60E+01	5.37E+02
1013			2.40E+01	2.75E+02
1014		6:00 AM	4.08E+01	5.35E+02
1015			5.63E+01	5.24E+02
1016			5.55E+01	4.91E+02
1011		10:00 AM	1.85E+01	4.43E+02
1012			2.01E+01	4.80E+02
1013			4.35E+00	1.27E+02
1014		12:00 PM	3.01E+01	4.92E+02
1015			3.21E+01	5.29E+02
1016			2.80E+01	3.98E+02
1061	Female	10:00 PM	6.53E+01	6.37E+02
1062			1.18E+02	6.54E+02
1063			6.16E+01	5.02E+02
1064		12:00 AM	1.35E+02	7.33E+02
1065			8.56E+01	7.75E+02
1066			7.63E+01	5.87E+02
1061		4:00 AM	4.29E+01	6.11E+02
1062			7.42E+01	7.71E+02
1063			6.58E+01	7.11E+02
1064		6:00 AM	8.63E+01	9.55E+02
1065			6.45E+01	6.08E+02
1066			6.88E+01	5.04E+02
1061		10:00 AM	4.03E+01	6.16E+02
1062			6.03E+01	8.04E+02
1063			5.64E+01	7.08E+02
1064		12:00 PM	4.46E+01	5.35E+02
1065			2.86E+01	6.17E+02
1066			5.22E+00	4.08E+02

Table 15 – E8M and E8F (8 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
1111	Male	10:00 PM	1.48E+02	1.58E+03
1112			1.43E+02	1.22E+03
1113			1.62E+02	1.97E+03
1114		12:00 AM	1.44E+02	1.39E+03
1115			1.83E+02	1.84E+03
1116			1.67E+02	1.58E+03
1111		4:00 AM	1.25E+02	2.16E+03
1112			1.55E+02	1.82E+03
1113			Sample Not Received	
1114		6:00 AM	1.97E+02	1.65E+03
1115			9.70E+01	1.16E+03
1116			2.20E+02	1.86E+03
1111		10:00 AM	1.12E+02	2.16E+03
1112			1.45E+02	2.08E+03
1113			Sample Not Received	
1114		12:00 PM	1.03E+02	1.56E+03
1115			8.63E+01	1.13E+03
1116			1.55E+02	2.03E+03
1161	Female	10:00 PM	1.57E+02	2.07E+03
1162			1.62E+02	1.69E+03
1163			1.94E+02	2.14E+03
1164		12:00 AM	1.49E+02	1.60E+03
1165			1.86E+02	2.73E+03
1166			1.92E+02	1.66E+03
1161		4:00 AM	1.36E+02	1.77E+03
1162			1.03E+02	1.48E+03
1163			2.01E+02	2.12E+03
1164		6:00 AM	1.89E+02	1.58E+03
1165			9.25E+01	2.41E+03
1166			1.25E+02	1.77E+03
1161		10:00 AM	1.36E+02	2.03E+03
1162			1.36E+02	1.16E+03
1163			1.37E+02	1.84E+03
1164		12:00 PM	1.42E+02	1.61E+03
1165			1.55E+02	1.89E+03
1166			7.58E+01	1.38E+03

Table 16 – E20M and E20F (20 mg/kg/day) Results

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
1211	Male	10:00 PM	3.25E+02	2.73E+03
1212			2.75E+02	3.34E+03
1213			2.62E+02	3.00E+03
1214		12:00 AM	3.15E+02	3.23E+03
1215			3.22E+02	3.11E+03
1216			2.60E+02	3.02E+03
1211		4:00 AM	2.26E+02	3.42E+03
1212			2.97E+02	3.78E+03
1213			2.92E+02	2.76E+03
1214		6:00 AM	3.06E+02	3.27E+03
1215			2.61E+02	2.96E+03
1216			2.60E+02	3.47E+03
1211		10:00 AM	1.21E+02	3.11E+03
1212			8.06E+01	2.90E+03
1213			2.73E+02	2.97E+03
1214		12:00 PM	2.43E+02	2.75E+03
1215			3.22E+02	3.16E+03
1216			1.29E+02	3.50E+03
1261	Female	10:00 PM	4.09E+02	2.86E+03
1262			3.36E+02	3.40E+03
1263			3.55E+02	3.56E+03
1264		12:00 AM	3.56E+02	3.80E+03
1265			3.71E+02	3.69E+03
1266			2.00E+02	3.60E+03
1261		4:00 AM	ALOQ <sup>1,3</sup>	3.19E+03
1262			ALOQ <sup>2,3</sup>	3.10E+03
1263			7.89E+01	2.42E+03
1264		6:00 AM	2.55E+02	3.65E+03
1265			2.30E+02	3.09E+03
1266			2.62E+02	3.86E+03
1261		10:00 AM	2.56E+02	3.34E+03
1262			3.68E+02	2.86E+03
1263			3.06E+02	2.11E+03
1264		12:00 PM	2.77E+02	3.16E+03
1265			2.36E+02	2.69E+03
1266			2.55E+02	3.39E+03

1. The extrapolated corrected concentration was 4.00E+02 ng/mL.

2. The extrapolated corrected concentration was 4.23E+02 ng/mL.

3. Samples mistakenly not reanalyzed. No adverse impact on data.

**Table 17 – NT20M and NT20F (20 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
211	Male	12:00 AM	2.10E+02	2.82E+03
212			2.33E+02	1.99E+03
213			2.57E+02	3.57E+03
214			2.53E+02	3.39E+03
215			4.19E+02	3.68E+03
261	Female	12:00 AM	3.46E+02	4.23E+03
262			3.03E+02	3.59E+03
263			3.63E+02	4.17E+03
264			2.74E+02	2.86E+03
265			3.08E+02	3.27E+03

**Table 18 – B0.2M and B0.2F (0.2 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
411	Male	12:00 AM	6.80E+00	6.60E+01
412			5.00E+00	5.30E+01
413			5.50E+00	4.30E+01
414			5.60E+00	4.70E+01
415			4.70E+00	4.30E+01
461	Female	12:00 AM	6.80E+00	4.80E+01
462			7.20E+00	6.10E+01
463			2.80E+00	4.30E+01
464			3.60E+00	5.10E+01
465			6.50E+00	5.90E+01

**Table 19 – B2M and B2F (2 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
511	Male	12:00 AM	4.93E+01	5.76E+02
512			5.08E+01	5.23E+02
513			2.86E+01	4.12E+02
514			4.89E+01	4.50E+02
515			4.22E+01	4.96E+02
561	Female	12:00 AM	4.56E+01	4.49E+02
562			6.37E+01	7.03E+02
563			2.16E+01	4.08E+02
564			1.59E+01	2.64E+02
565			6.51E+01	5.44E+02

**Table 20 – B8M and B8F (8 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
611	Male	12:00 AM	1.70E+02	1.40E+03
612			1.50E+02	1.34E+03
613			1.64E+02	1.16E+03
614			1.47E+02	2.14E+03
615			2.56E+02	1.99E+03
661	Female	12:00 AM	2.59E+02	1.92E+03
662			1.48E+02	1.79E+03
663			2.27E+02	2.18E+03
664			1.68E+02	1.30E+03
665			1.33E+02	1.99E+03

**Table 21 – B20M and B20F (20 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
711	Male	12:00 AM	2.63E+02	2.40E+03
712			3.85E+02	4.12E+03
714			3.01E+02	3.72E+03
715			3.38E+02	4.05E+03
716			3.32E+02	4.39E+03
761	Female	12:00 AM	2.48E+02	3.10E+03
762			3.17E+02	4.86E+03
763			4.82E+02	4.98E+03
764			2.88E+02	4.30E+03
765			5.72E+02	5.06E+03

**Table 22 – E0.2M and E0.2F (0.2 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
911	Male	12:00 AM	8.00E+00	4.80E+01
912			4.60E+00	4.50E+01
913			4.70E+00	4.50E+01
914			5.10E+00	5.10E+01
915			5.90E+00	4.90E+01
961	Female	12:00 AM	4.90E+00	5.70E+01
962			4.40E+00	4.80E+01
963			4.80E+00	4.40E+01
964			2.30E+00	4.00E+01
965			1.60E+00	4.60E+01

**Table 23 – E2M and E2F (2 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
1011	Male	12:00 AM	5.72E+01	5.81E+02
1012			5.68E+01	5.57E+02
1013			7.17E+01	5.78E+02
1014			5.50E+00	3.03E+02
1015			4.34E+01	6.04E+02
1061	Female	12:00 AM	6.63E+01	6.70E+02
1062			1.30E+02	7.28E+02
1063			1.29E+02	9.94E+02
1064			2.22E+01	3.92E+02
1065			8.58E+01	6.96E+02

**Table 24 – E8M and E8F (8 mg/kg/day) Results**

<b>Animal ID</b>	<b>Sex</b>	<b>Target Time Point</b>	<b>Nicotine Concentration (ng/mL)</b>	<b>Cotinine Concentration (ng/mL)</b>
1111	Male	12:00 AM	1.81E+02	1.69E+03
1112			1.44E+02	1.26E+03
1114			1.62E+02	1.30E+03
1115			1.60E+02	2.04E+03
1116			2.19E+02	1.96E+03
1161	Female	12:00 AM	1.11E+02	1.31E+03
1162			1.27E+02	1.45E+03
1163			1.53E+02	2.32E+03
1164			1.24E+02	2.07E+03
1165			4.20E+01	1.41E+03

**Table 25 – E20M and E20F (20 mg/kg/day) Results**

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
1211	Male	12:00 AM	2.08E+02	3.26E+03
1212			2.64E+02	2.58E+03
1213			2.37E+02	2.85E+03
1214			3.26E+02	2.77E+03
1215			3.03E+02	2.56E+03
1261	Female	12:00 AM	4.28E+02	3.67E+03
1262			2.89E+02	2.99E+03
1263			3.15E+02	3.47E+03
1264			4.02E+02	4.16E+03
1265			2.23E+02	2.90E+03

**Table 26 – Sentinels (0 mg/kg/day) Results**

Animal ID	Sex	Target Time Point	Nicotine Concentration (ng/mL)	Cotinine Concentration (ng/mL)
1406	Male	12:00 AM	BLOQ	BLOQ
1407			BLOQ	BLOQ
1408			BLOQ	BLOQ
1409			BLOQ	BLOQ
1410			BLOQ	BLOQ
1456	Female	12:00 AM	BLOQ	BLOQ
1457			BLOQ	BLOQ
1458			BLOQ	BLOQ
1459			BLOQ	BLOQ
1460			BLOQ	BLOQ

## V. KINETICS

### A. METHODS/RESULTS

The test system used was the male and female Wistar Han rats. For TK evaluation, animals received oral administration of nicotine tartrate, tobacco blend, or tobacco extract for at least 28 consecutive days at nicotine target doses of 20 mg/kg/day for nicotine tartrate, 0.2, 2, 8, and 20 mg/kg/day for tobacco blend and tobacco extract. Blood samples were collected from three rats/sex/group on Days 13 and 14 at target times of 10:00 PM, 12:00 AM, 4:00 AM, 6:00 AM, 10:00 AM, and 12:00 PM. Based on the Days 13 and 14 concentration time profiles, a single sampling time point was selected on Day 28 to be at 12:00 AM. Several of the animals on Day 28 did not have samples collected within the target time criteria of 12:00 AM. However, the samples taken outside the criteria were believed to be sufficiently close to be used in the analysis. TK analysis was performed using the target dose (mg/kg), target sample collection time (clock time), and the measured concentrations of nicotine and cotinine (ng/mL).

Figure 7 through Figure 17 show the group mean plasma concentration-time profiles for male and female rats on Days 13 and 14. Figure 18 and Figure 19 represent the group mean plasma concentration-time overlay profiles for male and female rats on Days 13 and 14. Observed  $T_{max}$  values were varied and often with no discernable peak concentration, i.e., multiple potential times to reach  $C_{max}$ . For nicotine, seven of the nine male dose groups and four of the nine female dose groups had 12:00 AM as the  $T_{max}$  or one of multiple possible  $T_{max}$  values. For cotinine, six of the nine male dose groups and four of the nine female dose groups had 12:00 AM as the  $T_{max}$  or one of multiple possible  $T_{max}$  values (Table 27).

**Table 27 – Summary of Peak Concentration Time Points**

Group	Dosage (mg/kg/day)	Analyte	Sex	Time Point(s)
NT20	20	Nicotine	M	10:00 PM; 12:00 AM; 4:00 AM; 6:00 AM; 12:00 PM <sup>a</sup>
			F	12:00 AM
		Cotinine	M	All Time Points <sup>a</sup>
			F	12:00 AM
B0.2	0.2	Nicotine	M	12:00 AM
			F	10:00 PM
		Cotinine	M	4:00 AM; 6:00 AM <sup>a</sup>
			F	10:00 AM
B2	2	Nicotine	M	4:00 AM
			F	10:00 PM
		Cotinine	M	12:00 AM; 10:00 AM <sup>a</sup>
			F	10:00 PM; 4:00 AM; 10:00 AM <sup>a</sup>
B8	8	Nicotine	M	12:00 AM
			F	10:00 PM
		Cotinine	M	12:00 AM
			F	10:00 PM; 4:00 AM <sup>a</sup>
B20	20	Nicotine	M	6:00 AM
			F	12:00 AM
		Cotinine	M	All Time Points <sup>a</sup>
			F	10:00 PM
E0.2	0.2	Nicotine	M	12:00 AM
			F	10:00 PM
		Cotinine	M	12:00 AM; 6:00 AM <sup>a</sup>
			F	6:00 AM
E2	2	Nicotine	M	12:00 AM
			F	12:00 AM
		Cotinine	M	12:00 AM; 6:00 AM <sup>a</sup>
			F	12:00 AM; 4:00 AM; 6:00 AM; 10:00 AM <sup>a</sup>

**Table 27 – Summary of Peak Concentration Time Points (Continued)**

Group	Dosage (mg/kg/day)	Analyte	Sex	Time Point(s)
E8	8	Nicotine	M	12:00 AM; 6:00 AM <sup>a</sup>
			F	10:00 PM; 12:00 AM <sup>a</sup>
		Cotinine	M	4:00 AM; 10:00 AM <sup>a</sup>
			F	10:00 PM; 12:00 AM; 6:00 AM <sup>a</sup>
E20	20	Nicotine	M	10:00 PM; 12:00 AM <sup>a</sup>
			F	10:00 PM
		Cotinine	M	4:00 AM; 6:00 AM; 12:00 AM; 12:00 PM <sup>a</sup>
			F	12:00 AM; 6:00 AM <sup>a</sup>

a. Variability allows more than one time point to be considered.

Group mean  $C_{max}$  values determined at 12:00 AM on Day 28 are reported in Table 28. Both the tobacco blend and tobacco extract had increasing  $C_{max}$  values for nicotine and cotinine with increasing dose. Male and female rats had similar  $C_{max}$  values (within two-fold) for all dose groups for both nicotine and cotinine. The tobacco blend and tobacco extract groups had mean  $C_{max}$  values that were similar when comparing the same dose (approximately within two-fold). Cotinine  $C_{max}$  values were between eight- to 15-fold greater than nicotine for the males and females (Figure 20 and Figure 21).

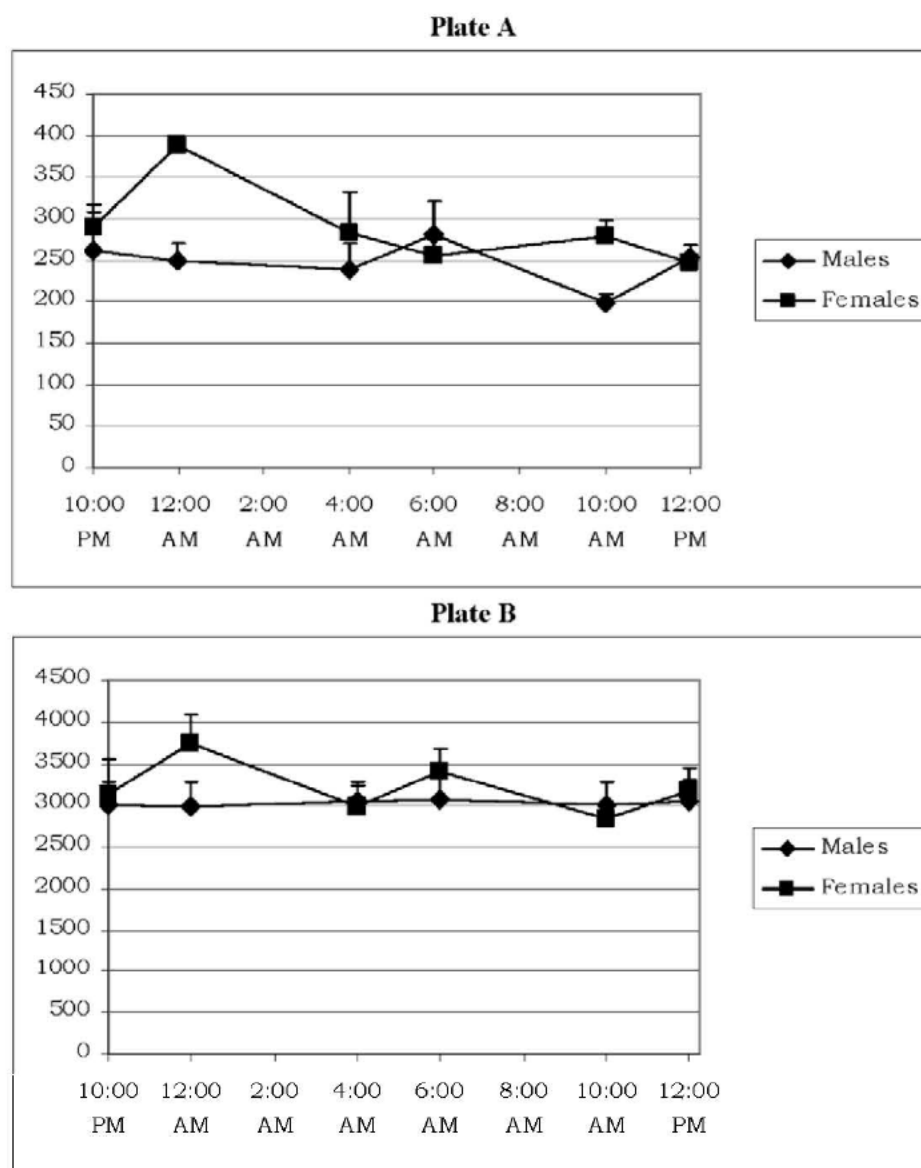
**Table 28 – Day 28  $C_{max}$  Values**

Group	Gender	Nicotine $C_{max}$ (ng/mL)	Cotinine $C_{max}$ (ng/mL)
NT20	Male	274 ± 37	3090 ± 310
	Female	319 ± 16	3620 ± 260
B0.2	Male	5.52 ± 0.36	50.4 ± 4.3
	Female	5.38 ± 0.91	52.4 ± 3.4
B2	Male	44.0 ± 4.1	491 ± 28
	Female	42.4 ± 10.3	474 ± 73
B8	Male	177 ± 20	1610 ± 190
	Female	187 ± 24	1840 ± 150
B20	Male	324 ± 20	3740 ± 350
	Female	381 ± 62	4460 ± 370
E0.2	Male	5.66 ± 0.63	47.6 ± 1.2
	Female	3.60 ± 0.69	47.0 ± 2.8
E2	Male	46.9 ± 11.3	525 ± 56
	Female	86.7 ± 20.3	696 ± 96
E8	Male	173 ± 13	1650 ± 160
	Female	111 ± 19	1710 ± 200
E20	Male	268 ± 21	2800 ± 130
	Female	331 ± 38	3440 ± 230

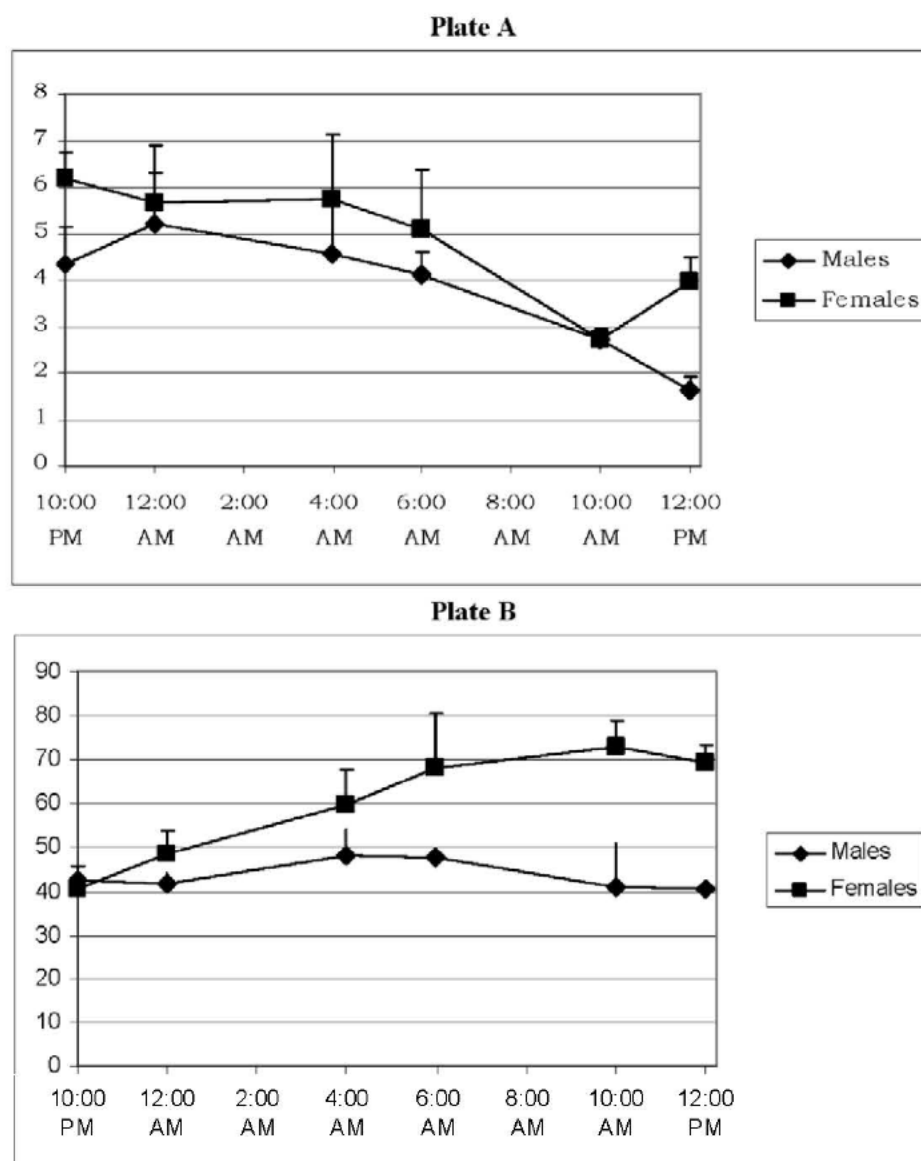
**B. CONCLUSIONS**

$T_{max}$  was determined by selecting the most common Day 14  $T_{max}$  among male and females rats of all dose groups. The variability of the eating habits of the rats led to increased variability in the group mean  $C_{max}$  determinations resulting in many dose groups with multiple time points that could be considered as potential  $T_{max}$  values. The time of 12:00 AM was chosen as it occurred with the highest frequency among the dose groups, both male and female. Among dose groups that had only one discernable  $T_{max}$ , 12:00 AM again occurred with the highest frequency.

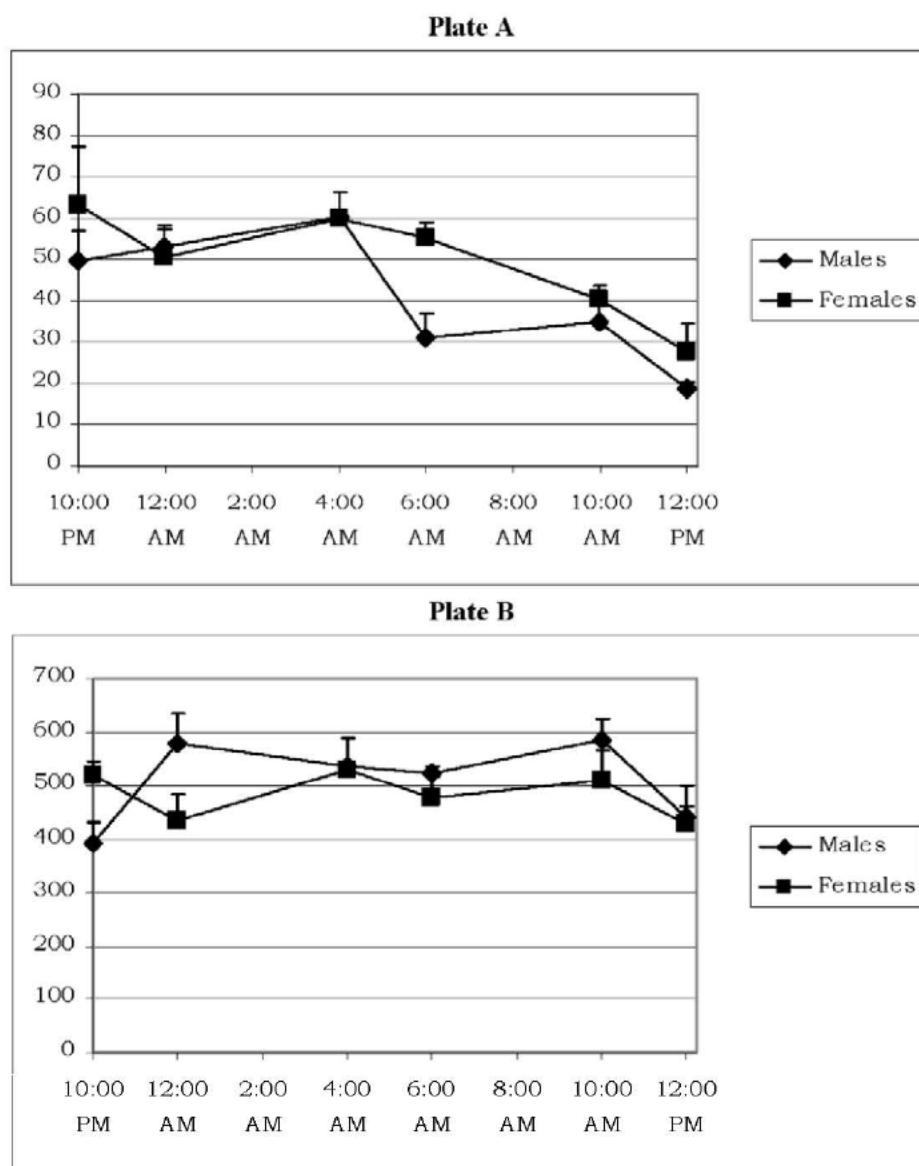
Evaluation of  $C_{max}$  values on Day 28 showed no gender effects as values were similar between the genders for all dose groups for nicotine and cotinine. There were no formulation effects as tobacco extract and tobacco blend with the same nicotine target dosages had similar  $C_{max}$  values for both males and females. The  $C_{max}$  values increased proportionally with an increase in dose for both the tobacco extract and tobacco blend except for the E2F, which was about two-fold higher than expected. However, this was not considered biologically relevant as the  $C_{max}$  values for the E8F and E20F both increased proportionally when compared with the E0.2F.



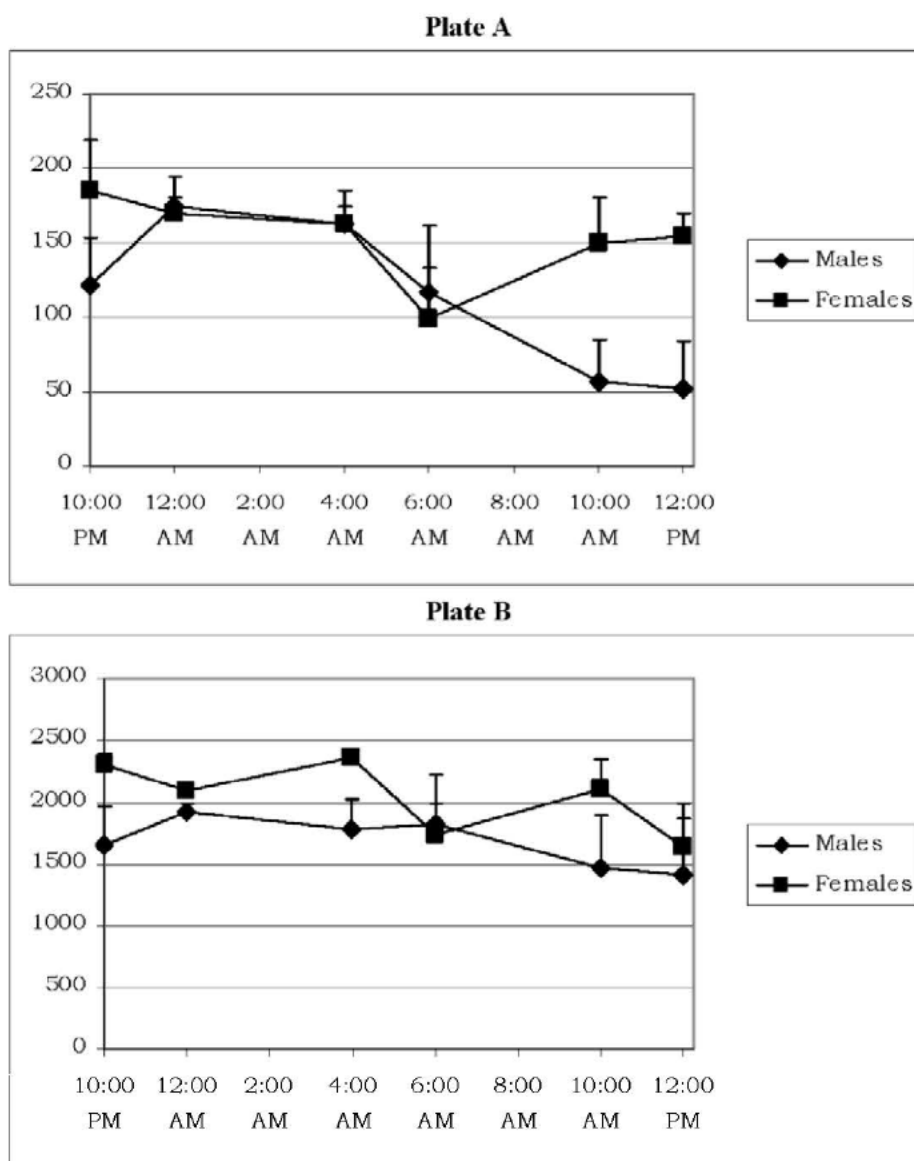
**Figure 7 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Nicotine Hydrogen Tartrate (20 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



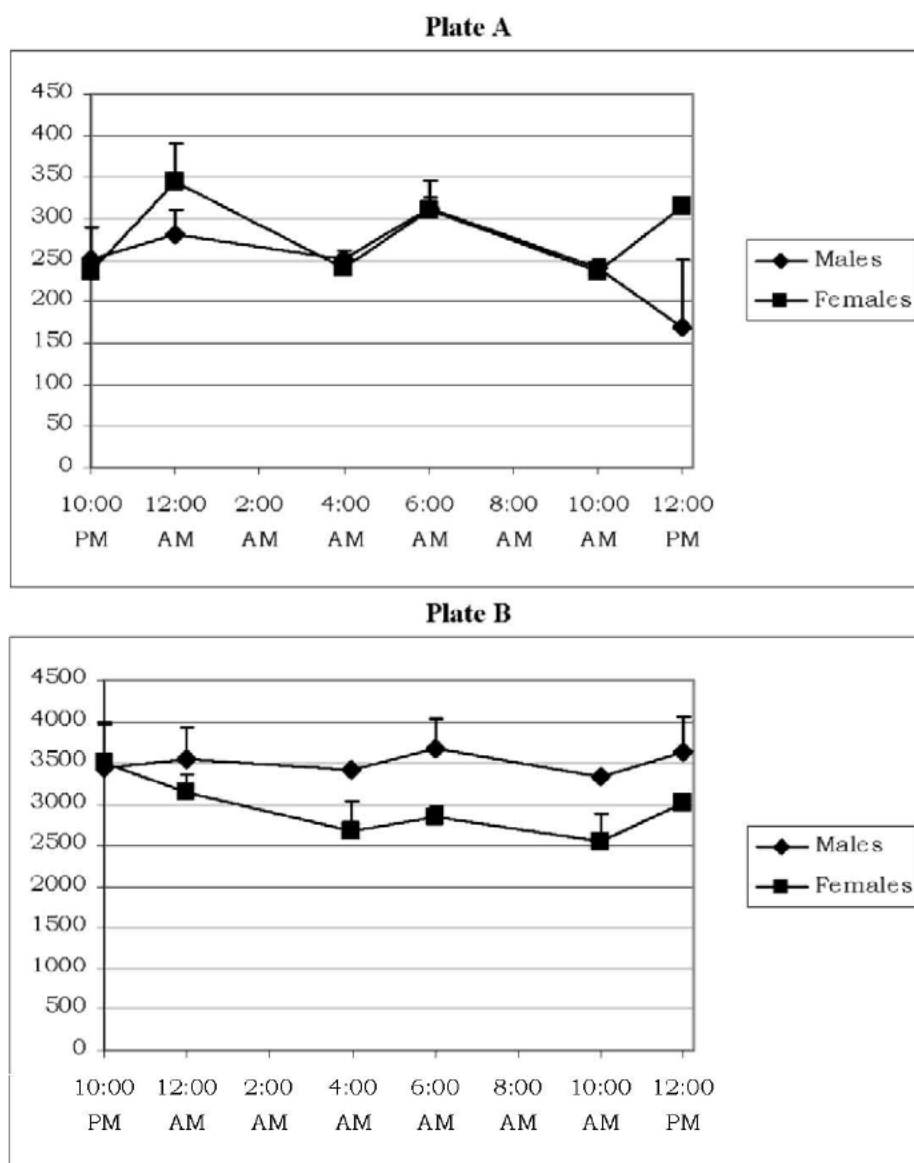
**Figure 8 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Blend (0.2 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



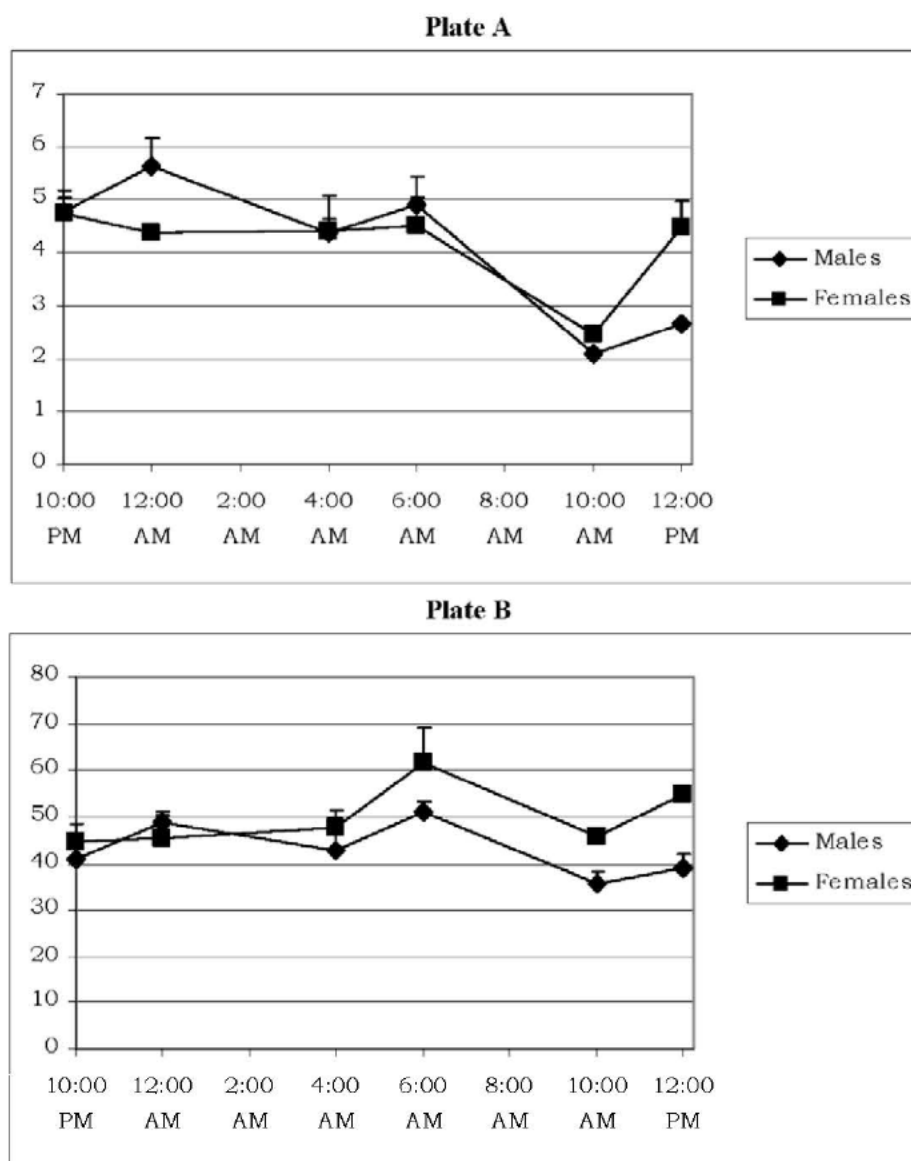
**Figure 9 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Blend (2 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



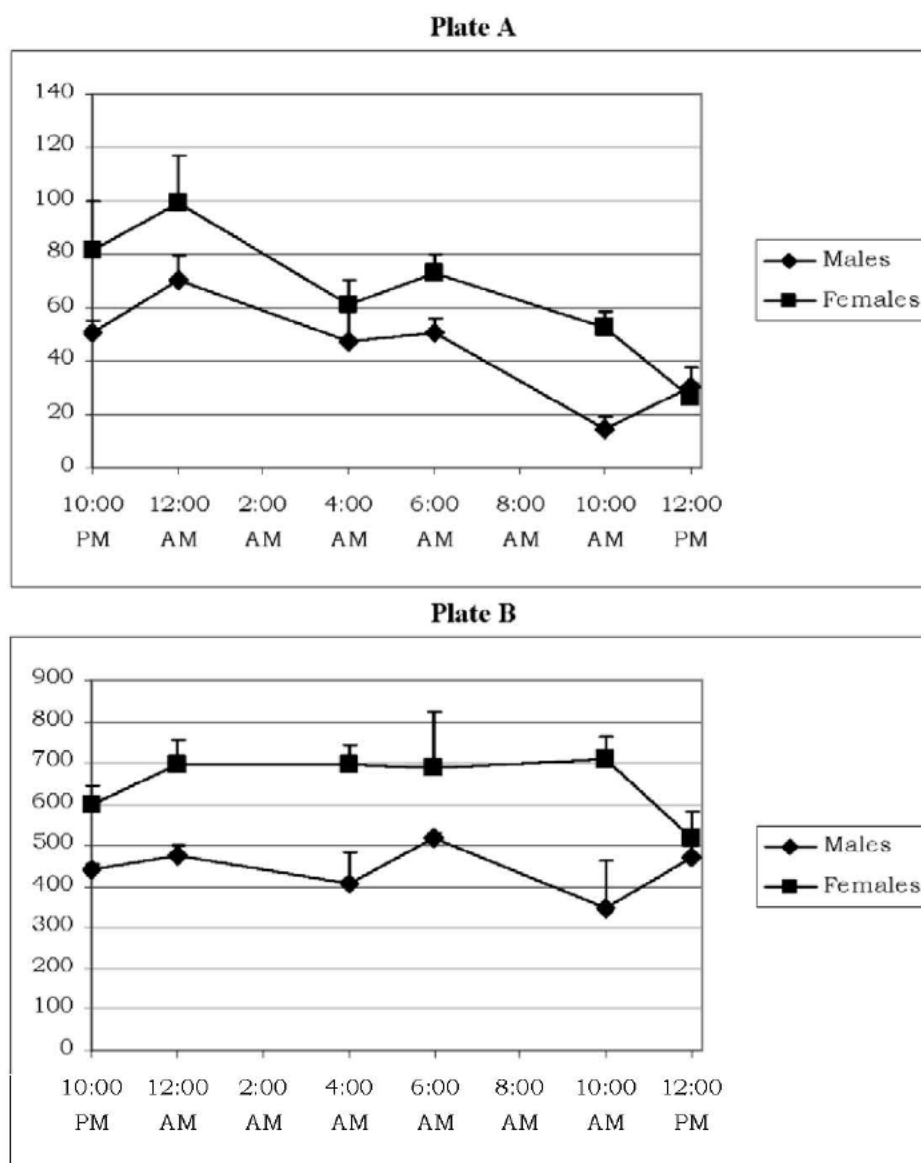
**Figure 10 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Blend (8 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



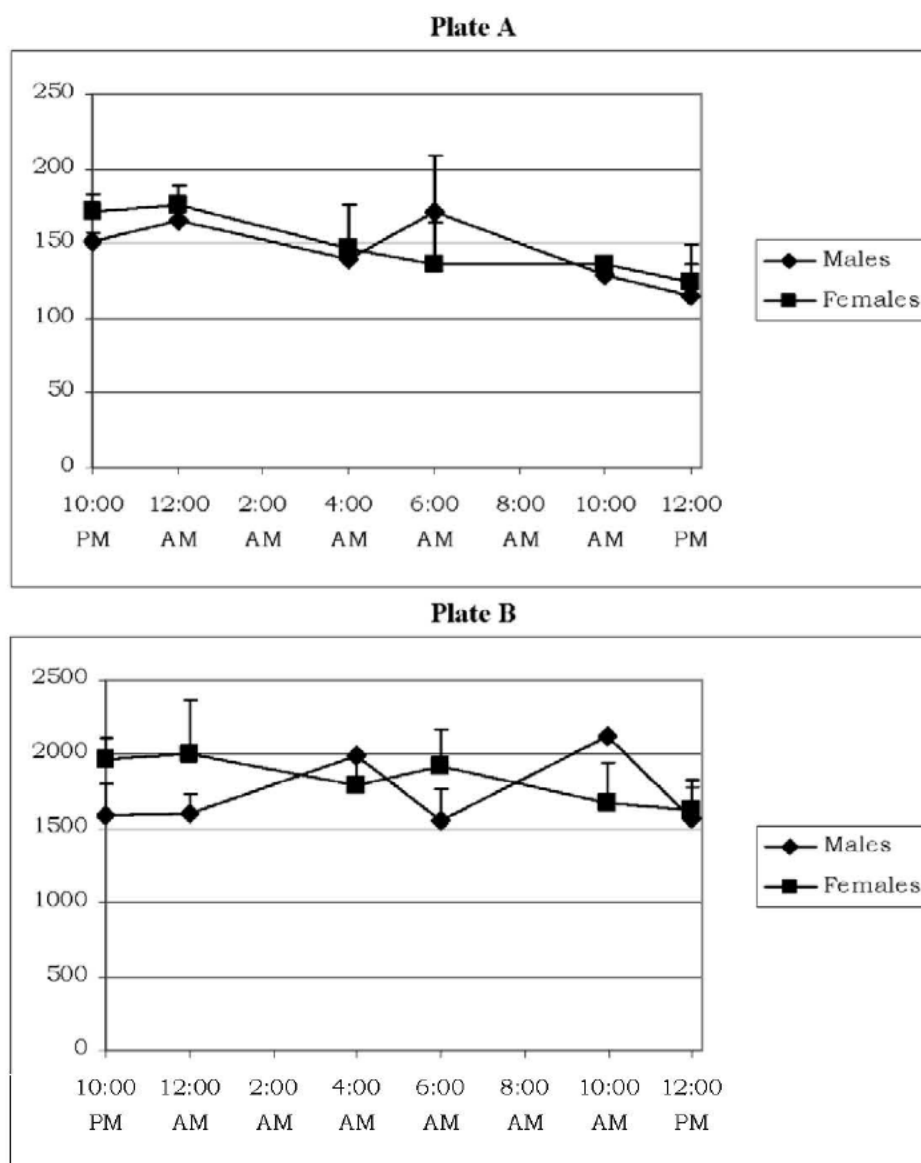
**Figure 11 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Blend (20 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



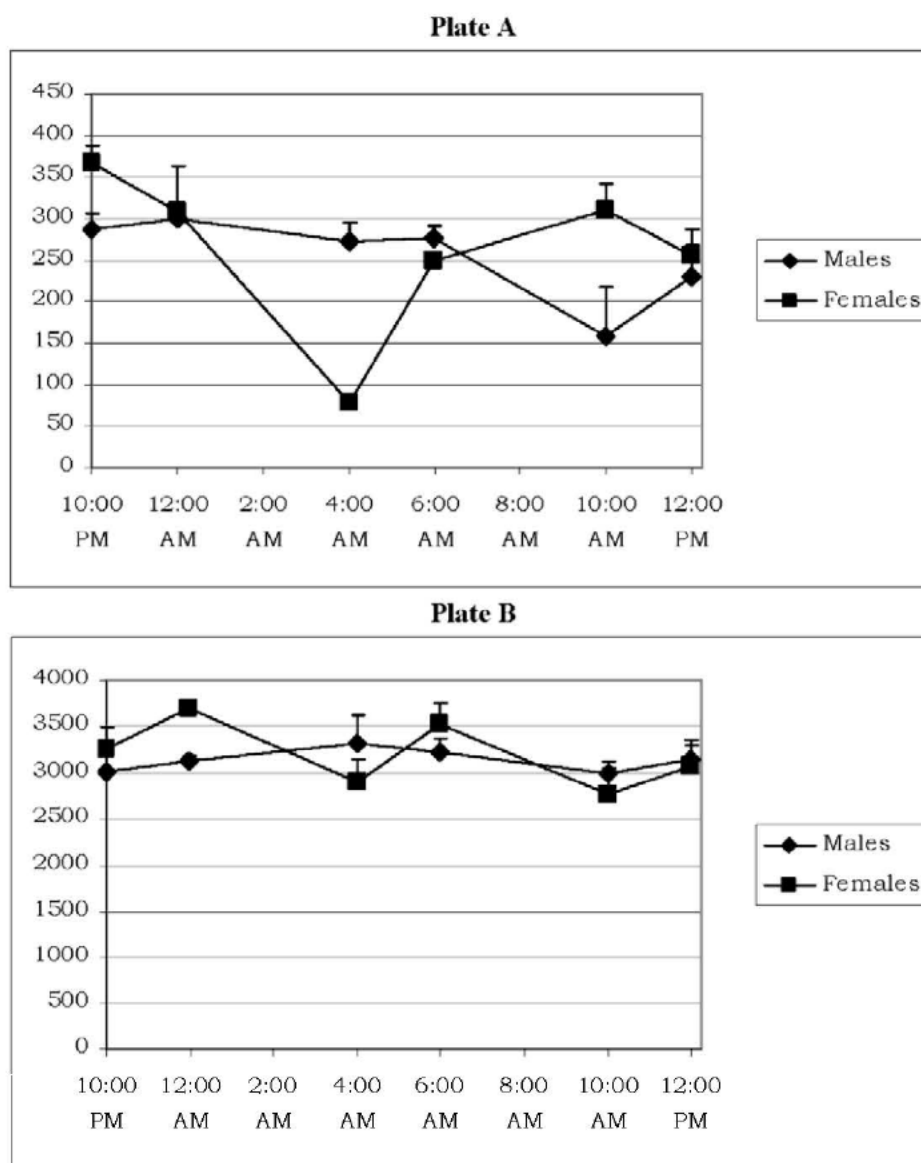
**Figure 12 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Extract (0.2 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



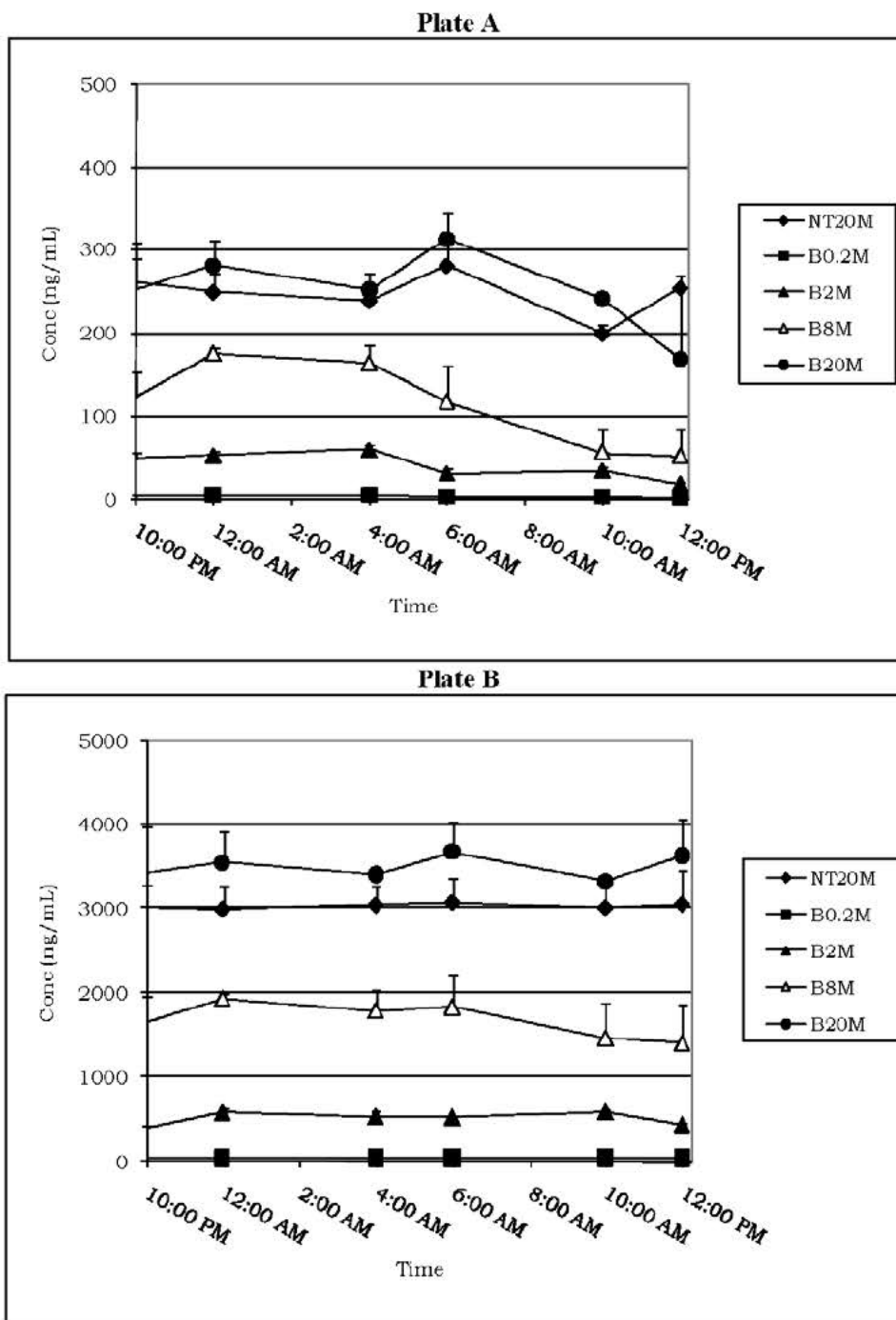
**Figure 13 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Extract (2 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



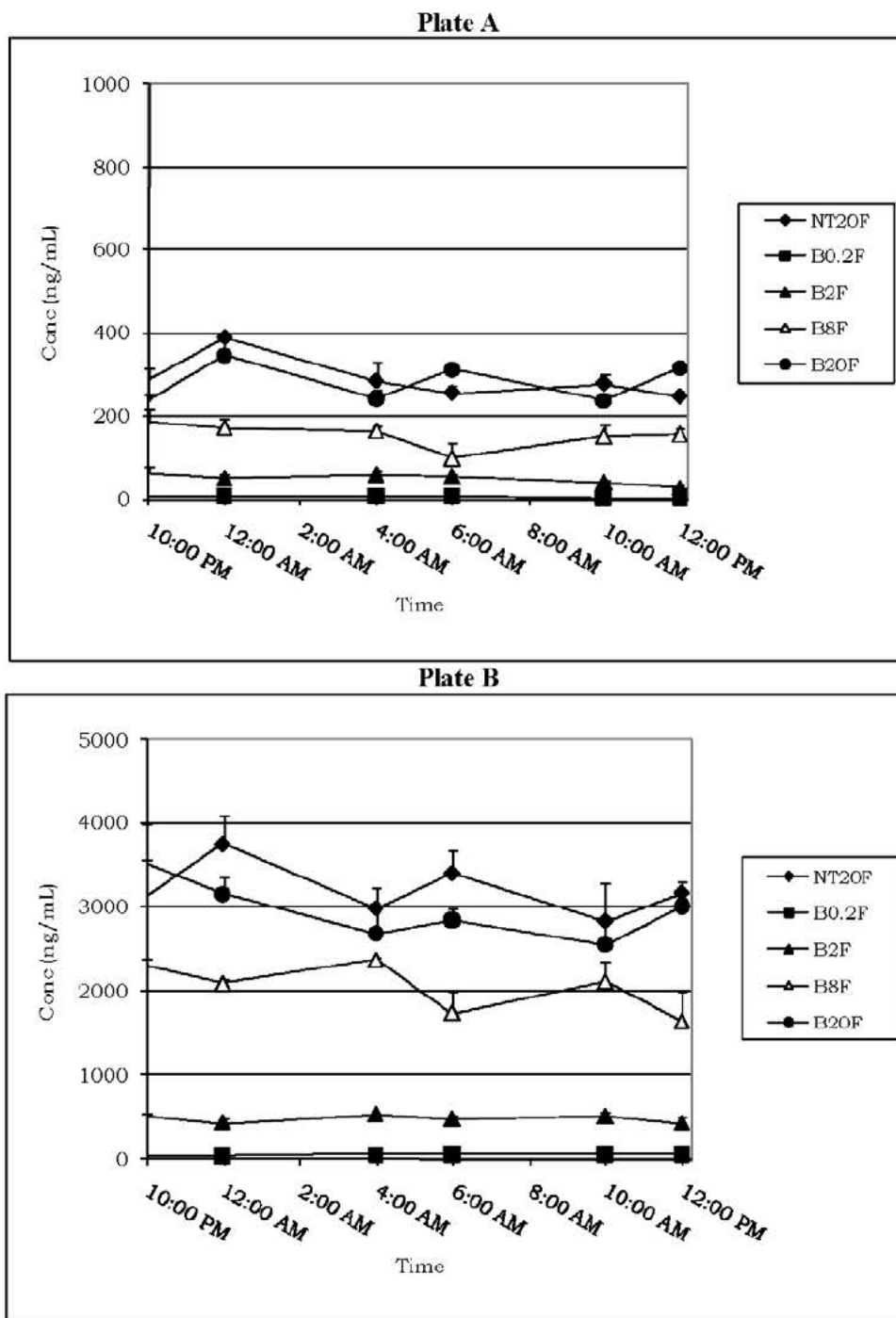
**Figure 14 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Extract (8 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**



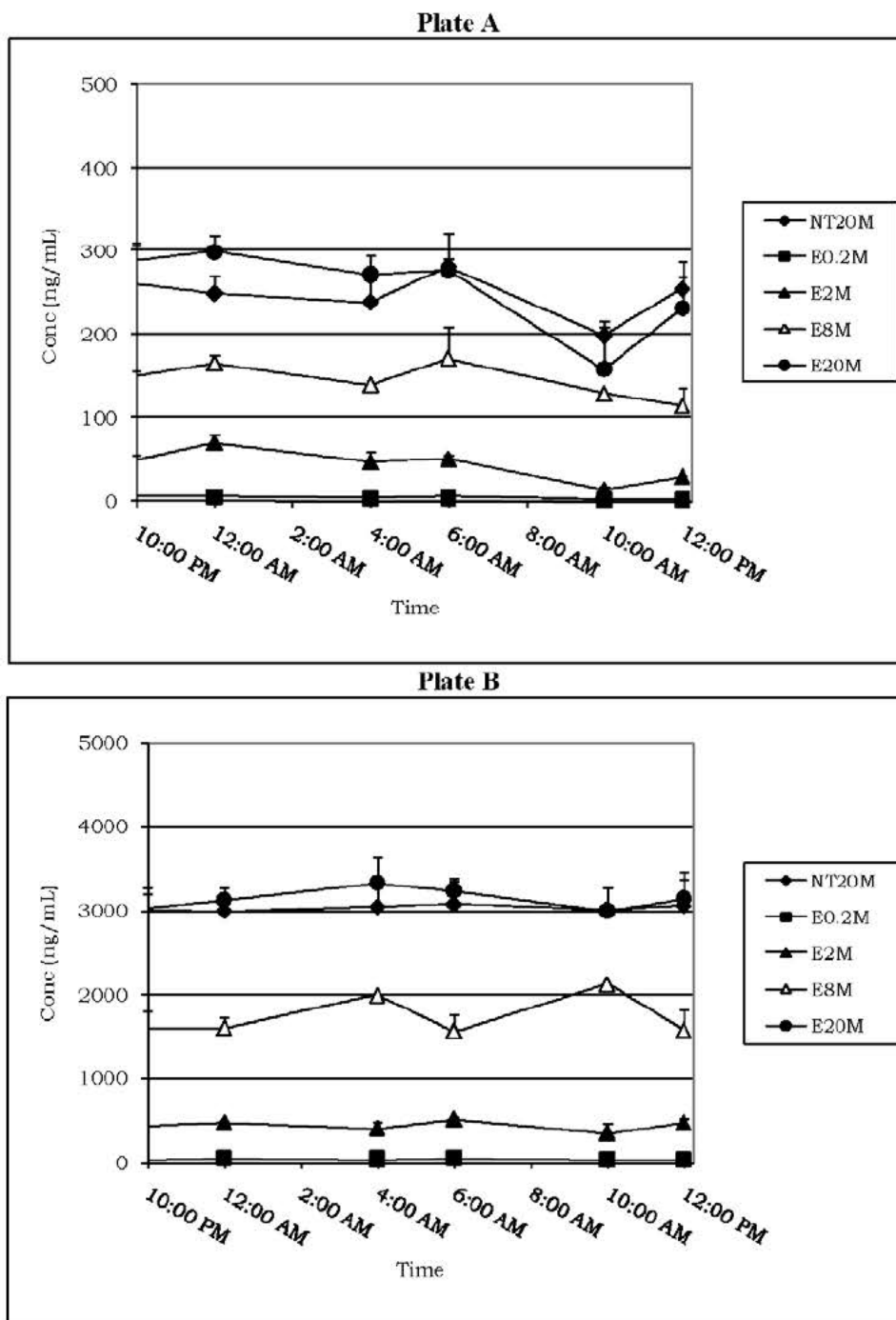
**Figure 15 – Plasma Concentration (ng/mL, Mean + SEM)-Time Profile for Male and Female Rats on Days 13 and 14 After Daily Oral Exposure of Tobacco Extract (20 mg/kg) – Nicotine (Plate A) and Cotinine (Plate B)**

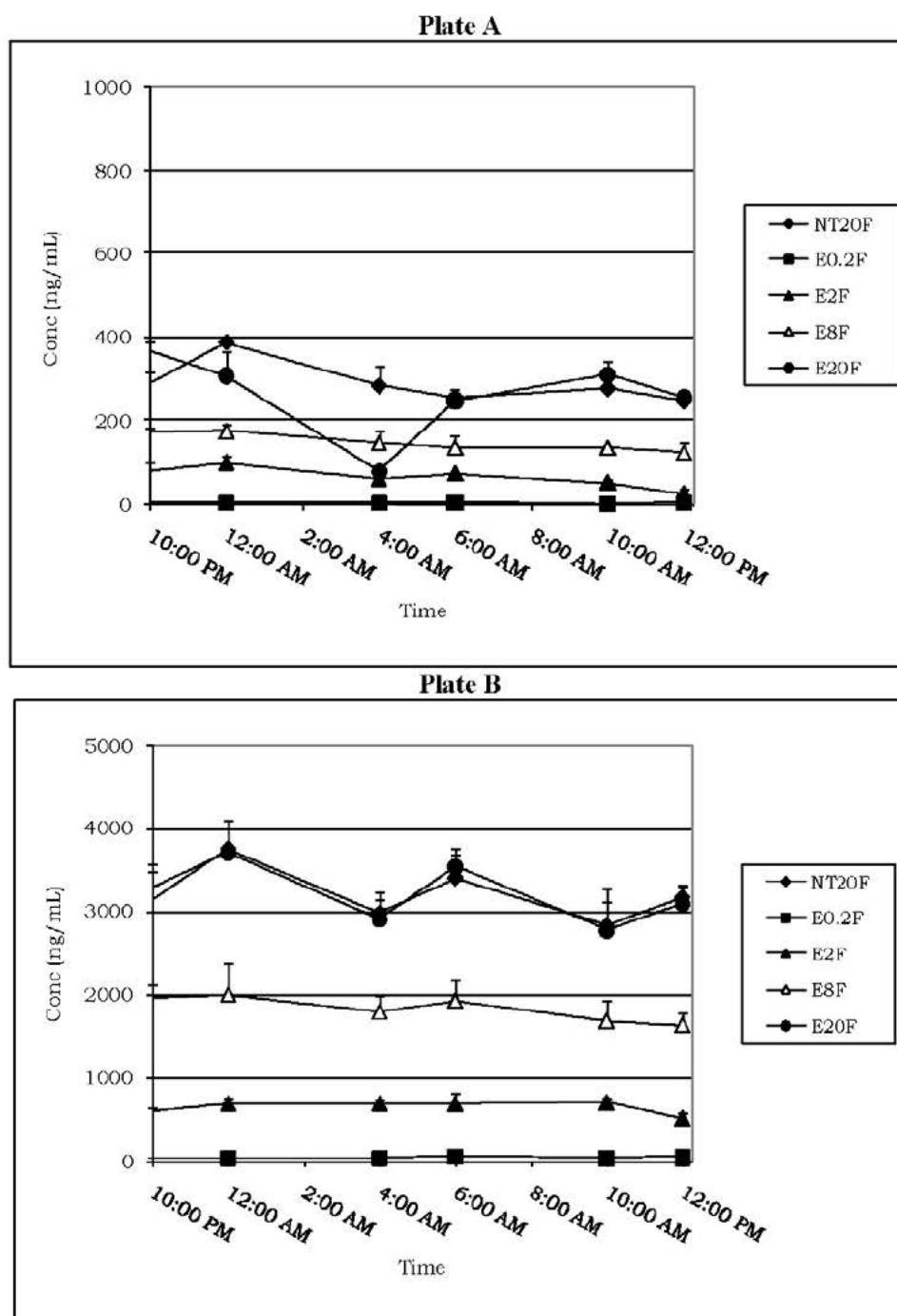


**Figure 16 – Plasma Concentration (Mean + SEM)-Time Profiles for Male Rats on Days 13 and 14 After Daily Oral Exposure of Nicotine Hydrogen Tartrate or Tobacco Blend – Nicotine (Plate A) and Cotinine (Plate B)**

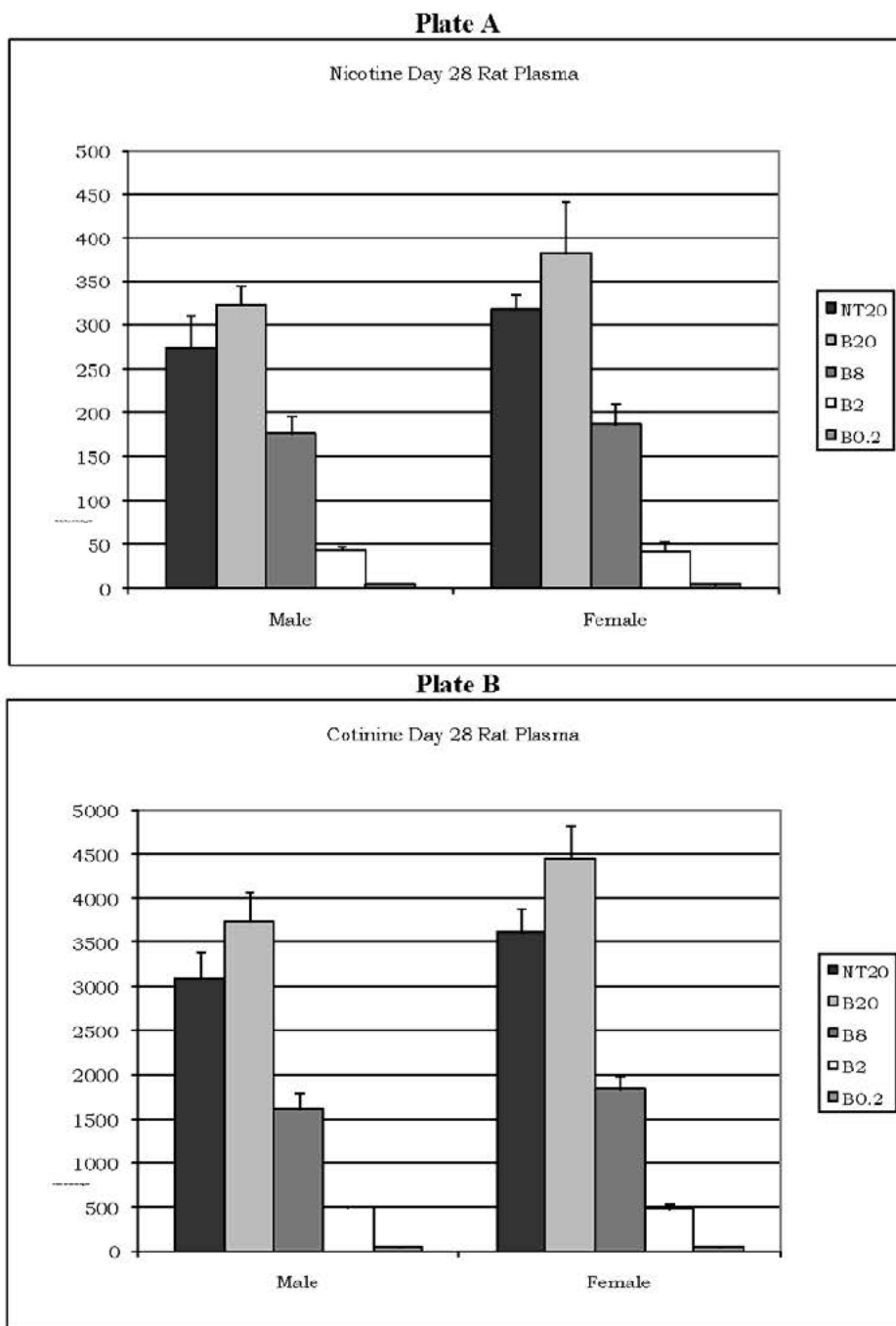


**Figure 17 – Plasma Concentration (Mean + SEM)-Time Profiles for Female Rats on Days 13 and 14 After Daily Oral Exposure of Nicotine Hydrogen Tartrate or Tobacco Blend – Nicotine (Plate A) and Cotinine (Plate B)**

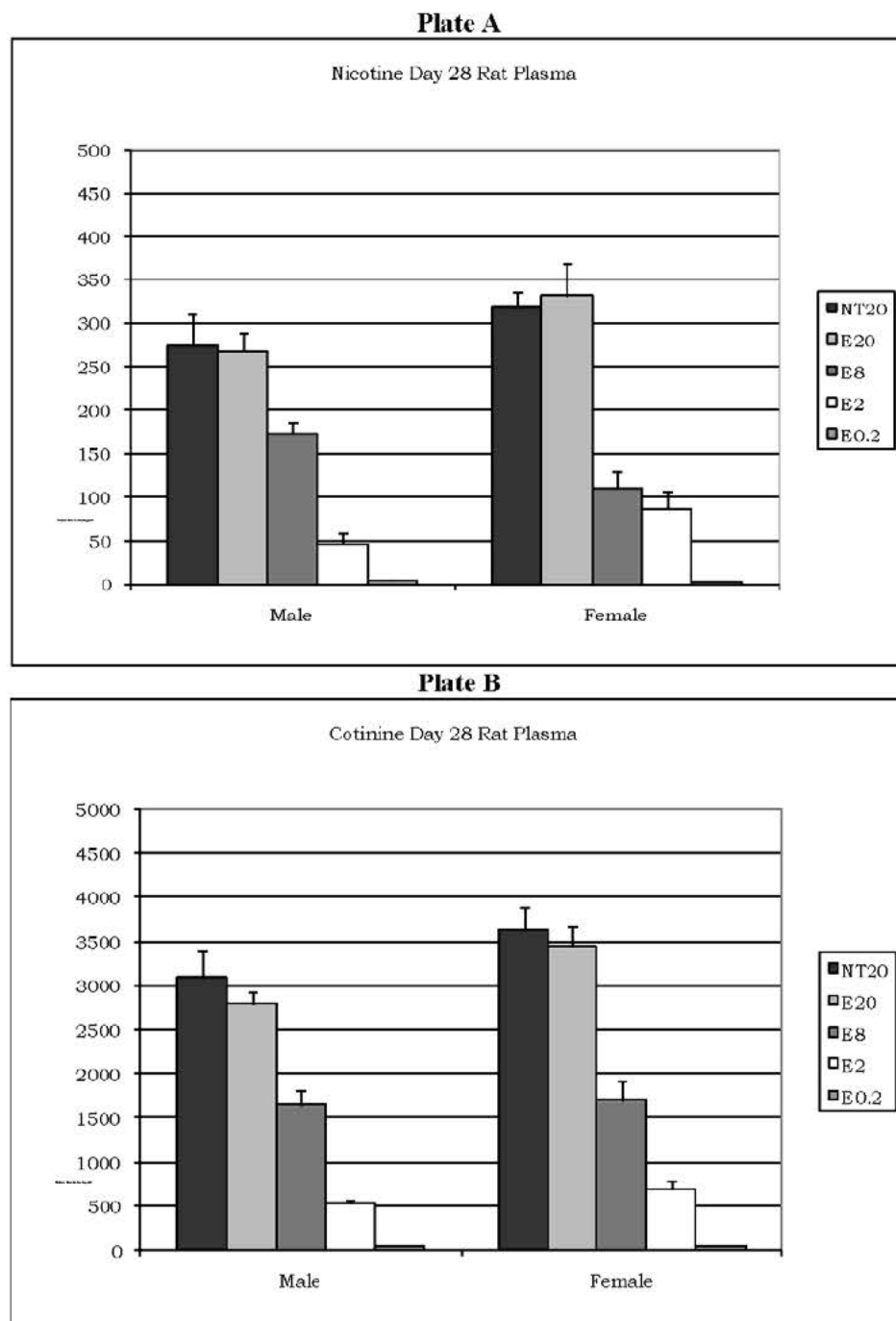




**Figure 19 – Plasma Concentration (Mean + SEM)-Time Profiles for Female Rats on Days 13 and 14 After Daily Oral Exposure of Nicotine Hydrogen Tartrate or Tobacco Extract – Nicotine (Plate A) and Cotinine (Plate B)**



**Figure 20 –  $C_{max}$  (Mean + SEM) for Male and Female Rats on Day 28 After Daily Oral Exposure of Nicotine Hydrogen Tartrate or Tobacco Blend – Nicotine (Plate A) and Cotinine (Plate B)**



**Figure 21 –  $C_{max}$  (Mean + SEM) for Male and Female Rats on Day 28 After Daily Oral Exposure of Nicotine Hydrogen Tartrate or Tobacco Extract – Nicotine (Plate A) and Cotinine (Plate B)**

**VI. ACKNOWLEDGEMENTS**

Jim Hoskinson, Dan Burnham, and Pat South performed the analytical work. Ed Psurny wrote this report. Drs. Seth Gibbs and Jerry D. Johnson provided the kinetic analysis and report section. Maria Evascu reviewed the data and report for completeness and accuracy.

**APPENDIX A – ANALYSIS DOCUMENTATION FORM**

Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

Page 1 of 14

**DOCUMENTATION FORM FOR THE ANALYSIS OF NICOTINE AND COTININE  
IN RAT PLASMA BY LC-MS**

**I. SCOPE**

The scope of this work is to determine the concentration of nicotine and cotinine in rat plasma samples. Plasma calibration standards are prepared from two independently prepared stock solutions. The calibration standards, blanks, and Quality Control (QC) samples are processed by liquid-liquid extraction followed by analysis using liquid chromatography with mass spectrometry (LC-MS). Nicotine and cotinine concentrations are calculated using area response ratios and a regression line constructed from the concentrations and peak area response ratios of the calibrations standards.

**II. PURPOSE**

The purpose of this documentation form is to provide instructions for conducting the analysis of nicotine and cotinine in rat plasma.

**III. REFERENCES**

- Current SOP for Labeling Reagents, Solutions, Test and Control Articles, and Specimens
- Current SOP for Using Electronic Balances
- Current SOP for Recording, Reviewing, and Correcting Raw Data
- Current SOP for Using Pipettors
- Current SOP for Using HPLCs
- Current SOP for Using Mass Spectrometers
- Current SOP for Numeric Data and Calculations
- Current SOP for Using Refrigerators and Freezers
- Current SOP for the Use and Training for Analyst Software

**IV. DEFINITIONS**

None

Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**V. PROCEDURE****A. GENERAL INSTRUCTIONS**

USE TWO PAIR OF DISSIMILAR GLOVES DURING NEAT CHEMICAL HANDLING.

Calibrate all required balances according to the SOP on balance usage.

Make equivalent dilutions when the volume needed varies from the volume stated in the method.

Label all standard and reagent solutions as specified in the appropriate SOP.

Document all materials, equipment, and the chromatographic parameters. Initial on the top of each page of this document to signify that you have followed the instructions as written, all materials and reagents are current, and all equipment has been properly calibrated.

Initial and date the top of the page on the day that the work for that page was begun. Other entries made by the analyst on a later date or entries made by another person will be initialed and dated near the data entry.

The procedures are written in general chronological order. However, it is not essential that all sections be performed sequentially. The analyst may determine the order for conducting the task in the most efficient manner, unless the order for certain activities is specified.

Line through any section that is not needed for a specific task.

**B. SAMPLES**

See attached form for sample list and dilution of samples.

Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**C. MATERIALS**

(b) (4)



Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**D. EQUIPMENT**(b) (4)  


Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**E. PREPARATION OF SOLUTIONS**

(b) (4)



Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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(b) (4)  


Study Number: CN49730C

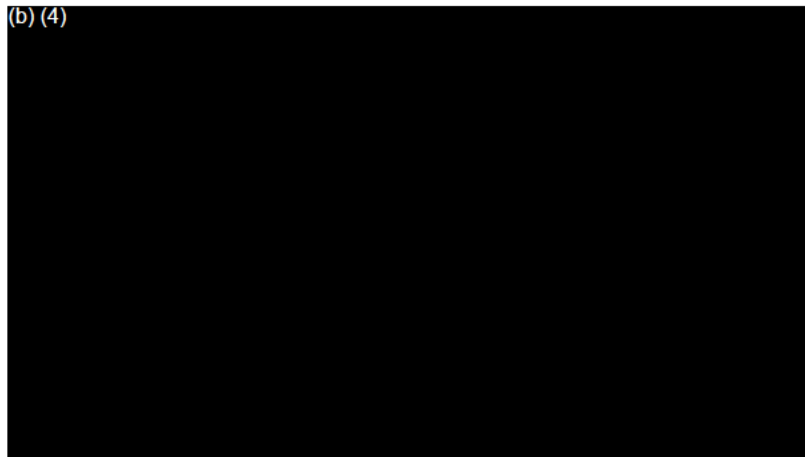
Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**G. PREPARATION OF PLASMA CALIBRATION STANDARDS**

(b) (4)

**H. PREPARATION OF BLANKS**

(b) (4)



Study Number: CN49730C

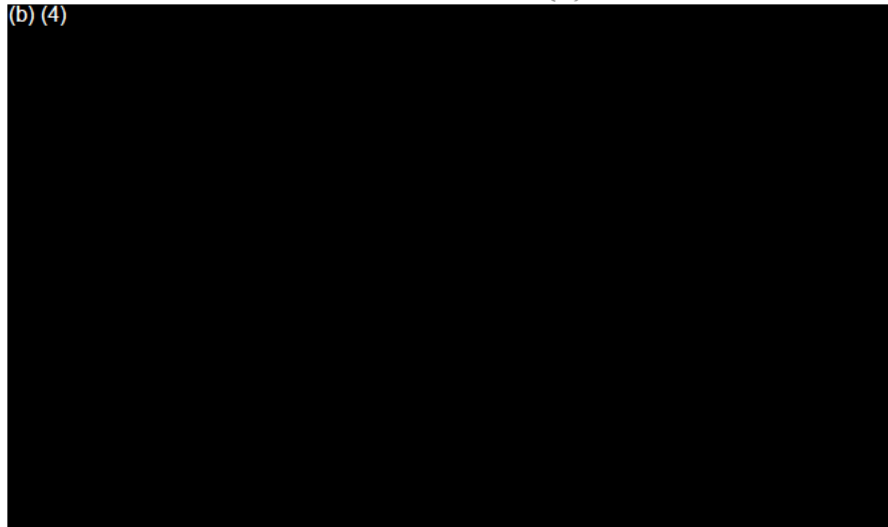
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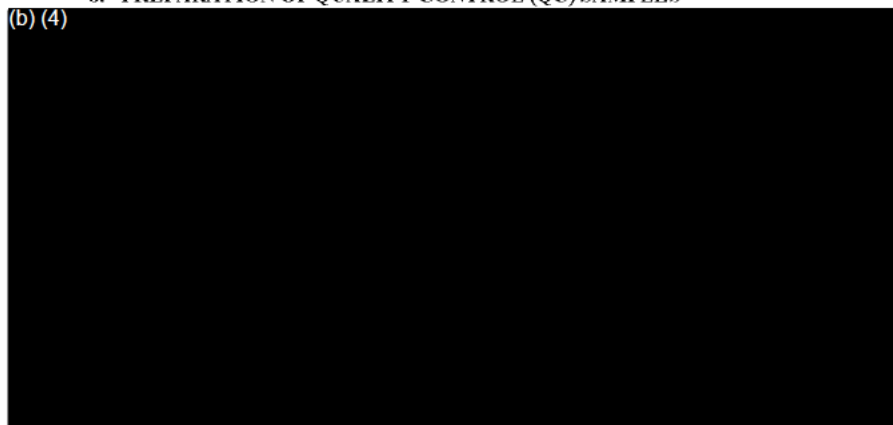
Page 8 of 14

**I. PREPARATION OF INTERNAL STANDARD (IS) SOLUTIONS**

(b) (4)

**J. PREPARATION OF QUALITY CONTROL (QC) SAMPLES**

(b) (4)



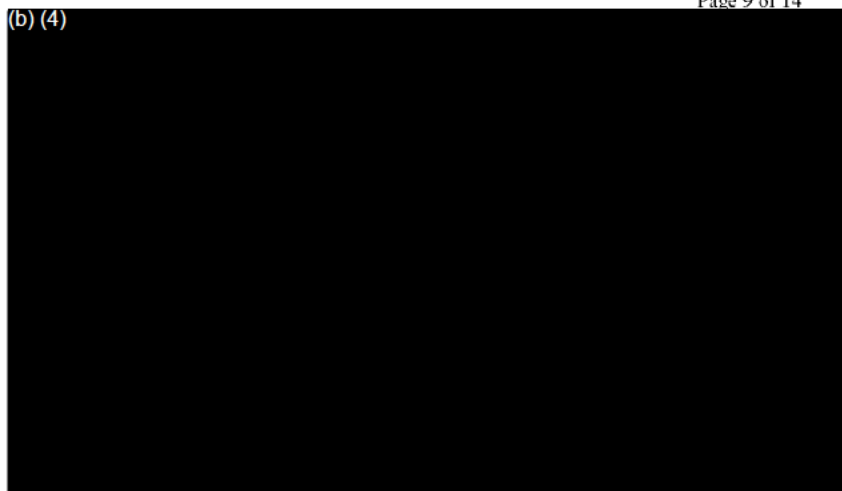
Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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(b) (4)



**K. PREPARATION OF PLASMA STANDARDS, BLANKS, QCS, AND  
SAMPLES**

(b) (4)



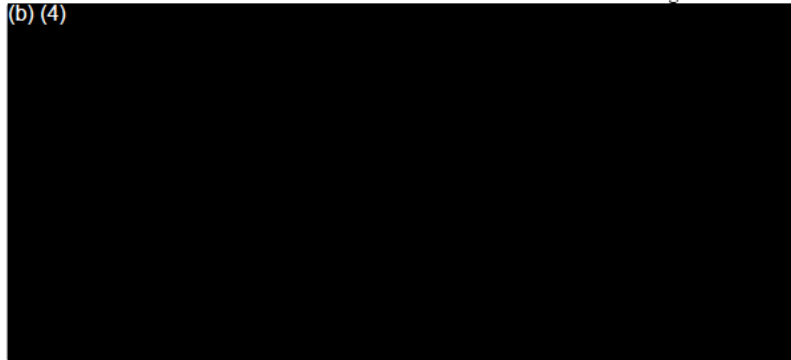
Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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(b) (4)



Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**L. ANALYSIS OF STANDARDS, BLANKS, SAMPLES, AND QCS**(b) (4)  


Study Number: CN49730C

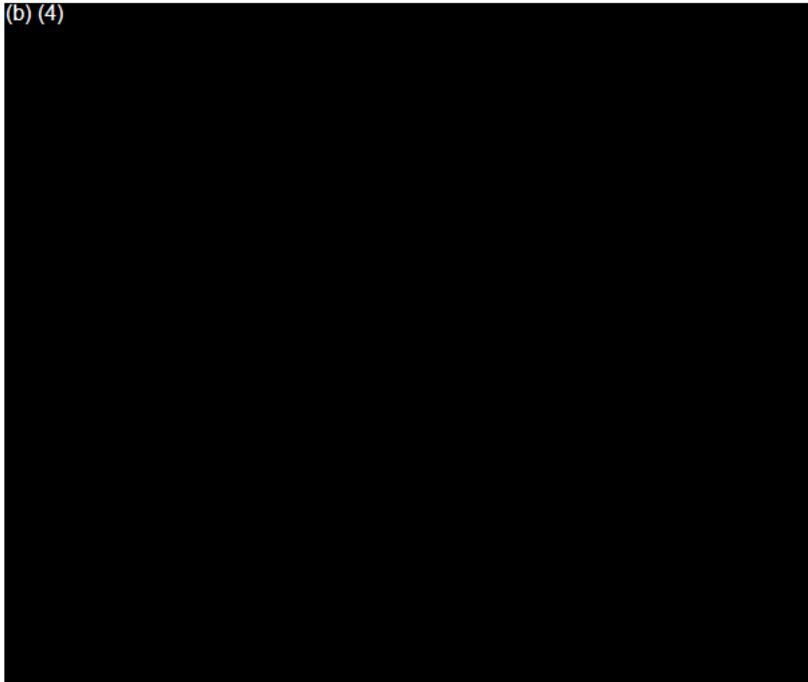
Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**VI. CALCULATIONS**

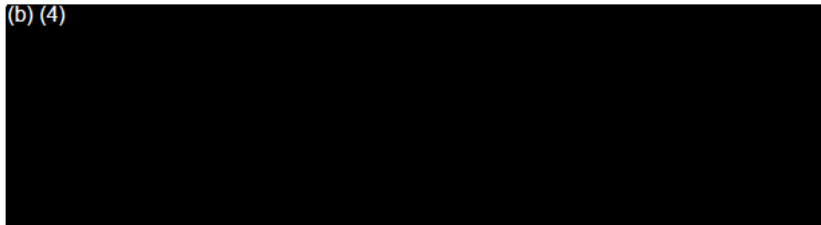
(b) (4)

**VII. RESULTS**

Include printouts of the acquisition method, HPLC method, calibration curve, chromatograms, summary report, data processing parameters, and spreadsheets in the data packet.

**VIII. ACCEPTANCE CRITERIA**

(b) (4)



Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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(b) (4)

**IX. COMMENTS/CONCLUSIONS**

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**X. DATA REVIEW****Technical Review**

Review at least the following to assure they are acceptable: rejection of calibration standards, integration of chromatograms, chromatography data processing and acquisition parameters, calibration standard concentrations, and regression model

**Data Accuracy Review**

Review at least the following: completeness and correctness of data entry, formulas used to calculate all values, accuracy of calculations, and compliance of data with acceptance criteria.

Study Number: CN49730C

Date: \_\_\_\_\_

Analyst: \_\_\_\_\_

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**XI. SIGNATURES**

Technical Review Signature/Date:

\_\_\_\_\_  
\_\_\_\_\_

Signature of the technical reviewer will be considered documentation that all modifications and/or changes to this SOP (documented during the course of conducting this task) are technically acceptable and have no adverse technical impact unless otherwise noted. Changes or deviations to the acceptance criteria section require independent assessment by the technical reviewer.

Data Accuracy Review Signature/Date:

\_\_\_\_\_  
\_\_\_\_\_

**APPENDIX I: SEROLOGY REPORTS**



**FINAL REPORT OF LABORATORY EXAMINATION**  
**MU Research Animal Diagnostic Laboratory**  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu

**CASE NUMBER: 14075-2008**

**RECEIVED ON: 6/20/2008**

**COMPLETED ON: 6/23/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7-1-20  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

**SPECIMEN DESCRIPTION:**

**SPECIES:** rat  
**DESCRIPTION:** serum samples, diluted  
**NUMBER OF SPECIMENS:** 10  
**FACILITY CODE:** COM

**PURCHASE ORDER #:** V103399000627

ID	Client ID	Investigator	Room #	Sex
1	CN49730C-1401	M. Hejtmacik	7C-074	M
2	CN49730C-1402	M. Hejtmacik	7C-074	M
3	CN49730C-1403	M. Hejtmacik	7C-074	M
4	CN49730C-1404	M. Hejtmacik	7C-074	M
5	CN49730C-1405	M. Hejtmacik	7C-074	M
6	CN49730C-1451	M. Hejtmacik	7C-074	F
7	CN49730C-1452	M. Hejtmacik	7C-074	F
8	CN49730C-1453	M. Hejtmacik	7C-074	F
9	CN49730C-1454	M. Hejtmacik	7C-074	F
10	CN49730C-1455	M. Hejtmacik	7C-074	F

**TESTS PERFORMED:** Basic Serology Profile - rat

**Serologic evaluation for antibodies to:** H1, KRV, LCM, *M. pulmonis*, Parvo NS-1, PVM, RCV/SDAV, REO3, RMV, RPV, RTV, Sendai, TMEV GDVII

**SUMMARY:** All test results were negative.

**If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at radil@missouri.edu.**

Technical Review TAB 7/7/08

QC: BMB 7-7-08

CN49730C

Case Number: 14075-2008

Page 2

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
LCM	MFI ( > 500)	-	-	-	-	-	-	-	-	-	-
<i>M. pulmonis</i>	MFI ( > 1,190)	-	-	-	-	-	-	-	-	-	-
Parvo NS-1	MFI ( > 4,095)	-	-	-	-	-	-	-	-	-	-
H1	MFI ( > 2,940)	-	-	-	-	-	-	-	-	-	-
KRV	MFI ( > 2,915)	-	-	-	-	-	-	-	-	-	-
RMV	MFI ( > 1,225)	-	-	-	-	-	-	-	-	-	-
RPV	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
PVM	MFI ( > 325)	-	-	-	-	-	-	-	-	-	-
RCV/SDAV	MFI ( > 2,610)	-	-	-	-	-	-	-	-	-	-
REO3	MFI ( > 860)	-	-	-	-	-	-	-	-	-	-
RTV	MFI ( > 2,400)	-	-	-	-	-	-	-	-	-	-
TMEV GDVII	MFI ( > 2,280)	-	-	-	-	-	-	-	-	-	-
Sendai	MFI ( > 865)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture active W = weak positive WB = Western Blot confirmatory analysis pending)

① reactive

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.

① rewritten because hole punch destroyed original entry. B&B 7-14-08



**FINAL REPORT OF LABORATORY EXAMINATION**  
**MU Research Animal Diagnostic Laboratory**  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu

**CASE NUMBER: 14075-2008**

**RECEIVED ON: 6/20/2008**

**COMPLETED ON: 6/23/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7120  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

**SPECIMEN DESCRIPTION:**

**SPECIES:** rat

**DESCRIPTION:** serum samples, diluted

**NUMBER OF SPECIMENS:** 10

**FACILITY CODE:** COM

**PURCHASE ORDER #:** V103399000627

ID	Client ID	Investigator	Room #	Sex
1	CN49730C-1401	M. Hejtmacik	7C-074	M
2	CN49730C-1402	M. Hejtmacik	7C-074	M
3	CN49730C-1403	M. Hejtmacik	7C-074	M
4	CN49730C-1404	M. Hejtmacik	7C-074	M
5	CN49730C-1405	M. Hejtmacik	7C-074	M
6	CN49730C-1451	M. Hejtmacik	7C-074	F
7	CN49730C-1452	M. Hejtmacik	7C-074	F
8	CN49730C-1453	M. Hejtmacik	7C-074	F
9	CN49730C-1454	M. Hejtmacik	7C-074	F
10	CN49730C-1455	M. Hejtmacik	7C-074	F

**TESTS PERFORMED:** Basic Serology Profile - rat

**Serologic evaluation for antibodies to:** H1, KRV, LCM, *M. pulmonis*, Parvo NS-1, PVM, RCV/SDAV, REO3, RMV, RPV, RTV, Sendai, TMEV GDVII

**SUMMARY:** All test results were negative.

If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at radil@missouri.edu.

Technical Review  
JPP 11/6/08  
QC Review: BAS 11-11-08

Case Number: 14075-2008

Page 2

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
LCM	MFI ( > 500)	-	-	-	-	-	-	-	-	-	-
<i>M. pulmonis</i>	MFI ( > 1,190)	-	-	-	-	-	-	-	-	-	-
Parvo NS-1	MFI ( > 4,095)	-	-	-	-	-	-	-	-	-	-
H1	MFI ( > 2,940)	-	-	-	-	-	-	-	-	-	-
KRV	MFI ( > 2,915)	-	-	-	-	-	-	-	-	-	-
RMV	MFI ( > 1,225)	-	-	-	-	-	-	-	-	-	-
RPV	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
PVM	MFI ( > 325)	-	-	-	-	-	-	-	-	-	-
RCV/SDAV	MFI ( > 2,610)	-	-	-	-	-	-	-	-	-	-
REO3	MFI ( > 860)	-	-	-	-	-	-	-	-	-	-
RTV	MFI ( > 2,400)	-	-	-	-	-	-	-	-	-	-
TMEV GDVII	MFI ( > 2,280)	-	-	-	-	-	-	-	-	-	-
Sendai	MFI ( > 865)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture reactive W = weak positive WB = Western Blot confirmatory analysis pending)

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.



**ADDENDUM to  
FINAL REPORT OF LABORATORY EXAMINATION  
MU Research Animal Diagnostic Laboratory  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu**

**CASE NUMBER: 14075-2008**

**RECEIVED ON: 6/20/2008**

**COMPLETED ON: 6/23/2008**

**ADDENDUM DATED: 9/10/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7120  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
CAR bacillus	MFI ( > 2,210)	-	-	-	-	-	-	-	-	-	-
<i>E. cuniculi</i>	MFI ( > 1,360)	-	-	-	-	-	-	-	-	-	-
Hantaan	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
MAD 1	MFI ( > 2,780)	-	-	-	-	-	-	-	-	-	-
MAD 2	MFI ( > 3,000)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture reactive W = weak positive WB = Western Blot confirmatory analysis pending)

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.

**If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at  
radil@missouri.edu.**



**FINAL REPORT OF LABORATORY EXAMINATION**  
**MU Research Animal Diagnostic Laboratory**  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu

**CASE NUMBER: 16480-2008**

**RECEIVED ON: 8/7/2008**

**COMPLETED ON: 8/8/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7-1-20  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

CN49730C

**SPECIMEN DESCRIPTION:**

**SPECIES:** rat  
**DESCRIPTION:** serum samples, diluted  
**NUMBER OF SPECIMENS:** 10  
**FACILITY CODE:** COM

**PURCHASE ORDER #:** V103399000688

ID	Client ID	Investigator	Room #	Sex
1	CN49730C-1406	M. Hejtmancik	7C-074	M
2	CN49730C-1407	M. Hejtmancik	7C-074	M
3	CN49730C-1408	M. Hejtmancik	7C-074	M
4	CN49730C-1409	M. Hejtmancik	7C-074	M
5	CN49730C-1410	M. Hejtmancik	7C-074	M
6	CN49730C-1456	M. Hejtmancik	7C-074	F
7	CN49730C-1457	M. Hejtmancik	7C-074	F
8	CN49730C-1458	M. Hejtmancik	7C-074	F
9	CN49730C-1459	M. Hejtmancik	7C-074	F
10	CN49730C-1460	M. Hejtmancik	7C-074	F

**TESTS PERFORMED:** Basic Serology Profile - rat

**Serologic evaluation for antibodies to:** H1, KRV, LCM, *M. pulmonis*, Parvo NS-1, PVM, RCV/SDAV, REO3, RMV, RPV, RTV, Sendai, TMEV GDVII

**GENERAL COMMENTS:** If any positive or reactive in any assay appears, even if the data is preliminary, please notify Dr. Tracy Peace with a verbal immediately. Alternate contact for information is Katie Hardin.

**SUMMARY:** All test results were negative.

If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at radil@missouri.edu.

Technical Review *TP* 9/8/08  
QC: BAB 4-26-08

Case Number: 16480-2008  
Page 2

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
LCM	MFI ( > 500)	-	-	-	-	-	-	-	-	-	-
<i>M. pulmonis</i>	MFI ( > 2,485)	-	-	-	-	-	-	-	-	-	-
Parvo NS-1	MFI ( > 4,095)	-	-	-	-	-	-	-	-	-	-
H1	MFI ( > 2,940)	-	-	-	-	-	-	-	-	-	-
KRV	MFI ( > 2,915)	-	-	-	-	-	-	-	-	-	-
RMV	MFI ( > 1,225)	-	-	-	-	-	-	-	-	-	-
RPV	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
PVM	MFI ( > 325)	-	-	-	-	-	-	-	-	-	-
RCV/SDAV	MFI ( > 2,610)	-	-	-	-	-	-	-	-	-	-
REO3	MFI ( > 1,250)	-	-	-	-	-	-	-	-	-	-
RTV	MFI ( > 2,400)	-	-	-	-	-	-	-	-	-	-
TMEV GDVII	MFI ( > 2,280)	-	-	-	-	-	-	-	-	-	-
Sendai	MFI ( > 1,665)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture reactive W = weak positive WB = Western Blot confirmatory analysis pending)

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.

CN49730/C

Hyphen not needed.

BA 2-16-08



**FINAL REPORT OF LABORATORY EXAMINATION**  
**MU Research Animal Diagnostic Laboratory**  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu

**CASE NUMBER: 16480-2008**

**RECEIVED ON: 8/7/2008**

**COMPLETED ON: 8/8/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7120  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

**SPECIMEN DESCRIPTION:**

**SPECIES:** rat

**DESCRIPTION:** serum samples, diluted

**NUMBER OF SPECIMENS:** 10

**FACILITY CODE:** COM

**PURCHASE ORDER #:** V103399000688

ID	Client ID	Investigator	Room #	Sex
1	CN49730C-1406	M. Hejtmancik	7C-074	M
2	CN49730C-1407	M. Hejtmancik	7C-074	M
3	CN49730C-1408	M. Hejtmancik	7C-074	M
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5	CN49730C-1410	M. Hejtmancik	7C-074	M
6	CN49730C-1456	M. Hejtmancik	7C-074	F
7	CN49730C-1457	M. Hejtmancik	7C-074	F
8	CN49730C-1458	M. Hejtmancik	7C-074	F
9	CN49730C-1459	M. Hejtmancik	7C-074	F
10	CN49730C-1460	M. Hejtmancik	7C-074	F

**TESTS PERFORMED:** Basic Serology Profile - rat

**Serologic evaluation for antibodies to:** H1, KRV, LCM, *M. pulmonis*, Parvo NS-1, PVM, RCV/SDAV, REO3, RMV, RPV, RTV, Sendai, TMEV GDVII

**GENERAL COMMENTS:** If any positive or reactive in any assay appears, even if the data is preliminary, please notify Dr. Tracy Peace with a verbal immediately. Alternate contact for information is Katie Hardin.

**SUMMARY:** All test results were negative.

If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at radil@missouri.edu.

Technical Review JPP 11/6/08  
QC Review: BAE 11-11-08  
CN49730C

Case Number: 16480-2008  
Page 2

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
LCM	MFI ( > 500)	-	-	-	-	-	-	-	-	-	-
<i>M. pulmonis</i>	MFI ( > 2,485)	-	-	-	-	-	-	-	-	-	-
Parvo NS-1	MFI ( > 4,095)	-	-	-	-	-	-	-	-	-	-
H1	MFI ( > 2,940)	-	-	-	-	-	-	-	-	-	-
KRV	MFI ( > 2,915)	-	-	-	-	-	-	-	-	-	-
RMV	MFI ( > 1,225)	-	-	-	-	-	-	-	-	-	-
RPV	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
PVM	MFI ( > 325)	-	-	-	-	-	-	-	-	-	-
RCV/SDAV	MFI ( > 2,610)	-	-	-	-	-	-	-	-	-	-
REO3	MFI ( > 1,250)	-	-	-	-	-	-	-	-	-	-
RTV	MFI ( > 2,400)	-	-	-	-	-	-	-	-	-	-
TMEV GDVII	MFI ( > 2,280)	-	-	-	-	-	-	-	-	-	-
Sendai	MFI ( > 1,665)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture reactive W = weak positive WB = Western Blot confirmatory analysis pending)

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.



**ADDENDUM to  
FINAL REPORT OF LABORATORY EXAMINATION  
MU Research Animal Diagnostic Laboratory  
1600 East Rollins, Columbia MO 65211 1-800-669-0825 1-573-882-5983  
radil@missouri.edu www.radil.missouri.edu**

**CASE NUMBER: 16480-2008**

**RECEIVED ON: 8/7/2008**

**COMPLETED ON: 8/8/2008**

**ADDENDUM DATED: 9/9/2008**

**SUBMITTED BY:**

Katherine M. Hardin  
Battelle Memorial Institute  
505 King Ave. Room 7120  
Columbus, OH 43201  
(614) 424-6328  
[614] 458-6328 (fax)

**SEROLOGY:**

		1	2	3	4	5	6	7	8	9	10
CAR bacillus	MFI ( > 2,210)	-	-	-	-	-	-	-	-	-	-
<i>E. cuniculi</i>	MFI ( > 1,360)	-	-	-	-	-	-	-	-	-	-
Hantaan	MFI ( > 1,200)	-	-	-	-	-	-	-	-	-	-
MAD 1	MFI ( > 2,780)	-	-	-	-	-	-	-	-	-	-
MAD 2	MFI ( > 3,000)	-	-	-	-	-	-	-	-	-	-

(LEGEND: \* = borderline + = positive - = negative blank = test not performed C = cell antigen reactor EQ = equivocal HE = hemolysis precluded testing I = insufficient INC = inconclusive finding NA = non-specific adherence NF = non-specific fluorescence NH = non-specific hemagglutination NR = sample not received NT = not tested S = suspect TC = tissue culture reactive W = weak positive WB = Western Blot confirmatory analysis pending)

Positive MFI results are reported as "+" followed by a number from 1 to 33 in thousands rounded off to the nearest thousand.

**If you have questions, please call our toll free number at 1-800-669-0825 or e-mail us at  
radil@missouri.edu.**