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Title Page

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Volume 1 of 2

Study Report for Task Order No. UIC-15B

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Sponsor: US Army Medical Materiel Development Activity

Test Article: WR238605 Succinate

Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

February 2, 1996

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This study evaluated the toxicity of WR238605 Succinate in rats following six months of daily oral (gavage) administration. WR238605 Succinate is an 8-aminoquinoline derivative which has demonstrated antimalarial potential in preclinical studies. Dose levels studied were 0 (vehicle control), 0.5, 2.0 and 9.0 mg base/kg/day, and were based on a three month toxicity study with a three month recovery period in rats (UIC/TRL Study No. 098) in which anemia and lung lesions were seen at 6 and 18 mg base/kg/day whereas 0.5 mg base/kg/day was the no-observed effect level. In the present study, the animals were ≈ 7 weeks old, and weighed 216 - 289 g (males) and 160 - 204 g (females) upon initiation of drug treatment.

The primary toxicities of WR238605 Succinate were to RBCs, the lungs and the liver. Mortality occurred in one high dose male rat. Treatment-related clinical signs in high dose animals included rough coat, hunched posture, labored breathing (males), and piloerection (females). Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. High dose males, and mid and high dose females had decreased RBC counts, HCT and HGB concentration, suggestive of mild anemia. The anemia may have been hemolytic in origin due to the presence of Heinz bodies and increased methemoglobin levels. Microscopic lesions observed in the spleen, bone marrow, kidneys and adrenal glands may have been secondary to anemia and/or hemolysis. High dose animals had elevations in mature neutrophil and lymphocyte numbers. Mild thrombocytopenia was seen in mid and high dose males. Pulmonary lesions in male and female rats in the mid and high dose groups consisted of foamy macrophage accumulation, chronic interstitial inflammation, and hemorrhage (high dose groups only). Apoptosis, pigmentation and fatty change in the centrilobular region of the liver were seen in high dose males, but not in females, and were accompanied by decreased serum GLOB, BUN and increased TBA. Similar clinical chemistry changes were seen in high dose females. The no-effect level (NOEL) for WR238605 Succinate is considered to be at or near the low dose of 0.5 mg base/kg/day.

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STATEMENT OF COMPLIANCE

Study No. 152 entitled "Six Month Oral Toxicity Study of WR238605 Succinate in Rats" was conducted in compliance with the Good Laboratory Practices regulations as published in 21 CFR 58, 40 CFR 160 and 40 CFR 792 in all material aspects.

The protocol for this study was approved by the UIC Animal Care Committee.

Signature

Study Director

_____ _____

Barry S. Levine, D.Sc., D.A.B.T. Date

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QUALITY ASSURANCE STATEMENT

STUDY TITLE: SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

STUDY NUMBER: 152

STUDY DIRECTOR: BARRY S. LEVINE

INITIATION DATE: 5/15/95

This study has been divided into a series of phases. Using a random sampling approach, Quality Assurance personnel monitors each of these phases over a series of studies. Procedures, equipment, documentation, etc., are examined in order to assure that the study is performed in accordance with the Good Laboratory Practice regulations of the Food and Drug Administration and the Environmental Protection Agency to assure that the study is conducted according to the protocol.

The following are the inspection dates, phases inspected, and report dates of QA inspections of the study.

INSPECT ON 5/15/95, TO STUDY DIR 5/15/95, TO MGMT 5/15/95
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INSPECT ON 7/19/95, TO STUDY DIR 7/19/95, TO MGMT 7/20/95
PHASES: ANIMAL RECEIPT
INSPECT ON 8/2/95, TO STUDY DIR 8/2/95, TO MGMT 8/3/95
PHASES: BODY WEIGHT, DOSING, CLINICAL OBSERVATION, FOOD CONSUMPTION, ROOM ENVIRONMENT AND ANIMAL IDENTIFICATION
INSPECT ON 9/11-12/95, TO STUDY DIR 9/12/95, TO MGMT 9/12/95
PHASES: RAW DATA AND DRAFT REPORT FROM THE ANALYTICAL LABORATORY
INSPECT ON 9/19/95, TO STUDY DIR 9/20/95, TO MGMT 9/21/95
PHASES: TEST ARTICLE ANALYSIS
INSPECT ON 1/30/96, TO STUDY DIR 1/31/96, TO MGMT 2/5/96
PHASES: OPTHALMIC EXAMINATION
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SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Test Article.: WR238605 Succinate

Sponsor: US Army Medical Materiel
Development Activity
Fort Detrick
Frederick, MD 21702-5009

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Testing Facility: TOXICOLOGY RESEARCH LABORATORY (TRL)
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Barry S. Levine, D.Sc., D.A.B.T. Date
Study Director

Study Initiation: May 15, 1995
Dosing Initiation: August 02, 1995
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1. SUMMARY

This study evaluated the toxicity of WR238605 Succinate in rats following six months of daily oral (gavage) administration. WR238605 Succinate is an 8-aminoquinoline derivative which has demonstrated antimalarial potential in preclinical studies. Dose levels studied were 0 (vehicle control), 0.5, 2.0 and 9.0 mg base/kg/day, and were based on a three month toxicity study with a three month recovery period in rats (UIC/TRL Study No. 098) in which anemia and lung lesions were seen at 6 and 18 mg base/kg/day whereas 0.5 mg base/kg/day was the no-observed effect level. In the present study, the animals were ≈ 7 weeks old, and weighed 216 - 289 g (males) and 160 - 204 g (females) upon initiation of drug treatment. The results are summarized in Table 1.

The primary toxicities of WR238605 Succinate were to RBCs, the lungs and the liver. Mortality occurred in one high dose male rat. Treatment-related clinical signs in high dose animals included rough coat, hunched posture, labored breathing (males), and piloerection (females). Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. High dose males, and mid and high dose females had decreased RBC counts, HCT and HGB concentration, suggestive of mild anemia. The anemia may have been hemolytic in origin due to the presence of Heinz bodies and increased methemoglobin levels. Microscopic lesions observed in the spleen, bone marrow, kidneys and adrenal glands may have been secondary to anemia and/or hemolysis. High dose animals had elevations in mature neutrophil and lymphocyte numbers. Mild thrombocytopenia was seen in mid and high dose males. Pulmonary lesions in male and female rats in the mid and high dose groups consisted of foamy macrophage accumulation, chronic interstitial inflammation, and hemorrhage (high dose groups only). Apoptosis, pigmentation and fatty change in the centrilobular region of the liver were seen in high dose males, but not in females, and were accompanied by decreased serum GLOB, BUN and increased TBA. Similar clinical chemistry changes were seen in high dose females. The no-effect level (NOEL) for WR238605 Succinate is considered to be at or near the low dose of 0.5 mg base/kg/day.

2. INTRODUCTION

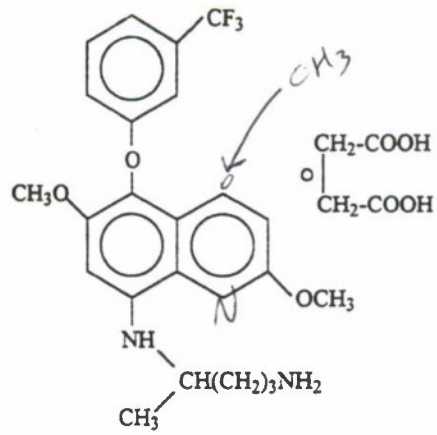
This study was conducted to determine the specific target organ toxicity, dose-response relationships and a no observed adverse effect level of WR238605 succinate in rats following six months of daily oral administration. WR238605 Succinate is an 8-aminoquinoline derivative which has demonstrated antimalarial potential in preclinical studies. WR238605 was discovered at WRAIR, and is being developed as a prophylactic to replace primaquine. The study was conducted in accordance with the specifications of the Sponsor as described in Task Order No. UIC-15. The rats used in the study are a standard and accepted rodent species for regulatory toxicology studies, and was specified by the Sponsor. Oral administration is the intended clinical route and was also specified by the Sponsor. All methods and procedures were conducted in accordance with the Quality Assurance Programs of the Toxicology Research Laboratory, University of Illinois at Chicago and Pathology Associates, Intl., designed to conform with FDA Good Laboratory Practices Regulations. No unforeseen circumstances affected the integrity of the study. Dosing was initiated on August 02, 1995 and the in-life portion was terminated on February 02, 1996.

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3. MATERIALS AND METHODS

3.1 Test Article

WR238605 Succinate (Bottle No. BM12562), a pale yellow powder, was provided by the Sponsor. It was received on December July 10, 1995 from Herner & Co., and was assigned an in-house chemical number (0720614). The chemical name of the test article is 8-[(4-Amino-1-methylbutyl)amino]-2,6-dimethoxy-4-methyl-5-(3-trifluoromethyl-phenoxy)quinoline succinate and the mole fraction of the base is 0.8. It was stored at 2 to 8°C and ambient humidity, and protected from light in an amber bottle. The chemical structure follows.



WR238605
Succinate

The Analytical Chemistry Report is contained in Appendix A. The test article was initially identified by GC-MS and the purity was determined to be 99.52% ± 0.21%. The purity was re-determined following completion of the in-life portion of the study. At that time, the purity was 99.98% ± 0.02%. Thus, the test article was stable under storage conditions.

3.2 Animals

One hundred and twenty-five male and one hundred and twenty-six female CD® Virus Antibody Free (VAF) rats were obtained from Charles River Breeding Laboratories (Kingston, NY) on July 19, 1995. The animals were approximately 6 weeks old (date of birth June 10, 1995) upon arrival at the UIC AAALAC-accredited animal facility. Each animal was given a study-unique quarantine/pretest number following placement in cages. Animals were singly housed in polycarbonate cages with Anderson bed-o-cob® bedding (Heinold, Kankakee, IL) in a temperature (65-78°F) and humidity (30-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm^2 area and 20 cm height, was adequate to house rats at the upper weight range as described in the *Guide for the Care and Use of Laboratory Animals*, DHEW (NIH) No. 86.23. All animals were routinely transferred to clean cages with fresh bedding weekly.

Certified Rodent Chow No. 5002 (PMI Feeds Inc., St. Louis, MO) was provided *ad libitum* from arrival until termination. Tap water from an automatic watering system in which the room distribution lines were flushed daily was provided *ad libitum*. The water

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was not treated with additional chlorine or HCl. There were no known contaminants in the feed or water which were expected to influence the study. The results of the bimonthly comprehensive chemical analyses of Chicago water performed by the City of Chicago are documented in files maintained by Quality Assurance.

3.3 Experimental Design

All animals were quarantined for approximately two weeks. During that time, the animals were observed daily for signs of illness, and all unusual observations were reported to the Study Director or Clinical Veterinarian. Hematology, clinical chemistry and coagulation parameters measured in five rats/sex indicated that the shipment was suitable for use (Appendix K). These rats, however, were not used in the dosing portion of the study. Animals were examined and approved for use by the Clinical Veterinarian during the quarantine period prior to being placed on test. Near the end of the quarantine/pretest period, 100 animals of each sex were randomized by sex into the groups shown in the following table using a computer-generated randomization program, stratified on the basis of body weight.

Treatment Group	Dose Level (mg base/kg/day	Dose Conc. (mg base/ml)	Dose Volume (ml/kg/day)	Number of Males	Number of Females
1	0	0	5	20 + 5*	20 + 5*
2	0.5	0.1	5	20 + 5*	20 + 5*
3	2.0	0.4	5	20 + 5*	20 + 5*
4	9.0	1.8	5	20 + 5*	20 + 5*

* Five satellite rats/sex/dose were utilized for the collection of blood samples for plasma drug level analysis and were euthanized after the last set of samples were collected in week 25. All other observations, tests and measurements were performed on these animals except for the collection of blood samples for clinical pathology measurements, ophthalmology examinations and pathology evaluations. The remaining 20 rats/sex/dose were used in the core toxicity study.

During the test animal selection process, each animal was assigned an animal number unique to it within the population making up the study. This number was coded on a subcutaneously implanted microchip and also appeared on a cage card visible on the front of each cage. The cage card additionally contained the study number, test article identification, sex, treatment group number, and dose level. Cage cards were color-coded as a function of treatment group.

The test article dosage formulation was administered by gavage once daily for at least 26 weeks beginning on August 2, 1995 (day 1). Control animals received the test article vehicle (aqueous 1% methylcellulose/0.2% Tween 80). All animals received the vehicle by gavage for at least 3 days during week -1 to acclimate them to the procedure. The animals were dosed up to and including the day prior to scheduled necropsy on days 183,

184, and 185. Dosing volume was 5 ml/kg/day, adjusted on the basis of each animal's most recent body weight. Gavage needles were cleaned with 100% ethanol and rinsed with deionized distilled water after each day's use. The rats weighed 216 - 289 g (males) and 160 - 204 g (females) on day 1 and were approximately seven weeks old at initiation of treatment.

Dosing formulation calculations of the test article were adjusted for purity of the test article and the base mole fraction. The control materials were assumed to be 100% pure for dosing calculations. Formulations were prepared weekly and were administered daily by gavage, at 5 ml/kg/day, 7 days a week. The 1% methylcellulose/0.2% Tween 80 vehicle was prepared at least weekly by placing the required amount of deionized distilled water in a beaker and then adding the required amount of methylcellulose and volume of Tween 80, using its specific gravity of 1.08 (1.0 g of methylcellulose and 0.2 g Tween 80 per 100 ml of deionized water). One lot no. each of methylcellulose and Tween 80 was used. The mixture was stirred while being heated until homogenous and then refrigerated.

The test article dosing suspensions were prepared weekly. Stability data from a previously conducted dog toxicity study by gastric intubation demonstrated that WR238605 Succinate suspensions were stable for at least 28 days (UIC/TRL Study No. 47). Homogeneity data also obtained from UIC/TRL Study No. 047 demonstrated that the test article suspensions were homogenous (coefficients of variations for sampling in the top, middle and bottom of several test suspensions were typically less than 4%).

Each test article dosing suspension was prepared individually by adding the appropriate amount of WR238605 Succinate to the required volume of the 1.0% methylcellulose/0.2% Tween 80 vehicle in a pre-calibrated beaker. The contents were mixed with an Omni-Mixer homogenizer, for at least 5 minutes. All suspensions were stored at 2 - 8°C. All suspensions were allowed to warm to room temperature and stirred continuously before and during gavage administration. Samples of all dosing suspensions prepared weekly were analyzed, and only suspensions within 10% of their target concentration were used. Weekly samples were also analyzed for test article concentration after use. Tolerance of sample analysis after use was also 10%, i.e., of the "before use" assay value.

Non-fasted body weights were recorded in week -1, on day 1, weekly thereafter and at scheduled necropsy. Clinical signs were observed and recorded for all animals once daily, approximately 1 - 2 hours after dosing. The general behavior, posture, locomotion, breathing pattern and coat were observed for all animals. The animals were also observed immediately prior to dosing and in the afternoon for moribundity/mortality. Physical examinations (clinical observations) which included examination of eyes and all orifices were conducted weekly starting in week -1. Food consumption was measured for all animals weekly commencing with week -1. Core study rats were examined by indirect ophthalmoscopy prior to study initiation (week -1), and during week 13 and week 26. The animals were treated with 1% atropine sulfate eye drops prior to the examination.

Hematology and clinical chemistry parameters were measured for 10 animals/sex/group in the core toxicity study during weeks 4, 13 and 26. The same animals were used throughout the study, with the exception of animal no. 558 (Group 4-M) which was found dead on December 16, 1995 (Day 137) and replaced with animal no. 561. The non-fasted animals were anesthetized by carbon dioxide inhalation (70% CO_2:30% O_2),

and approximately 1.5 - 2.0 ml of blood was collected from the orbital sinus to measure the following parameters. The samples were processed in the same random order as collected. Clinical pathology methodology is contained in Appendix B.

Hematology

[a]Erythrocyte count and morphology	Mean corpuscular volume (MCV)
Hematocrit	Mean corpuscular hemoglobin (MCH)
Hemoglobin	Mean corpuscular hemoglobin concentration (MCHC)
Leukocyte count, total and differential	Heinz bodies
Reticulocyte count	Platelet count
	[b]Methemoglobin

[a]Includes nucleated RBCs

[b]Measured with a Co-oximeter (Instrumentation Laboratory Model 282). The assay was performed within one hour of sample collection. The specimens were kept on wet ice prior to analysis.

Clinical Chemistry

Alanine aminotransferase (ALT)	Inorganic phosphorus
Albumin	Lactate dehydrogenase (LDH)
Albumin/Globulin ratio (calc.)	Potassium
Alkaline phosphatase (ALKP)	Sodium
Calcium	Sorbitol dehydrogenase (SDH)
Chloride	Total bile acids
Creatinine	Total Protein
Creatine kinase	Urea nitrogen (BUN)
Glucose	

Activated partial thromboplastin time (APTT) was measured in all rats for which clinical pathology measurements were done. The blood samples for the APTT measurements were collected from the vena cava at scheduled necropsy in week 27.

Blood samples (1.0 - 2.0 ml) were collected from the orbital sinus from the 5 satellite rats/sex/group designated for the determination of plasma drug levels in week -1, approximately 24 hours after the first day of dosing, and approximately 24 hours after dosing at the following timepoints: weeks 3, 7, 18 and 25. Blood samples were collected immediately prior to dosing, i.e., approximately 24 hours after the previous dose, due to the anticipated long half-life of the test article. The plasma samples were stored at -65° to -70°C, and sent in two shipments as directed by the Sponsor to Dr. Emil Lin, University of California at San Francisco (UCSF) for measurement of plasma drug levels. As indicated by the Sponsor, the UCSF plasma drug level results will not be included in this report.

All animals which died on test were necropsied on that day. The surviving animals were killed and necropsied in random order over three consecutive days at the onset of week 27 (days 183 - 185). Euthanasia was accomplished by carbon dioxide asphyxiation, and

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an extensive necropsy was performed under the direction and supervision of the pathologist. Terminal body weights were collected prior to routine sacrifice.

The necropsy procedure was a thorough and systematic examination and dissection of the animal viscera and carcass, and collection and fixation of the following tissues/organs in 10% neutral buffered formalin (NBF). The subcutaneously implanted microchip was also saved from each animal with the NBF-fixed tissues.

*Adrenal glands	Pancreas
*Brain (fore-, mid-, hind-)	Pituitary
Cecum	Prostate
Colon	Rib with costochondral junction
Diaphragm	Salivary gland (submaxillary)
Duodenum	Sciatic nerve
Esophagus	Skeletal muscle
Eyes with harderian glands	Skin with mammary gland
Femur with marrow	Spinal cord (thoracic)
Gross lesions	*Spleen
*Heart	Sternum with marrow
Ileum	Stomach
Jejunum	*Testes with epididymides
*Kidneys	Thymus
*Liver	Thyroid gland/Parathyroids
* Lungs/Bronchi	Tongue
Lymph node (mesenteric)	Trachea
*Ovaries	Urinary bladder
	Uterus

*Weighed at scheduled necropsy. Paired organs were weighed as a unit.

All tissues and organs collected at necropsy were examined microscopically in all control and high dose animals. If treatment-related lesions were observed, those tissues/organs were examined microscopically within sex for mid and low dose animals. The one high dose male found dead was also processed for microscopic examination. Gross lesions were examined microscopically in all animals.

Femoral bone marrow smears were prepared from all animals at scheduled necropsy. The myeloid:erythroid (M:E) ratio was determined in control and high dose animals. Since treatment-related changes were not seen (Section 4.8, Pathology), M:E ratios were not determined in mid and low dose animals.

3.4 Statistical Analyses

For each sex, Analysis of Variance tests were conducted on body weight, weekly body weight gains, food consumption, hematology, clinical chemistry and organ weight data. Organ weight analyses considered weights relative to brain weight. If a significant F ratio was obtained from an ANOVA test ($p \leq 0.05$), Dunnett's t test was used for pair-wise

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comparisons with the concurrent control group (Dunnett, 1964). The level of significance was $p \leq 0.05$. All statistical analyses compared treated to control animals at each time point. Data were not corrected for baseline values, except that body weight analysis included absolute values, weekly changes and total weight changes. Dose levels for all summary and individual data are expressed on the basis of mg base/kg/day.

Statistical analyses was performed on an IBM™ compatible computer using the commercially available LabCat® computer program.

Quantitative data were tabulated and are presented in the report. In addition to the written report, summary data tables of parameters and variability were transmitted to the Sponsor on magnetic media (computer diskette) in "ASCII" form. The transcribed data on disk were no longer considered GLP compliant.

4. RESULTS

4.1 Dosage Formulation Analyses

The Analytical Chemistry Report is contained in Appendix A. Dosage formulation analyses are shown in Table 2.

Test article dosage formulations were within 10% of their respective target concentrations both prior to and essentially after dosing. Minor exceptions were in week 14 (0.1 mg base/ml postdose dosage formulation was 129.5% of the predose value and 123% of the target concentration), week 22 (1.8 mg base/ml postdose dosage formulation was 111.1% of the predose value, but 107.1%, i.e., within range, of target concentration), and week 25 (0.4 mg base/ml postdose dosage formulation was 110.9% of the predose value, but 109.0%, i.e., within range, of target concentration). Thus, out of 78 post-dosing analyses, only one sample was slightly (13%) out of predose or target concentration range.

4.2 Mortality and Clinical Signs/Observations

Summaries of clinical signs and clinical observations are presented in Table 3. Individual clinical signs and daily incidence of clinical signs are contained in Appendix C.

One high dose male (No. 558) was found dead on day 137. One day prior to its demise, labored breathing was seen. Treatment-related clinical signs in surviving high dose animals included rough coat, hunched posture, labored breathing (one surviving male), and piloerection (females). These signs were generally seen during the middle-to-latter part of the study. Clinical signs of toxicity were not apparent in mid and low dose animals. Hunched posture seen in one low dose male on one occasion and rough coat in one low dose female on three occasions were considered spurious observations, as it was not apparent in mid dose animals.

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4.3 Body Weight

Summaries of body weights and body weight gains are presented in Tables 4 and 5, respectively. Individual body weights are contained in Appendix D. In addition, summaries of body weights are graphically depicted in Figures 1 (males) and 2 (females).

Body weights and body weight gains were significantly reduced in high dose animals and mid dose males. Reductions in weight gain were first noted in high dose males after one week of dosing. For high dose females, this was first apparent on day 22. Beginning on days 15 and 22, and continuing until the end of the study, body weights of high dose male and female rats, respectively, were significantly less than the corresponding vehicle control group. Beginning on day 85 and continuing until the end of the study, body weights of the mid dose male rats were significantly less than the corresponding vehicle control group. Total body weight gain for the 6 month period was decreased 12% and 39% in the mid and high dose male rats, respectively. Total body weight gain in the high dose female rats was decreased 32% over the same period.

4.4 Food Consumption

Summaries of food consumption are in Table 6. Individual food consumption data are in Appendix E.

Food consumption in high dose male rats was significantly less than the control group during the first study week and generally throughout the study. Food consumption in high dose female rats was also less than the control group during week 1 and was periodically decreased throughout the rest of the study.

4.5 Clinical Pathology

Summaries of clinical chemistry tests are presented in Table 7. Individual clinical chemistry data are in Appendix F. Summaries of hematology tests are presented in Table 8. Individual hematology data are in Appendix G.

Clinical Chemistry

Serum globulin content was decreased 10% in week 13 in high dose males, resulting in a 12% increase in the A/G ratio. Total protein concentration, however, was not significantly altered. Similar changes in globulin and the A/G ratio were noted in high dose females in week 26 and total protein was decreased slightly, however, these results may have been incidental as significant changes in these parameters were also seen in low but not mid dose female rats. In week 26, significant elevations occurred in total bile acids in high dose males. Corresponding increases in high dose females occurred, however significant variability may have been responsible for the lack of statistical significance.

Serum BUN concentrations were slightly, but significantly reduced in high dose males in weeks 4, 13 and 26, and in high dose females in week 26. This suggests a drug-related affect on urea synthesis by the liver.

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No other clinical chemistry changes were considered related to treatment. Sporadic increases and decreases were seen, but were not considered biologically significant.

Hematology

High dose animals and mid dose females had changes in erythrocyte parameters suggestive of anemia. Erythrocyte counts were decreased 4 - 7% and 5 - 11% in the mid and high dose females, respectively, in weeks 4, 13 and 26. During the study, the hematocrit (absolute) was decreased 1.7 - 2.5% and 2.0 - 3.8% in the mid and high dose females, respectively. Similar decreases in RBC counts and hematocrit were seen in week 4 in the high dose males. Hemoglobin content was decreased 7 - 10% in the high dose females during the study and 5% in week 13 in the mid dose group. Hemoglobin content was decreased 5 - 10% in the high dose males in weeks 4, 13 and 26. MCHC was decreased in week 13 in the high dose females. High dose males had decreased MCHC in weeks 13 and 26, and decreased MCH in week 26. Reticulocyte counts were elevated slightly during the study in high dose animals, and Heinz bodies were present in week 13 in the high-dose males, and in weeks 13 and 26 in the high dose females. Heinz bodies are formed by precipitation of oxidatively denatured hemoglobin. WR238605 administration produced methemoglobin in a dose-dependent fashion throughout the study. Slight increases in erythrocyte anisocytosis were seen in WR238605-treated males and high dose females.

Male and female rats exposed to 9.0 mg base/kg/day of WR238605 had changes in white blood cell parameters. Total leukocyte counts in high dose males were elevated 59%, 62% and 77% in weeks 4, 13 and 26, respectively. Total leukocyte counts in the high dose females were elevated to a similar extent during the study. These changes were due primarily to increases in mature neutrophils and lymphocytes. A slight increase of immature neutrophils was seen in weeks 4 and 13 in the high dose females.

In week 13, platelet counts were decreased 10% and 15% in the mid and high dose males, respectively.

No other hematologic changes were considered related to treatment. Sporadic increases and decreases were seen, but were not considered biologically significant.

4.6 Ophthalmology

The ophthalmology report is contained in Appendix H. No treatment-related changes were seen.

4.7 Organ Weights

The summary of organ weights expressed as relative values (% brain weight) are presented in Table 9. Individual organ weight data are contained in Appendix I.

WR238605 administration resulted in increased relative weights of the kidneys, lungs/bronchi, spleen and adrenal glands. The relative weight of the kidneys were increased 10% and 13% in mid and high dose males, respectively. The relative weights

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of the lungs/bronchi were increased 46% and 100% for mid and high dose males, respectively, and 55% and 97% for mid and high dose females, respectively. The relative weight of the spleen was increased 25% and 168% in mid and high dose males, respectively, and 19% and 127% in mid and high dose females, respectively. The relative weight of the adrenal glands was increased 34% in high dose females. Mid and high dose males and high dose females had relative weights of the heart decreased 8 - 10%.

4.8 Pathology

The Pathology Report is contained in Appendix J. A summary of gross and microscopic lesions is shown in Table 10.

Male and female rats in the high dose group had pulmonary lesions consisting of hemorrhage, foamy macrophage accumulation, and chronic interstitial inflammation. Animals in the mid dose group had foamy macrophage accumulation and chronic interstitial inflammation. Hemorrhage was characterized by the presence of free erythrocytes and fibrin in the lumen of alveoli in the affected region. Foamy macrophage accumulation was diagnosed when lumenal macrophages were very large with copious foamy cytoplasm. Chronic interstitial inflammation was characterized by the presence of alveolar macrophages in alveolar lumens and thickened alveolar walls which stained more basophilic than normal in the affected region. Minimal changes in the lungs were seen in the low dose groups (foamy macrophage accumulation in 2/20 males) compared to the control animals.

Both male and female rats in the mid and high dose groups had pigmentation in the cortex of the kidney, with lesions being more prevalent and severe in the high dose animals. Pigmentation in renal cortex was characterized by the presence of brown granular pigment in the cytoplasm of renal tubule epithelial cells. The pattern of pigmented cell distribution was most consistent with specific accumulation in proximal convoluted tubules. Pigmentation of cortical epithelial cells was considered to be a sensitive indicator of chronic hemoglobin resorption by the kidney.

Male and female rats in the high dose group had increased congestion in the spleen which was characterized by increased prominence of red pulp regions due to pooling of erythrocytes in the splenic sinusoids. In male rats, there appeared to be a mild dose-dependent increase in splenic erythropoiesis and pigmentation. Erythropoiesis was characterized by increased number and size of erythrocyte precursor cell colonies in the red pulp of the spleen. Pigmentation was characterized by the increased presence of focal groups of macrophages that contained dark brown granular material in their cytoplasm. Splenic hyperplasia of reticuloendothelial cells was seen in the high dose males and one high dose female, and was characterized by an increased thickness and prominence of the lightly basophilic zone of cells at the interface between the red and white pulp.

Apoptosis, pigmentation, and fatty change were observed in the centrilobular region of the liver from high dose males, but were not seen in female rats. Apoptosis was characterized by the presence of condensed, deeply eosinophilic round bodies in the centrilobular region of the liver. Pigmentation was characterized by the presence of brown granular material in the cytoplasm of the hepatocytes. Fatty change was diagnosed

when cells contained discrete round vacuoles in their cytoplasm. These vacuoles were generally empty, but sometimes contained lightly eosinophilic homogenous material and displaced the nucleus to the outer margin of the cell. Centrilobular fatty change was also seen to a lesser extent in mid dose males. Congestion in the centrilobular region was seen in 2 males in the mid and high dose groups each, and was diagnosed when blood filled sinusoids were observed in centrilobular regions that are generally occupied by hepatocytes.

Pigmentation in the zona reticularis region of the adrenal cortex was notably present in high dose animals and was seen to a lesser extent in the low and mid dose groups. Pigmentation was characterized by the presence of cells that contained a variable amount of brown granular pigment in their cytoplasm. Adrenal gland congestion was increased in high dose females in comparison to the other female dose groups. Congestion was diagnosed when vessels in the adrenal cortex were dilated and filled with erythrocytes.

Bone marrow hyperplasia occurred in a dose-dependent fashion in both the male and female dose groups. Hyperplasia was diagnosed when blood precursor cells were increased at the expense of lipid cells. Bone marrow granulopoiesis was observed in one high dose female and the high dose male that was found dead on day 137. Granulopoiesis was diagnosed when the number of myeloid cells was increased at the expense of lipid cells and suggests that an inflammatory response occurred at some site within 1 to 2 weeks prior to necropsy. No treatment-related effect on bone marrow Myeloid:Erythroid (M:E) ratios were seen in the study.

5. DISCUSSION/CONCLUSION

This study evaluated the toxicity of WR238605 Succinate in rats following six months of daily oral (gavage) administration. Dose levels studied were 0 (vehicle control), 0.5, 2.0 and 9.0 mg base/kg/day. The results are summarized in Table 1. One high dose male rat was found dead on day 137. Labored breathing was seen one day prior to its demise. Treatment-related clinical signs in surviving high dose animals included rough coat, hunched posture, labored breathing (one surviving male), and piloerection (females). These signs were generally seen during the middle-to-latter part of the study. Clinical signs of toxicity were not apparent in mid and low dose animals. Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. Treatment-related ophthalmic lesions were not seen.

High dose males, and mid and high dose females had changes in erythrocyte parameters suggestive of mild anemia. These changes included decreased RBC counts, hematocrit and hemoglobin concentration. As a result of the mild anemia, compensatory increases in reticulocyte counts were seen in high dose animals. The anemia may have been hemolytic in origin as Heinz bodies were present in high dose animals. Heinz bodies are formed by the precipitation of oxidatively denatured hemoglobin. Also, methemoglobin was observed in mid and high dose animals. The production of methemoglobin indicates an oxidant nature of the drug, and further supports the mild anemia as being hemolytic in origin. WR238605 administration resulted in bone marrow hyperplasia in a dose-dependent fashion in the male and female rats, and is a compensatory response to the anemia. However, no treatment related effects on bone marrow M:E ratios were seen. Male and female rats in the high dose group had increased congestion in

the spleen which may have accounted for the increase in splenic weights. Mid dose animals also exhibited splenomegaly. Splenic hyperplasia of reticuloendothelial cells was also seen in the high dose animals. In male rats, there appeared to be a mild dose-dependent increase in splenic erythropoiesis and pigmentation. The increase in splenic erythropoiesis may be an adaptive response to the anemia.

Treatment with WR238605 resulted in leukocytosis. Male and female rats in the high dose group had elevations in total leukocyte counts in weeks 4, 13 and 26 which were due primarily to increases in mature neutrophil and lymphocyte numbers. WR238605 administration also resulted in mild thrombocytopenia in mid and high dose males.

Administration of WR238605 for 6 months resulted in pulmonary lesions in male and female rats in the mid and high dose groups. These lesions consisted of hemorrhage (high dose groups only), foamy macrophage accumulation, and chronic interstitial inflammation and are most likely responsible for the increased lung weights. Minimal changes in the lungs were seen in the low dose group. The pathogenesis of the pulmonary lesions is unknown. A possible mechanism could be a primary lesion to the endothelium and/or type 1 alveolar cells resulting in hemorrhage. The presence of erythrocytes and blood protein could result in accumulation of macrophages in the alveolar lumen. Macrophages may develop copious foamy cytoplasm as they attempt to digest the lipid membrane component of the erythrocytes and may release mediators into the alveolar lumen resulting in interstitial inflammation.

Administration of WR238605 resulted in hepatotoxicity. Changes in clinical chemistry parameters were suggestive of mild liver dysfunction. Serum globulin content was decreased and the A/G ratio was correspondingly increased in high dose males, and low and high dose females. Total bile acids were also elevated in high dose males. Serum BUN concentrations were slightly reduced in high dose animals, suggestive of a drug-related effect on urea synthesis by the liver. Clinical chemistry changes were supported by histopathologic evidence of liver injury in high dose males, but not females, and consisted of apoptosis, pigmentation and fatty change in the centrilobular region. Centrilobular fatty change was seen to a lesser extent in mid dose males. The centrilobular lesions are consistent with classic cases of chronic congestion. However, congestion was only seen in 2 male rats in the mid and high dose groups each. Alternatively, these hepatic lesions may have arisen due to circulating free hemoglobin in the blood or direct test article toxicity.

Both male and female rats in the mid and high dose groups had increased kidney weights, accompanied by pigmentation in the cortex, with lesions being more prevalent and severe in the high dose animals. The pigment is most likely hemosiderin arising from the reuptake of free hemoglobin by the renal glomeruli. Circulating hemoglobin may have arisen from the pulmonary hemorrhages upon hemoglobin release and return to the blood via direct resorption or lymphatic return. Hemolytic anemia would also result in circulating free hemoglobin.

WR238605 administration resulted in pigmentation of the zona reticularis region of the adrenal cortex in a dose-dependent fashion in male and female rats. The identity of the pigment is unknown, but may be either lipofuscin or hemosiderin. Adrenal gland congestion was increased in the high dose females and may have accounted for the increased weight of the adrenal glands in this dose group.

Decreased heart weights were seen in mid dose males and high dose animals. The significance of these changes are unclear as corresponding histopathologic lesions were not observed.

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In summary, the primary toxicities of WR238605 Succinate were to RBCs, the lungs and the liver. Mortality occurred in one high dose male rat. Treatment-related clinical signs in high dose animals included rough coat, hunched posture, labored breathing (males), and piloerection (females). Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. High dose males, and mid and high dose females had decreased RBC counts, HCT and HGB concentration, suggestive of mild anemia. The anemia may have been hemolytic in origin due to the presence of Heinz bodies and increased methemoglobin levels. Microscopic lesions observed in the spleen, bone marrow, kidneys and adrenal glands may have been secondary to anemia and/or hemolysis. High dose animals had elevations in mature neutrophil and lymphocyte numbers. Mild thrombocytopenia was seen in mid and high dose males. Pulmonary lesions in male and female rats in the mid and high dose groups consisted of foamy macrophage accumulation, chronic interstitial inflammation, and hemorrhage (high dose groups only). Apoptosis, pigmentation and fatty change in the centrilobular region of the liver were seen in high dose males, but not in females, and were accompanied by decreased serum GLOB, BUN and increased TBA. Similar clinical chemistry changes were seen in high dose females. The no-effect level (NOEL) for WR238605 Succinate is considered to be at or near the low dose of 0.5 mg base/kg/day.

PERSONNEL

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7. ARCHIVES

The raw data, specimens, test article reserves, and final report are archived at the Toxicology Research Laboratory (TRL), University of Illinois at Chicago (UIC), Department of Pharmacology, 1940 W. Taylor St., Chicago, IL 60612-7353.

8. REFERENCE

Dunnett, C.W., 1964. New tables for multiple comparisons with a control. *Biometrics* 20:482-491.

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Table 1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

Summary of Toxic Responses

Dose (mg base/kg/day)	0	0.5	2.0	9.0
Rats/Sex	20 + 5[a]	20 + 5[a]	20 + 5[a]	20 + 5[a]
Deaths	0	0	0	1M (day 137)
Body Weight Gains	-	NE	↓M	↓M/F
Food Consumption	-	NE	NE	↓M/F
Clinical Observations (Signs)	-	Hunched Posture (1M) Rough Coat (1F)	NE	Hunched Posture (3M/1F) Rough Coat (5M/2F) Labored Breathing (2M) Piloerection (7F)
Clinical Chemistry[b]	-	↓GLOB (F) ↑A/G (F) ↓TP (F)	NE	↓GLOB ↓TP (F) ↑A/G ↓BUN ↑TBA (M/F?)
Hematology[c]	-	NE	↓RBC (F) ↓HCT (F) ↓HGB (F) ↑METHGB ↓PLT (M)	↓RBC ↓HCT ↓HGB ↓MCHC ↓MCH (M) ↑RETICS ↑HEINZ ↑METHGB ↑LEUK ↑MNEUT ↑INEUT (F) ↑LYMPH ↑MONO ↓PLT (M)
Organ Weights	-	NE	↓Heart (M) ↑Kidneys (M) ↑Lungs/Bronchi ↑Spleen	↓Heart ↑Kidneys (M) ↑Lungs/Bronchi ↑Spleen ↑Adrenals (F)
Histopathology	-	Lung - Accumulation, foamy macrophages (2M) Spleen - Pigmentation (4M) - Erythropoiesis (4M) Adrenal gland - Pigmentation, zona reticularis (1M/1F) Bone marrow - Hyperplasia (5M/4F)	Lung - Hemorrhage (4M/9F) - Accumulation, foamy macrophages (20M/20F) - Chronic interstitial inflammation (20M/20F) Liver - Fatty change (6M) - Congestion (2M) Spleen - Pigmentation (8M) - Erythropoiesis (8M) Kidney - Pigmentation, cortex (4M/7F) Bone Marrow - Hyperplasia (11M/7F) Adrenal Gland - Pigmentation, zona reticularis (3M/2F)	Lung - Hemorrhage (20M/20F) - Accumulation, foamy macrophages (20M/20F) - Chronic interstitial inflammation (20M/20F) Liver - Apoptosis (11M) - Pigmentation (11M) - Fatty change (10M) - Congestion (2M) Spleen - Congestion (18M/17F) - Hyperplasia, reticuloendothelial cell (4M/1F) - Pigmentation (11M) - Erythropoiesis (8M) Kidney - Pigmentation, cortex (16M/20F) Bone Marrow - Hyperplasia (19M/13F) - Granulopoiesis (1M/1F) Adrenal Gland - Pigmentation, zona reticularis (10M/18F) - Congestion (18F)

CONCLUSIONS: The primary toxicities of WR238605 Succinate were to RBCs, the lungs and the liver. Mortality occurred in one high dose male rat. Treatment-related clinical signs in high dose animals included rough coat, hunched posture, labored breathing (males), and piloerection (females). Body weight gains were significantly reduced in high dose animals and mid dose males. Also, food consumption was decreased in high dose animals. High dose males, and mid and high dose females had decreased RBC counts, HCT and HGB concentration, suggestive of mild anemia. The anemia may have been hemolytic in origin due to the presence of Heinz bodies and increased methemoglobin levels. Microscopic lesions observed in the spleen, bone marrow, kidneys and adrenal glands may have been secondary to anemia and/or hemolysis. High dose animals had elevations in mature neutrophil and lymphocyte numbers. Mild thrombocytopenia was seen in mid and high dose males. Pulmonary lesions in male and female rats in the mid and high dose groups consisted of foamy macrophage accumulation, chronic interstitial inflammation, and hemorrhage (high dose groups only). Apoptosis, pigmentation and fatty change in the centrilobular region of the liver were seen in high dose males, but not in females, and were accompanied by decreased serum GLOB, BUN and increased TBA. Similar clinical chemistry changes were seen in high dose females. The no-effect level (NOEL) for WR238605 Succinate is considered to be at or near the low dose of 0.5 mg base/kg/day.

[a]Satellite rats for plasma drug level analysis

[b]TP = total protein, GLOB = globulin, TBA = total bile acids, BUN = blood urea nitrogen, A/G = Albumin/globulin ratio.

[c]RBC = red blood cell counts, HGB = hemoglobin, HCT = hematocrit, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, RETICS = reticulocytes, HEINZ = Heinz bodies, METHGB = methemoglobin, PLT = platelets, LEUK = leukocytes, MNEUT = mature neutrophils, INEUT = immature neutrophils, LYMPH = lymphocytes, MONO = monocytes

? = Possible or marginal effect NE = No effect M = Male F = Female

Table 2

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Dosage Formulation Analyses

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
1	0.0	08/01/95	0	-	08/08/95	0	-
	0.1		0.105 ± 0.001	105.0		0.106 ± 0.002	101.0
	0.4		0.409 ± 0.002	102.3		0.385 ± 0.024	94.1
	1.8		1.770 ± 0.069	98.3		1.777 ± 0.019	100.4
2	0.0	08/08/95	0	-	08/15/95	0	-
	0.1		0.100 ± 0.001	100.0		0.098 ± 0.003	98.0
	0.4		0.391 ± 0.002	97.8		0.397 ± 0.007	101.5
	1.8		1.789 ± 0.012	99.4		1.822 ± 0.071	101.8
3	0.0	08/15/95	0	-	08/22/95	0	-
	0.1		0.100 ± 0.001	100.0		0.099 ± 0.002	99.0
	0.4		0.411 ± 0.004	102.8		0.401 ± 0.001	97.6
	1.8		1.909 ± 0.009	106.1		1.818 ± 0.016	95.2
4	0.0	08/22/95	0	-	08/29/95	0	-
	0.1		0.098 ± 0.001	98.0		0.098± 0.001	100.0
	0.4		0.388 ± 0.004	97.0		0.387 ± 0.007	99.7
	1.8		1.790 ± 0.003	99.4		1.781 ± 0.029	99.5
5	0.0	08/29/95	0	-	09/05/95	0	-
	0.1		0.100 ± 0.002	100.0		0.104 ± 0.009	104.0
	0.4		0.400 ± 0.006	100.0		0.395 ± 0.002	98.8
	1.8		1.818 ± 0.039	101.0		1.825 ± 0.027	100.4
6	0.0	09/05/95	0	-	09/12/95	0	-
	0.1		0.096 ± 0.003	96.0		0.101 ± 0.005	105.2
	0.4		0.406 ± 0.006	101.5		0.397 ± 0.013	97.8
	1.8		1.799 ± 0.022	99.9		1.882 ± 0.069	104.6
7	0.0	09/12/95	0	-	09/19/95	0	-
	0.1		0.098 ± 0.009	98.0		0.105 ± 0.001	107.1
	0.4		0.405 ± 0.012	101.3		0.433 ± 0.007	106.9
	1.8		1.787 ± 0.031	99.3		1.866 ± 0.026	104.4
8	0.0	09/19/95	0	-	09/26/95	0	-
	0.1		0.100 ± 0.006	100.0		0.093 ± 0.004	93.0
	0.4		0.406 ± 0.005	101.5		0.391 ± 0.003	96.3
	1.8		1.873 ± 0.042	104.1		2.037 ± 0.038	108.8
9	0.0	09/26/95	0	-	10/03/95	0	-
	0.1		0.096 ± 0.001	96.0		0.097 ± 0.005	101.0
	0.4		0.395 ± 0.011	98.8		0.404 ± 0.004	102.3
	1.8		1.720 ± 0.034	95.6		1.876 ± 0.055	109.1
10	0.0	10/03/95	0	-	10/10/95	0	-
	0.1		0.093 ± 0.001	93.0		0.098 ± 0.003	108.6
	0.4		0.404 ± 0.004	101.0		0.405 ± 0.004	100.2
	1.8		1.844 ± 0.003	102.4		1.788 ± 0.036	97.0
11	0.0	10/10/95	0	-	10/17/95	0	-
	0.1		0.103 ± 0.006	103.0		0.101 ± 0.003	91.8
	0.4		0.400 ± 0.006	100.0		0.391 ± 0.005	97.8
	1.8		1.788 ± 0.003	99.3		1.728 ± 0.015	103.5
12	0.0	10/17/95	0	-	10/24/95	0	-
	0.1		0.110 ± 0.001	110.0		0.099 ± 0.002	90.0
	0.4		0.395 ± 0.006	98.8		0.395 ± 0.004	100.0
	1.8		1.827 ± 0.003	101.5		1.849 ± 0.011	101.2

Table 2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

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Dosage Formulation Analyses

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
13	0.0	10/24/95	0	-	10/31/95	0	-
	0.1		0.099 ± 0.001	99.0		0.096 ± 0.001	97.0
	0.4		0.389 ± 0.003	97.3		0.372 ± 0.008	95.6
	1.8		1.788 ± 0.009	99.3		1.786 ± 0.017	99.9
14	0.0	10/31/95	0	-	11/07/95	0	-
	0.1		0.095 ± 0.002	95.0		0.123 ± 0.008	129.5
	0.4		0.432 ± 0.006	108.0		0.453 ± 0.009	104.9
	1.8		1.707 ± 0.035	94.8		1.854 ± 0.040	108.6
15	0.0	11/07/95	0	-	11/14/95	0	-
	0.1		0.102 ± 0.001	102.0		0.104 ± 0.007	102.0
	0.4		0.403 ± 0.007	100.8		0.394 ± 0.010	97.8
	1.8		1.672 ± 0.024	92.9		1.739 ± 0.041	104.0
16	0.0	11/14/95	0	-	11/21/95	0	-
	0.1		0.101 ± 0.004	101.0		0.104 ± 0.004	103.0
	0.4		0.412 ± 0.050	103.0		0.420 ± 0.001	101.9
	1.8		1.768 ± 0.050	98.2		1.890 ± 0.024	106.9
17	0.0	11/21/95	0	-	11/28/95	0	-
	0.1		0.106 ± 0.002	106.0		0.106 ± 0.006	100.0
	0.4		0.413 ± 0.001	103.3		0.392 ± 0.034	94.9
	1.8		1.842 ± 0.011	102.3		1.774 ± 0.026	96.3
18	0.0	11/28/95	0	-	12/05/95	0	-
	0.1		0.106 ± 0.001	106.0		0.100 ± 0.001	94.3
	0.4		0.408 ± 0.007	102.0		0.398 ± 0.001	97.5
	1.8		1.861 ± 0.033	103.3		1.737 ± 0.023	93.4
19	0.0	12/05/95	0	-	12/12/95	0	-
	0.1		0.102 ± 0.001	102.0		0.103 ± 0.002	101.0
	0.4		0.377 ± 0.001	94.3		0.381 ± 0.004	101.1
	1.8		1.910 ± 0.034	106.1		1.877 ± 0.036	98.3
20	0.0	12/12/95	0	-	12/19/95	0	-
	0.1		0.098 ± 0.002	98.0		0.101 ± 0.003	103.1
	0.4		0.390 ± 0.019	97.5		0.412 ± 0.009	105.6
	1.8		1.828 ± 0.001	101.6		1.873 ± 0.018	102.5
21	0.0	12/19/95	0	-	12/27/95	0	-
	0.1		0.102 ± 0.006	102.0		0.111 ± 0.004	108.8
	0.4		0.414 ± 0.009	103.5		0.396 ± 0.009	95.7
	1.8		1.831 ± 0.027	101.7		1.816 ± 0.018	99.2
22	0.0	12/27/95	0	-	01/03/96	0	-
	0.1		0.098 ± 0.004	98.0		0.096 ± 0.004	98.0
	0.4		0.417 ± 0.009	104.3		0.398 ± 0.012	95.4
	1.8		1.735 ± 0.099	96.4		1.928 ± 0.041	111.1
23	0.0	01/03/96	0	-	01/09/96	0	-
	0.1		0.094 ± 0.006	94.0		0.103 ± 0.006	109.6
	0.4		0.411 ± 0.011	102.8		0.403 ± 0.024	98.1
	1.8		1.798 ± 0.037	99.9		1.795 ± 0.022	99.8
24	0.0	01/09/96	0	-	01/16/96	0	-
	0.1		0.098 ± 0.005	98.0		0.099 ± 0.008	101.0
	0.4		0.396 ± 0.010	99.0		0.392 ± 0.004	99.0
	1.8		1.803 ± 0.059	100.2		1.805 ± 0.041	100.1

Table 2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

Dosage Formulation Analyses

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
25	0.0	01/16/96	0	-	01/23/96	0	-
	0.1		0.105 ± 0.002	105.0		0.104 ± 0.067	99.0
	0.4		0.392 ± 0.005	98.3		0.436 ± 0.004	110.9
	1.8		1.845 ± 0.036	102.5		1.709 ± 0.034	92.6
26	0.0	01/23/96	0	-	02/02/96	0	-
	0.1		0.102 ± 0.002	102.0		0.100 ± 0.002	98.0
	0.4		0.421 ± 0.006	105.3		0.397 ± 0.007	94.3
	1.8		1.708 ± 0.007	94.9		1.774 ± 0.010	103.9

Table 3

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

Summary of Clinical Signs (Males)

DOSE (mg base/kg/day): GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
Scheduled Sacrifice	20	20	20	20
Animal Found Dead	0	0	0	1 (137)[a]
Hunched Posture	0	1 (11)	0	3 (62-84, 136, 169, 171-181)
Labored Breathing	0	0	0	2 (136, 167)
Rough Coat	0	0	0	5 (48-102,104,117,124-125,134,173-176)
Total Number of Animals[b]	25	25	25	25

Summary of Clinical Signs (Females)

DOSE (mg base/kg/day): GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
Scheduled Sacrifice	20	20	20	20
Hunched Posture	0	0	0	1 (92-96)[a]
Piloerection	0	0	0	7 (67-73, 76-77, 86, 94, 100-102, 126-128)
Rough Coat	0	1 (156, 158-159)	0	2 (92-97, 132)
Total Number of Animals[b]	25	25	25	25

[a]Number(s) in parentheses indicate the day(s) the adverse sign was observed
[b]Includes 5 satellite animals/sex/group

DRAFT

Table 4.1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

PERIOD	DOSE: / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M	mg base/kg/day
DAY 1	MEAN	252	249	248	248	
	S.D.	16.6	13.5	12.8	14.6	
	N	25	25	25	25	
DAY 8	MEAN	306	298	299	291	
	S.D.	20.7	24.5	15.7	18.1	
	N	25	25	25	25	
DAY 15	MEAN	353	342	342	320*	
	S.D.	26.9	28.0	18.9	19.4	
	N	25	25	25	25	
DAY 22	MEAN	390	378	379	338*	
	S.D.	29.6	33.2	20.6	23.8	
	N	25	25	25	25	
DAY 29	MEAN	419	409	411	358*	
	S.D.	34.9	36.7	24.8	29.7	
	N	25	25	25	25	
DAY 36	MEAN	446	438	438	373*	
	S.D.	38.5	38.9	29.3	32.5	
	N	25	25	25	25	
DAY 43	MEAN	485	472	466	395*	
	S.D.	44.1	41.0	31.4	36.5	
	N	25	25	25	25	
DAY 50	MEAN	506	496	482	402*	
	S.D.	46.8	40.0	30.6	38.4	
	N	25	25	25	25	
DAY 57	MEAN	530	521	502	414*	
	S.D.	51.0	41.9	30.9	46.2	
	N	25	25	25	25	
DAY 64	MEAN	548	544	521	426*	
	S.D.	53.3	42.7	32.6	53.8	
	N	25	25	25	25	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

Table 4.1 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

PERIOD	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 mg base/kg/day 4-M
DAY 71	MEAN	570	566	537	437*
	S.D.	54.2	45.0	34.1	60.2
	N	25	25	25	25
DAY 78	MEAN	583	581	552	444*
	S.D.	60.7	44.8	34.7	55.2
	N	25	25	25	25
DAY 85	MEAN	599	598	563*	458*
	S.D.	61.7	46.7	36.5	50.8
	N	25	25	25	25
DAY 92	MEAN	606	600	564*	459*
	S.D.	65.1	50.6	37.4	49.4
	N	25	25	25	25
DAY 99	MEAN	622	622	577*	474*
	S.D.	63.7	53.5	39.4	52.8
	N	25	25	25	25
DAY 106	MEAN	630	631	582*	475*
	S.D.	64.1	56.1	40.9	49.7
	N	25	25	25	25
DAY 113	MEAN	644	642	592*	488*
	S.D.	64.7	57.4	39.4	53.2
	N	25	25	25	25
DAY 120	MEAN	650	653	596*	492*
	S.D.	62.6	56.9	40.4	53.9
	N	25	25	25	25
DAY 127	MEAN	653	659	598*	494*
	S.D.	63.4	59.4	37.8	53.2
	N	25	25	25	25
DAY 134	MEAN	662	668	607*	499*
	S.D.	65.5	60.4	39.0	58.3
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

Table 4.1 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: MALE

PERIOD	DOSE: / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M	mg base/kg/day
DAY 141	MEAN	673	682	618*	510*	
	S.D.	67.2	63.4	40.3	56.8	
	N	25	25	25	24	
DAY 148	MEAN	683	693	628*	522*	
	S.D.	65.5	65.5	42.1	57.7	
	N	25	25	25	24	
DAY 155	MEAN	696	703	642*	530*	
	S.D.	68.4	67.6	43.8	58.9	
	N	25	25	25	24	
DAY 162	MEAN	703	709	647*	528*	
	S.D.	73.0	71.4	44.1	58.9	
	N	25	25	25	24	
DAY 169	MEAN	705	709	652*	527*	
	S.D.	76.2	75.7	46.1	61.1	
	N	25	25	25	24	
DAY 176	MEAN	715	714	656*	534*	
	S.D.	73.9	78.1	46.2	61.5	
	N	25	25	25	24	
DAY 182	MEAN	717	700	659*	530*	
	S.D.	56.9	62.2	52.1	61.7	
	N	20	20	20	19	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

Table 4.2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F	mg base/kg/day
DAY 1	MEAN	182	182	182	179	
	S.D.	10.2	11.0	10.3	10.6	
	N	25	25	25	25	
DAY 8	MEAN	204	203	202	198	
	S.D.	12.6	13.8	12.6	9.8	
	N	25	25	25	25	
DAY 15	MEAN	222	221	221	212	
	S.D.	12.7	16.0	14.5	12.6	
	N	25	25	25	25	
DAY 22	MEAN	236	234	235	223*	
	S.D.	14.4	16.7	15.4	13.3	
	N	25	25	25	25	
DAY 29	MEAN	247	247	249	237	
	S.D.	15.4	18.5	19.4	14.0	
	N	25	25	25	25	
DAY 36	MEAN	252	253	252	236*	
	S.D.	16.1	19.3	20.0	14.4	
	N	25	25	25	25	
DAY 43	MEAN	268	269	267	251*	
	S.D.	16.0	22.6	22.4	15.6	
	N	25	25	25	25	
DAY 50	MEAN	273	276	277	254*	
	S.D.	18.5	25.8	24.4	15.1	
	N	25	25	25	25	
DAY 57	MEAN	284	287	285	260*	
	S.D.	20.9	27.8	27.6	15.7	
	N	25	25	25	25	
DAY 64	MEAN	294	293	294	267*	
	S.D.	22.2	26.9	29.8	15.4	
	N	25	25	25	25	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 mg base/kg/day 4-F
DAY 71	MEAN	299	298	298	270*
	S.D.	22.7	28.4	32.3	16.2
	N	25	25	25	25
DAY 78	MEAN	305	306	301	274*
	S.D.	24.9	29.9	34.9	16.6
	N	25	25	25	25
DAY 85	MEAN	313	312	308	280*
	S.D.	26.2	32.0	34.2	18.2
	N	25	25	25	25
DAY 92	MEAN	317	313	311	277*
	S.D.	27.5	31.1	31.4	22.1
	N	25	25	25	25
DAY 99	MEAN	315	312	308	281*
	S.D.	26.7	30.8	32.8	17.7
	N	25	25	25	25
DAY 106	MEAN	316	314	311	280*
	S.D.	27.2	30.3	31.2	18.6
	N	25	25	25	25
DAY 113	MEAN	330	330	324	290*
	S.D.	27.6	33.5	33.3	17.5
	N	25	25	25	25
DAY 120	MEAN	337	333	330	292*
	S.D.	30.9	34.7	36.6	18.7
	N	25	25	25	25
DAY 127	MEAN	341	337	335	291*
	S.D.	31.9	36.5	39.3	16.9
	N	25	25	25	25
DAY 134	MEAN	347	342	343	295*
	S.D.	33.8	35.5	41.3	18.6
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

Table 4.2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 mg base/kg/day 4-F
DAY 141	MEAN	353	348	347	296*
	S.D.	34.7	36.9	41.8	17.8
	N	25	25	25	25
DAY 148	MEAN	358	352	353	300*
	S.D.	38.7	38.7	42.3	18.9
	N	25	25	25	25
DAY 155	MEAN	364	353	358	305*
	S.D.	40.D	42.1	46.0	18.3
	N	25	25	25	25
DAY 162	MEAN	360	353	355	304*
	S.D.	40.7	42.4	45.5	21.1
	N	25	25	25	25
DAY 169	MEAN	365	359	359	307*
	S.D.	42.6	42.3	44.0	21.3
	N	25	25	25	25
DAY 176	MEAN	375	369	367	312*
	S.D.	46.4	44.5	48.1	22.9
	N	25	25	25	25
DAY 182	MEAN	386	370	374	317*
	S.D.	44.4	51.9	44.6	17.4
	N	20	20	20	20

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

Table 5.1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: MALE

PERIOD [a]	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M mg base/kg/day
DAY 8 [b]	MEAN	54	49	50	43*
	S.D.	6.1	17.0	6.9	7.3
	N	25	25	25	25
DAY 15	MEAN	46	44	44	29*
	S.D.	7.7	6.4	5.2	6.6
	N	25	25	25	25
DAY 22	MEAN	38	36	36	18*
	S.D.	6.2	7.0	4.3	8.7
	N	25	25	25	25
DAY 29	MEAN	29	31	32	20*
	S.D.	10.9	10.3	8.6	15.2
	N	25	25	25	25
DAY 36	MEAN	27	29	26	15*
	S.D.	9.2	5.9	11.1	12.9
	N	25	25	25	25
DAY 43	MEAN	39	35	28*	22*
	S.D.	9.3	7.5	7.0	9.3
	N	25	25	25	25
DAY 50	MEAN	21	24	17	7*
	S.D.	6.7	6.5	7.2	8.8
	N	25	25	25	25
DAY 57	MEAN	24	25	20	13*
	S.D.	7.6	6.8	5.5	10.6
	N	25	25	25	25
DAY 64	MEAN	18	23	19	12*
	S.D.	9.6	3.3	5.0	12.5
	N	25	25	25	25
DAY 71	MEAN	22	22	16*	11*
	S.D.	10.4	5.0	5.8	13.3
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a] Weight gains compared to the previous period
[b] Baseline is day 1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: MALE

PERIOD[a]	DOSE: / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 mg base/kg/day 4-M
DAY 78	MEAN	14	15	15	7
	S.D.	21.2	7.1	6.8	23.8
	N	25	25	25	25
DAY 85	MEAN	16	17	11	13
	S.D.	6.3	5.9	5.6	21.1
	N	25	25	25	25
DAY 92	MEAN	6	1	1	2
	S.D.	23.4	26.6	8.3	13.4
	N	25	25	25	25
DAY 99	MEAN	17	22	13	14
	S.D.	10.5	23.9	8.2	8.3
	N	25	25	25	25
DAY 106	MEAN	8	9	5	2*
	S.D.	8.2	9.5	8.6	8.0
	N	25	25	25	25
DAY 113	MEAN	14	11	9	13
	S.D.	6.9	6.9	7.2	6.5
	N	25	25	25	25
DAY 120	MEAN	6	11	4	3
	S.D.	17.1	5.9	9.6	8.3
	N	25	25	25	25
DAY 127	MEAN	3	6	2	2
	S.D.	5.3	7.8	9.6	8.9
	N	25	25	25	25
DAY 134	MEAN	9	9	9	6
	S.D.	10.7	4.8	4.7	10.4
	N	25	25	25	25
DAY 141	MEAN	11	15	11	7
	S.D.	7.6	6.5	5.8	7.4
	N	25	25	25	24

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: MALE

PERIOD[a]	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M	mg base/kg/day
DAY 148	MEAN	11	11	11	12	
	S.D.	4.7	7.6	5.4	5.3	
	N	25	25	25	24	
DAY 155	MEAN	13	10	13	8	
	S.D.	6.5	7.4	5.4	9.4	
	N	25	25	25	24	
DAY 162	MEAN	7	6	5	-2*	
	S.D.	8.3	8.7	8.0	8.3	
	N	25	25	25	24	
DAY 169	MEAN	2	-1	4	-1	
	S.D.	7.1	25.2	6.3	21.7	
	N	25	25	25	24	
DAY 176	MEAN	9	5	5	7	
	S.D.	9.7	8.9	8.6	10.0	
	N	25	25	25	24	
DAY 182	MEAN	6	3	3	9	
	S.D.	4.9	7.3	7.2	11.9	
	N	20	20	20	19	
TOTAL GAIN	MEAN	466	453	412*	286*	
	S.D.	49.2	57.9	52.0	55.3	
	N	20	20	20	19	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period

Table 5.2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD[a]	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 mg base/kg/day 4-F
DAY 8[b]	MEAN	22	21	20	19
	S.D.	6.4	4.5	4.5	4.9
	N	25	25	25	25
DAY 15	MEAN	17	18	19	14
	S.D.	5.7	4.3	4.2	5.9
	N	25	25	25	25
DAY 22	MEAN	14	13	14	11*
	S.D.	4.9	4.0	5.3	4.9
	N	25	25	25	25
DAY 29	MEAN	11	13	14	13
	S.D.	6.2	4.1	6.3	3.4
	N	25	25	25	25
DAY 36	MEAN	6	6	3	-1*
	S.D.	5.9	6.0	6.3	6.9
	N	25	25	25	25
DAY 43	MEAN	16	16	15	15
	S.D.	8.4	6.5	8.0	5.7
	N	25	25	25	25
DAY 50	MEAN	5	7	10	3
	S.D.	5.8	6.7	8.0	5.6
	N	25	25	25	25
DAY 57	MEAN	10	11	8	6*
	S.D.	5.7	4.7	7.2	6.2
	N	25	25	25	25
DAY 64	MEAN	10	6	9	6
	S.D.	5.0	6.9	5.5	4.3
	N	25	25	25	25
DAY 71	MEAN	5	5	4	3
	S.D.	3.7	5.2	6.3	3.5
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period
[b]Baseline is day 1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD [a]	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 mg base/kg/day 4-F
DAY 78	MEAN	6	8	3	4
	S.D.	5.0	4.9	5.1	3.8
	N	25	25	25	25
DAY 85	MEAN	7	6	7	6
	S.D.	6.3	5.6	3.9	3.7
	N	25	25	25	25
DAY 92	MEAN	4	2	3	-2*
	S.D.	5.6	4.6	5.4	10.6
	N	25	25	25	25
DAY 99	MEAN	-2	-2	-3	4
	S.D.	10.2	4.8	8.6	10.1
	N	25	25	25	25
DAY 106	MEAN	1	3	3	-1
	S.D.	7.2	5.4	8.6	6.0
	N	25	25	25	25
DAY 113	MEAN	14	15	13	10
	S.D.	11.6	7.2	6.2	5.0
	N	25	25	25	25
DAY 120	MEAN	7	4	6	2
	S.D.	8.9	5.6	6.8	4.4
	N	25	25	25	25
DAY 127	MEAN	4	3	5	0*
	S.D.	5.8	6.7	5.7	6.1
	N	25	25	25	25
DAY 134	MEAN	6	5	7	4
	S.D.	5.8	4.7	5.4	8.0
	N	25	25	25	25
DAY 141	MEAN	6	6	4	0*
	S.D.	6.1	6.9	4.3	5.3
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Weight gains compared to the previous period

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 152 SEX: FEMALE

PERIOD [a]	DOSE: / GROUP:	0 mg base/kg/day 1-F	0.5 mg base/kg/day 2-F	2.0 mg base/kg/day 3-F	9.0 mg base/kg/day 4-F
DAY 148	MEAN	5	4	6	4
	S.D.	8.3	5.1	4.5	5.8
	N	25	25	25	25
DAY 155	MEAN	6	1	5	5
	S.D.	7.3	7.3	7.9	7.1
	N	25	25	25	25
DAY 162	MEAN	-4	0	-3	-1
	S.D.	10.5	5.2	7.1	6.5
	N	25	25	25	25
DAY 169	MEAN	4	5	3	3
	S.D.	7.3	4.6	5.5	5.5
	N	25	25	25	25
DAY 176	MEAN	11	10	9	5
	S.D.	9.3	7.1	8.5	6.4
	N	25	25	25	25
DAY 182	MEAN	5	5	4	3
	S.D.	9.5	10.4	6.7	5.5
	N	20	20	20	20
TOTAL GAIN	MEAN	203	190	192	138*
	S.D.	38.7	46.1	37.6	15.9
	N	20	20	20	20

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a] Weight gains compared to the previous period

Table 6.1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

PERIOD[a]	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 mg base/kg/day 4-M
DAY 1[b]	INTAKE (g)	24.3	24.3	24.3	23.8
	S.D.	2.26	2.01	2.36	2.05
	N	25	25	25	25
DAY 8	INTAKE (g)	25.1	24.3	24.5	22.5*
	S.D.	1.81	3.58	1.47	2.25
	N	25	25	25	25
DAY 15	INTAKE (g)	26.2	24.9	25.3	20.7*
	S.O.	2.28	3.15	1.68	1.68
	N	25	25	25	25
OAY 22	INTAKE (g)	26.5	25.8	26.6	20.3*
	S.O.	1.80	2.32	1.91	1.99
	N	25	24	25	25
DAY 29	INTAKE (g)	26.1	26.2	25.8	20.1*
	S.O.	2.67	3.56	1.96	2.51
	N	25	25	25	25
DAY 36	INTAKE (g)	26.4	25.3	26.1	20.3*
	S.D.	2.92	2.71	3.84	2.66
	N	25	25	25	25
DAY 43	INTAKE (g)	28.7	27.1	27.1	22.1*
	S.O.	3.06	2.63	2.25	2.74
	N	25	25	25	25
OAY 50	INTAKE (g)	28.4	28.4	26.8	22.4*
	S.D.	3.06	2.59	1.98	3.44
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals
[b]Baseline is day -6

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

PERIOD[a]	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 mg base/kg/day 4-M
DAY 57	INTAKE (g)	29.4	29.2	27.6	21.6*
	S.D.	3.44	2.56	1.77	3.56
	N	25	25	25	25
DAY 64	INTAKE (g)	28.5	28.5	27.8	21.1*
	S.D.	2.96	2.52	1.89	4.22
	N	25	25	25	25
DAY 71	INTAKE (g)	28.8	29.3	27.8	21.8*
	S.D.	2.90	2.85	1.83	4.90
	N	25	25	25	25
DAY 78	INTAKE (g)	29.2	29.4	28.8	22.9*
	S.D.	5.19	2.63	1.88	4.00
	N	25	25	25	25
DAY 85	INTAKE (g)	28.4	29.0	29.0	24.2*
	S.D.	3.27	2.80	2.95	2.72
	N	25	25	25	25
DAY 92	INTAKE (g)	27.3	26.6	26.1	20.9*
	S.D.	3.75	5.07	2.22	3.27
	N	25	25	25	25
DAY 99	INTAKE (g)	27.4	28.0	26.3	22.5*
	S.D.	2.94	3.04	2.24	3.41
	N	25	25	25	25
DAY 106	INTAKE (g)	26.9	27.1	26.6	22.2*
	S.D.	2.51	3.39	2.88	3.24
	N	25	25	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals

Table 6.1 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

PERIOD [a]	DOSE: GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M	mg base/kg/day
DAY 113	INTAKE (g)	27.1	27.2	27.2	23.5*	
	S.D.	2.72	2.87	2.14	2.82	
	N	25	25	25	25	
DAY 120	INTAKE (g)	27.1	27.5	26.1	22.8*	
	S.D.	3.55	2.47	2.68	3.01	
	N	25	25	25	25	
DAY 127	INTAKE (g)	25.8	26.8	25.1	22.0*	
	S.D.	2.73	2.53	2.09	2.55	
	N	25	25	25	25	
DAY 134	INTAKE (g)	26.3	26.6	26.6	21.8*	
	S.D.	2.78	2.01	2.06	4.61	
	N	25	25	25	25	
DAY 141	INTAKE (g)	26.1	27.8	27.3	22.7*	
	S.D.	2.77	2.89	1.99	3.36	
	N	25	25	25	24	
DAY 148	INTAKE (g)	27.6	27.8	27.7	25.7	
	S.D.	2.43	3.72	1.95	3.68	
	N	25	25	25	24	
DAY 155	INTAKE (g)	28.0	28.0	27.9	24.3*	
	S.D.	2.41	2.98	1.88	3.30	
	N	25	25	25	24	
DAY 162	INTAKE (g)	26.0	26.1	25.7	22.0*	
	S.D.	2.98	3.51	2.20	2.38	
	N	25	25	25	24	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a] Calculated daily food consumption for successive period intervals

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: MALE

PERIOD[a]	DOSE: / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 mg base/kg/day 4-M
DAY 169	INTAKE (g)	25.6	25.7	25.6	21.8*
	S.D.	3.03	3.70	2.02	2.80
	N	25	25	25	24
DAY 176	INTAKE (g)	26.3	25.2	26.2	22.8*
	S.D.	2.84	4.29	2.09	3.58
	N	25	25	25	24
DAY 182	INTAKE (g)	27.2	25.9	27.4	25.8
	S.D.	2.30	3.49	2.92	3.17
	N	20	20	20	19

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals

Table 6.2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

PERIOD[a]	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F	mg base/kg/day
DAY 1[b]	INTAKE (g)	20.6	19.4	18.3	18.2	
	S.D.	7.21	2.87	2.49	2.55	
	N	25	25	25	25	
DAY 8	INTAKE (g)	18.6	17.7	17.8	15.9*	
	S.D.	2.69	1.67	3.06	1.55	
	N	25	25	25	25	
DAY 15	INTAKE (g)	18.1	17.7	18.4	17.7	
	S.D.	2.65	1.94	4.21	3.09	
	N	25	25	25	25	
DAY 22	INTAKE (g)	19.0	18.4	19.6	16.2*	
	S.D.	3.59	3.10	3.62	1.77	
	N	25	25	25	25	
DAY 29	INTAKE (g)	17.5	17.8	18.3	16.2*	
	S.D.	2.05	1.66	2.24	1.25	
	N	25	25	25	25	
DAY 36	INTAKE (g)	17.8	16.9	18.6	15.9	
	S.D.	3.14	1.53	4.12	2.39	
	N	25	25	25	25	
DAY 43	INTAKE (g)	17.7	19.4*	19.2*	17.1	
	S.D.	2.07	1.95	1.89	1.65	
	N	24	25	25	25	
DAY 50	INTAKE (g)	19.0	19.0	19.7	19.5	
	S.D.	3.77	2.18	2.86	3.41	
	N	25	25	25	25	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals
[b]Baseline is day -6

Table 6.2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

PERIOD [a]	DOSE: GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F	mg base/kg/day
DAY 57	INTAKE (g)	19.6	19.6	19.6	16.8	
	S.D.	2.65	2.08	1.97	1.99	
	N	25	25	25	25	
DAY 64	INTAKE (g)	19.4	19.1	19.4	16.7*	
	S.D.	2.34	2.55	2.12	1.35	
	N	25	25	25	25	
DAY 71	INTAKE (g)	18.9	18.6	18.8	16.7*	
	S.D.	2.59	2.22	2.13	1.45	
	N	25	25	25	25	
DAY 78	INTAKE (g)	21.2	20.7	20.6	18.3*	
	S.D.	5.52	2.44	2.73	2.17	
	N	25	25	25	24	
DAY 85	INTAKE (g)	20.6	19.9	20.3	18.7	
	S.D.	3.47	2.32	2.05	3.25	
	N	25	25	25	25	
DAY 92	INTAKE (g)	19.3	18.8	18.9	15.1*	
	S.D.	6.11	3.30	3.41	2.25	
	N	25	25	25	25	
DAY 99	INTAKE (g)	17.8	17.1	17.5	15.6*	
	S.D.	4.14	1.56	2.44	1.37	
	N	25	25	25	25	
DAY 106	INTAKE (g)	17.8	18.6	18.3	16.0	
	S.D.	5.21	2.67	2.52	2.01	
	N	25	24	25	25	

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a] Calculated daily food consumption for successive period intervals

Table 6.2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

PERIOD[a]	DOSE: / GROUP:	0 mg base/kg/day 1-F	0.5 mg base/kg/day 2-F	2.0 mg base/kg/day 3-F	9.0 mg base/kg/day 4-F
DAY 113	INTAKE (g)	18.9	19.4	20.2	17.8
	S.D.	4.69	2.20	3.28	1.83
	N	25	25	25	25
DAY 120	INTAKE (g)	19.4	19.1	20.0	17.6*
	S.D.	2.33	2.08	2.53	2.99
	N	25	25	25	25
DAY 127	INTAKE (g)	18.7	18.3	19.2	16.0*
	S.D.	1.95	1.72	2.09	1.26
	N	25	25	25	25
DAY 134	INTAKE (g)	19.7	18.9	20.0	16.6*
	S.D.	3.74	1.80	2.55	2.52
	N	25	25	25	25
DAY 141	INTAKE (g)	18.9	19.1	20.6	16.5*
	S.D.	3.00	1.78	3.29	2.67
	N	25	25	25	25
DAY 148	INTAKE (g)	19.9	19.6	22.0	20.0
	S.D.	3.83	1.95	4.63	4.57
	N	25	25	25	25
DAY 155	INTAKE (g)	19.5	18.6	20.3	17.5
	S.D.	4.81	2.44	2.58	2.05
	N	25	23	25	25
DAY 162	INTAKE (g)	16.0	17.2	17.6	15.8
	S.D.	3.81	2.42	3.31	1.87
	N	25	23	25	25

* P less than .05 Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals

Table 6.2 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF DAILY MEAN FOOD CONSUMPTION (Grams)

STUDY: 152 SEX: FEMALE

PERIOD[a]	DOSE: / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 mg base/kg/day 4-F
DAY 169	INTAKE (g)	17.2	17.5	18.3	16.2
	S.D.	4.14	2.52	2.29	1.82
	N	25	25	25	25
DAY 176	INTAKE (g)	19.0	19.0	19.6	17.4
	S.D.	3.14	1.90	2.53	1.86
	N	25	25	25	25
DAY 182	INTAKE (g)	21.1	20.9	23.1	20.1
	S.D.	3.53	2.92	3.17	2.64
	N	20	20	20	20

Analysis of Variance using DUNNETT'S Procedure

[a]Calculated daily food consumption for successive period intervals

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	ALT IU/L	SDH IU/L	TP g/dL	ALB g/dL	GLOB g/dL	A/G -	TBA umol/L	ALKP IU/L	LDH IU/L
Group: 1 M : 0 mg base/kg/day									
MEAN	53	15.5	7.7	4.0	3.8	1.07	24.7	368	171
SD	8.7	8.40	0.78	0.36	0.49	0.097	7.58	98.7	146.3
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	52	18.7	7.8	3.9	3.9	1.02	34.1	340	163
SD	9.8	8.53	0.48	0.23	0.34	0.089	24.94	41.0	101.5
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	53	16.3	7.7	4.1	3.6	1.13	33.8	364	176
SD	7.2	10.71	0.41	0.25	0.44	0.200	20.01	122.7	159.6
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	48	19.0	7.9	4.1	3.8	1.09	33.0	325	188
SD	6.3	6.02	0.45	0.15	0.41	0.132	11.72	96.8	111.1
N	10	10	10	10	10	10	10	10	10

Table 7.2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 4

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1 M : 0 mg base/kg/day									
MEAN	242	18.3	0.54	144.3	6.20	105.2	11.3	9.6	161
SD	173.4	1.67	0.069	3.47	0.489	2.53	0.49	0.57	39.1
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	304	17.3	0.56	146.9	6.18	104.1	11.4	9.4	145
SD	293.8	1.62	0.094	3.35	0.552	4.09	0.51	0.58	11.1
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	170	17.0	0.52	145.3	5.67	106.5	11.1	9.6	151
SD	140.2	1.31	0.042	2.21	0.476	2.92	0.34	0.54	23.8
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	167	15.8*	0.59	147.9	6.40	104.7	11.1	9.2	135
SD	182.7	2.52	0.125	3.67	0.515	2.36	0.33	0.90	11.7
N	10	10	10	10	10	10	10	10	10

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*-Significant Difference from Control P < .05

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALT	SDH	TP	ALB	GLOB	A/G	TBA	ALKP	LDH
UNITS:	IU/L	IU/L	g/dL	g/dL	g/dL	-	umol/L	IU/L	IU/L
Group: 1-F : 0 mg base/kg/day									
MEAN	51	14.9	7.3	4.1	3.2	1.27	25.6	213	253
SD	7.3	3.48	0.41	0.29	0.26	0.133	13.51	44.4	211.0
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	48	14.8	7.2	4.0	3.2	1.24	22.7	237	240
SD	8.4	1.60	0.56	0.28	0.35	0.104	7.13	70.5	110.8
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	49	15.2	7.4	4.1	3.3	1.23	29.5	242	392
SD	3.5	6.40	0.40	0.26	0.19	0.065	16.51	116.7	254.2
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	57	18.8	7.2	4.0	3.3	1.21	36.8	260	183
SD	9.3	2.49	0.41	0.28	0.20	0.083	18.47	100.6	86.7
N	10	10	10	10	10	10	10	10	10

Table 7.4

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0 mg base/kg/day									
MEAN	211	18.4	0.55	144.1	5.47	103.5	10.8	7.8	129
SD	167.9	1.50	0.028	1.20	0.241	3.63	0.33	0.88	18.2
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	147	18.3	0.56	143.9	5.46	103.7	10.8	8.0	133
SD	47.2	1.85	0.047	1.29	0.288	3.74	0.23	0.52	14.7
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	260	19.5	0.57	143.8	5.69	104.6	10.9	8.4	146
SD	216.3	1.72	0.054	1.75	0.417	2.91	0.41	0.97	24.4
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	149	18.0	0.57	143.7	5.63	104.2	10.9	8.3	139
SD	48.7	2.44	0.023	1.06	0.272	3.16	0.37	0.63	23.3
N	10	10	10	10	10	10	10	10	10

Table 7.5

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALT	SDH	TP	ALB	GLOB	A/G	TBA	ALKP	LDH
UNITS:	IU/L	IU/L	g/dL	g/dL	g/dL	-	umol/L	IU/L	IU/L
Group: 1 M : 0 mg base/kg/day									
MEAN	65	20.1	8.3	4.3	4.0	1.07	44.4	236	473
SD	14.3	13.31	0.60	0.40	0.31	0.108	20.18	80.9	515.2
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	62	16.4	7.9	4.1	3.8	1.09	46.3	222	413
SD	13.1	7.08	0.37	0.21	0.27	0.088	24.88	46.8	289.8
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	60	18.2	8.0	4.2	3.8	1.11	67.3	236	333
SD	9.4	8.55	0.57	0.36	0.32	0.101	26.35	98.0	142.3
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	77	16.7	7.9	4.3	3.6*	1.20*	62.2	222	460
SD	20.7	6.10	0.49	0.26	0.33	0.101	26.53	54.0	193.4
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7.6

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1 M : 0 mg base/kg/day									
MEAN	312	21.0	0.57	145.1	6.01	105.7	10.9	7.8	170
SD	249.1	3.61	0.071	1.20	0.493	5.14	0.41	0.98	51.3
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	456	17.0*	0.52	145.2	5.88	99.9*	10.9	7.4	143
SD	392.0	2.73	0.044	1.48	0.559	4.38	0.34	0.74	47.3
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	381	18.1	0.58	145.3	5.75	105.8	10.8	8.0	165
SD	335.6	2.91	0.079	1.34	0.533	5.73	0.40	0.44	34.2
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	226	15.4*	0.57	144.3	5.95	108.6	10.5	8.1	134
SD	159.0	2.54	0.055	1.42	0.446	5.64	0.24	0.93	19.6
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7.7

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALT	SOH	TP	ALB	GLOB	A/G	TBA	ALKP	LDH
UNITS:	IU/L	IU/L	g/dL	g/dL	g/dL	-	umol/L	IU/L	IU/L
Group: 1-F : 0 mg base/kg/day									
MEAN	64	12.2	7.7	4.6	3.2	1.46	45.1	128	444
SD	13.4	4.18	0.65	0.30	0.44	0.188	30.14	26.5	197.3
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	60	13.1	8.0	4.6	3.5	1.34	86.6	176	457
SD	8.6	6.69	0.55	0.40	0.36	0.189	89.41	90.7	242.7
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	68	18.7*	7.7	4.5	3.2	1.42	59.7	151	320
SD	11.4	8.11	0.73	0.43	0.50	0.253	25.49	79.6	163.4
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	71	17.4	7.7	4.4	3.2	1.40	90.2	171	375
SD	15.6	2.40	0.65	0.33	0.47	0.198	38.40	76.5	190.0
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7.8

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0 mg base/kg/day									
MEAN	427	16.8	0.60	144.8	5.81	99.4	11.0	7.9	142
SD	461.4	3.18	0.088	1.69	0.438	2.46	0.66	1.08	30.3
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	489	18.3	0.55	144.9	5.45	100.6	11.0	7.7	144
SD	525.6	3.89	0.107	1.52	0.391	2.80	0.56	0.73	23.9
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	408	18.8	0.63	146.1	5.47	102.3	11.2	8.2	166
SD	242.1	2.26	0.075	2.85	0.457	2.91	0.47	0.54	43.0
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	240	15.6	0.57	143.8	5.54	101.7	11.1	8.0	147
SD	142.1	2.76	0.074	2.39	0.214	2.79	0.34	0.96	45.1
N	10	10	10	10	10	10	10	10	10

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALT	SDH	TP	ALB	GLOB	A/G	TBA	ALKP	LDH
UNITS:	IU/L	IU/L	g/dL	g/dL	g/dL	-	umol/L	IU/L	IU/L
Group: 1 M : 0 mg base/kg/day									
MEAN	75	13.0	7.6	4.2	3.4	1.32	59.8	204	516
SD	15.7	4.44	0.56	0.28	0.78	0.375	35.22	76.0	359.7
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	81	16.0	7.3	4.0	3.3	1.26	48.2	173	421
SD	42.5	7.60	0.61	0.24	0.75	0.327	19.59	56.5	321.1
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	65	12.4	7.6	4.1	3.5	1.25	60.3	191	405
SD	14.4	6.57	0.45	0.31	0.65	0.365	31.87	90.1	210.9
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	89	15.8	7.3	4.1	3.2	1.34	95.0*	203	460
SD	29.7	7.62	0.48	0.21	0.60	0.324	37.05	55.5	255.3
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1 M : 0 mg base/kg/day									
MEAN	502	18.1	0.60	146.6	5.89	103.1	11.5	8.6	192
SD	397.4	2.48	0.046	1.43	0.387	2.73	0.47	0.90	43.4
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	378	15.5	0.57	146.4	5.80	103.1	11.7	8.5	184
SD	358.6	3.38	0.049	1.35	0.316	3.67	0.31	1.06	52.5
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	333	15.8	0.62	145.8	5.84	105.3	11.6	8.8	186
SD	380.8	1.95	0.102	2.04	0.418	3.02	0.37	1.33	54.3
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	606	14.0*	0.58	144.4*	5.60	105.6	11.3	8.4	161
SD	654.3	2.23	0.042	1.17	0.251	4.40	0.32	0.90	32.6
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7.11

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALT	SDH	TP	ALB	GLOB	A/G	TBA	ALKP	LDH
UNITS:	IU/L	IU/L	g/dL	g/dL	g/dL	-	umol/L	IU/L	IU/L
Group: 1-F : 0 mg base/kg/day									
MEAN	113	8.7	9.9	4.7	5.2	0.91	93.9	110	483
SD	51.6	6.12	0.85	0.28	0.76	0.121	44.84	36.5	270.4
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	98	8.7	9.2*	4.6	4.5*	1.03*	82.3	114	550
SD	72.3	4.19	0.51	0.23	0.47	0.123	34.15	50.0	249.7
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	117	7.0	9.8	4.7	5.1	0.94	82.5	136	486
SD	73.2	5.30	0.56	0.20	0.49	0.089	38.92	93.3	243.2
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	89	5.8	9.1*	4.7	4.4*	1.06*	153.9	153	487
SD	28.6	5.70	0.58	0.31	0.37	0.085	164.18	62.3	218.5
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7.12

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF CLINICAL CHEMISTRY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	BUN	CREAT	NA	K	CL	CA	IP	GLU
UNITS:	IU/L	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0 mg base/kg/day									
MEAN	298	18.8	0.65	145.5	5.61	104.4	11.1	9.2	153
SD	232.5	1.96	0.096	2.07	0.671	3.86	0.32	0.84	32.5
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	479	18.1	0.65	146.3	5.58	102.5	11.0	8.6	139
SD	462.0	2.18	0.066	1.64	0.448	1.58	0.32	1.13	26.5
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	653	18.8	0.67	146.1	5.51	104.7	10.9	9.1	157
SD	921.2	2.10	0.065	1.45	0.465	5.38	0.24	1.12	38.9
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	589	15.9*	0.63	144.6	5.74	102.1	10.9	9.0	137
SD	707.0	1.72	0.086	1.26	0.413	1.91	0.31	0.91	31.7
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control $P < .05$

Table 8.1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	RBC 10^6/mm^3	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETICS % RBCs	HEINZ BOD. % RBCs	% METHGB % HGB
Group: 1-M : 0 mg base/kg/day									
MEAN	7.56	15.7	44.2	58.5	21.0	36.0	0.7	0.0	0.6
SD	0.460	0.73	2.19	1.41	1.23	1.48	0.28	0.00	0.25
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	7.69	15.9	45.8	59.6	21.6	36.0	0.8	0.0	0.7
SD	0.270	0.67	1.34	2.44	1.37	2.10	0.25	0.00	0.27
N	10	10	10	10	10	10	10	1D	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	7.31	15.4	43.7	59.7	21.3	35.6	0.8	0.0	1.2
SD	0.183	0.38	1.91	2.07	0.87	1.23	0.38	0.00	0.19
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	7.19*	14.2*	42.1*	58.5	20.7	35.3	1.6*	0.0	6.5*
SD	0.350	0.66	1.75	2.34	0.82	1.12	0.46	0.00	1.22
N	10	10	10	10	10	10	10	10	10

6.5-9 13-71 40-5 0-1.5

*-Significant Difference from Control P < .05

Table 8.2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-M : 0 mg base/kg/day									
MEAN	16.5	0	2.8	0.0	13.1	0.5	0.1	0.0	955
SD	3.01	0.0	1.26	0.04	2.56	0.19	0.22	0.00	99.1
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	17.0	0	2.2	0.0	14.0	0.7	0.1	0.0	1019
SD	3.43	0.0	0.85	0.00	2.85	0.50	0.20	0.00	108.7
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	18.8	0	3.6	0.1	14.7	0.5	0.0	0.0	945
SD	3.07	0.0	1.66	0.10	2.03	0.37	0.06	0.00	85.0
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	26.3*	0	4.1	0.0	21.2*	0.9	0.1	0.0	998
SD	6.28	0.0	1.88	0.00	4.98	0.48	0.13	0.00	108.6
N	10	10	10	10	10	10	10	10	10

9-18

800-1400

WBC corrected for NRBC = or > 10

*-Significant Difference from Control P < .05

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	RBC	HGB	HCT	MCV	MCH	MCHC	RETICS	HEINZ BOD.	% METHGB
UNITS:	10^6/mm^3	g/dL	%	fL	pg	g/dL	% RBCs	% RBCs	% HGB
Group: 1-F : 0 mg base/kg/day									
MEAN	7.39	16.0	42.9	58.0	21.6	37.3	0.6	0.0	0.8
SD	0.201	0.52	1.91	1.37	0.66	1.23	0.19	0.00	0.14
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	7.41	15.7	42.5	57.4	21.1	36.9	0.7	0.0	0.7
SD	0.275	0.51	1.35	1.70	0.49	0.95	0.23	0.00	0.21
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	7.12	15.4	40.7*	57.2	21.7	37.9	0.9	0.0	1.2
SD	0.290	0.77	1.97	1.04	0.48	0.66	0.38	0.00	0.26
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	6.61*	14.4*	39.1*	59.2	21.9	37.0	1.4*	0.0	5.9*
SD	0.248	0.40	1.67	1.97	0.75	0.85	0.51	0.00	1.39
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 8.4

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 4

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-F : 0 mg base/kg/day									
MEAN	15.9	0	2.7	0.0	12.8	0.3	0.2	0.0	1089
SD	3.41	0.0	1.72	0.06	2.26	0.18	0.14	0.06	139.2
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	15.9	0	1.7	0.0	13.7	0.4	0.1	0.0	1066
SD	2.91	0.3	1.07	0.00	2.51	0.41	0.08	0.00	130.9
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	14.9	0	2.0	0.0	12.5	0.3	0.2	0.0	950
SD	2.63	0.3	0.93	0.00	2.03	0.15	0.21	0.00	216.9
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	27.6*	0	4.4*	0.1	22.4*	0.7*	0.1	0.0	1118
SD	6.01	0.0	1.30	0.19	6.05	0.48	0.11	0.00	97.6
N	10	10	10	10	10	10	10	10	10

6-15

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05

Table 8.5

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	RBC	HGB	HCT	MCV	MCH	MCHC	RETICS	HEINZ BOD.	% METHGB
UNITS:	10^6/mm^3	g/dL	%	fL	pg	g/dL	% RBCs	% RBCs	% HGB
Group: 1-M : 0 mg base/kg/day									
MEAN	8.26	15.7	43.6	52.8	19.0	36.0	0.4	0.0	0.8
SD	0.556	0.89	2.65	0.94	0.51	0.48	0.25	0.00	0.23
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	8.31	16.2	45.5	54.8	19.5	35.7	0.7	0.0	0.8
SD	0.387	0.56	2.18	2.75	0.75	0.70	0.42	0.00	0.34
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	8.13	16.0	45.2	55.6	19.7	35.4	0.5	0.0	2.4*
SD	0.184	0.39	1.03	2.16	0.63	0.66	0.28	0.00	0.59
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	7.99	14.9*	43.0	53.9	18.7	34.6*	1.1*	0.1*	7.3*
SD	0.645	0.65	1.85	2.95	0.79	0.65	0.52	0.15	1.47
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 8.6

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-M : 0 mg base/kg/day									
MEAN	16.5	0	2.3	0.1	13.8	0.3	0.1	0.0	1041
SD	3.08	0.0	0.98	0.13	3.27	0.12	0.09	0.00	100.4
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	17.1	0	2.5	0.0	14.1	0.4	0.1	0.0	986
SD	3.62	0.0	1.10	0.06	3.15	0.28	0.21	0.00	100.9
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	20.6	0	3.2	0.0	16.8	0.4	0.1	0.0	932*
SD	2.70	0.3	0.73	0.06	2.70	0.34	0.15	0.00	91.4
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	26.7*	0	4.4*	0.0	21.6*	0.7	0.1	0.0	886*
SD	5.95	0.3	1.44	0.09	5.57	0.59	0.15	0.00	106.0
N	10	10	10	10	10	10	10	10	10

9-18

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05

Table 8.7

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 13

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	RBC	HGB	HCT	MCV	MCH	MCHC	RETICS	HEINZ BOD.	% METHGB
UNITS:	10^6/mm^3	g/dL	%	fL	pg	g/dL	% RBCs	% RBCs	% HGB
Group: 1-F : 0 mg base/kg/day									
MEAN	7.90	15.8	43.6	55.3	20.1	36.3	0.5	0.0	0.4
SD	0.375	0.62	1.89	2.07	0.68	0.66	0.21	0.03	0.27
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	7.76	15.4	43.0	55.4	19.9	35.9	0.6	0.0	0.5
SD	0.509	0.59	1.57	2.07	0.64	0.92	0.27	0.03	0.34
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	7.38*	15.0*	41.1*	55.8	20.2	36.3	0.6	0.0	1.6*
SD	0.400	0.91	2.31	1.60	0.64	0.61	0.47	0.00	0.32
N	10	9	10	10	9	9	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	7.28*	14.6*	41.6	57.2	20.1	35.2*	1.0*	0.1*	7.0*
SD	0.355	0.63	2.31	2.36	0.71	0.72	0.48	0.13	1.15
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 8.8

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 13

DRAFT

STUDY IO: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-F : 0 mg base/kg/day									
MEAN	15.3	0	1.6	0.0	13.3	0.3	0.1	0.0	954
SD	4.16	0.0	0.95	0.00	3.47	0.15	0.12	0.00	158.7
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	15.4	0	1.4	0.0	13.5	0.3	0.1	0.0	950
SD	3.79	0.0	0.69	0.00	3.56	0.24	0.09	0.00	139.7
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	13.9	0	2.4	0.0	11.2	0.3	0.1	0.0	887
SD	2.10	0.0	0.58	0.03	2.07	0.18	0.13	0.00	79.0
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	26.2*	0	2.8*	0.1*	22.9*	0.5	0.1	0.0	1054
SD	6.74	0.0	1.36	0.14	6.65	0.39	0.21	0.00	162.9
N	10	10	10	10	10	10	10	10	10

6-15

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05

Table 8.9

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	RBC	HGB	HCT	MCV	MCH	MCHC	RETICS	HEINZ BOD.	% METHGB
UNITS:	10^6/mm^3	g/dL	%	fL	pg	g/dL	% RBCs	% RBCs	% HGB
Group: 1-M : 0 mg base/kg/day									
MEAN	8.39	15.2	44.3	52.9	18.1	34.3	0.7	0.0	0.6
SD	0.308	0.47	1.59	1.11	0.50	0.66	0.24	0.00	0.12
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	8.26	15.5	45.1	54.7	18.7	34.3	0.6	0.0	0.6
SD	0.434	0.76	2.23	2.79	0.89	0.65	0.39	0.08	0.24
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	8.28	15.4	45.8	55.4	18.7	33.7	0.7	0.0	2.3*
SD	0.240	0.45	2.09	2.61	0.59	0.67	0.25	0.06	0.33
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	8.35	14.3*	42.8	51.4	17.2*	33.3*	1.3*	0.0	7.4*
SD	0.479	0.42	0.81	2.76	0.80	0.51	0.55	0.03	1.43
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 8.10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-M : 0 mg base/kg/day									
MEAN	14.9	0	2.1	0.0	12.3	0.3	0.3	0.0	1001
SD	2.40	0.0	0.83	0.00	3.15	0.21	0.23	0.00	187.1
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.5 mg base/kg/day									
MEAN	17.2	0	3.4	0.0	13.2	0.4	0.2	0.0	974
SD	4.21	0.3	1.44	0.00	3.04	0.31	0.23	0.00	116.8
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 2.0 mg base/kg/day									
MEAN	19.3	0	3.2	0.0	15.7	0.2	0.1	0.0	971
SD	3.54	0.4	1.60	0.00	2.37	0.18	0.20	0.00	158.6
N	10	10	10	10	10	10	10	10	10
Group: 4-M : 9.0 mg base/kg/day									
MEAN	26.3*	0	4.2*	0.0	21.1*	0.8*	0.1	0.0	824
SD	6.44	0.6	0.92	0.09	5.63	0.41	0.19	0.00	154.9
N	10	10	10	10	10	10	10	10	10

9-18

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-158
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	NRBC	M. Neutrop	I. Neutrop	Lymphocyte	Monocytes	Eosinophil	Basophils	PLT
UNITS:	10^3/mm^3	COUNT	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3	10^3/mm^3
Group: 1-F : 0 mg base/kg/day									
MEAN	12.6	0	2.2	0.0	10.1	0.2	0.1	0.0	980
SD	3.82	0.7	1.37	0.00	2.97	0.17	0.11	0.00	133.1
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	11.0	0	1.4	0.0	9.3	0.2	0.1	0.0	903
SD	3.01	1.0	0.87	0.00	2.46	0.09	0.07	0.00	146.2
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	11.0	0	2.5	0.0	8.3	0.2	0.1	0.0	942
SD	1.55	0.3	0.69	0.00	1.24	0.18	0.08	0.00	94.9
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	20.8*	0	3.5*	0.0	17.0*	0.2	0.1	0.0	980
SD	3.37	0.4	1.17	0.00	3.53	0.24	0.13	0.00	133.1
N	10	10	10	10	10	10	10	10	10

6-15

WBC corrected for NRBC = or > 10
*-Significant Difference from Control P < .05

Table 8.12

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 26

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	RBC	HGB	HCT	MCV	MCH	MCHC	RETICS	HEINZ BOD.	% METHGB
UNITS:	10^6/mm^3	g/dL	%	fL	pg	g/dL	% RBCs	% RBCs	% HGB
Group: 1-F : 0 mg base/kg/day									
MEAN	7.69	15.2	43.8	57.0	19.8	34.8	1.1	0.0	0.6
SD	0.367	0.50	1.74	1.99	0.58	0.73	0.22	0.00	0.51
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.5 mg base/kg/day									
MEAN	7.54	15.0	43.2	57.3	19.9	34.7	1.0	0.0	0.6
SD	0.272	0.26	0.77	2.31	0.69	0.62	0.36	0.00	0.32
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 2.0 mg base/kg/day									
MEAN	7.33*	14.8	42.1	57.5	20.2	35.1	0.9	0.0	1.8
SD	0.261	0.40	1.44	1.49	0.50	0.75	0.44	0.00	0.60
N	10	10	10	10	10	10	10	10	10
Group: 4-F : 9.0 mg base/kg/day									
MEAN	7.34*	14.1*	41.6*	56.7	19.3	34.0	1.7*	0.1*	8.0*
SD	0.358	0.76	2.58	3.03	0.84	0.76	0.47	0.16	2.04
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 27

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	APTT
UNITS:	sec
Group: 1-M : 0 mg base/kg/day	
MEAN	18.2
SD	3.54
N	10
Group: 2-M : 0.5 mg base/kg/day	
MEAN	19.8
SD	1.21
N	10
Group: 3-M : 2.0 mg base/kg/day	
MEAN	19.3
SD	1.21
N	10
Group: 4-M : 9.0 mg base/kg/day	
MEAN	17.3
SD	1.24
N	10

Table 8.14

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

SUMMARY OF HEMATOLOGY TESTS
PERIOD: Week 27

DRAFT

STUDY ID: UIC-15B
STUDY NO: 152

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	APTT
UNITS:	sec
Group: 1-F : 0 mg base/kg/day	
MEAN	16.3
SD	1.93
N	10
Group: 2-F : 0.5 mg base/kg/day	
MEAN	18.4
SD	5.16
N	10
Group: 3-F : 2.0 mg base/kg/day	
MEAN	18.9
SD	3.40
N	10
Group: 4-F : 9.0 mg base/kg/day	
MEAN	17.0
SD	3.13
N	10

Table 9.1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: MALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

GROUP:	(1) 1-M	(2) 2-M	(3) 3-M	(4) 4-M
Adrenal Glands (% BRAIN WEIGHT)				
MEAN	2.77	2.98	2.72	3.18
SD	0.319	0.591	0.822	0.812
N	20	20	20	19
Heart (% BRAIN WEIGHT)				
MEAN	82.49	79.13	75.69*	74.17*
SD	9.525	7.466	6.856	10.710
N	20	20	20	19
Kidneys (% BRAIN WEIGHT)				
MEAN	187.63	188.21	205.99*	211.31*
SD	15.277	18.890	20.407	34.564
N	20	20	20	19
Lungs/Bronchi (% BRAIN WEIGHT)				
MEAN	104.54	111.26	205.18*	209.40*
SD	13.301	15.623	231.794	43.117
N	20	20	20	19
Liver (% BRAIN WEIGHT)				
MEAN	1129.25	1090.79	1100.10	1041.70
SD	106.800	131.674	267.811	188.636
N	20	20	20	19
Spleen (% BRAIN WEIGHT)				
MEAN	43.44	43.05	54.38	116.23*
SD	5.976	5.915	7.282	31.092
N	20	20	20	19
Testes with Epididymides (% BRAIN WEIGHT)				
MEAN	242.33	239.63	248.22	241.23
SD	25.829	19.127	24.124	31.324
N	20	20	20	19

(1)-0 mg base/kg/day
(2)-0.5 mg base/kg/day
(3)-2.0 mg base/kg/day
(4)-9.0 mg base/kg/day
* - Significant difference P<.05

Table 9.1 (contd.)

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: 152
SEX: FEMALE

ALL FATES DAYS: 183-185 ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

DRAFT

GROUP:	(5) 1-F	(6) 2-F	(7) 3-F	(8) 4-F
Adrenal Glands (% BRAIN WEIGHT)				
MEAN	3.49	4.01	3.60	4.69*
SD	0.867	0.701	0.881	0.713
N	20	20	20	20
Heart (% BRAIN WEIGHT)				
MEAN	55.29	58.95	53.54	50.78*
SD	5.677	7.725	4.921	5.148
N	20	20	20	20
Kidneys (% BRAIN WEIGHT)				
MEAN	127.15	125.04	126.85	135.90
SD	15.763	15.598	13.871	15.535
N	20	20	20	20
Lungs/Bronchi (% BRAIN WEIGHT)				
MEAN	84.71	87.16	131.50*	167.28*
SD	8.564	10.243	18.434	29.464
N	20	20	20	20
Liver (% BRAIN WEIGHT)				
MEAN	650.58	658.46	653.34	637.60
SD	80.273	104.675	93.187	82.022
N	20	20	20	20
Ovaries (% BRAIN WEIGHT)				
MEAN	5.02	5.59	5.63	5.56
SD	1.204	1.684	1.812	1.504
N	20	20	20	20
Spleen (% BRAIN WEIGHT)				
MEAN	28.11	29.09	33.39*	63.93*
SD	4.591	4.392	4.672	11.515
N	20	20	20	20

(5)-0 mg base/kg/day
(6)-0.5 mg base/kg/day
(7)-2.0 mg base/kg/day
(8)-9.0 mg base/kg/day
* - Significant difference P<.05

DRAFT

Table 10

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

Summary of Treatment-Related Lesions

		Dose (mg base/kg/day)			
ORGAN - lesion		0	0.5	2.0	9.0
LUNG					
- Hemorrhage	M	2/20 (0.09)*	1/20 (0.06)	4/20 (0.30)	20/20 (1.50)
	F	6/20 (0.14)	9/20 (0.30)	9/20 (0.25)	20/20 (2.10)
- Accumulation, foamy macrophage	M	0/20 (0.00)	2/20 (0.05)	20/20 (1.80)	20/20 (2.65)
	F	0/20 (0.00)	0/20 (0.00)	20/20 (1.95)	20/20 (1.85)
- Inflammation, chronic, interstitium	M	2/20 (0.03)	3/20 (0.06)	20/20 (1.20)	20/20 (2.40)
	F	3/20 (0.05)	0/20 (0.00)	20/20 (1.40)	20/20 (1.90)
LIVER					
- Apoptosis, centrilobular	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	11/20 (0.70)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Pigmentation, centrilobular	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	11/20 (0.60)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Fatty change, centrilobular	M	2/20 (0.10)	3/20 (0.10)	6/20 (0.30)	10/20 (0.50)
	F	0/20 (0.00)	-	-	0/20 (0.00)
- Congestion, centrilobular	M	0/20 (0.00)	0/20 (0.00)	2/20 (0.10)	2/20 (0.13)
	F	0/20 (0.00)	-	-	0/20 (0.00)
SPLEEN					
- Erythropoiesis	M	2/20 (0.10)	4/20 (0.20)	8/20 (0.50)	8/20 (0.55)
	F	10/20 (0.70)	11/20 (0.90)	14/20 (1.25)	8/20 (0.60)
- Pigmentation	M	1/20 (0.10)	4/20 (0.20)	8/20 (0.45)	11/20 (0.80)
	F	17/20 (1.15)	20/20 (1.90)	18/20 (1.80)	17/20 (1.20)
- Congestion	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	18/20 (1.90)
	F	0/20 (0.00)	1/20 (0.05)	1/20 (0.05)	17/20 (1.45)
- Hyperplasia, reticuloendothelial cell	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	4/20 (0.30)
	F	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.10)
STERNUM WITH MARROW					
- Hyperplasia, bone marrow	M	0/20 (0.00)	5/20 (0.30)	11/20 (0.60)	19/20 (1.25)
	F	0/20 (0.00)	4/20 (0.20)	7/20 (0.40)	13/20 (0.90)
- Granulopoiesis	M	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.10)
	F	0/20 (0.00)	0/20 (0.00)	0/20 (0.00)	1/20 (0.05)
KIDNEY					
- Pigmentation, cortex	M	0/20 (0.00)	0/20 (0.00)	4/20 (0.20)	16/19 (1.11)
	F	0/20 (0.00)	0/20 (0.00)	7/20 (0.35)	20/20 (1.60)
ADRENAL GLAND					
- Pigmentation, zona reticularis	M	0/20 (0.00)	1/20 (0.05)	3/20 (0.15)	10/20 (0.60)
	F	0/20 (0.00)	1/20 (0.05)	2/20 (0.10)	18/20 (1.55)
- Congestion	M	1/20 (0.05)	1/20 (0.05)	4/20 (0.25)	2/20 (0.10)
	F	7/20 (0.35)	3/20 (0.15)	7/20 (0.40)	18/20 (1.50)

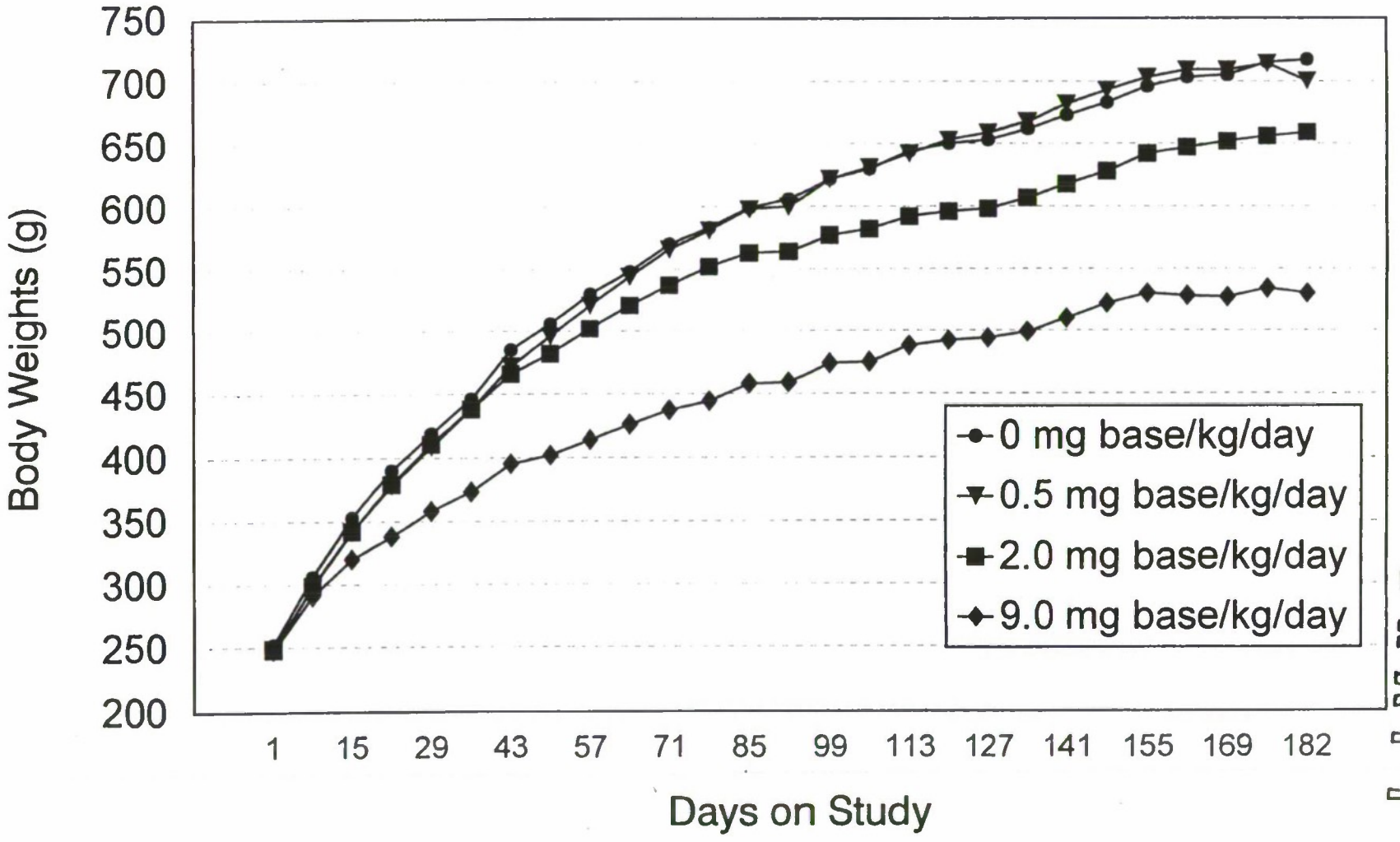
*Incidence (mean group severity score) - Not examined

Lesion severity as modified by distribution is defined in Pathology Report (page J-15).

Figure 1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

Summary of Male Body Weights



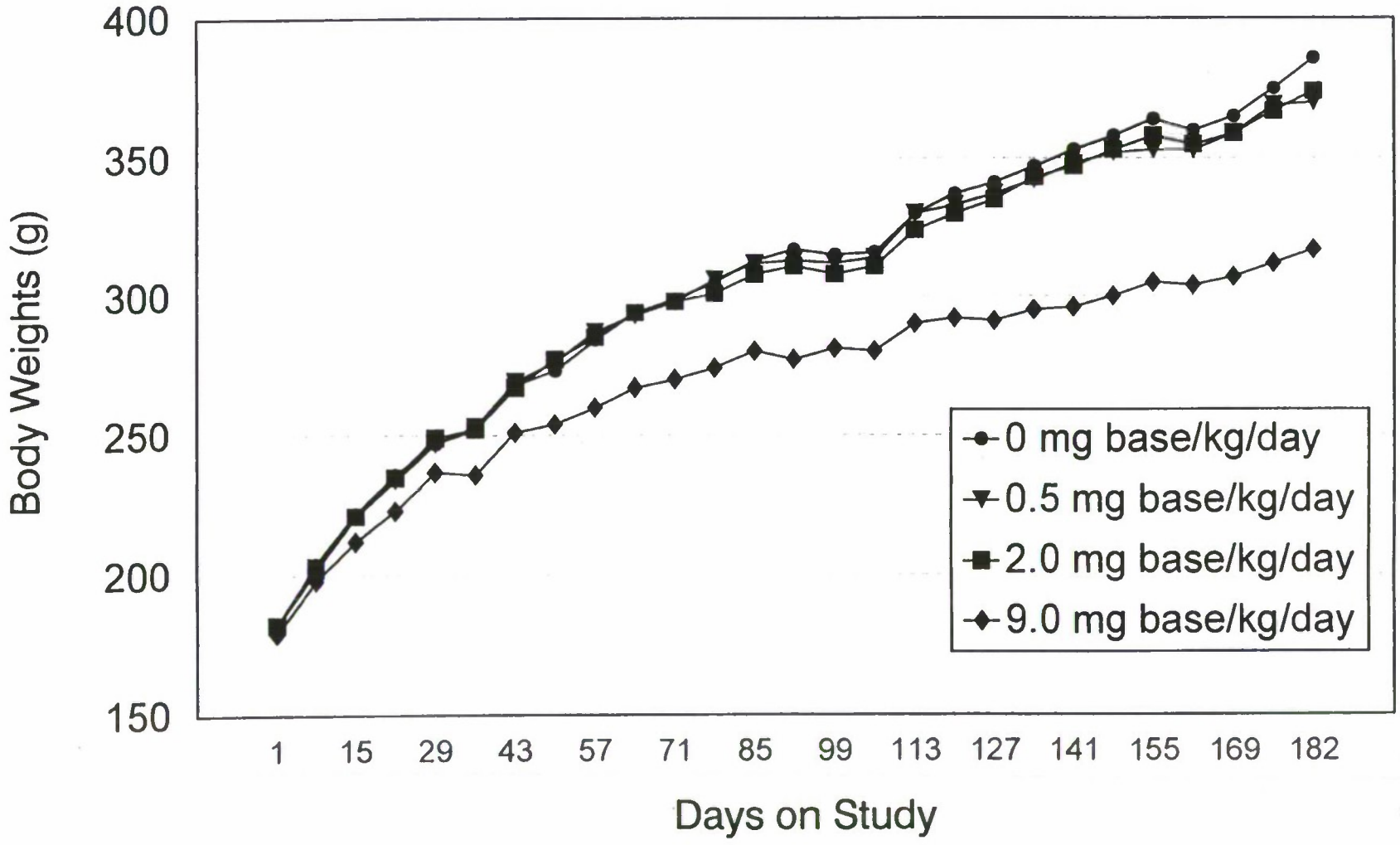
DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-15B
UIC/TRL Study No.: 152

Figure 2

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

Summary of Female Body Weights



DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-15B
UIC/TRL Study No.: 152

DRAFT

APPENDIX A

ANALYTICAL CHEMISTRY REPORT

Six Month Oral Toxicity Study of
WR238605 Succinate In Rats
UIC/TRL Study Number 152

DRAFT

Part I: **Identity, Purity and Stability of Neat WR238605 Succinate**

Part II: **Dosing Formulations Analysis of WR238605 Succinate in 1% Methylcellulose/0.2% Tween 80**

Analysts: Adam Negrusz
A. Karl Larsen, Jr.
Thomas Tolhurst

Study Site: Drug Disposition Research Laboratory
College of Pharmacy
University of Illinois at Chicago
Chicago, Illinois 60612

Sponsor: Toxicology Research Laboratory
University of Illinois at Chicago
Chicago, Illinois 60612

Report Prepared by: Thomas Tolhurst T. Tolhurst

Report Prepared: March 30, 1996

Approved: April 10, 1996
Eugene F. Woods
Drug Disposition Research Laboratory E. Woods

Part 1: Identity, Purity and Stability of Neat WR238605 Succinate

Objective

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The objective of this study was to confirm the identity and establish the purity and stability of neat WR238605 Succinate (Bottle No. BM 12562).

Identification

GC-MS System

Gas Chromatograph:	Hewlett-Packard Model 5890 Series II
Mass Selective Detector:	Hewlett-Packard Model 5970
Analytical Column:	30 m x 0.25 mm ID, DB-1 with a 3 micron film thickness.
GC Parameters:	Injector temp. 250°C, oven temp. 70°C initial, 270°C final, 15°C/minute ramp, carrier gas - helium, flow rate 2 ml/minute, split ratio 10:1

Procedure

Subject sample (WR238605 succinate) was submitted by the Toxicology Research Laboratory. The sample was dissolved in hexane:ethanol (4:1) to a concentration of 0.8 µg base/ml and a 2 µl aliquot was injected on the column. The MSD scanned from 40 amu to 475 amu at a rate of 1 scan per second.

Results - GC-MS

The mass spectrum indicates a molecular ion m/e 463 (M^+ free base) and m/e 405 [M^+ free base minus $(CH_2)_3$ NH_2]. This pattern is consistent with the structural formula and corresponds to the finding by SRI International (see SRI International Report No. 469, May 9, 1994).

The mass spectrum of the WR238605 sample was previously reported (see Analytical Chemistry Report of UIC/TRL Study No. 097 and Study No. 098 from August 19, 1993) and it is shown in Figure 1.

Purity/Stability

The subject sample (WR238605 Succinate) was supplied by the Toxicology Research Laboratory (TRL) and stored at 0-4° C when not being analyzed.

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Description

A fine pale yellow powder, no obvious odor.

HPLC System

Solvent Delivery:	Perkin Elmer, Model 3B
Injector:	Rheodyne 7125 with 20μl sample loop
Analytical Column:	Bondclone ODS, 10μ, 300 mm x 3.9 mm (Phenomenex)
Detector:	Kratos, Spectroflow 773 UV Detector, 268 nm
Integrator:	Perkin Elmer LCI-100 Integrator
Mobile Phase:	75% methanol: 25% deionized water containing 6.9 grams of sodium acetate and 8 ml of 85% o-phosphoric acid; flow rate 1.5 ml/min

Procedure

Six solutions of WR238605 were prepared as follows. Twenty-five mg of WR238605 was weighed into each of six 25 ml volumetric flasks. The samples were dissolved in and the volume brought to mark with mobile phase. A 20 μl aliquot of each solution was chromatographed at 268 nm for purity determination.

Calculation of Purity

Quantitations were based on the assumption of equal detector response per unit weight of all UV-absorbing components. Areas of WR238605 and other detectable components in the subject sample chromatograms were employed in the following equation to calculate the percentage of WR238605 present in the sample:

$$\%\text{PURITY} = (\text{area of WR238605/total area}) \times 100$$

Stability

The stability of neat WR238605 Succinate was assessed by comparing the percent purity of WR238605 samples submitted for analysis prior to and following completion of Study Number 152. A change in purity greater than 10% was considered to represent a significant loss of potency.

Results

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Typical chromatograms are shown in Figure 2. The subject samples were found to contain less than 1% of UV-absorbing impurities. The percent purity of the initial and terminal WR238605 samples were 99.52 $\pm$ 0.21 and 99.98 $\pm$ 0.02, respectively, and the assay results are presented in Tables 1 and 2. No loss of potency was found to have occurred over the period during which Study Number 152 was conducted.

Figure 1

Mass Spectrum of WR238605 Sample

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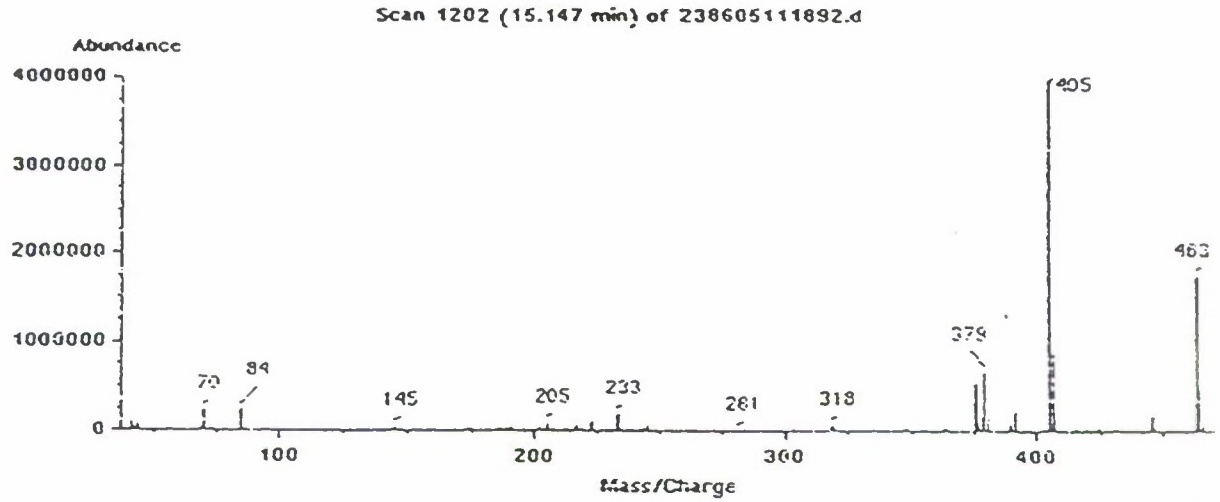
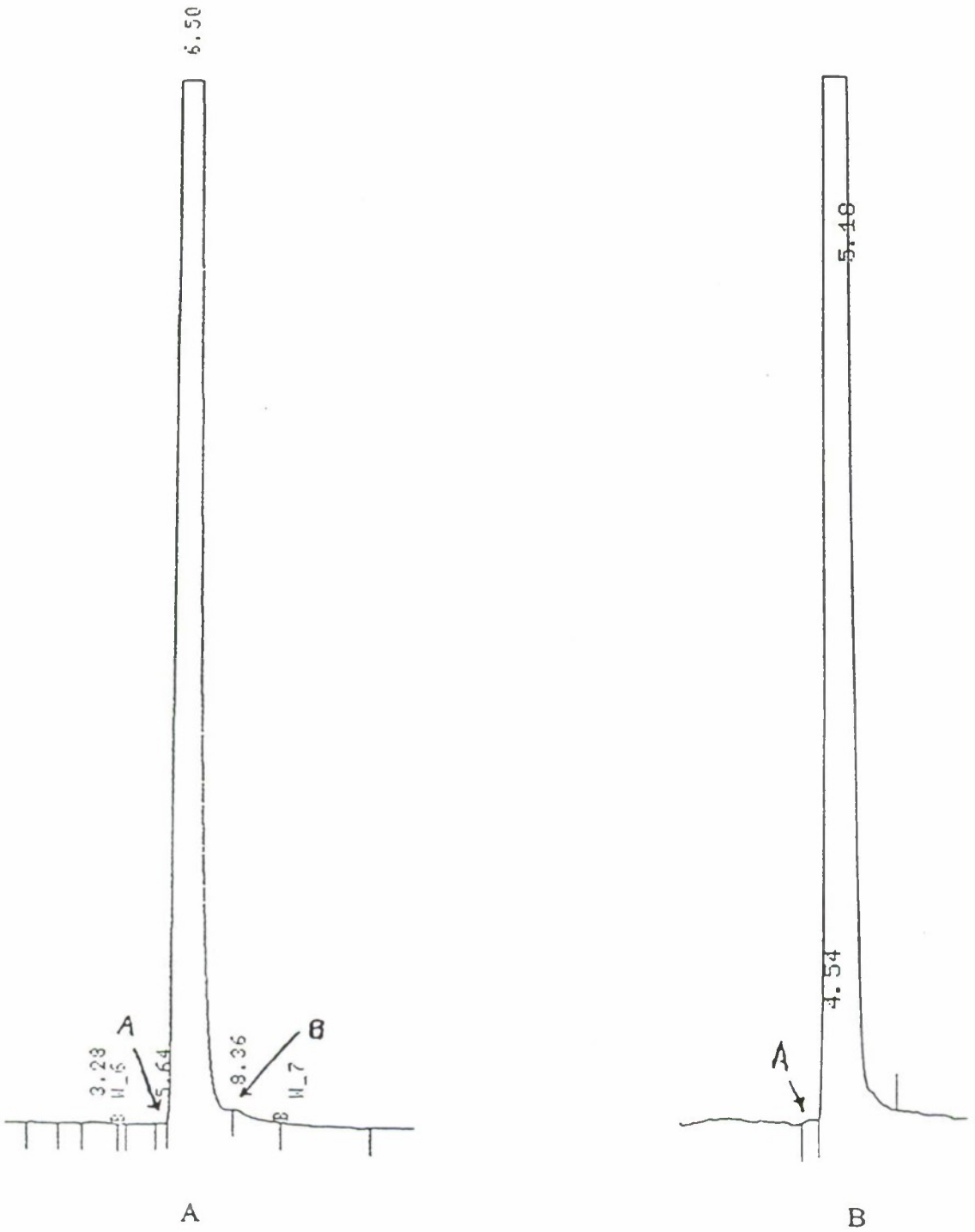


Figure 2

Chromatograms of WR238605 (Conc. 0.8 mg/ml, 268 nm)
A - Initial Sample, B - Terminal Sample

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A B

Table 1

Purity Data for WR238605 Succinate
Initial Sample

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Solutions

Peak Identity	1	2	3	4	5	6
A	5571	____[1]	1743	2792	2890	____
B	81818	111201	108637	133756	97545	____
WR238605	21209642	21198802	21123542	21199894	21095026	21150796
% Purity	99.52	99.40	99.44	99.36	99.48	99.93

[1] - peak not integrated
Mean ± s.d. 99.52 ± 0.21

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Table 2

Purity Data for WR238605 Succinate
Terminal Sample

Solutions

Peak Identity	1	2	3	4	5	6
A	2105	1188	1221	4620	____	____
WR238605	10257841	12416867	12394351	9416609	11784722	8730453
% Purity	99.98	99.99	99.99	99.95	100	100

Mean $\pm$ s.d. 99.98 $\pm$ 0.02

Part II: Dosing Formulations Analysis of WR238605 Succinate in 1% Methylcellulose/0.2% Tween 80

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Introduction:

Sample from UIC/TRL Study No. 152 were submitted by the Toxicology Research Laboratory to the Drug Disposition Research Laboratory for the quantitation of WR238605 free base in dosing formulations. All samples submitted were analyzed by HPLC using an existing analytical method (SOP No. 01MA10-01).

Analytical Method

Regents

Subject sample (WR238605 Succinate) was supplied by the Toxicology Research Laboratory. HPLC grade methanol, 85% O-phosphoric acid and sodium acetate were purchased from Fisher Scientific. HPLC grade water was acquired through a Millipore, MILLI-Q Reagent Water System which was supplied with distilled water.

Standards

All WR238605 concentrations reflect free base value. A 0.8 mg base/ml WR238605 stock solution was prepared by weighing 100 mg of the drug (mole fraction = 0.8) into a 100 ml volumetric flask. The content was dissolved in and the volume brought to mark with mobile phase. A working calibration standard solution of 80μg base/ml was prepared by transferring 10.0 ml of the 0.80 mg base/ml stock solution to a 100 ml volumetric flask and diluting to mark with mobile phase. The remaining working calibration standards were prepared from the 80 μg base/ml WR238605 solution as follows:

Volume Transferred (ml)	Flask Volume (ml)	Final Concentration (μg base/ml)
1.0	10	8
2.0	10	16
4.0	10	32
6.0	10	48
8.0	10	64

Controls

Control A (0.8 mg base/ml) and control B (2.4 mg base/ml) were prepared by weighing 25 mg and 75 mg, respectively, of WR238605 Succinate salt into two 25 ml volumetric flasks. The contents were dissolved in and diluted to mark with mobile phase.

Sample Preparation

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Triplicate dilutions of each suspension were prepared in mobile phase prior to HPLC analysis. The vehicle and the 0.1 mg base/ml suspension were diluted 1:5 and the 0.4 mg base/ml and the 1.8 mg base/ml suspension were diluted 1:10 and 1:50, respectively.

HPLC System

See part I: HPLC System

Calculations

A standard curve was run at the beginning and end of each assay day. Final concentration for controls and samples were determined using a composite standard curve. The composite standard curve was determined by linear least squared regression analysis of the peak areas for WR238605 free base as a function of concentration. WR238605 concentrations (mg base/ml) for controls and samples were determined using the following equation:

$$\text{WR238605 Conc.} = (Y-B)/M \times (d.f./1000)$$

Y = peak height

B = Y-intercept from composite standard curve

M = slope from composite standard curve

d.f. = dilution factor

The standard curves were linear over the range of WR238605 assayed (8 μg base/ml - 80 μg base/ml) and had correlation coefficients greater than 0.998. A representative standard curve is shown in Figure 3.

Results

Result of dosing formulations analysis for UIC/TRL Study No. 152 are presented in Table 3. Test article dosage formulations were within 10% of their respective target concentrations both prior to and essentially after dosing. Minor exceptions were in week 14 (0.1 mg base/ml dosage formulation was 129.5% of the predose value and 123% of the target concentration), week 22 (1.8 mg base/ml dosage formulation was 111.1% of the predose value, but 107.1%, i.e., within range, of target concentration), and week 25 (0.4 mg base/ml dosage formulation was 110.9% of the predose value, but 109.0%, i.e., within range, of target concentration). Thus, out of 78 post-dosing analyses, only one sample was slightly (13%) out of predose or target concentration range.

Figure 3

Standard Curve of WR238606

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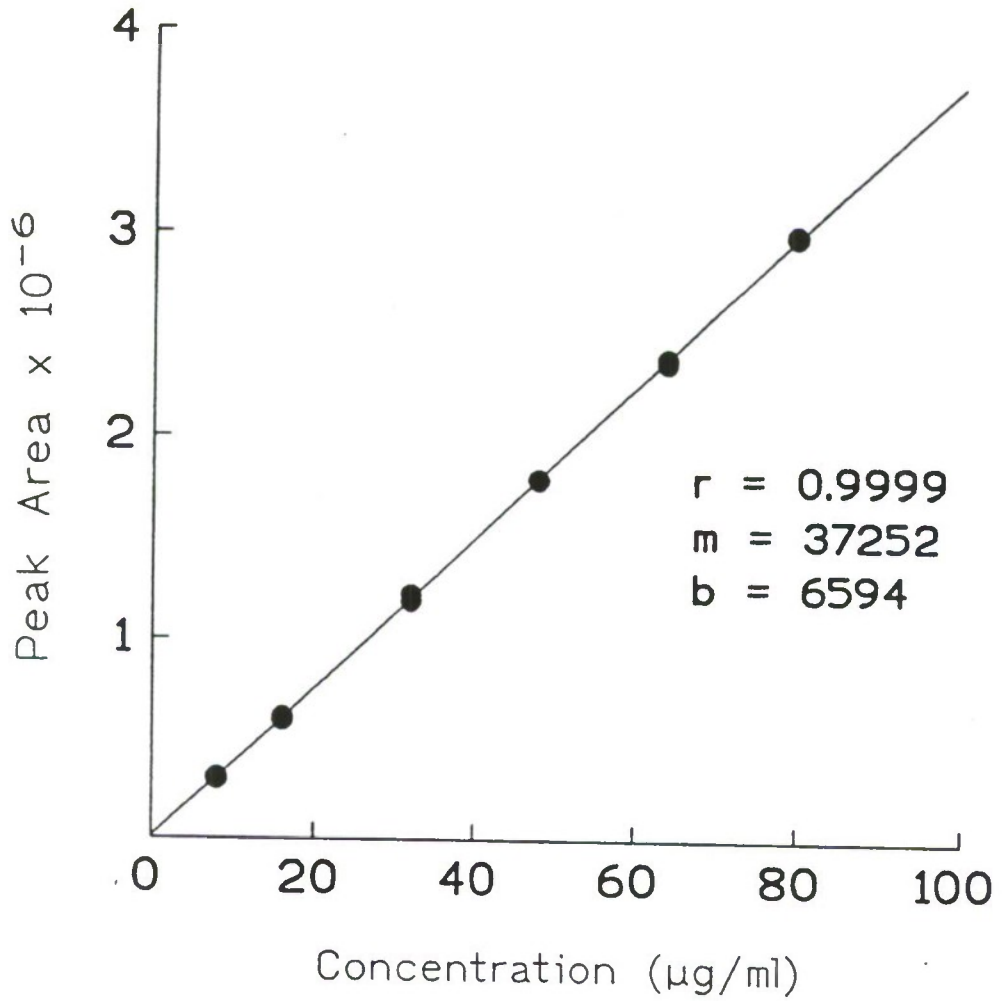


Table 3

Results Of Dosing Formulations Analysis for UIC/TRL Study Number 152

DRAFT

Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
1	0.0	08/01/95	0	-	08/08/95	0	-
	0.1		0.105 ± 0.001	105.0		0.106 ± 0.002	101.0
	0.4		0.409 ± 0.002	102.3		0.385 ± 0.024	94.1
	1.8		1.770 ± 0.069	98.3		1.777 ± 0.019	100.4
2	0.0	08/08/95	0	-	08/15/95	0	-
	0.1		0.100 ± 0.001	100.0		0.098 ± 0.003	98.0
	0.4		0.391 ± 0.002	97.8		0.397 ± 0.007	101.5
	1.8		1.789 ± 0.012	99.4		1.822 ± 0.071	101.8
3	0.0	08/15/95	0	-	08/22/95	0	-
	0.1		0.100 ± 0.001	100.0		0.099 ± 0.002	99.0
	0.4		0.411 ± 0.004	102.8		0.401 ± 0.001	97.6
	1.8		1.909 ± 0.009	106.1		1.818 ± 0.016	95.2
4	0.0	08/22/95	0	-	08/29/95	0	-
	0.1		0.098 ± 0.001	98.0		0.098± 0.001	100.0
	0.4		0.388 ± 0.004	97.0		0.387 ± 0.007	99.7
	1.8		1.790 ± 0.003	99.4		1.781 ± 0.029	99.5
5	0.0	08/29/95	0	-	09/05/95	0	-
	0.1		0.100 ± 0.002	100.0		0.104 ± 0.009	104.0
	0.4		0.400 ± 0.006	100.0		0.395 ± 0.002	98.8
	1.8		1.818 ± 0.039	101.0		1.825 ± 0.027	100.4
6	0.0	09/05/95	0	-	09/12/95	0	-
	0.1		0.096 ± 0.003	96.0		0.101 ± 0.005	105.2
	0.4		0.406 ± 0.006	101.5		0.397 ± 0.013	97.8
	1.8		1.799 ± 0.022	99.9		1.882 ± 0.069	104.6
7	0.0	09/12/95	0	-	09/19/95	0	-
	0.1		0.098 ± 0.009	98.0		0.105 ± 0.001	107.1
	0.4		0.405 ± 0.012	101.3		0.433 ± 0.007	106.9
	1.8		1.787 ± 0.031	99.3		1.866 ± 0.026	104.4
8	0.0	09/19/95	0	-	09/26/95	0	-
	0.1		0.100 ± 0.006	100.0		0.093 ± 0.004	93.0
	0.4		0.406 ± 0.005	101.5		0.391 ± 0.003	96.3
	1.8		1.873 ± 0.042	104.1		2.037 ± 0.038	108.8
9	0.0	09/26/95	0	-	10/03/95	0	-
	0.1		0.096 ± 0.001	96.0		0.097 ± 0.005	101.0
	0.4		0.395 ± 0.011	98.8		0.404 ± 0.004	102.3
	1.8		1.720 ± 0.034	95.6		1.876 ± 0.055	109.1
10	0.0	10/03/95	0	-	10/10/95	0	-
	0.1		0.093 ± 0.001	93.0		0.098 ± 0.003	108.6
	0.4		0.404 ± 0.004	101.0		0.405 ± 0.004	100.2
	1.8		1.844 ± 0.003	102.4		1.788 ± 0.036	97.0
11	0.0	10/10/95	0	-	10/17/95	0	-
	0.1		0.103 ± 0.006	103.0		0.101 ± 0.003	91.8
	0.4		0.400 ± 0.006	100.0		0.391 ± 0.005	97.8
	1.8		1.788 ± 0.003	99.3		1.728 ± 0.015	103.5
12	0.0	10/17/95	0	-	10/24/95	0	-
	0.1		0.110 ± 0.001	110.0		0.099 ± 0.002	90.0
	0.4		0.395 ± 0.006	98.8		0.395 ± 0.004	100.0
	1.8		1.827 ± 0.003	101.5		1.849 ± 0.011	101.2

Table 3

Results Of Dosing Formulations Analysis for UIC/TRL Study Number 152

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Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
13	0.0	10/24/95	0	-	10/31/95	0	-
	0.1		0.099 ± 0.001	99.0		0.096 ± 0.001	97.0
	0.4		0.389 ± 0.003	97.3		0.372 ± 0.008	95.6
	1.8		1.788 ± 0.009	99.3		1.786 ± 0.017	99.9
14	0.0	10/31/95	0	-	11/07/95	0	-
	0.1		0.095 ± 0.002	95.0		0.123 ± 0.008	129.5
	0.4		0.432 ± 0.006	108.0		0.453 ± 0.009	104.9
	1.8		1.707 ± 0.035	94.8		1.854 ± 0.040	108.6
15	0.0	11/07/95	0	-	11/14/95	0	-
	0.1		0.102 ± 0.001	102.0		0.104 ± 0.007	102.0
	0.4		0.403 ± 0.007	100.8		0.394 ± 0.010	97.8
	1.8		1.672 ± 0.024	92.9		1.739 ± 0.041	104.0
16	0.0	11/14/95	0	-	11/21/95	0	-
	0.1		0.101 ± 0.004	101.0		0.104 ± 0.004	103.0
	0.4		0.412 ± 0.050	103.0		0.420 ± 0.001	101.9
	1.8		1.768 ± 0.050	98.2		1.890 ± 0.024	106.9
17	0.0	11/21/95	0	-	11/28/95	0	-
	0.1		0.106 ± 0.002	106.0		0.106 ± 0.006	100.0
	0.4		0.413 ± 0.001	103.3		0.392 ± 0.034	94.9
	1.8		1.842 ± 0.011	102.3		1.774 ± 0.026	96.3
18	0.0	11/28/95	0	-	12/05/95	0	-
	0.1		0.106 ± 0.001	106.0		0.100 ± 0.001	94.3
	0.4		0.408 ± 0.007	102.0		0.398 ± 0.001	97.5
	1.8		1.861 ± 0.033	103.3		1.737 ± 0.023	93.4
19	0.0	12/05/95	0	-	12/12/95	0	-
	0.1		0.102 ± 0.001	102.0		0.103 ± 0.002	101.0
	0.4		0.377 ± 0.001	94.3		0.381 ± 0.004	101.1
	1.8		1.910 ± 0.034	106.1		1.877 ± 0.036	98.3
20	0.0	12/12/95	0	-	12/19/95	0	-
	0.1		0.098 ± 0.002	98.0		0.101 ± 0.003	103.1
	0.4		0.390 ± 0.019	97.5		0.412 ± 0.009	105.6
	1.8		1.828 ± 0.001	101.6		1.873 ± 0.018	102.5
21	0.0	12/19/95	0	-	12/27/95	0	-
	0.1		0.102 ± 0.006	102.0		0.111 ± 0.004	108.8
	0.4		0.414 ± 0.009	103.5		0.396 ± 0.009	95.7
	1.8		1.831 ± 0.027	101.7		1.816 ± 0.018	99.2
22	0.0	12/27/95	0	-	01/03/96	0	-
	0.1		0.098 ± 0.004	98.0		0.096 ± 0.004	98.0
	0.4		0.417 ± 0.009	104.3		0.398 ± 0.012	95.4
	1.8		1.735 ± 0.099	96.4		1.928 ± 0.041	111.1
23	0.0	01/03/96	0	-	01/09/96	0	-
	0.1		0.094 ± 0.006	94.0		0.103 ± 0.006	109.6
	0.4		0.411 ± 0.011	102.8		0.403 ± 0.024	98.1
	1.8		1.798 ± 0.037	99.9		1.795 ± 0.022	99.8
24	0.0	01/09/96	0	-	01/16/96	0	-
	0.1		0.098 ± 0.005	98.0		0.099 ± 0.008	101.0
	0.4		0.396 ± 0.010	99.0		0.392 ± 0.004	99.0
	1.8		1.803 ± 0.059	100.2		1.805 ± 0.041	100.1

Table 3

Results Of Dosing Formulations Analysis for UIC/TRL Study Number 152

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Study Week	Target Concentration (mg base/ml)	Predose Analysis			Postdose Analysis		
		Date	(mg base/ml)	% Target	Date	(mg base/ml)	% Predose
25	0.0	01/16/96	0	-	01/23/96	0	-
	0.1		0.105 ± 0.002	105.0		0.104 ± 0.067	99.0
	0.4		0.392 ± 0.005	98.3		0.436 ± 0.004	110.9
	1.8		1.845 ± 0.036	102.5		1.709 ± 0.034	92.6
26	0.0	01/23/96	0	-	02/02/96	0	-
	0.1		0.102 ± 0.002	102.0		0.100 ± 0.002	98.0
	0.4		0.421 ± 0.006	105.3		0.397 ± 0.007	94.3
	1.8		1.708 ± 0.007	94.9		1.774 ± 0.010	103.9

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APPENDIX B

CLINICAL PATHOLOGY METHODOLOGY

CLINICAL CHEMISTRY

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Alanine Aminotransferase (ALT/GPT)

Modified Wroblewski & La Due procedure
Ciba-Corning 550 Express Clinical Chemistry System
Henry, R.J., Chiamori, N., Golub, O.J. and Berkman, S.
Am. J. Clin. Path., 34, 381, 1960.

Albumin

Bromocresol green method
Ciba-Corning 550 Express Clinical Chemistry System
Doumas, B.T. and Biggs, H.G.
Standard Methods of Clinical Chemistry, 7, 175, 1972.

Alkaline Phosphatase

Modified Bessey-Lowry procedure
Ciba-Corning 550 Express Clinical Chemistry System
Neumann, H. and Von Vreedendaal
M. Clin. Chem. Acta., 17, 183, 1967.

Calcium

Modified alizarin procedure
Ciba-Corning 550 Express Clinical Chemistry System
Frings, C.S., et. al.
Clin. Chem., 16, 816, 1970.

Chloride

Mecuric thiocyanate procedure
Ciba-Corning 550 Express Clinical Chemistry System
Zall, O.M., Fisher, D. and Garner, M.Q.
Anal. Chem, 28, 1065, 1956.

Creatinine

Jaffe method
Ciba-Corning 550 Express Clinical Chemistry System
Larsen. K.
Clin. Chem. Acta, 41, 209, 1972

Creatine Kinase (CK)

Modification of Szasz *et al.* procedure
Ciba-Corning 550 Express Clinical Chemistry System
Clin. Chem. 22, 650-656, 1976.

Glucose

Hexokinase method
Ciba-Corning 550 Express Clinical Chemistry System
Bondar, J.L. and Mead, D.C.
Clin. Chem. 20, 586, 1974.

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Phosphorus, Inorganic

Ammonium molybdate method
Ciba-Corning 550 Express Clinical Chemistry System
Fiske, C.H. and Subbarow, Y.
J. Biol. Chem. 66, 325, 1925.

Lactate Dehydrogenase

L → P technique
Ciba-Corning 550 Express Clinical Chemistry System
Wacker, W.E.C., Ulmer, D.D., Valle, B.L.
New England J Med. 225, 449, 1956.

Na+, K+

Ion specific electrodes
Model 614 ISE Na+/K+ Analyzer (Ciba Corning)

Sorbitol Dehydrogenase

Fructose → Sorbitol oxidase reaction
Ciba-Corning 550 Express Clinical Chemistry System
Asada, M. and Galanbos J.T.
Gastroenterology 44, 578, 1963.
Wiesner, I.S. *et al.*
Am. J. Dig. Dis. 10, 147, 1965.

Total Bile Acids

3α- Hydroxy bile acid oxidation procedure (Sigma Diagnostic kit)
Ciba-Corning 550 Express Clinical Chemistry System
Mashige, F. *et al.*
Clin Chem. 27, 1352-1356, 1981.

Total Protein

Biuret technique
Ciba-Corning 550 Express Clinical Chemistry System
Kingsley, G.R.
J. Biol. Chem. 131, 197, 1939.

Urea Nitrogen (BUN)

Modified urease technique
Ciba-Corning 550 Express Clinical Chemistry System
Talke, H. and Schubert, G.E.
Klin. Wchnschr. 43, 174, 1965.

HEMATOLOGY

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Erythrocyte Count
Electronic counting procedure
Sysmex K1000 Hematology Analyzer

Hemoglobin
Cyanomethemoglobin method
Sysmex K1000 Hematology Analyzer

Hematocrit
Indirect method; calculated value based on volume of red cells and volume of blood

Mean Corpuscular Volume (MCV)
Indirect method; calculated value based on hematocrit and red blood cell count

Mean Corpuscular Hemoglobin (MCH)
Indirect method; calculated value based on erythrocyte count and hemoglobin

Mean Corpuscular Hemoglobin Concentration (MCHC)
Indirect method; calculated value based on hematocrit and hemoglobin

Methemoglobin (% METHGB)
Co-oximeter (Instrumentation Laboratory Model 282)

Reticulocyte Count
New methylene blue staining procedure
Brecher, G., Am. J. Clin. Path., 19, 895, 1949.

Platelet Count
Electronic counting procedure
Sysmex K1000 Hematology Analyzer

Activated Partial Thromboplastin Time (APTT)
Electra 700 coagulation machine

Leukocyte Count
Electronic counting procedure
Sysmex K1000 Hematology Analyzer

Leukocyte Differential Count
Neutrophils - Immature (bands)
Neutrophils - Mature (segs)
Monocytes
Basophils
Lymphocytes
Eosinophils
Wright stain procedure
Schalm, O.W., Jain, N.C. and Carroll, E.J. Veterinary Hematology, Color Plates Chapter, 3rd Edition, Lee and Febiger, 1975.

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Nucleated RBCs

Wright stain procedure

Schalm, O.W., Jain, N.C. and Carroll, E.J. Veterinary Hematology, Color Plates Chapter, 3rd Edition, Lee and Febiger, 1975.

RBC Morphology

Wright stain procedure

Schalm, O.W., Jain, N.C. and Carroll, E.J. Veterinary Hematology, Color Plates Chapter, 3rd Edition, Lee and Febiger, 1975.

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APPENDIX C

INDIVIDUAL OBSERVATIONS (Clinical Signs)

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-M SEX: MALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
401	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 176
	Normal			DAY 178-DAY 183
	Scheduled Sacrifice			DAY 184
402	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
403	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
404	Dark Material Around Eyes			DAY 177
	Dark Material Around Nose			DAY 72
	Normal			DAY 1-DAY 71
	Normal			DAY 73-DAY 176
	Normal			DAY 178-DAY 183
	Scheduled Sacrifice			DAY 184
405	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
406	Normal			DAY 1-DAY 68
	Normal			DAY 70-DAY 183
	Scheduled Sacrifice			DAY 184
407	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 27
	Normal			DAY 31-DAY 176
	Normal			DAY 178-DAY 182
	Swollen Left Eye			DAY 28-DAY 30
	Scheduled Sacrifice			DAY 183
408	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
409	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-M SEX: MALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
410	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
411	Normal Scheduled Sacrifice			DAY 1-DAY 183 DAY 184
412	Normal Scheduled Sacrifice			DAY 1-DAY 183 DAY 184
413	Normal Scheduled Sacrifice			DAY 1-DAY 183 DAY 184
414	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
415	Normal Scheduled Sacrifice			DAY 1-DAY 183 DAY 184
416	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
417	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
418	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
419	Normal Scheduled Sacrifice			DAY 1-DAY 182 DAY 183
420	Normal Scheduled Sacrifice			DAY 1-DAY 183 DAY 184
421	Normal Animal Removed From Study			DAY 1-DAY 175 DAY 176
422	Normal Animal Removed From Study			DAY 1-DAY 175 DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-M SEX: MALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
423	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
424	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
425	Dark Material Around Eyes			DAY 156
	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 155
	Normal			DAY 157-DAY 174
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-M SEX: MALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
451	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 183
	Scheduled Sacrifice			DAY 184
452	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 176
	Normal			DAY 178-DAY 182
	Scheduled Sacrifice			DAY 183
453	Dark Material Around Eyes			DAY 167
	Dark Material Around Eyes			DAY 177
	Dark Material Around Mouth			DAY 167
	Dark Material Around Mouth			DAY 169-DAY 173
	Dark Material Around Nose			DAY 167-DAY 168
	Normal			DAY 1-DAY 166
	Normal			DAY 174-DAY 176
	Normal			DAY 178-DAY 182
	Nasal Discharge			DAY 167
	Scheduled Sacrifice			DAY 183
454	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
455	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
456	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
457	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
458	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
459	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-M SEX: MALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
460	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 69
	Normal			DAY 71-DAY 176
	Normal			DAY 178-DAY 183
	Scheduled Sacrifice			DAY 184
461	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
462	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
463	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
464	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
465	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
466	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
467	Hunched Posture			DAY 11
	Normal			DAY 1-DAY 10
	Normal			DAY 12-DAY 182
	Scheduled Sacrifice			DAY 183
468	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
469	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
470	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-M SEX: MALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
471	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
472	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
473	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
474	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
475	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-M SEX: MALE
DAY 1-DAY 185 DOSE: 2.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
501	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
502	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
503	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
504	Dark Material Around Eyes			DAY 177-DAY 179
	Normal			DAY 1-DAY 176
	Normal			DAY 182-DAY 183
	Swollen Left Eye			DAY 178-DAY 181
	Scheduled Sacrifice			DAY 184
505	Dark Material Around Eyes			DAY 177-DAY 178
	Normal			DAY 1-DAY 176
	Normal			DAY 179-DAY 182
	Scheduled Sacrifice			DAY 183
506	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 183
	Scheduled Sacrifice			DAY 184
507	Dark Material Around Eyes			DAY 177-DAY 178
	Normal			DAY 1-DAY 176
	Normal			DAY 179-DAY 182
	Scheduled Sacrifice			DAY 183
508	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
509	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
510	Dark Material Around Eyes			DAY 86

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-M SEX: MALE
DAY 1-DAY 185 DOSE: 2.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 85
	Normal			DAY 87-DAY 176
	Normal			DAY 178-DAY 182
	Scheduled Sacrifice			DAY 183
511	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
512	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
513	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
514	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
515	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
516	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
517	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
518	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
519	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
520	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
521	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-M SEX: MALE
DAY 1-DAY 185 DOSE: 2.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
522	Dark Material Around Eyes			DAY 165
	Dark Material Around Eyes			DAY 168-DAY 175
	Normal			DAY 1-DAY 164
	Normal			DAY 166-DAY 167
	Animal Removed From Study			DAY 176
523	Dark Material Around Mouth			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176
524	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176
525	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-M SEX: MALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
551	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
552	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
553	Dark Material Around Eyes			DAY 178-DAY 179
	Normal			DAY 1-DAY 177
	Normal			DAY 180-DAY 183
	Scheduled Sacrifice			DAY 184
554	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
555	Dark Material Around Eyes			DAY 177-DAY 178
	Normal			DAY 1-DAY 60
	Normal			DAY 62
	Normal			DAY 76-DAY 85
	Normal			DAY 103
	Normal			DAY 105-DAY 116
	Normal			DAY 118-DAY 176
	Normal			DAY 179-DAY 182
	Rough Coat			DAY 61
	Rough Coat			DAY 63-DAY 75
	Rough Coat			DAY 86-DAY 102
	Rough Coat			DAY 104
	Rough Coat			DAY 117
	Scheduled Sacrifice			DAY 183
556	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 182
	Scheduled Sacrifice			DAY 183
557	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-M SEX: MALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
558	Dark Material Around Nose			DAY 134
	Dark Material Around Nose			DAY 136
	Animal Found Dead			DAY 137
	Hunched Posture			DAY 62-DAY 78
	Hunched Posture			DAY 136
	Labored Breathing			DAY 136
	Normal			DAY 1-DAY 47
	Normal			DAY 79
	Normal			DAY 85-DAY 103
	Normal			DAY 105-DAY 123
	Normal			DAY 126-DAY 133
	Normal			DAY 135
	Rough Coat			DAY 48-DAY 78
	Rough Coat			DAY 80-DAY 84
	Rough Coat			DAY 104
	Rough Coat			DAY 124-DAY 125
	Rough Coat			DAY 134
559	Dark Material Around Eyes			DAY 177
	Normal			DAY 1-DAY 176
	Normal			DAY 178-DAY 182
	Scheduled Sacrifice			DAY 183
560	Dark Material Around Eyes			DAY 181
	Normal			DAY 1-DAY 180
	Normal			DAY 182
	Scheduled Sacrifice			DAY 183
561	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
562	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
563	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
564	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-M SEX: MALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
565	Dark Material Around Eyes			DAY 167
	Dark Material Around Mouth			DAY 169
	Dark Material Around Nose			DAY 167
	Hunched Posture			DAY 169
	Hunched Posture			DAY 171-DAY 181
	Labored Breathing			DAY 167
	Normal			DAY 1-DAY 166
	Normal			DAY 168
	Normal			DAY 170
	Normal			DAY 182-DAY 183
	Nasal Discharge			DAY 167
	Rough Coat			DAY 173-DAY 176
	Scheduled Sacrifice			DAY 184
566	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
567	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
568	Hunched Posture			DAY 68-DAY 84
	Normal			DAY 1-DAY 63
	Normal			DAY 86-DAY 182
	Rough Coat			DAY 64-DAY 85
	Scheduled Sacrifice			DAY 183
569	Normal			DAY 1-DAY 81
	Normal			DAY 84-DAY 183
	Rough Coat			DAY 82-DAY 83
	Scheduled Sacrifice			DAY 184
570	Normal			DAY 1-DAY 182
	Scheduled Sacrifice			DAY 183
571	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
572	Dark Material Around Eyes			DAY 57-DAY 60

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-M SEX: MALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 56
	Normal			DAY 61-DAY 174
	Animal Removed From Study			DAY 176
573	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
574	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
575	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
426	Dark Material Around Eyes			DAY 179-DAY 181
	Normal			DAY 1-DAY 178
	Normal			DAY 182-DAY 184
	Scheduled Sacrifice			DAY 185
427	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
428	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 183
	Scheduled Sacrifice			DAY 184
429	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
430	Dark Material Around Eyes			DAY 179-DAY 180
	Normal			DAY 1-DAY 178
	Normal			DAY 181-DAY 184
	Scheduled Sacrifice			DAY 185
431	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 183
	Scheduled Sacrifice			DAY 184
432	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
433	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
434	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
435	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
436	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
437	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
438	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
439	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
440	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
441	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
442	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
443	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
444	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
445	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
446	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176
447	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
448	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 1-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
449	Normal			DAY 1-DAY 147
	Normal			DAY 149-DAY 175
	Animal Removed From Study			DAY 176
450	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
476	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
477	Dark Material Around Eyes			DAY 178-DAY 179
	Normal			DAY 1-DAY 177
	Normal			DAY 180-DAY 183
	Scheduled Sacrifice			DAY 184
478	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
479	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
480	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 184
	Scheduled Sacrifice			DAY 185
481	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
482	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 155
	Normal			DAY 157
	Normal			DAY 160-DAY 177
	Normal			DAY 179-DAY 184
	Rough Coat			DAY 156
	Rough Coat			DAY 158-DAY 159
	Scheduled Sacrifice			DAY 185
483	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
484	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
485	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 184
	Scheduled Sacrifice			DAY 185
486	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
487	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
488	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
489	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
490	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
491	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
492	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
493	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
494	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
495	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
496	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 2-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 0.5 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
497	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
498	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
499	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
500	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 2.0(mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
526	Dark Material Around Eyes			DAY 178-DAY 179
	Normal			DAY 1-DAY 177
	Normal			DAY 180-DAY 184
	Scheduled Sacrifice			DAY 185
527	Dark Material Around Eyes			DAY 181
	Normal			DAY 1-DAY 180
	Normal			DAY 182-DAY 184
	Scheduled Sacrifice			DAY 185
528	Dark Material Around Eyes			DAY 179
	Normal			DAY 1-DAY 178
	Normal			DAY 180-DAY 183
	Scheduled Sacrifice			DAY 184
529	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
530	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
531	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
532	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 184
	Scheduled Sacrifice			DAY 185
533	Normal			DAY 1-DAY 177
	Normal			DAY 180-DAY 184
	Swollen Left Eye			DAY 178-DAY 179
	Scheduled Sacrifice			DAY 185
534	Dark Material Around Eyes			DAY 179
	Normal			DAY 1-DAY 178
	Normal			DAY 180-DAY 183
	Scheduled Sacrifice			DAY 184

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 2.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
535	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
536	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
537	Normal			DAY 1-DAY 67
	Normal			DAY 69-DAY 184
	Scheduled Sacrifice			DAY 185
538	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
539	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
540	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
541	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
542	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
543	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
544	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
545	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
546	Normal			DAY 1-DAY 67
	Normal			DAY 69-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 3-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 2.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
547	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176
548	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
549	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
550	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
576	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
577	Dark Material Around Eyes			DAY 178-DAY 179
	Normal			DAY 1-DAY 177
	Normal			DAY 181-DAY 184
	Swollen Left Eye			DAY 178-DAY 180
	Scheduled Sacrifice			DAY 185
578	Dark Material Around Eyes			DAY 181
	Normal			DAY 1-DAY 180
	Normal			DAY 183-DAY 184
	Swollen Left Eye			DAY 181-DAY 182
	Scheduled Sacrifice			DAY 185
579	Dark Material Around Eyes			DAY 181-DAY 183
	Normal			DAY 1-DAY 180
	Normal			DAY 184
	Scheduled Sacrifice			DAY 185
580	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
581	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 184
	Scheduled Sacrifice			DAY 185
582	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
583	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
584	Dark Material Around Eyes			DAY 178
	Normal			DAY 1-DAY 177
	Normal			DAY 179-DAY 183
	Scheduled Sacrifice			DAY 184

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
585	Dark Material Around Eyes			DAY 178-DAY 180
	Normal			DAY 1-DAY 177
	Normal			DAY 181-DAY 184
	Scheduled Sacrifice			DAY 185
586	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
587	Normal			DAY 1-DAY 99
	Normal			DAY 103-DAY 184
	Piloerection			DAY 100-DAY 102
	Scheduled Sacrifice			DAY 185
588	Normal			DAY 1-DAY 68
	Normal			DAY 70-DAY 131
	Normal			DAY 133-DAY 184
	Piloerection			DAY 69
	Rough Coat			DAY 132
	Scheduled Sacrifice			DAY 185
589	Normal			DAY 1-DAY 183
	Scheduled Sacrifice			DAY 184
590	Normal			DAY 1-DAY 93
	Normal			DAY 95-DAY 184
	Piloerection			DAY 94
	Scheduled Sacrifice			DAY 185
591	Normal			DAY 1-DAY 125
	Normal			DAY 129-DAY 184
	Piloerection			DAY 126-DAY 128
	Scheduled Sacrifice			DAY 185
592	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
593	Hunched Posture			DAY 92-DAY 96
	Normal			DAY 1-DAY 91

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 9.0 (mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
593 (contd.)	Normal			DAY 98-DAY 99
	Normal			DAY 103-DAY 184
	Piloerection			DAY 100-DAY 102
	Rough Coat			DAY 92-DAY 97
	Scheduled Sacrifice			DAY 185
594	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
595	Normal			DAY 1-DAY 184
	Scheduled Sacrifice			DAY 185
596	Normal			DAY 1-DAY 72
	Normal			DAY 74-DAY 175
	Piloerection			DAY 73
	Animal Removed From Study			DAY 176
597	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
598	Normal			DAY 1-DAY 175
	Animal Removed From Study			DAY 176
599	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 174
	Animal Removed From Study			DAY 176

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INDIVIDUAL CLINICAL SIGNS

STUDY: 152 GROUP: 4-F SEX: FEMALE
DAY 1-DAY 185 DOSE: 9.0(mg base/kg/day)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	TIME OCCURRED
600	Dark Material Around Eyes			DAY 49
	Dark Material Around Eyes			DAY 175
	Normal			DAY 1-DAY 48
	Normal			DAY 50-DAY 66
	Normal			DAY 73-DAY 75
	Normal			DAY 78-DAY 85
	Normal			DAY 87-DAY 174
	Piloerection			DAY 67-DAY 72
	Piloerection			DAY 76-DAY 77
	Piloerection			DAY 86
	Animal Removed From Study			DAY 176

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 1					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 2					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 3					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 4					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 5					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 6					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 7					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 8					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 9					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 10					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152

SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 11					
No. Observed		25	25	25	25
Normal		25 100%	24 96%	25 100%	25 100%
Hunched Posture		0	1 4%	0	0
DAY 12					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 13					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 14					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 15					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 16					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 17					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 18					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 19					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 20					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 21					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 22					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 23					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 24					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 25					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 26					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 27					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 28					
No. Observed		25	25	25	25
Normal		24 96%	25 100%	25 100%	25 100%
Swollen Left Eye		1 4%	0	0	0
DAY 29					
No. Observed		25	25	25	25
Normal		24 96%	25 100%	25 100%	25 100%
Swollen Left Eye		1 4%	0	0	0
DAY 30					
No. Observed		25	25	25	25
Normal		24 96%	25 100%	25 100%	25 100%
Swollen Left Eye		1 4%	0	0	0

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 31					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 32					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 33					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 34					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 35					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 36					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 37					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 38					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 39					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 40					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 41					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 42					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 43					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 44					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 45					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 46					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 47					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 48					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 49					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 50					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152

SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 51					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 52					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 53					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 54					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 55					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 56					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 57					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Dark Material Around Eyes	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 58					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Dark Material Around Eyes	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 59					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Dark Material Around Eyes	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 60					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Dark Material Around Eyes	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 61					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Rough Coat	0	0	0	2 8%
DAY 62					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 63					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	2 8%
DAY 64					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%
DAY 65					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 66					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%
DAY 67					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%
DAY 68					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 69					
	No. Observed	24	25	25	25
	Normal	24 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 70					
	No. Observed	25	24	25	25
	Normal	25 100%	24 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 71					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 72					
	No. Observed	25	25	25	25
	Normal	24 96%	25 100%	25 100%	22 88%
	Dark Material Around Nose	1 4%	0	0	0
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 73					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 74					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 75					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	3 12%
DAY 76					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	2 8%
DAY 77					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	2 8%
DAY 78					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	2 8%
	Rough Coat	0	0	0	2 8%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE: (mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 79					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 80					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	2 8%
DAY 81					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	2 8%
DAY 82					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%
DAY 83					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	22 88%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	3 12%
DAY 84					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	2 8%
DAY 85					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE: (mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 86					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	24 96%	24 96%
	Dark Material Around Eyes	0	0	1 4%	0
	Rough Coat	0	0	0	1 4%
DAY 87					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 88					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 89					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 90					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 91					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 92					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 93					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 94					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 95					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 96					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 97					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 98					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 99					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 100					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 101					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE: (mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 102					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 103					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 104					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	23 92%
Rough Coat		0	0	0	2 8%
DAY 105					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 106					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 107					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 108					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 109					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 110					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 111					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 112					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 113					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 114					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 115					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 116					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 117					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 118					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 119					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 120					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 121					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

DRAFT

INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE: (mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 122					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 123					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 124					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 125					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%
DAY 126					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 127					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 128					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 129					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 130					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 131					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 132					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 133					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 134					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Dark Material Around Nose	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%
DAY 135					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 136					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Dark Material Around Nose	0	0	0	1 4%
	Hunched Posture	0	0	0	1 4%
	Labored Breathing	0	0	0	1 4%
DAY 137					
	No. Observed	25	25	25	25
	Animal Found Dead	0	0	0	1 4%
	Normal	25 100%	25 100%	25 100%	24 96%
DAY 138					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 139					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 140					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 141					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 142					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 143					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 144					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 145					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 146					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 147					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 148					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
DAY 149					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%
OAY 150					
No. Observed		25	25	25	24
Normal		25 100%	25 100%	25 100%	24 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 151					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 152					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 153					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 154					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 155					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 156					
	No. Observed	25	25	25	24
	Normal	24 96%	25 100%	25 100%	24 100%
	Dark Material Around Eyes	1 4%	0	0	0
DAY 157					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 158					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 159					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 160					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 161					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 162					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 163					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 164					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 165					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	24 96%	24 100%
	Dark Material Around Eyes	0	0	1 4%	0
DAY 166					
	No. Observed	25	25	25	24
	Normal	25 100%	25 100%	25 100%	24 100%
DAY 167					
	No. Observed	25	25	25	24
	Normal	25 100%	24 96%	25 100%	23 96%
	Dark Material Around Eyes	0	1 4%	0	1 4%
	Dark Material Around Nose	0	1 4%	0	1 4%
	Labored Breathing	0	0	0	1 4%
	Nasal Discharge	0	1 4%	0	1 4%
	Dark Material Around Mouth	0	1 4%	0	0
DAY 168					
	No. Observed	25	25	25	24
	Normal	25 100%	24 96%	24 96%	24 100%
	Dark Material Around Eyes	0	0	1 4%	0
	Dark Material Around Nose	0	1 4%	0	0

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 169					
	No. Observed	25	25	25	24
	Normal	25 100%	24 96%	24 96%	23 96%
	Dark Material Around Eyes	0	0	1 4%	0
	Hunched Posture	0	0	0	1 4%
	Dark Material Around Mouth	0	1 4%	0	1 4%
DAY 17D					
	No. Observed	25	25	25	24
	Normal	25 1DD%	24 96%	24 96%	24 1D0%
	Dark Material Around Eyes	0	0	1 4%	0
	Dark Material Around Mouth	0	1 4%	0	0
DAY 171					
	No. Observed	25	25	25	24
	Normal	25 100%	24 96%	24 96%	23 96%
	Dark Material Around Eyes	0	0	1 4%	0
	Hunched Posture	D	D	0	1 4%
	Dark Material Around Mouth	0	1 4%	0	0
DAY 172					
	No. Observed	25	25	25	24
	Normal	25 100%	24 96%	24 96%	23 96%
	Dark Material Around Eyes	0	0	1 4%	D
	Hunched Posture	0	0	0	1 4%
	Dark Material Around Mouth	0	1 4%	0	0
DAY 173					
	No. Dbserved	25	25	25	24
	Normal	25 1D0%	24 96%	24 96%	23 96%
	Dark Material Around Eyes	D	0	1 4%	D
	Hunched Posture	0	D	0	1 4%
	Rough Coat	D	0	D	1 4%
	Dark Material Around Mouth	0	1 4%	0	0
DAY 174					
	No. Dbserved	25	25	25	24
	Normal	25 100%	25 100%	24 96%	23 96%
	Dark Material Around Eyes	0	0	1 4%	0
	Hunched Posture	0	0	0	1 4%
	Rough Coat	0	0	0	1 4%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-M		0.5 2-M		2.0 3-M		9.0 4-M	
DAY 175									
	No. Observed	25		25		25		24	
	Normal	24	96%	25	100%	21	84%	21	88%
	Dark Material Around Eyes	1	4%	0		3	12%	2	8%
	Hunched Posture	0		0		0		1	4%
	Rough Coat	0		0		0		1	4%
	Dark Material Around Mouth	0		0		1	4%	0	
DAY 176									
	No. Observed	25		25		25		24	
	Normal	20	80%	20	80%	20	80%	18	75%
	Hunched Posture	0		0		0		1	4%
	Rough Coat	0		0		0		1	4%
	Animal Removed From Study	5	20%	5	20%	5	20%	5	21%
DAY 177									
	No. Observed	20		20		20		19	
	Normal	17	85%	17	85%	16	80%	16	84%
	Dark Material Around Eyes	3	15%	3	15%	4	20%	2	11%
	Hunched Posture	0		0		0		1	5%
DAY 178									
	No. Observed	20		20		20		19	
	Normal	20	100%	19	95%	16	80%	15	79%
	Dark Material Around Eyes	0		1	5%	4	20%	3	16%
	Hunched Posture	0		0		0		1	5%
	Swollen Left Eye	0		0		1	5%	0	
DAY 179									
	No. Observed	20		20		20		19	
	Normal	20	100%	20	100%	19	95%	17	89%
	Dark Material Around Eyes	0		0		1	5%	1	5%
	Hunched Posture	0		0		0		1	5%
	Swollen Left Eye	0		0		1	5%	0	
DAY 180									
	No. Observed	20		20		20		19	
	Normal	20	100%	20	100%	19	95%	18	95%
	Hunched Posture	0		0		0		1	5%
	Swollen Left Eye	0		0		1	5%	0	

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: MALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-M	0.5 2-M	2.0 3-M	9.0 4-M
DAY 181					
	No. Observed	20	20	20	19
	Normal	20 100%	20 100%	19 95%	17 89%
	Dark Material Around Eyes	0	0	0	1 5%
	Hunched Posture	0	0	0	1 5%
	Swollen Left Eye	0	0	1 5%	0
DAY 182					
	No. Observed	20	20	20	19
	Normal	20 100%	20 100%	20 100%	19 100%
DAY 183					
	No. Observed	20	20	20	19
	Scheduled Sacrifice	11 55%	14 70%	14 70%	13 68%
	Normal	9 45%	6 30%	6 30%	6 32%
DAY 184					
	No. Observed	9	6	6	6
	Scheduled Sacrifice	9 100%	6 100%	6 100%	6 100%

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 1					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 2					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 3					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 4					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 5					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 6					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 7					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 8					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 9					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 10					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 11					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 12					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 13					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 14					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 15					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 16					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 17					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 18					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 19					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 20					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 21					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 22					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 23					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 24					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 25					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 26					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 27					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 28					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 29					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 30					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 31					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 32					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 33					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 34					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 35					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 36					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 37					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 38					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 39					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 40					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 41					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 42					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 43					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 44					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 45					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 46					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 47					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 48					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 49					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Dark Material Around Eyes	0	0	0	1 4%
DAY 50					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 51					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 52					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 53					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 54					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 55					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 56					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 57					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 58					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 59					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 60					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 61					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 62					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 63					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 64					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 65					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 66					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 67					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 68					
No. Observed		25	25	23	25
Normal		25 100%	25 100%	23 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 69					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	23 92%
Piloerection		0	0	0	2 8%
DAY 70					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 71					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 72					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 73					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 74					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 75					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 76					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 77					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 78					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 79					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 80					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 81					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 82					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 83					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 84					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 85					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 86					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 87					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 88					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 89					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 90					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 91					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 92					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Hunched Posture		0	0	0	1 4%
Rough Coat		0	0	0	1 4%
DAY 93					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Hunched Posture		0	0	0	1 4%
Rough Coat		0	0	0	1 4%
DAY 94					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	23 92%
Hunched Posture		0	0	0	1 4%
Piloerection		0	0	0	1 4%
Rough Coat		0	0	0	1 4%
DAY 95					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Hunched Posture		0	0	0	1 4%
Rough Coat		0	0	0	1 4%
DAY 96					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Hunched Posture		0	0	0	1 4%
Rough Coat		0	0	0	1 4%
DAY 97					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Rough Coat		0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 98					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 99					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 100					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Piloerection	0	0	0	2 8%
DAY 101					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Piloerection	0	0	0	2 8%
DAY 102					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	23 92%
	Piloerection	0	0	0	2 8%
DAY 103					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 104					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 105					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 106					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DDSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 107					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 108					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 109					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 110					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 111					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 112					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 113					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 114					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 115					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 116					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 117					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 118					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 119					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 120					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 121					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 122					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 123					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 124					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 125					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 126					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%
DAY 127					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	24 96%
Piloerection		0	0	0	1 4%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 128					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Piloerection	0	0	0	1 4%
DAY 129					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 130					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 131					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 132					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	24 96%
	Rough Coat	0	0	0	1 4%
DAY 133					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 134					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 135					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 136					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

SIX MONTH ORAL TOXICITY STUDY OF WR238605 SUCCINATE IN RATS

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 137					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 138					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 139					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 140					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 141					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 142					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 143					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 144					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 145					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 146					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 147					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 148					
No. Observed		24	25	25	25
Normal		24 100%	25 100%	25 100%	25 100%
DAY 149					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 150					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 151					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 152					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 153					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 154					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 155					
No. Observed		25	25	25	25
Normal		25 100%	25 100%	25 100%	25 100%
DAY 156					
No. Observed		25	25	25	25
Normal		25 100%	24 96%	25 100%	25 100%
Rough Coat		0	1 4%	0	0

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 157					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 158					
	No. Observed	25	25	25	25
	Normal	25 100%	24 96%	25 100%	25 100%
	Rough Coat	0	1 4%	0	0
DAY 159					
	No. Observed	25	25	25	25
	Normal	25 100%	24 96%	25 100%	25 100%
	Rough Coat	0	1 4%	0	0
DAY 160					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 161					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 162					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 163					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 164					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 165					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 166					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%

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INCIDENCE OF CLINICAL SIGNS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 167					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 168					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 169					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 170					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 171					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 172					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 173					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 174					
	No. Observed	25	25	25	25
	Normal	25 100%	25 100%	25 100%	25 100%
DAY 175					
	No. Observed	25	25	25	25
	Normal	24 96%	25 100%	24 96%	23 92%
	Dark Material Around Eyes	1 4%	0	1 4%	2 8%
DAY 176					
	No. Observed	25	25	25	25
	Normal	20 80%	20 80%	20 80%	20 80%
	Animal Removed From Study	5 20%	5 20%	5 20%	5 20%

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INCIDENCE OF OBSERVATIONS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 177					
	No. Observed	20	20	20	20
	Normal	20 100%	20 100%	20 100%	20 100%
DAY 178					
	No. Observed	20	20	20	20
	Normal	18 90%	16 80%	17 85%	16 80%
	Dark Material Around Eyes	2 10%	4 20%	2 10%	4 20%
	Swollen Left Eye	0	0	1 5%	1 5%
DAY 179					
	No. Observed	20	20	20	20
	Normal	18 90%	19 95%	16 80%	18 90%
	Dark Material Around Eyes	2 10%	1 5%	3 15%	2 10%
	Swollen Left Eye	0	0	1 5%	1 5%
DAY 180					
	No. Observed	20	20	20	20
	Normal	18 90%	20 100%	20 100%	18 90%
	Dark Material Around Eyes	2 10%	0	0	1 5%
	Swollen Left Eye	0	0	0	1 5%
DAY 181					
	No. Observed	20	20	20	20
	Normal	19 95%	20 100%	19 95%	18 90%
	Dark Material Around Eyes	1 5%	0	1 5%	2 10%
	Swollen Left Eye	0	0	0	1 5%
DAY 182					
	No. Observed	20	20	20	20
	Normal	20 100%	20 100%	20 100%	18 90%
	Dark Material Around Eyes	0	0	0	1 5%
	Swollen Left Eye	0	0	0	1 5%
DAY 183					
	No. Observed	20	20	20	20
	Normal	20 100%	20 100%	20 100%	19 95%
	Dark Material Around Eyes	0	0	0	1 5%

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INCIDENCE OF CLINICAL SIGNS

STUDY: 152 SEX: FEMALE

PERIOD	DOSE:(mg base/kg/day) / GROUP:	0 1-F	0.5 2-F	2.0 3-F	9.0 4-F
DAY 184					
	No. Observed	20	20	20	20
	Scheduled Sacrifice	9 45%	7 35%	7 35%	3 15%
	Normal	11 55%	13 65%	13 65%	17 85%
DAY 185					
	No. Observed	11	12	13	17
	Scheduled Sacrifice	11 100%	12 100%	13 100%	17 100%

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APPENDIX D

INDIVIDUAL BODY WEIGHTS AND BODY WEIGHT GAINS

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1 M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
401	276	341	390	423	447	464	490	524	557	574	594	620
402	246	298	345	394	413	436	481	504	524	555	573	591
403	219	269	307	341	364	392	426	446	472	489	509	520
404	238	290	334	374	399	420	476	502	529	552	576	491
405	249	302	335	372	392	420	461	484	511	533	551	564
406	258	308	356	402	433	471	509	548	569	591	622	637
407	264	323	376	416	424	449	498	516	519	549	573	596
408	258	318	368	410	426	467	514	543	579	589	620	641
409	266	321	371	422	448	488	546	567	591	620	640	652
410	244	299	339	377	390	422	458	477	502	519	547	572
411	246	298	330	357	384	416	442	464	482	497	506	518
412	246	299	343	383	398	427	466	487	507	517	533	544
413	249	312	362	406	440	466	507	528	553	573	594	610
414	260	317	360	390	424	455	490	511	537	518	583	604
415	245	293	334	366	392	397	425	443	456	468	483	493
416	265	328	380	423	466	491	538	558	586	607	621	648
417	231	278	322	356	383	414	440	454	474	497	514	531
418	267	330	383	419	454	476	527	538	567	581	602	617
419	253	307	352	390	425	466	502	521	545	569	582	603
420	242	285	328	365	401	419	449	468	495	514	531	549
421	238	290	333	367	402	416	450	460	470	484	510	521
422	240	292	339	374	416	438	471	488	517	539	560	578
423	232	276	318	343	367	380	414	424	443	456	478	492
424	283	345	414	453	508	536	587	608	643	663	685	710
425	289	338	397	434	478	515	556	584	616	638	657	682
MEAN	252	306	353	390	419	446	485	506	530	548	570	583
S.D.	16.6	20.7	26.9	29.6	34.9	38.5	44.1	46.8	51.0	53.3	54.2	60.7
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

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INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
401	631	637	656	659	676	677	681	681	686	700	707	715
402	603	606	616	621	636	646	649	658	669	680	689	699
403	533	545	566	573	581	590	596	605	606	623	634	648
404	515	545	579	588	619	630	642	652	667	673	684	699
405	582	492	548	583	597	625	630	631	629	647	656	670
406	659	675	691	711	728	657	668	714	732	748	769	776
407	602	603	628	629	652	669	671	682	698	709	725	729
408	655	623	638	652	665	677	676	682	702	706	719	724
409	667	667	693	702	721	728	735	740	744	751	764	781
410	598	606	617	627	649	658	665	672	695	705	721	732
411	534	549	560	559	573	573	576	589	600	611	622	622
412	567	573	580	592	611	610	605	619	629	642	640	653
413	622	636	648	647	653	665	666	672	689	699	710	715
414	613	622	633	654	656	661	663	687	704	704	722	716
415	505	514	527	524	530	538	541	546	558	565	579	578
416	665	684	692	696	706	714	722	743	741	746	769	779
417	541	552	561	570	581	594	594	586	608	618	625	610
418	635	640	663	668	682	690	695	705	720	726	732	744
419	610	644	656	665	674	678	687	695	704	715	736	734
420	554	574	584	590	601	611	613	602	609	629	646	653
421	543	556	567	575	581	586	575	584	590	605	622	625
422	597	612	624	630	654	667	664	669	680	691	698	701
423	506	513	523	522	538	546	552	563	557	571	575	574
424	729	751	768	773	780	795	790	793	808	820	830	851
425	711	719	737	741	762	767	775	785	795	802	829	848
MEAN	599	606	622	630	644	650	653	662	673	683	696	703
S.D.	61.7	65.1	63.7	64.1	64.7	62.6	63.4	65.5	67.2	65.5	68.4	73.0
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

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INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
401	713	711	730
402	700	716	718
403	648	654	659
404	696	715	720
405	672	686	691
406	785	787	792
407	730	731	729
408	726	739	742
409	789	796	806
410	733	746	747
411	630	636	638
412	655	674	679
413	702	712	724
414	723	730	733
415	574	581	592
416	779	801	805
417	592	633	645
418	748	757	762
419	737	746	756
420	664	668	673
421	628	619	--
422	702	708	--
423	578	592	--
424	857	858	--
425	866	867	--
MEAN	705	715	717
S.D.	76.2	73.9	56.9
N	25	25	20

--: Data Unavailable

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INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5(mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
451	244	303	348	383	401	436	483	518	540	563	586	605
452	264	307	346	379	398	422	455	476	491	514	531	539
453	243	294	338	369	381	405	447	467	495	522	544	564
454	246	295	338	373	379	418	465	481	504	531	550	569
455	245	297	346	388	423	463	497	529	562	587	614	615
456	243	301	339	373	395	426	468	496	519	540	557	586
457	266	332	385	432	463	496	543	564	590	613	642	655
458	245	298	341	375	402	434	475	506	527	549	567	568
459	249	308	350	382	414	437	477	496	522	541	558	568
460	240	286	327	362	385	414	438	457	489	512	538	554
461	254	306	339	376	415	446	469	493	513	540	552	567
462	266	324	365	401	434	460	494	517	544	572	598	604
463	264	318	363	403	438	467	493	509	531	552	577	591
464	256	312	358	398	436	467	495	508	547	570	584	604
465	232	282	335	358	392	417	452	469	487	512	534	547
466	261	323	363	414	451	483	514	539	553	570	593	606
467	240	213	242	258	295	323	353	386	414	436	458	482
468	230	278	322	354	381	408	443	473	502	522	549	565
469	234	276	317	356	385	412	443	476	503	526	546	565
470	216	262	301	339	365	377	398	422	440	455	469	484
471	251	301	346	379	424	447	475	496	529	549	575	591
472	243	285	336	372	406	435	469	486	502	520	541	552
473	274	326	379	422	468	499	531	554	586	612	632	663
474	262	316	363	398	448	480	521	537	563	586	612	628
475	251	300	357	399	434	471	511	543	582	604	636	652
MEAN	249	298	342	378	409	438	472	496	521	544	566	581
S.D.	13.5	24.5	28.0	33.2	36.7	38.9	41.0	40.0	41.9	42.7	45.0	44.8
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
451	629	643	663	670	678	701	711	717	737	751	745	749
452	551	558	573	578	595	598	606	610	625	637	651	656
453	581	591	608	618	628	641	649	659	670	684	698	708
454	586	585	595	601	604	621	625	624	637	655	669	653
455	629	640	660	665	663	682	689	697	712	729	742	748
456	601	608	622	627	641	653	648	655	680	684	693	705
457	666	673	690	699	706	718	734	735	749	757	771	781
458	593	596	619	622	631	646	659	661	673	690	699	706
459	580	557	600	597	608	621	624	631	641	641	647	651
460	571	583	596	608	615	630	633	641	650	634	641	656
461	592	602	618	622	636	649	641	655	676	686	686	695
462	625	631	651	650	664	679	684	691	707	717	726	738
463	603	618	615	641	643	643	653	667	676	692	685	688
464	616	626	636	638	651	667	681	694	701	714	726	717
465	558	570	585	601	612	623	633	649	659	661	672	688
466	629	628	648	664	668	678	675	685	699	716	736	739
467	497	501	510	514	520	535	526	531	545	560	561	564
468	583	602	617	630	649	652	660	670	682	702	724	735
469	588	514	590	597	618	633	642	648	668	676	684	698
470	496	508	520	519	530	540	545	559	564	572	582	573
471	621	624	642	655	667	676	680	693	719	732	750	755
472	557	566	555	579	597	599	603	608	614	619	632	635
473	685	710	741	756	768	776	766	785	816	830	852	878
474	644	670	694	691	706	706	720	731	750	760	775	776
475	673	585	694	731	762	770	790	799	810	826	833	844
MEAN	598	600	622	631	642	653	659	668	682	693	703	709
S.D.	46.7	50.6	53.5	56.1	57.4	56.9	59.4	60.4	63.4	65.5	67.6	71.4
N	25	25	25	25	25	25	25	25	25	25	25	25

: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
451	768	784	764
452	648	667	667
453	590	565	558
454	655	665	673
455	746	757	761
456	710	714	717
457	781	784	785
458	715	722	728
459	668	677	685
460	657	672	674
461	699	704	711
462	743	750	752
463	692	693	695
464	727	723	734
465	694	698	703
466	743	755	756
467	569	568	584
468	737	738	746
469	690	708	709
470	582	584	592
471	752	750	--
472	640	643	--
473	881	884	--
474	776	788	--
475	855	860	--
MEAN	709	714	700
S.D.	75.7	78.1	62.2
N	25	25	20

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
501	235	284	326	360	385	419	438	453	475	498	512	530
502	235	281	318	354	386	406	435	457	473	495	508	525
503	238	296	344	379	407	432	472	489	508	527	545	554
504	223	275	314	349	373	408	425	448	470	492	504	513
505	254	308	359	396	421	448	466	474	494	508	526	539
506	251	301	338	375	401	420	455	474	499	520	538	544
507	263	325	374	413	451	483	507	527	544	566	566	587
508	256	306	349	384	398	429	459	480	491	509	532	555
509	284	335	377	411	431	444	471	477	495	513	523	542
510	235	288	336	363	385	401	416	440	449	474	491	507
511	238	286	321	357	390	416	443	475	500	525	542	566
512	263	325	374	419	470	514	550	574	590	617	647	648
513	242	300	347	388	426	457	493	509	532	558	566	581
514	246	292	333	369	402	433	457	475	498	516	534	548
515	253	311	362	404	448	492	522	536	558	580	598	618
516	253	307	357	385	421	441	470	481	492	511	525	531
517	244	292	339	377	414	445	478	492	512	532	546	560
518	242	287	324	355	388	416	448	470	493	506	525	548
519	257	311	353	384	416	440	457	472	492	502	509	515
520	243	294	343	386	422	449	474	497	514	522	542	560
521	263	310	354	393	437	454	483	480	498	520	534	552
522	247	279	313	347	373	403	430	450	475	486	503	520
523	262	304	352	393	429	464	498	508	541	559	580	609
524	238	276	319	356	401	432	460	472	489	506	525	537
525	246	293	335	373	406	394	434	447	476	490	506	513
MEAN	248	299	342	379	411	438	466	482	502	521	537	552
S.D.	12.8	15.7	18.9	20.6	24.8	29.3	31.4	30.6	30.9	32.6	34.1	34.7
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
501	544	533	557	558	572	581	591	608	626	640	654	658
502	537	532	544	545	560	560	566	576	587	596	602	600
503	561	570	570	572	582	568	557	571	584	593	598	596
504	523	523	537	556	556	569	580	585	589	598	603	617
505	553	555	568	569	572	577	587	592	612	619	637	624
506	558	562	571	574	590	598	599	613	621	628	636	645
507	597	577	592	606	627	629	621	633	632	639	658	668
508	560	553	576	577	594	594	601	608	617	627	646	649
509	542	537	556	541	556	560	551	561	574	587	592	595
510	518	526	539	544	554	558	563	573	584	593	606	619
511	577	586	591	604	599	614	620	623	638	650	657	667
512	661	659	674	691	687	685	695	709	724	739	754	755
513	595	595	616	605	616	621	627	635	642	660	676	669
514	562	548	572	579	604	623	630	640	648	662	678	682
515	643	652	671	682	683	700	667	682	707	731	752	755
516	544	537	557	556	566	570	567	574	585	597	610	613
517	562	569	591	584	596	595	596	606	614	621	634	645
518	561	569	579	584	590	600	602	614	626	632	648	658
519	516	528	538	538	544	533	539	550	562	573	590	580
520	568	576	577	580	589	578	589	592	606	621	637	640
521	559	564	571	575	584	596	604	612	625	634	656	666
522	538	543	557	575	581	597	598	594	605	618	628	639
523	622	630	649	653	666	661	663	675	680	679	688	703
524	556	564	569	578	588	579	578	581	582	599	609	622
525	524	521	513	529	534	552	561	572	576	575	597	617
MEAN	563	564	577	582	592	596	598	607	618	628	642	647
S.D.	36.5	37.4	39.4	40.9	39.4	40.4	37.8	39.0	40.3	42.1	43.8	44.1
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0(mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
501	659	664	672
502	603	618	613
503	602	604	598
504	623	614	617
505	623	642	638
506	651	654	648
507	679	672	673
508	653	664	660
509	592	603	599
510	607	604	616
511	676	683	681
512	757	772	780
513	676	674	674
514	679	692	698
515	770	771	786
516	618	629	632
517	647	646	650
518	660	660	674
519	587	597	602
520	645	660	676
521	660	656	--
522	649	655	--
523	719	719	--
524	632	617	--
525	626	636	--
MEAN	652	656	659
S.D.	46.1	46.2	52.1
N	25	25	20

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
551	235	273	311	325	346	354	380	389	408	432	447	458
552	235	274	302	318	329	344	366	375	388	400	415	423
553	235	273	302	324	346	353	374	379	387	406	405	412
554	241	293	327	355	378	396	419	426	441	448	459	479
555	221	256	281	274	294	286	307	315	315	314	343	353
556	262	302	324	346	360	369	381	382	391	413	425	428
557	262	292	324	354	372	393	429	450	475	494	509	516
558	253	291	324	344	361	351	348	330	303	287	292	352
559	239	292	319	340	357	375	399	404	415	430	443	453
560	243	278	296	302	325	354	365	369	377	377	383	387
561	233	268	303	321	344	348	372	379	397	406	418	424
562	244	294	331	340	376	394	419	431	442	450	471	473
563	250	292	319	334	360	382	411	423	435	449	460	461
564	236	272	296	313	330	342	357	367	367	388	404	413
565	247	301	332	344	373	382	407	416	433	452	467	471
566	246	291	318	342	352	361	398	399	415	432	445	436
567	236	288	315	336	345	365	400	407	421	446	448	474
568	241	273	294	312	332	337	342	346	360	334	291	308
569	265	311	330	348	305	362	380	401	420	449	456	469
570	261	312	343	374	404	423	454	460	485	505	535	545
571	266	310	339	370	401	429	455	450	465	474	492	401
572	268	320	361	376	413	422	442	433	456	465	476	495
573	250	288	329	357	392	405	421	430	450	470	481	487
574	287	336	359	367	386	407	429	440	449	457	478	488
575	244	285	323	344	370	390	418	441	463	478	492	499
MEAN	248	291	320	338	358	373	395	402	414	426	437	444
S.D.	14.6	18.1	19.4	23.8	29.7	32.5	36.5	38.4	46.2	53.8	60.2	55.2
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
551	470	471	478	476	495	507	519	531	541	540	537	531
552	427	427	435	447	457	449	454	460	471	485	473	481
553	415	389	424	417	432	437	424	430	430	439	447	451
554	471	460	477	480	497	505	510	515	522	536	544	533
555	354	352	358	361	368	365	379	367	381	398	414	414
556	426	428	433	448	454	464	469	470	480	489	496	505
557	529	521	538	525	548	546	563	567	578	593	599	587
558	386	416	428	435	449	450	443	415	c	c	c	c
559	464	469	479	482	492	497	506	500	510	518	515	520
560	393	386	389	409	409	420	417	422	423	433	432	438
561	423	428	438	436	447	456	465	471	479	484	495	482
562	473	464	474	484	493	492	499	502	517	524	540	535
563	465	468	494	483	499	506	509	517	528	537	545	549
564	414	423	431	429	435	444	446	459	471	484	491	487
565	481	485	496	496	510	523	518	526	540	552	538	545
566	463	454	453	453	475	457	457	481	487	501	510	489
567	489	474	495	491	506	517	520	529	535	551	561	554
568	367	396	414	424	427	420	422	423	420	435	459	447
569	471	479	491	488	508	509	520	524	518	539	549	542
570	558	554	580	579	600	588	592	613	609	630	654	654
571	492	522	542	552	554	569	556	565	581	593	600	604
572	503	501	524	518	538	547	525	547	559	569	575	569
573	497	507	525	520	536	543	543	552	563	579	590	592
574	493	502	521	519	538	539	537	541	548	570	590	588
575	515	509	522	527	542	544	546	552	539	550	560	571
MEAN	458	459	474	475	488	492	494	499	510	522	530	528
S.D.	50.8	49.4	52.8	49.7	53.2	53.9	53.2	58.3	56.8	57.7	58.9	58.9
N	25	25	25	25	25	25	25	25	24	24	24	24

--: Data Unavailable c: Animal Found Dead

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
551	552	566	579
552	488	510	513
553	438	453	457
554	541	549	553
555	411	416	428
556	506	519	524
557	588	603	616
558	c	c	c
559	519	533	535
560	441	450	449
561	495	503	501
562	546	526	543
563	552	555	563
564	492	498	502
565	449	445	495
566	498	507	519
567	551	570	581
568	464	464	463
569	538	551	572
570	662	681	680
571	598	598	--
572	564	578	--
573	592	583	--
574	597	592	--
575	572	571	--
MEAN	527	534	530
S.D.	61.1	61.5	61.7
N	24	24	19

--: Data Unavailable c: Animal Found Dead

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
426	204	228	251	270	271	276	282	296	312	318	321	332
427	179	203	230	251	250	261	279	288	304	314	320	333
428	181	210	227	246	256	260	267	272	285	287	297	308
429	169	196	213	225	231	239	264	263	273	278	285	287
430	194	227	240	253	263	268	299	296	313	326	335	332
431	183	197	218	235	241	240	267	265	280	292	292	299
432	183	205	222	231	250	249	272	275	290	299	300	309
433	178	211	228	248	257	259	291	291	297	314	322	328
434	186	205	219	234	239	241	257	269	277	294	297	299
435	198	225	236	258	280	282	290	303	324	333	335	347
436	199	217	236	254	270	281	295	310	321	331	339	351
437	190	219	235	244	260	272	274	291	294	310	319	323
438	178	196	215	227	227	248	246	248	265	281	295	305
439	188	213	224	232	245	251	266	267	277	290	291	291
440	162	189	205	218	230	234	251	252	254	258	263	257
441	178	193	216	225	238	254	265	268	276	287	296	306
442	178	205	222	229	246	255	266	268	282	293	295	297
443	170	192	204	222	229	230	247	248	261	273	277	282
444	190	199	224	236	250	257	271	281	286	291	301	307
445	169	186	197	215	230	230	249	250	261	270	275	277
446	192	216	219	239	253	263	273	283	298	300	300	309
447	184	203	228	240	251	256	281	289	293	311	319	329
448	177	193	208	225	237	234	253	253	259	261	268	278
449	175	188	204	213	216	227	242	249	246	255	259	262
450	176	191	218	224	243	240	253	261	269	272	274	283
MEAN	182	204	222	236	247	252	268	273	284	294	299	305
S.D.	10.2	12.6	12.7	14.4	15.4	16.1	16.0	18.5	20.9	22.2	22.7	24.9
N	25	25	25	25	25	25	25	25	25	25	25	25

: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
426	341	335	332	323	356	366	372	382	386	384	385	364
427	339	338	331	330	346	363	365	373	377	397	394	384
428	311	314	344	333	322	323	333	336	340	367	374	347
429	298	302	300	292	306	311	325	325	323	333	332	322
430	344	340	339	328	349	346	355	362	366	372	384	378
431	310	313	303	307	324	336	336	348	357	360	364	357
432	323	333	323	326	341	351	349	370	371	377	377	373
433	338	339	335	344	365	377	387	392	385	397	401	406
434	312	317	304	303	319	328	326	335	336	346	338	339
435	357	363	356	352	376	396	402	404	421	430	432	424
436	345	363	349	352	369	381	388	399	413	432	452	462
437	326	337	331	332	357	362	365	376	387	390	392	381
438	325	331	333	336	351	355	366	378	389	396	407	409
439	303	313	298	309	327	317	325	333	331	331	344	334
440	257	263	267	273	287	297	301	295	302	308	302	307
441	316	322	321	321	335	341	343	342	351	349	363	352
442	301	306	296	307	331	321	331	342	342	338	346	339
443	281	284	276	274	288	290	297	303	310	307	318	300
444	308	301	318	337	315	346	337	340	337	341	342	343
445	284	287	290	288	298	297	306	309	314	319	325	323
446	318	327	323	328	345	346	350	356	367	365	384	375
447	343	351	361	365	361	371	370	371	376	383	392	406
448	277	277	278	274	291	291	284	293	299	288	292	294
449	276	276	274	268	290	293	290	287	299	297	307	325
450	282	283	294	293	300	310	312	321	337	341	357	361
MEAN	313	317	315	316	330	337	341	347	353	358	364	360
S.D.	26.2	27.5	26.7	27.2	27.6	30.9	31.9	33.8	34.7	38.7	40.0	40.7
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
426	361	389	400
427	392	397	408
428	352	354	384
429	329	347	350
430	383	392	390
431	359	378	376
432	383	394	412
433	407	421	428
434	343	363	356
435	429	457	457
436	478	492	494
437	385	414	417
438	414	426	424
439	341	348	350
440	315	326	345
441	360	359	353
442	350	367	359
443	303	305	313
444	348	357	358
445	330	334	341
446	377	391	--
447	404	404	--
448	300	301	--
449	300	302	--
450	371	368	--
MEAN	365	375	386
S.D.	42.6	46.4	44.4
N	25	25	20

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
476	195	222	237	259	273	278	301	306	322	339	341	353
477	177	197	214	228	234	239	264	264	273	279	278	289
478	161	181	194	207	215	227	234	237	247	253	254	263
479	196	220	241	252	262	272	290	302	316	317	319	335
480	177	206	226	243	251	266	281	289	297	317	315	334
481	186	210	233	239	252	263	284	294	309	323	339	353
482	167	187	200	213	227	227	235	247	256	258	261	267
483	160	169	188	199	208	206	217	222	239	244	241	251
484	186	205	221	230	247	253	265	268	276	288	289	299
485	180	200	212	224	234	237	257	261	273	279	288	290
486	171	187	208	217	233	237	252	246	258	269	268	272
487	192	221	242	250	265	267	286	291	294	304	308	317
488	180	199	221	237	247	250	266	283	292	293	304	308
489	186	204	216	231	238	245	252	259	270	272	274	280
490	176	200	221	232	251	255	270	280	294	306	315	326
491	190	213	234	248	266	275	292	314	329	316	325	334
492	187	209	221	240	254	264	284	284	288	298	305	302
493	190	206	223	238	252	257	278	281	288	292	296	306
494	170	185	197	213	224	226	244	245	248	254	258	265
495	186	208	232	241	250	258	278	286	296	298	306	317
496	203	227	253	269	290	288	314	335	359	355	352	360
497	194	216	236	252	267	272	292	295	310	310	324	328
498	187	205	223	239	253	244	262	261	275	286	296	298
499	180	198	210	226	244	262	259	272	285	292	296	309
500	173	197	217	223	239	254	265	273	285	292	295	299
MEAN	182	203	221	234	247	253	269	276	287	293	298	306
S.D.	11.0	13.8	16.0	16.7	18.5	19.3	22.6	25.8	27.8	26.9	28.4	29.9
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
476	375	378	372	369	397	404	423	424	434	441	442	433
477	287	294	291	293	314	311	314	319	325	328	329	332
478	265	267	262	266	279	287	285	291	297	298	290	293
479	341	341	336	339	356	359	357	359	382	373	373	370
480	342	336	335	333	355	366	371	382	378	383	377	379
481	354	348	345	358	378	392	401	404	413	429	443	444
482	270	270	273	277	277	281	287	290	292	287	269	267
483	254	253	256	266	271	275	280	286	290	293	301	299
484	306	309	297	289	316	321	326	336	343	343	344	329
485	302	302	299	301	318	320	330	329	332	336	334	335
486	278	284	281	282	295	305	310	320	323	331	334	339
487	319	315	320	315	333	324	334	342	337	344	343	340
488	316	308	311	315	341	334	347	351	366	370	364	361
489	284	285	288	285	299	302	301	316	314	316	315	312
490	335	332	342	348	367	369	378	379	390	397	400	399
491	337	339	335	341	358	361	368	371	375	380	375	377
492	307	310	308	315	333	331	326	337	345	355	363	363
493	306	311	306	317	330	329	326	326	344	346	342	348
494	267	272	268	269	283	286	282	292	297	302	298	296
495	311	314	311	317	336	339	340	337	339	343	356	352
496	368	367	367	360	376	385	374	382	378	379	389	395
497	332	343	339	338	346	354	350	360	357	368	378	383
498	308	314	304	310	321	321	328	328	332	336	340	346
499	323	328	326	333	338	347	348	356	368	373	380	389
500	307	313	316	320	323	333	331	332	341	352	356	353
MEAN	312	313	312	314	330	333	337	342	348	352	353	353
S.D.	32.0	31.1	30.8	30.3	33.5	34.7	36.5	35.5	36.9	38.7	42.1	42.4
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
476	437	460	461
477	332	339	336
478	300	321	309
479	382	402	397
480	391	408	412
481	446	459	486
482	267	275	289
483	303	308	302
484	342	352	354
485	343	349	358
486	349	354	359
487	350	352	369
488	356	380	390
489	317	328	321
490	409	416	422
491	378	390	395
492	373	375	402
493	353	359	358
494	302	308	315
495	354	369	369
496	398	406	--
497	383	396	--
498	354	352	--
499	391	398	--
500	360	359	--
MEAN	359	369	370
S.D.	42.3	44.5	51.9
N	25	25	20

--: Data Unavailable

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INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
526	198	221	249	265	287	300	307	329	351	358	363	372
527	166	179	199	213	214	224	233	252	249	252	268	264
528	183	205	222	231	243	249	271	281	280	292	297	301
529	182	203	222	236	249	254	264	273	279	292	300	295
530	180	201	213	223	239	234	246	263	268	282	282	280
531	177	197	213	225	239	238	256	253	264	265	262	267
532	196	224	250	258	280	280	310	320	341	357	362	369
533	192	214	236	251	272	276	296	311	326	332	347	359
534	189	213	233	256	272	271	288	303	311	329	337	340
535	172	186	206	217	211	218	234	236	245	255	257	258
536	182	197	217	232	249	240	266	265	274	283	272	265
537	189	214	236	246	254	266	283	302	296	301	309	320
538	179	209	229	250	266	275	284	298	297	305	316	315
539	185	209	224	247	259	255	275	269	285	300	295	303
540	187	214	233	244	259	264	288	288	304	316	325	328
541	184	204	224	234	249	249	269	269	278	285	284	287
542	162	180	198	217	224	231	246	260	260	276	281	285
543	179	194	220	236	247	247	269	270	287	297	302	305
544	191	207	223	236	253	268	266	282	289	288	296	305
545	159	182	196	209	223	226	237	250	259	264	267	272
546	190	209	227	249	268	264	286	305	312	328	339	343
547	167	183	200	217	235	237	237	254	260	258	264	266
548	193	209	222	236	252	255	274	278	291	301	306	306
549	177	196	213	215	233	239	244	251	254	260	258	253
550	186	203	214	237	251	243	250	261	269	273	269	276
MEAN	182	202	221	235	249	252	267	277	285	294	298	301
S.D.	10.3	12.6	14.5	15.4	19.4	20.0	22.4	24.4	27.6	29.8	32.3	34.9
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
526	379	371	371	378	397	397	411	419	415	419	435	424
527	277	280	277	277	293	285	296	294	298	301	313	309
528	306	307	299	302	322	325	328	339	343	352	348	341
529	302	307	303	310	314	319	322	328	330	330	331	323
530	290	298	287	294	305	309	306	326	327	335	333	339
531	275	276	280	287	294	297	300	304	308	314	320	323
532	381	373	374	378	390	410	421	438	449	455	465	468
533	360	359	373	359	382	394	411	416	422	427	439	428
534	344	342	338	335	349	355	361	369	371	380	378	378
535	263	269	265	268	274	277	286	288	292	304	292	298
536	273	288	278	284	305	316	326	334	331	341	341	336
537	323	319	323	319	332	330	337	347	348	346	360	349
538	326	332	328	336	343	338	344	353	355	362	369	364
539	310	317	288	310	324	330	338	339	352	359	352	336
540	336	338	324	329	345	353	366	375	380	387	402	398
541	296	303	296	292	308	313	311	315	326	335	326	322
542	288	293	281	290	309	322	328	344	348	360	370	360
543	314	315	307	310	324	332	327	335	342	347	358	357
544	310	308	304	319	327	335	344	353	358	373	380	379
545	279	283	286	286	294	296	299	308	309	308	316	309
546	340	348	350	331	351	371	376	387	395	407	416	421
547	271	270	281	291	287	286	290	295	294	296	305	302
548	319	328	327	337	353	367	364	365	372	371	378	389
549	259	267	269	264	278	285	284	282	293	301	302	301
550	289	289	291	286	302	305	305	314	318	321	317	329
MEAN	308	311	308	311	324	330	335	343	347	353	358	355
S.D.	34.2	31.4	32.8	31.2	33.3	36.6	39.3	41.3	41.8	42.3	46.0	45.5
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
526	427	442	439
527	310	317	318
528	346	347	358
529	325	332	333
530	340	347	352
531	326	323	327
532	465	471	478
533	424	443	455
534	370	390	389
535	306	311	319
536	344	372	365
537	355	371	369
538	367	369	372
539	352	360	378
540	404	416	415
541	336	343	349
542	365	363	374
543	362	378	371
544	385	395	394
545	310	314	325
546	419	425	--
547	296	292	--
548	396	420	--
549	308	305	--
550	331	338	--
MEAN	359	367	374
S.D.	44.0	48.1	44.6
N	25	25	20

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 1	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
576	187	209	228	237	250	239	262	262	281	282	280	288
577	180	202	215	226	235	242	248	255	266	263	266	272
578	201	215	235	244	255	263	275	275	284	290	295	298
579	168	189	208	216	229	228	248	253	262	269	273	278
580	184	204	222	229	245	237	251	260	262	269	275	279
581	177	187	201	208	216	221	234	240	246	252	257	256
582	175	199	198	211	226	225	240	242	245	253	249	258
583	172	194	208	219	228	239	251	247	254	263	269	278
584	168	183	195	211	222	231	232	240	248	253	254	257
585	174	196	208	224	241	238	252	267	271	273	274	281
586	172	192	209	226	241	242	259	268	276	279	283	290
587	187	208	230	234	257	253	271	269	283	289	293	299
588	187	202	209	217	231	222	244	242	248	258	261	262
589	181	205	212	228	243	230	250	253	258	263	265	273
590	184	208	224	223	235	241	259	253	259	267	269	267
591	184	201	220	236	246	250	259	265	273	281	285	279
592	164	180	192	197	209	214	227	227	233	236	243	247
593	175	196	206	213	232	235	248	250	251	262	260	260
594	191	211	217	231	245	245	257	258	261	267	272	272
595	170	182	194	207	220	210	223	229	235	242	250	251
596	199	208	231	247	263	256	278	281	286	293	299	303
597	164	186	200	208	221	212	225	236	239	246	240	248
598	163	191	201	211	225	218	244	236	250	255	261	264
599	184	202	223	231	246	246	268	275	259	280	285	289
600	192	204	226	246	255	255	274	270	280	284	289	295
MEAN	179	198	212	223	237	236	251	254	260	267	270	274
S.D.	10.6	9.8	12.6	13.3	14.0	14.4	15.6	15.1	15.7	15.4	16.2	16.6
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
576	302	302	296	299	309	305	307	318	321	319	319	323
577	281	280	275	275	287	282	288	292	294	291	293	291
578	302	305	307	305	319	324	316	318	314	318	333	325
579	287	285	285	275	291	292	296	280	290	300	304	298
580	281	283	286	286	293	298	300	279	290	299	304	308
581	257	259	268	267	275	270	280	289	285	287	303	304
582	265	256	269	260	271	278	279	281	285	288	287	293
583	282	278	286	279	288	291	294	302	302	312	313	306
584	265	268	277	267	277	278	282	289	288	291	293	283
585	285	282	288	287	300	300	304	307	303	310	314	313
586	300	304	301	302	313	314	318	323	319	328	326	326
587	305	303	301	294	311	312	303	321	321	331	321	322
588	266	265	270	261	283	281	278	289	285	292	289	290
589	284	271	275	275	285	290	290	293	295	295	309	300
590	275	274	283	276	291	288	293	298	283	296	308	308
591	286	289	290	295	301	303	297	298	299	305	319	316
592	249	249	250	261	270	262	273	273	272	278	281	278
593	265	216	262	267	272	275	275	274	278	285	284	289
594	278	282	283	282	286	293	284	291	301	290	303	303
595	254	252	248	254	267	268	268	273	273	278	287	289
596	304	298	299	306	311	317	304	315	316	321	320	328
597	247	250	246	241	252	256	249	257	257	249	263	248
598	267	274	272	266	276	282	283	287	286	290	293	283
599	296	299	299	306	304	313	306	311	311	309	318	331
600	306	305	308	309	313	319	320	329	328	328	343	347
MEAN	280	277	281	280	290	292	291	295	296	300	305	304
S.D.	18.2	22.1	17.7	18.6	17.5	18.7	16.9	18.6	17.8	18.9	18.3	21.1
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
576	326	346	349
577	299	296	305
578	338	346	340
579	306	310	314
580	306	314	320
581	310	300	300
582	291	300	309
583	315	315	327
584	293	304	306
585	316	332	330
586	330	341	349
587	328	333	329
588	288	296	306
589	301	308	321
590	314	321	321
591	318	316	319
592	289	295	292
593	286	287	289
594	305	313	310
595	286	290	295
596	325	335	--
597	250	250	--
598	280	289	--
599	321	322	--
600	348	347	--
MEAN	307	312	317
S.D.	21.3	22.9	17.4
N	25	25	20

--: Data Unavailable

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0(mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
401	65	49	33	24	17	26	34	33	17	20	26
402	52	47	49	19	23	45	23	20	31	18	18
403	50	38	34	23	28	34	20	26	17	20	11
404	52	44	40	25	21	56	26	27	23	24	-85
405	53	33	37	20	28	41	23	27	22	18	13
406	50	48	46	31	38	38	39	21	22	31	15
407	59	53	40	8	25	49	18	3	30	24	23
408	60	50	42	16	41	47	29	36	10	31	21
409	55	50	51	26	40	58	21	24	29	20	12
410	55	40	38	13	32	36	19	25	17	28	25
411	52	32	27	27	32	26	22	18	15	9	12
412	53	44	40	15	29	39	21	20	10	16	11
413	63	50	44	34	26	41	21	25	20	21	16
414	57	43	30	34	31	35	21	26	-19	65	21
415	48	41	32	26	5	28	18	13	12	15	10
416	63	52	43	43	25	47	20	28	21	14	27
417	47	44	34	27	31	26	14	20	23	17	17
418	63	53	36	35	22	51	11	29	14	21	15
419	54	45	38	35	41	36	19	24	24	13	21
420	43	43	37	36	18	30	19	27	19	17	18
421	52	43	34	35	14	34	10	10	14	26	11
422	52	47	35	42	22	33	17	29	22	21	18
423	44	42	25	24	13	34	10	19	13	22	14
424	62	69	39	55	28	51	21	35	20	22	25
425	49	59	37	44	37	41	28	32	22	19	25
MEAN	54	46	38	29	27	39	21	24	18	22	14
S.D.	6.1	7.7	6.2	10.9	9.2	9.3	6.7	7.6	9.6	10.4	21.2
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
401	11	6	19	3	17	1	4	0	5	14	7
402	12	3	10	5	15	10	3	9	11	11	9
403	13	12	21	7	8	9	6	9	1	17	11
404	24	30	34	9	31	11	12	10	15	6	11
405	18	-90	56	35	14	28	5	1	-2	18	9
406	22	16	16	20	17	-71	11	46	18	16	21
407	6	1	25	1	23	17	2	11	16	11	16
408	14	-32	15	14	13	12	-1	6	20	4	13
409	15	0	26	9	19	7	7	5	4	7	13
410	26	8	11	10	22	9	7	7	23	10	16
411	16	15	11	-1	14	0	3	13	11	11	11
412	23	6	7	12	19	-1	-5	14	10	13	-2
413	12	14	12	-1	6	12	1	6	17	10	11
414	9	9	11	21	2	5	2	24	17	0	18
415	12	9	13	-3	6	8	3	5	12	7	14
416	17	19	8	4	10	8	8	21	-2	5	23
417	10	11	9	9	11	13	0	-8	22	10	7
418	18	5	23	5	14	8	5	10	15	6	6
419	7	34	12	9	9	4	9	8	9	11	21
420	5	20	10	6	11	10	2	-11	7	20	17
421	22	13	11	8	6	5	-11	9	6	15	17
422	19	15	12	6	24	13	-3	5	11	11	7
423	14	7	10	-1	16	8	6	11	-6	14	4
424	19	22	17	5	7	15	-5	3	15	12	10
425	29	8	18	4	21	5	8	10	10	7	27
MEAN	16	6	17	8	14	6	3	9	11	11	13
S.D.	6.3	23.4	10.5	8.2	6.9	17.1	5.3	10.7	7.6	4.7	6.5
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
401	8	-2	-2	19	454
402	10	1	16	2	472
403	14	0	6	5	440
404	15	-3	19	5	482
405	14	2	14	5	442
406	7	9	2	5	534
407	4	1	1	-2	465
408	5	2	13	3	484
409	17	8	7	10	540
410	11	1	13	1	503
411	0	8	6	2	392
412	13	2	19	5	433
413	5	-13	10	12	475
414	-6	7	7	3	473
415	-1	-4	7	11	347
416	10	0	22	4	540
417	-15	-18	41	12	414
418	12	4	9	5	495
419	-2	3	9	10	503
420	7	11	4	5	431
421	3	3	-9	--	381
422	3	1	6	--	468
423	-1	4	14	--	360
424	21	6	1	--	575
425	19	18	1	--	578
MEAN	7	2	9	6	467
S.D.	8.3	7.1	9.7	4.9	60.8
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5(mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
451	59	45	35	18	35	47	35	22	23	23	19
452	43	39	33	19	24	33	21	15	23	17	8
453	51	44	31	12	24	42	20	28	27	22	20
454	49	43	35	6	39	47	16	23	27	19	19
455	52	49	42	35	40	34	32	33	25	27	1
456	58	38	34	22	31	42	28	23	21	17	29
457	66	53	47	31	33	47	21	26	23	29	13
458	53	43	34	27	32	41	31	21	22	18	1
459	59	42	32	32	23	40	19	26	19	17	10
460	46	41	35	23	29	24	19	32	23	26	16
461	52	33	37	39	31	23	24	20	27	12	15
462	58	41	36	33	26	34	23	27	28	26	6
463	54	45	40	35	29	26	16	22	21	25	14
464	56	46	40	38	31	28	13	39	23	14	20
465	50	53	23	34	25	35	17	18	25	22	13
466	62	40	51	37	32	31	25	14	17	23	13
467	-27	29	16	37	28	30	33	28	22	22	24
468	48	44	32	27	27	35	30	29	20	27	16
469	42	41	39	29	27	31	33	27	23	20	19
470	46	39	38	26	12	21	24	18	15	14	15
471	50	45	33	45	23	28	21	33	20	26	16
472	42	51	36	34	29	34	17	16	18	21	11
473	52	53	43	46	31	32	23	32	26	20	31
474	54	47	35	50	32	41	16	26	23	26	16
475	49	57	42	35	37	40	32	39	22	32	16
MEAN	49	44	36	31	29	35	24	25	23	22	15
S.D.	17.0	6.4	7.0	10.3	5.9	7.5	6.5	6.8	3.3	5.0	7.1
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a] Weight gains compared to the previous period
[b] Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
451	24	14	20	7	8	23	10	6	20	14	-6
452	12	7	15	5	17	3	8	4	15	12	14
453	17	10	17	10	10	13	8	10	11	14	14
454	17	-1	10	6	3	17	4	-1	13	18	14
455	14	11	20	5	-2	19	7	8	15	17	13
456	15	7	14	5	14	12	-5	7	25	4	9
457	11	7	17	9	7	12	16	1	14	8	14
458	25	3	23	3	9	15	13	2	12	17	9
459	12	-23	43	-3	11	13	3	7	10	0	6
460	17	12	13	12	7	15	3	8	9	-16	7
461	25	10	16	4	14	13	-8	14	21	10	0
462	21	6	20	-1	14	15	5	7	16	10	9
463	12	15	-3	26	2	0	10	14	9	16	-7
464	12	10	10	2	13	16	14	13	7	13	12
465	11	12	15	16	11	11	10	16	10	2	11
466	23	-1	20	16	4	10	-3	10	14	17	20
467	15	4	9	4	6	15	-9	5	14	15	1
468	18	19	15	13	19	3	8	10	12	20	22
469	23	-74	76	7	21	15	9	6	20	8	8
470	12	12	12	-1	11	10	5	14	5	8	10
471	30	3	18	13	12	9	4	13	26	13	18
472	5	9	-11	24	18	2	4	5	6	5	13
473	22	25	31	15	12	8	-10	19	31	14	22
474	16	26	24	-3	15	0	14	11	19	10	15
475	21	-88	109	37	31	8	20	9	11	16	7
MEAN	17	1	22	9	11	11	6	9	15	11	10
S.D.	5.9	26.6	23.9	9.5	6.9	5.9	7.8	4.8	6.5	7.6	7.4
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
451	4	19	16	-20	520
452	5	-8	19	0	403
453	10	-118	-25	-7	315
454	-16	2	10	8	427
455	6	-2	11	4	516
456	12	5	4	3	474
457	10	0	3	1	519
458	7	9	7	6	483
459	4	17	9	8	436
460	15	1	15	2	434
461	9	4	5	7	457
462	12	5	7	2	486
463	3	4	1	2	431
464	-9	10	-4	11	478
465	16	6	4	5	471
466	3	4	12	1	495
467	3	5	-1	16	344
468	11	2	1	8	516
469	14	-8	18	1	475
470	-9	9	2	8	376
471	5	-3	-2	--	499
472	3	5	3	--	400
473	26	3	3	--	610
474	1	0	12	--	526
475	11	11	5	--	609
MEAN	6	-1	5	3	468
S.D.	8.7	25.2	8.9	7.3	69.9
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
501	49	42	34	25	34	19	15	22	23	14	18
502	46	37	36	32	20	29	22	16	22	13	17
503	58	48	35	28	25	40	17	19	19	18	9
504	52	39	35	24	35	17	23	22	22	12	9
505	54	51	37	25	27	18	8	20	14	18	13
506	50	37	37	26	19	35	19	25	21	18	6
507	62	49	39	38	32	24	20	17	22	0	21
508	50	43	35	14	31	30	21	11	18	23	23
509	51	42	34	20	13	27	6	18	18	10	19
510	53	48	27	22	16	15	24	9	25	17	16
511	48	35	36	33	26	27	32	25	25	17	24
512	62	49	45	51	44	36	24	16	27	30	1
513	58	47	41	38	31	36	16	23	26	8	15
514	46	41	36	33	31	24	18	23	18	18	14
515	58	51	42	44	44	30	14	22	22	18	20
516	54	50	28	36	20	29	11	11	19	14	6
517	48	47	38	37	31	33	14	20	20	14	14
518	45	37	31	33	28	32	22	23	13	19	23
519	54	42	31	32	24	17	15	20	10	7	6
520	51	49	43	36	27	25	23	17	8	20	18
521	47	44	39	44	17	29	-3	18	22	14	18
522	32	34	34	26	30	27	20	25	11	17	17
523	42	48	41	36	35	34	10	33	18	21	29
524	38	43	37	45	31	28	12	17	17	19	12
525	47	42	38	33	-12	40	13	29	14	16	7
MEAN	50	44	36	32	26	28	17	20	19	16	15
S.D.	6.9	5.2	4.3	8.6	11.1	7.0	7.2	5.5	5.0	5.8	6.8
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
501	14	-11	24	1	14	9	10	17	18	14	14
502	12	-5	12	1	15	0	6	10	11	9	6
503	7	9	0	2	10	-14	-11	14	13	9	5
504	10	0	14	19	0	13	11	5	4	9	5
505	14	2	13	1	3	5	10	5	20	7	18
506	14	4	9	3	16	8	1	14	8	7	8
507	10	-20	15	14	21	2	-8	12	-1	7	19
508	5	-7	23	1	17	0	7	7	9	10	19
509	0	-5	19	-15	15	4	-9	10	13	13	5
510	11	8	13	5	10	4	5	10	11	9	13
511	11	9	5	13	-5	15	6	3	15	12	7
512	13	-2	15	17	-4	-2	10	14	15	15	15
513	14	0	21	-11	11	5	6	8	7	18	16
514	14	-14	24	7	25	19	7	10	8	14	16
515	25	9	19	11	1	17	-33	15	25	24	21
516	13	-7	20	-1	10	4	-3	7	11	12	13
517	2	7	22	-7	12	-1	1	10	8	7	13
518	13	8	10	5	6	10	2	12	12	6	16
519	1	12	10	0	6	-11	6	11	12	11	17
520	8	8	1	3	9	-11	11	3	14	15	16
521	7	5	7	4	9	12	8	8	13	9	22
522	18	5	14	18	6	16	1	-4	11	13	10
523	13	8	19	4	13	-5	2	12	5	-1	9
524	19	8	5	9	10	-9	-1	3	1	17	10
525	11	-3	-8	16	5	18	9	11	4	-1	22
MEAN	11	1	13	5	9	4	2	9	11	11	13
S.D.	5.6	8.3	8.2	8.6	7.2	9.6	9.6	4.7	5.8	5.4	5.4
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
501	4	1	5	8	437
502	-2	3	15	-5	378
503	-2	6	2	-6	360
504	14	6	-9	3	394
505	-13	-1	19	-4	384
506	9	6	3	-6	397
507	10	11	-7	1	410
508	3	4	11	-4	404
509	3	-3	11	-4	315
510	13	-12	-3	12	381
511	10	9	7	-2	443
512	1	2	15	8	517
513	-7	7	-2	0	432
514	4	-3	13	6	452
515	3	15	1	15	533
516	3	5	11	3	379
517	11	2	-1	4	406
518	10	2	0	14	432
519	-10	7	10	5	345
520	3	5	15	16	433
521	10	-6	-4	--	393
522	11	10	6	--	408
523	15	16	0	--	457
524	13	10	-15	--	379
525	20	9	10	--	390
MEAN	5	4	5	3	410
S.D.	8.0	6.3	8.6	7.2	48.0
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
551	38	38	14	21	8	26	9	19	24	15	11
552	39	28	16	11	15	22	9	13	12	15	8
553	38	29	22	22	7	21	5	8	19	-1	7
554	52	34	28	23	18	23	7	15	7	11	20
555	35	25	-7	20	-8	21	8	0	-1	29	10
556	40	22	22	14	9	12	1	9	22	12	3
557	30	32	30	18	21	36	21	25	19	15	7
558	38	33	20	17	-10	-3	-18	-27	-16	5	60
559	53	27	21	17	18	24	5	11	15	13	10
560	35	18	6	23	29	11	4	8	0	6	4
561	35	35	18	23	4	24	7	18	9	12	6
562	50	37	9	36	18	25	12	11	8	21	2
563	42	27	15	26	22	29	12	12	14	11	1
564	36	24	17	17	12	15	10	0	21	16	9
565	54	31	12	29	9	25	9	17	19	15	4
566	45	27	24	10	9	37	1	16	17	13	-9
567	52	27	21	9	20	35	7	14	25	2	26
568	32	21	18	20	5	5	4	14	-26	-43	17
569	46	19	18	-43	57	18	21	19	29	7	13
570	51	31	31	30	19	31	6	25	20	30	10
571	44	29	31	31	28	26	-5	15	9	18	-91
572	52	41	15	37	9	20	-9	23	9	11	19
573	38	41	28	35	13	16	9	20	20	11	6
574	49	23	8	19	21	22	11	9	8	21	10
575	41	38	21	26	20	28	23	22	15	14	7
MEAN	43	29	18	20	15	22	7	13	12	11	7
S.D.	7.3	6.6	8.7	15.2	12.9	9.3	8.8	10.6	12.5	13.3	23.8
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a] Weight gains compared to the previous period
[b] Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
551	12	1	7	-2	19	12	12	12	10	-1	-3
552	4	0	8	12	10	-8	5	6	11	14	-12
553	3	-26	35	-7	15	5	-13	6	0	9	8
554	-8	-11	17	3	17	8	5	5	7	14	8
555	1	-2	6	3	7	-3	14	-12	14	17	16
556	-2	2	5	15	6	10	5	1	1D	9	7
557	13	-8	17	-13	23	-2	17	4	11	15	6
558	34	30	12	7	14	1	-7	-28	c	c	c
559	11	5	1D	3	1D	5	9	-6	10	8	-3
560	6	-7	3	20	0	11	-3	5	1	10	-1
561	-1	5	10	-2	11	9	9	6	8	5	11
562	0	-9	10	10	9	-1	7	3	15	7	16
563	4	3	26	-11	16	7	3	8	11	9	8
564	1	9	8	-2	6	9	2	13	12	13	7
565	10	4	11	0	14	13	-5	8	14	12	-14
566	27	-9	-1	0	22	-18	0	24	6	14	9
567	15	-15	21	-4	15	11	3	9	6	16	10
568	59	29	18	10	3	-7	2	1	-3	15	24
569	2	8	12	-3	20	1	11	4	-6	21	10
570	13	-4	26	-1	21	-12	4	21	-4	21	24
571	91	30	20	10	2	15	-13	9	16	12	7
572	8	-2	23	-6	20	9	-22	22	12	1D	6
573	1D	1D	18	-5	16	7	0	9	11	16	11
574	5	9	19	-2	19	1	-2	4	7	22	20
575	16	-6	13	5	15	2	2	6	-13	11	1D
MEAN	13	2	14	2	13	3	2	6	7	12	8
S.D.	21.1	13.4	8.3	8.D	6.5	8.3	8.9	1D.4	7.4	5.3	9.4
N	25	25	25	25	25	25	25	25	24	24	24

--: Data Unavailable c: Animal Found Dead

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
551	-6	21	14	13	344
552	8	7	22	3	278
553	4	-13	15	4	222
554	-11	8	8	4	312
555	0	-3	5	12	207
556	9	1	13	5	262
557	-12	1	15	13	354
558	c	c	c	c	--
559	5	-1	14	2	296
560	6	3	9	-1	206
561	-13	13	8	-2	268
562	-5	11	-20	17	299
563	4	3	3	8	313
564	-4	5	6	4	266
565	7	-96	-4	50	248
566	-21	9	9	12	273
567	-7	-3	19	11	345
568	-12	17	0	-1	222
569	-7	-4	13	21	307
570	0	8	19	-1	419
571	4	-6	0	--	332
572	-6	-5	14	--	310
573	2	0	-9	--	333
574	-2	9	-5	--	305
575	11	1	-1	--	327
MEAN	-2	-1	7	9	294
S.D.	8.3	21.7	10.0	11.9	51.3
N	24	24	24	19	24

--: Data Unavailable c: Animal Found Dead

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
426	24	23	19	1	5	6	14	16	6	3	11
427	24	27	21	-1	11	18	9	16	10	6	13
428	29	17	19	10	4	7	5	13	2	10	11
429	27	17	12	6	8	25	-1	10	5	7	2
430	33	13	13	10	5	31	-3	17	13	9	-3
431	14	21	17	6	-1	27	-2	15	12	0	7
432	22	17	9	19	-1	23	3	15	9	1	9
433	33	17	20	9	2	32	0	6	17	8	6
434	19	14	15	5	2	16	12	8	17	3	2
435	27	11	22	22	2	8	13	21	9	2	12
436	18	19	18	16	11	14	15	11	10	8	12
437	29	16	9	16	12	2	17	3	16	9	4
438	18	19	12	0	21	-2	2	17	16	14	10
439	25	11	8	13	6	15	1	10	13	1	0
440	27	16	13	12	4	17	1	2	4	5	-6
441	15	23	9	13	16	11	3	8	11	9	10
442	27	17	7	17	9	11	2	14	11	2	2
443	22	12	18	7	1	17	1	13	12	4	5
444	9	25	12	14	7	14	10	5	5	10	6
445	17	11	18	15	0	19	1	11	9	5	2
446	24	3	20	14	10	10	10	15	2	0	9
447	19	25	12	11	5	25	8	4	18	8	10
448	16	15	17	12	-3	19	0	6	2	7	10
449	13	16	9	3	11	15	7	-3	9	4	3
450	15	27	6	19	-3	13	8	8	3	2	9
MEAN	22	17	14	11	6	16	5	10	10	5	6
S.D.	6.4	5.7	4.9	6.2	5.9	8.4	5.8	5.7	5.0	3.7	5.0
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
426	9	-6	-3	-9	33	10	6	10	4	-2	1
427	6	-1	-7	-1	16	17	2	8	4	20	-3
428	3	3	30	-11	-11	1	10	3	4	27	7
429	11	4	-2	-8	14	5	14	0	-2	10	-1
430	12	-4	-1	-11	21	-3	9	7	4	6	12
431	11	3	-10	4	17	12	0	12	9	3	4
432	14	10	-10	3	15	10	-2	21	1	6	0
433	10	1	-4	9	21	12	10	5	-7	12	4
434	13	5	-13	-1	16	9	-2	9	1	10	-8
435	10	6	-7	-4	24	20	6	2	17	9	2
436	-6	18	-14	3	17	12	7	11	14	19	20
437	3	11	-6	1	25	5	3	11	11	3	2
438	20	6	2	3	15	4	11	12	11	7	11
439	12	10	-15	11	18	-10	8	8	-2	0	13
440	0	6	4	6	14	10	4	-6	7	6	-6
441	10	6	-1	0	14	6	2	-1	9	-2	14
442	4	5	-10	11	24	-10	10	11	0	-4	8
443	-1	3	-8	-2	14	2	7	6	7	-3	11
444	1	-7	17	19	-22	31	-9	3	-3	4	1
445	7	3	3	-2	10	-1	9	3	5	5	6
446	9	9	-4	5	17	1	4	6	11	-2	19
447	14	8	10	4	-4	10	-1	1	5	7	9
448	-1	0	1	-4	17	0	-7	9	6	-11	4
449	14	0	-2	-6	22	3	-3	-3	12	-2	10
450	-1	1	11	-1	7	10	2	9	16	4	16
MEAN	7	4	-2	1	14	7	4	6	6	5	6
S.D.	6.3	5.6	10.2	7.2	11.6	8.9	5.8	5.8	6.1	8.3	7.3
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
426	-21	-3	28	11	196
427	-10	8	5	11	229
428	-27	5	2	30	203
429	-10	7	18	3	181
430	-6	5	9	-2	196
431	-7	2	19	-2	193
432	-4	10	11	18	229
433	5	1	14	7	250
434	1	4	20	-7	170
435	-8	5	28	0	259
436	10	16	14	2	295
437	-11	4	29	3	227
438	2	5	12	-2	246
439	-10	7	7	2	162
440	5	8	11	19	183
441	-11	8	-1	-6	175
442	-7	11	17	-8	181
443	-18	3	2	8	143
444	1	5	9	1	168
445	-2	7	4	7	172
446	-9	2	14	--	199
447	14	-2	0	--	220
448	2	6	1	--	124
449	18	-25	2	--	127
450	4	10	-3	--	192
MEAN	-4	4	11	5	197
S.D.	10.5	7.3	9.3	9.5	40.8
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
476	27	15	22	14	5	23	5	16	17	2	12
477	20	17	14	6	5	25	0	9	6	-1	11
478	20	13	13	8	12	7	3	10	6	1	9
479	24	21	11	10	10	18	12	14	1	2	16
480	29	20	17	8	15	15	8	8	20	-2	19
481	24	23	6	13	11	21	10	15	14	16	14
482	20	13	13	14	0	8	12	9	2	3	6
483	9	19	11	9	-2	11	5	17	5	-3	10
484	19	16	9	17	6	12	3	8	12	1	10
485	20	12	12	10	3	20	4	12	6	9	2
486	16	21	9	16	4	15	-6	12	11	-1	4
487	29	21	8	15	2	19	5	3	10	4	9
488	19	22	16	10	3	16	17	9	1	11	4
489	18	12	15	7	7	7	7	11	2	2	6
490	24	21	11	19	4	15	10	14	12	9	11
491	23	21	14	18	9	17	22	15	-13	9	9
492	22	12	19	14	10	20	0	4	10	7	-3
493	16	17	15	14	5	21	3	7	4	4	10
494	15	12	16	11	2	18	1	3	6	4	7
495	22	24	9	9	8	20	8	10	2	8	11
496	24	26	16	21	-2	26	21	24	-4	-3	8
497	22	20	16	15	5	20	3	15	0	14	4
498	18	18	16	14	-9	18	-1	14	11	10	2
499	18	12	16	18	18	-3	13	13	7	4	13
500	24	20	6	16	15	11	8	12	7	3	4
MEAN	21	18	13	13	6	16	7	11	6	5	8
S.D.	4.5	4.3	4.0	4.1	6.0	6.5	6.7	4.7	6.9	5.2	4.9
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
476	22	3	-6	-3	28	7	19	1	10	7	1
477	-2	7	-3	2	21	-3	3	5	6	3	1
478	2	2	-5	4	13	8	-2	6	6	1	-8
479	6	0	-5	3	17	3	-2	2	23	-9	0
480	8	-6	-1	-2	22	11	5	11	-4	5	-6
481	1	-6	-3	13	20	14	9	3	9	16	14
482	3	0	3	4	0	4	6	3	2	-5	-18
483	3	-1	3	10	5	4	5	6	4	3	8
484	7	3	-12	-8	27	5	5	10	7	0	1
485	12	0	-3	2	17	2	10	-1	3	4	-2
486	6	6	-3	1	13	10	5	10	3	8	3
487	2	-4	5	-5	18	-9	10	8	-5	7	-1
488	8	-8	3	4	26	-7	13	4	15	4	-6
489	4	1	3	-3	14	3	-1	15	-2	2	-1
490	9	-3	10	6	19	2	9	1	11	7	3
491	3	2	-4	6	17	3	7	3	4	5	-5
492	5	3	-2	7	18	-2	-5	11	8	10	8
493	0	5	-5	11	13	-1	-3	0	18	2	-4
494	2	5	-4	1	14	3	-4	10	5	5	-4
495	-6	3	-3	6	19	3	1	-3	2	4	13
496	8	-1	0	-7	16	9	-11	8	-4	1	10
497	4	11	-4	-1	8	8	-4	10	-3	11	10
498	10	6	-10	6	11	0	7	0	4	4	4
499	14	5	-2	7	5	9	1	8	12	5	7
500	8	6	3	4	3	10	-2	1	9	11	4
MEAN	6	2	-2	3	15	4	3	5	6	4	1
S.D.	5.6	4.6	4.8	5.4	7.2	5.6	6.7	4.7	6.9	5.1	7.3
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
476	-9	4	23	1	266
477	3	0	7	-3	159
478	3	7	21	-12	148
479	-3	12	20	-5	201
480	2	12	17	4	235
481	1	2	13	27	300
482	-2	0	8	14	122
483	-2	4	5	-6	142
484	-15	13	10	2	168
485	1	8	6	9	178
486	5	10	5	5	188
487	-3	10	2	17	177
488	-3	-5	24	10	210
489	-3	5	11	-7	135
490	-1	10	7	6	246
491	2	1	12	5	205
492	0	10	2	27	215
493	6	5	6	-1	168
494	-2	6	6	7	145
495	-4	2	15	0	183
496	6	3	8	--	203
497	5	0	13	--	202
498	6	8	-2	--	165
499	9	2	7	--	218
500	-3	7	-1	--	186
MEAN	0	5	10	5	191
S.D.	5.2	4.6	7.1	10.4	41.9
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
526	23	28	16	22	13	7	22	22	7	5	9
527	13	20	14	1	10	9	19	-3	3	16	-4
528	22	17	9	12	6	22	10	-1	12	5	4
529	21	19	14	13	5	10	9	6	13	8	-5
530	21	12	10	16	-5	12	17	5	14	0	-2
531	20	16	12	14	-1	18	-3	11	1	-3	5
532	28	26	8	22	0	30	10	21	16	5	7
533	22	22	15	21	4	20	15	15	6	15	12
534	24	20	23	16	-1	17	15	8	18	8	3
535	14	20	11	-6	7	16	2	9	10	2	1
536	15	20	15	17	-9	26	-1	9	9	-11	-7
537	25	22	10	8	12	17	19	-6	5	8	11
538	30	20	21	16	9	9	14	-1	8	11	-1
539	24	15	23	12	-4	20	-6	16	15	-5	8
540	27	19	11	15	5	24	0	16	12	9	3
541	20	20	10	15	0	20	0	9	7	-1	3
542	18	18	19	7	7	15	14	0	16	5	4
543	15	26	16	11	0	22	1	17	10	5	3
544	16	16	13	17	15	-2	16	7	-1	8	9
545	23	14	13	14	3	11	13	9	5	3	5
546	19	18	22	19	-4	22	19	7	16	11	4
547	16	17	17	18	2	D	17	6	-2	6	2
548	16	13	14	16	3	19	4	13	10	5	0
549	19	17	2	18	6	5	7	3	6	-2	-5
550	17	11	23	14	-8	7	11	8	4	-4	7
MEAN	20	19	14	14	3	15	10	8	9	4	3
S.D.	4.5	4.2	5.3	6.3	6.3	8.0	8.0	7.2	5.5	6.3	5.1
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
526	7	-8	0	7	19	0	14	8	-4	4	16
527	13	3	-3	0	16	-8	11	-2	4	3	12
528	5	1	-8	3	20	3	3	11	4	9	-4
529	7	5	-4	7	4	5	3	6	2	0	1
530	10	8	-11	7	11	4	-3	20	1	8	-2
531	8	1	4	7	7	3	3	4	4	6	6
532	12	-8	1	4	12	20	11	17	11	6	10
533	1	-1	14	-14	23	12	17	5	6	5	12
534	4	-2	-4	-3	14	6	6	8	2	9	-2
535	5	6	-4	3	6	3	9	2	4	12	-12
536	8	15	-10	6	21	11	10	8	-3	10	0
537	3	-4	4	-4	13	-2	7	10	1	-2	14
538	11	6	-4	8	7	-5	6	9	2	7	7
539	7	7	-29	22	14	6	8	1	13	7	-7
540	8	2	-14	5	16	8	13	9	5	7	15
541	9	7	-7	-4	16	5	-2	4	11	9	-9
542	3	5	-12	9	19	13	6	16	4	12	10
543	9	1	-8	3	14	8	-5	8	7	5	11
544	5	-2	-4	15	8	8	9	9	5	15	7
545	7	4	3	0	8	2	3	9	1	-1	8
546	-3	8	2	-19	20	20	5	11	8	12	9
547	5	-1	11	10	-4	-1	4	5	-1	2	9
548	13	9	-1	10	16	14	-3	1	7	-1	7
549	6	8	2	-5	14	7	-1	-2	11	8	1
550	13	0	2	-5	16	3	0	9	4	3	-4
MEAN	7	3	-3	3	13	6	5	7	4	6	5
S.D.	3.9	5.4	8.6	8.6	6.2	6.8	5.7	5.4	4.3	4.5	7.9
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
526	-11	3	15	-3	241
527	-4	1	7	1	152
528	-7	5	1	11	175
529	-8	2	7	1	151
530	6	1	7	5	172
531	3	3	-3	4	150
532	3	-3	6	7	282
533	-11	-4	19	12	263
534	0	-8	20	-1	200
535	6	8	5	8	147
536	-5	8	28	-7	183
537	-11	6	16	-2	180
538	-5	3	2	3	193
539	-16	16	8	18	193
540	-4	6	12	-1	228
541	-4	14	7	6	165
542	-10	5	-2	11	212
543	-1	5	16	-7	192
544	-1	6	10	-1	203
545	-7	1	4	11	166
546	5	-2	6	--	235
547	-3	-6	-4	--	125
548	11	7	24	--	227
549	-1	7	-3	--	128
550	12	2	7	--	152
MEAN	-3	3	9	4	189
S.D.	7.1	5.5	8.5	6.7	40.7
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 8[b]	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
576	22	19	9	13	-11	23	0	19	1	-2	8
577	22	13	11	9	7	6	7	11	-3	3	6
578	14	20	9	11	8	12	0	9	6	5	3
579	21	19	8	13	-1	20	5	9	7	4	5
580	20	18	7	16	-8	14	9	2	7	6	4
581	10	14	7	8	5	13	6	6	6	5	-1
582	24	-1	13	15	-1	15	2	3	8	-4	9
583	22	14	11	9	11	12	-4	7	9	6	9
584	15	12	16	11	9	1	8	8	5	1	3
585	22	12	16	17	-3	14	15	4	2	1	7
586	20	17	17	15	1	17	9	8	3	4	7
587	21	22	4	23	-4	18	-2	14	6	4	6
588	15	7	8	14	-9	22	-2	6	10	3	1
589	24	7	16	15	-13	20	3	5	5	2	8
590	24	16	-1	12	6	18	-6	6	8	2	-2
591	17	19	16	10	4	9	6	8	8	4	-6
592	16	12	5	12	5	13	0	6	3	7	4
593	21	10	7	19	3	13	2	1	11	-2	0
594	20	6	14	14	0	12	1	3	6	5	0
595	12	12	13	13	-10	13	6	6	7	8	1
596	9	23	16	16	-7	22	3	5	7	6	4
597	22	14	8	13	-9	13	11	3	7	-6	8
598	28	10	10	14	-7	26	-8	14	5	6	3
599	18	21	8	15	0	22	7	-16	21	5	4
600	12	22	20	9	0	19	-4	10	4	5	6
MEAN	19	14	11	13	-1	15	3	6	6	3	4
S.D.	4.9	5.9	4.9	3.4	6.9	5.7	5.6	6.2	4.3	3.5	3.8
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period
[b]Baseline is day 1

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155
576	14	0	-6	3	10	-4	2	11	3	-2	0
577	9	-1	-5	0	12	-5	6	4	2	-3	2
578	4	3	2	-2	14	5	-8	2	-4	4	15
579	9	-2	0	-10	16	1	4	-16	10	10	4
580	2	2	3	0	7	5	2	-21	11	9	5
581	1	2	9	-1	8	-5	10	9	-4	2	16
582	7	-9	13	-9	11	7	1	2	4	3	-1
583	4	-4	8	-7	9	3	3	8	0	10	1
584	8	3	9	-10	10	1	4	7	-1	3	2
585	4	-3	6	-1	13	0	4	3	-4	7	4
586	10	4	-3	1	11	1	4	5	-4	9	-2
587	6	-2	-2	-7	17	1	-9	18	0	10	-10
588	4	-1	5	-9	22	-2	-3	11	-4	7	-3
589	11	-13	4	0	10	5	0	3	2	0	14
590	8	-1	9	-7	15	-3	5	5	-15	13	12
591	7	3	1	5	6	2	-6	1	1	6	14
592	2	0	1	11	9	-8	11	0	-1	6	3
593	5	-49	46	5	5	3	0	-1	4	7	-1
594	6	4	1	-1	4	7	-9	7	10	-11	13
595	3	-2	-4	6	13	1	0	5	0	5	9
596	1	-6	1	7	5	6	-13	11	1	5	-1
597	-1	3	-4	-5	11	4	-7	8	0	-8	14
598	3	7	-2	-6	10	6	1	4	-1	4	3
599	7	3	0	7	-2	9	-7	5	0	-2	9
600	11	-1	3	1	4	6	1	9	-1	0	15
MEAN	6	-2	4	-1	10	2	0	4	0	4	5
S.D.	3.7	10.6	10.1	6.0	5.0	4.4	6.1	8.0	5.3	5.8	7.1
N	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)[a]

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0(mg base/kg/day)

ANIMAL #	DAY 162	DAY 169	DAY 176	DAY 182	TOTAL GAIN
576	4	3	20	3	162
577	-2	8	-3	9	125
578	-8	13	8	-6	139
579	-6	8	4	4	146
580	4	-2	8	6	136
581	1	6	-10	0	123
582	6	-2	9	9	134
583	-7	9	0	12	155
584	-10	10	11	2	138
585	-1	3	16	-2	156
586	0	4	11	8	177
587	1	6	5	-4	142
588	1	-2	8	10	119
589	-9	1	7	13	140
590	0	6	7	0	137
591	-3	2	-2	3	135
592	-3	11	6	-3	128
593	5	-3	1	2	114
594	0	2	8	-3	119
595	2	-3	4	5	125
596	8	-3	10	--	136
597	-15	2	0	--	86
598	-10	-3	9	--	126
599	13	-10	1	--	138
600	4	1	-1	--	155
MEAN	-1	3	5	3	136
S.D.	6.5	5.5	6.4	5.5	18.0
N	25	25	25	20	25

--: Data Unavailable

[a]Weight gains compared to the previous period

DRAFT

APPENDIX E

INDIVIDUAL FOOD CONSUMPTION DATA

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
401	24.7	27.9	30.3	27.3	26.6	22.9	24.6	28.4	30.0	29.3	29.7	30.6
402	24.2	26.6	29.9	29.3	33.3	25.3	30.9	30.6	36.7	30.3	31.7	36.3
403	22.8	27.4	25.0	26.1	25.7	23.4	30.7	28.0	33.0	26.7	27.3	27.9
404	22.2	23.9	24.6	26.6	24.6	25.0	30.9	30.7	31.1	29.9	30.3	9.0
405	23.8	25.3	25.4	25.7	24.9	25.4	28.9	29.7	30.7	30.0	29.9	30.4
406	24.5	23.9	25.9	27.9	28.6	28.1	31.6	32.9	30.6	30.6	31.9	31.3
407	23.5	24.9	26.9	26.9	25.1	23.0	28.0	28.6	24.4	26.7	28.4	29.3
408	23.5	24.7	27.0	27.6	25.0	25.7	34.9	30.9	32.9	29.1	30.9	31.9
409	27.0	26.7	27.6	28.4	27.6	33.9	33.1	32.9	32.6	33.0	32.3	31.4
410	23.3	24.1	25.9	26.1	26.0	25.9	28.4	27.3	27.6	27.1	29.1	30.4
411	26.2	25.7	24.3	23.7	23.3	23.9	26.3	26.1	26.1	25.3	24.7	25.7
412	22.7	24.0	24.9	25.3	22.1	27.6	26.0	26.3	26.6	25.6	25.3	26.7
413	23.2	24.9	26.1	27.0	26.7	26.4	28.6	28.1	27.7	30.6	28.4	33.1
414	23.8	24.6	26.0	26.3	25.4	30.0	28.7	27.9	30.3	30.7	30.7	31.3
415	23.7	24.0	24.0	25.0	23.7	25.1	24.7	24.1	23.9	23.6	23.6	25.0
416	24.2	25.4	27.3	27.9	28.6	27.4	30.6	29.0	30.3	29.0	29.3	31.4
417	33.0	21.0	22.4	23.3	23.9	28.3	26.0	22.3	25.0	25.0	24.4	26.6
418	24.3	26.4	28.6	28.6	28.7	28.1	32.4	30.6	31.1	31.4	31.1	31.6
419	24.8	25.6	25.6	25.3	26.3	26.3	28.1	27.4	28.7	28.0	28.1	28.6
420	21.5	23.6	24.6	25.0	25.1	24.0	25.3	26.0	28.0	27.3	26.9	28.3
421	21.7	23.4	24.4	25.4	24.0	22.6	25.0	25.9	24.7	24.1	26.4	27.1
422	22.3	24.9	26.1	26.6	25.9	29.1	26.3	26.9	28.3	28.9	29.1	30.3
423	25.2	22.9	23.3	23.6	22.4	22.0	24.0	23.4	25.4	23.3	23.7	25.6
424	25.5	30.0	32.4	30.6	32.0	31.3	32.7	33.1	34.1	33.6	32.3	35.3
425	25.5	25.7	27.3	28.1	27.7	29.1	30.9	34.0	34.0	33.1	34.1	35.1
MEAN	24.3	25.1	26.2	26.5	26.1	26.4	28.7	28.4	29.4	28.5	28.8	29.2
S.D.	2.26	1.81	2.28	1.80	2.67	2.92	3.06	3.06	3.44	2.96	2.90	5.19
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
401	28.0	26.6	26.4	24.3	23.7	23.9	24.1	22.0	23.0	26.1	26.4	23.4
402	30.4	30.4	28.7	27.0	27.4	28.9	27.6	26.1	27.3	28.9	28.3	26.9
403	28.1	28.1	26.7	29.6	25.9	27.1	24.7	24.6	24.4	27.7	27.0	25.9
404	18.0	29.6	28.6	26.9	30.0	30.6	27.9	26.6	26.1	26.7	27.9	25.4
405	29.0	14.4	20.7	29.9	30.0	29.7	26.9	26.6	24.4	27.4	28.1	28.1
406	31.4	30.9	29.0	30.1	31.7	15.7	19.6	30.6	30.3	29.6	31.7	28.7
407	26.3	25.7	25.7	26.4	28.1	28.9	27.3	26.4	28.9	28.4	29.4	26.0
408	30.1	23.1	24.4	23.6	24.7	27.3	23.6	24.7	26.0	26.7	27.9	25.1
409	30.7	29.3	30.7	29.6	30.1	30.3	30.4	30.1	25.7	29.7	30.1	29.6
410	30.6	28.6	29.0	27.9	29.1	29.7	27.0	27.6	28.0	29.0	29.6	27.6
411	25.3	25.7	25.1	23.1	23.4	23.7	22.9	24.3	23.1	25.3	25.6	23.3
412	27.3	26.1	25.3	25.4	27.3	25.7	23.6	25.3	26.3	26.1	26.7	24.1
413	28.3	28.1	27.4	25.4	26.3	27.7	26.1	28.3	27.9	28.9	28.6	26.3
414	29.7	28.1	28.1	27.6	27.0	27.1	25.4	28.9	29.4	28.0	29.4	25.6
415	24.9	24.7	23.9	22.7	22.3	22.9	21.9	22.1	22.0	22.7	23.1	21.7
416	29.7	29.9	28.0	26.4	27.0	28.0	26.6	28.9	25.3	27.6	30.4	27.3
417	26.1	24.9	24.7	24.1	23.7	24.0	23.3	22.7	23.4	22.7	24.7	18.1
418	32.0	30.7	31.4	29.7	30.6	31.7	29.1	30.7	30.7	30.9	29.9	29.0
419	27.0	28.0	28.6	26.7	26.0	26.9	26.0	26.1	26.9	27.3	28.4	25.1
420	26.3	25.4	26.1	25.0	24.7	25.4	23.9	21.9	20.7	26.9	26.9	26.0
421	27.9	26.4	27.3	26.3	24.9	25.7	23.4	23.6	24.3	26.0	25.4	24.7
422	30.3	29.6	28.0	29.1	28.6	28.7	27.6	26.1	27.6	29.9	28.1	23.1
423	25.6	23.9	23.7	23.9	24.1	25.0	24.6	24.4	22.7	23.9	23.7	25.1
424	32.9	33.3	33.7	31.1	29.4	31.7	30.3	28.0	28.3	30.6	30.9	30.4
425	34.3	32.1	32.6	30.0	31.3	32.0	30.0	30.9	30.3	32.7	32.9	32.6
MEAN	28.4	27.3	27.4	26.9	27.1	27.1	25.8	26.3	26.1	27.6	28.0	26.0
S.D.	3.27	3.75	2.94	2.51	2.72	3.55	2.73	2.78	2.77	2.43	2.41	2.98
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-M SEX: MALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
401	21.9	20.4	23.5
402	26.0	28.9	28.7
403	24.0	24.9	25.0
404	25.3	26.6	26.8
405	26.1	27.9	28.0
406	27.9	27.3	27.5
407	26.4	23.6	26.5
408	25.4	27.7	27.3
409	29.9	30.0	30.5
410	27.7	28.0	27.7
411	23.4	23.3	23.3
412	25.1	26.7	27.8
413	24.3	26.4	29.0
414	26.4	26.0	28.2
415	20.1	20.6	22.3
416	25.6	29.6	29.8
417	19.6	24.7	26.0
418	28.9	29.9	31.0
419	23.7	25.0	27.8
420	26.6	24.6	26.3
421	23.3	23.6	--
422	26.3	27.9	--
423	22.1	24.3	--
424	32.1	30.7	--
425	30.7	30.1	--
MEAN	25.6	26.3	27.2
S.D.	3.03	2.84	2.30
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
451	31.3	25.1	25.6	25.9	24.7	25.1	28.4	30.0	28.4	28.6	28.7	30.9
452	23.7	23.4	23.4	23.3	22.4	20.6	24.1	25.6	25.1	25.6	25.3	26.3
453	23.8	25.4	25.7	25.6	23.6	22.4	25.9	27.3	29.9	29.0	29.4	30.3
454	24.8	26.3	26.9	26.4	23.4	26.3	29.1	28.7	29.9	29.1	31.0	31.3
455	23.0	23.7	25.3	26.9	26.3	25.3	27.3	31.0	33.0	31.3	33.0	30.0
456	22.2	25.0	25.1	24.9	24.3	25.3	28.1	28.6	29.0	28.0	28.7	28.9
457	22.8	29.3	30.3	30.1	28.7	28.6	30.6	32.0	31.9	31.4	32.6	30.6
458	23.8	25.6	26.6	25.6	25.6	26.3	30.9	30.0	30.9	30.1	30.9	27.7
459	22.5	23.3	23.9	24.3	24.4	23.4	26.1	26.1	27.3	26.0	27.4	27.6
460	26.5	23.4	24.4	25.4	24.6	24.7	26.0	27.9	28.9	28.6	30.4	29.9
461	24.8	25.6	23.9	25.1	28.7	26.1	25.0	28.0	28.4	28.4	27.3	29.6
462	24.8	27.7	27.7	27.0	26.1	26.9	28.0	30.6	32.9	32.1	32.4	33.6
463	23.8	27.7	27.3	27.3	33.3	27.3	27.3	28.3	28.9	29.3	30.4	30.0
464	25.3	25.9	27.1	27.4	29.4	27.4	28.3	27.7	31.9	30.6	30.7	31.6
465	20.8	21.9	23.0	23.6	24.7	24.1	25.1	25.6	26.3	26.3	26.6	26.4
466	26.2	28.3	27.3	28.1	30.1	28.9	29.4	29.3	29.4	29.6	31.0	26.7
467	23.0	10.9	13.3	18.9	18.1	20.0	22.0	23.7	24.7	24.3	24.4	26.6
468	25.3	25.7	23.9	24.7	25.1	24.9	26.9	28.9	30.4	28.6	29.6	29.7
469	23.7	22.9	23.1	24.0	25.6	24.1	25.9	27.6	29.1	28.0	29.7	30.0
470	23.8	19.1	21.1	--	21.6	19.4	20.3	22.6	23.1	22.0	21.9	23.6
471	23.0	23.3	24.0	25.1	26.4	25.9	27.1	28.4	28.6	27.0	26.9	27.7
472	22.3	23.4	25.1	26.7	26.6	25.0	27.1	27.6	28.6	27.1	28.4	27.7
473	25.2	26.1	28.4	30.7	32.1	31.0	32.0	31.6	33.4	33.7	34.0	36.3
474	25.2	26.4	26.1	26.3	27.3	27.4	28.6	28.6	28.6	28.4	30.4	29.6
475	25.8	22.7	24.1	26.1	33.1	26.3	29.1	34.7	30.7	30.0	32.0	32.1
MEAN	24.3	24.3	24.9	25.8	26.2	25.3	27.1	28.4	29.2	28.5	29.3	29.4
S.D.	2.01	3.58	3.15	2.32	3.56	2.71	2.63	2.59	2.56	2.52	2.85	2.63
N	25	25	25	24	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5(mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
451	31.0	29.4	28.9	27.7	26.4	28.6	28.6	26.0	29.0	29.3	25.3	25.4
452	25.3	24.3	25.7	24.3	25.4	24.0	25.3	24.3	25.3	26.4	25.6	24.7
453	30.0	27.6	28.4	26.6	27.3	28.4	28.1	26.9	27.1	27.6	28.0	26.3
454	31.7	27.4	26.7	28.0	25.3	29.0	27.1	26.7	26.3	28.7	29.3	25.6
455	31.6	28.6	28.6	27.7	25.1	30.3	29.1	29.4	33.0	31.7	32.6	27.1
456	28.6	24.9	25.9	24.1	24.0	24.6	24.3	24.0	27.4	26.9	25.7	26.9
457	28.9	28.0	29.0	27.3	27.0	28.9	29.1	26.6	27.6	28.6	28.6	28.0
458	29.7	26.4	29.0	27.1	26.6	27.1	27.7	27.3	26.6	29.0	28.3	28.0
459	26.0	22.9	26.1	23.6	24.9	25.4	24.7	25.3	25.1	19.6	27.4	23.1
460	29.1	27.7	27.6	27.0	27.6	27.6	26.7	27.9	28.6	18.4	26.4	24.3
461	28.4	27.9	27.9	24.7	25.1	26.0	24.7	25.4	27.3	27.7	27.0	23.7
462	31.0	31.1	29.1	28.4	29.7	29.0	28.7	28.0	30.0	29.9	29.3	28.1
463	29.6	37.4	27.1	30.7	28.7	27.1	27.1	28.1	28.6	29.0	27.0	22.9
464	30.4	28.7	28.0	26.6	28.4	29.6	29.6	29.1	28.4	29.3	29.6	26.3
465	25.3	25.0	25.4	24.4	26.1	25.9	25.1	26.7	25.9	26.0	24.3	23.9
466	31.4	28.4	29.9	30.3	28.9	28.0	26.4	27.6	27.9	29.6	30.7	26.9
467	25.7	24.6	23.7	23.4	23.7	23.9	21.0	22.9	24.9	26.0	23.1	21.4
468	29.6	28.9	29.3	29.1	29.4	27.3	26.9	27.4	27.7	29.3	31.1	28.3
469	30.1	13.7	30.3	25.9	28.7	27.9	27.0	26.6	26.9	27.3	28.1	25.6
470	22.4	22.9	22.0	21.1	21.9	22.9	22.0	21.9	21.9	22.6	22.4	18.7
471	27.4	23.1	26.4	26.6	27.6	26.4	24.3	27.1	30.4	27.9	28.4	28.9
472	25.7	27.9	24.3	24.7	26.9	27.3	27.1	23.9	25.3	26.0	26.4	24.6
473	35.4	35.1	37.1	34.0	32.3	32.4	30.7	29.0	37.0	36.4	36.4	37.3
474	29.4	29.1	30.0	27.1	28.0	26.3	27.3	26.3	27.3	28.3	28.4	25.1
475	32.1	14.4	33.1	37.0	36.0	33.3	32.0	29.7	29.1	33.1	29.9	31.4
MEAN	29.0	26.6	28.0	27.1	27.2	27.5	26.8	26.6	27.8	27.8	28.0	26.1
S.D.	2.80	5.07	3.04	3.39	2.87	2.47	2.53	2.01	2.89	3.72	2.98	3.51
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-M SEX: MALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
451	27.4	28.6	20.8
452	22.7	25.4	26.0
453	13.7	9.0	14.5
454	22.3	27.3	27.8
455	26.0	28.3	29.2
456	26.3	24.7	24.2
457	26.4	24.4	26.3
458	28.6	26.7	28.8
459	24.9	25.0	26.3
460	24.9	25.3	29.0
461	23.6	22.3	26.2
462	28.0	27.9	29.5
463	26.4	24.4	26.7
464	27.9	26.4	27.8
465	25.0	25.7	26.5
466	27.4	26.9	27.5
467	23.7	22.9	25.0
468	28.7	24.7	28.0
469	25.9	26.4	25.8
470	20.6	19.6	22.2
471	26.0	24.9	--
472	24.7	25.0	--
473	34.1	33.4	--
474	25.9	26.0	--
475	30.4	30.0	--
MEAN	25.7	25.2	25.9
S.D.	3.70	4.29	3.49
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
501	20.8	21.4	22.9	24.3	23.9	23.0	24.7	24.6	26.0	25.6	27.3	28.3
502	23.7	22.6	21.6	28.4	24.7	23.4	25.6	25.4	27.3	26.1	25.7	31.4
503	23.2	24.4	24.9	26.3	25.6	24.6	27.7	27.4	28.6	29.1	28.9	29.6
504	22.0	23.9	23.7	24.6	23.3	23.6	24.7	25.9	27.0	26.3	25.7	26.4
505	23.0	25.0	26.3	26.9	25.7	24.3	25.9	24.3	27.1	26.0	27.9	28.3
506	24.5	24.6	24.7	27.0	26.3	25.6	29.1	27.1	28.9	29.6	28.3	28.7
507	25.0	26.3	27.0	28.4	28.7	27.4	30.0	28.7	29.7	29.3	27.1	28.9
508	22.5	24.1	25.4	26.4	24.3	23.1	25.1	25.4	26.0	26.7	28.6	29.6
509	24.8	25.6	26.1	26.6	24.1	22.0	24.7	24.0	24.7	24.7	25.4	25.9
510	22.2	24.4	25.9	24.7	23.7	20.9	22.4	24.1	24.0	24.3	26.1	27.1
511	26.0	24.0	24.3	25.1	25.6	25.4	28.7	30.1	29.7	30.1	30.3	32.3
512	26.7	27.4	29.0	30.1	31.3	33.0	33.0	31.9	30.7	32.0	33.4	31.1
513	22.7	24.0	25.1	27.3	26.6	27.3	29.0	29.0	30.0	30.1	29.4	31.3
514	27.3	24.0	24.4	25.9	25.0	24.6	27.3	26.1	27.1	27.3	27.6	27.1
515	25.0	26.4	27.9	28.0	28.7	30.7	29.4	28.6	28.9	28.9	29.7	29.7
516	24.0	23.4	25.1	24.3	24.7	24.0	25.7	24.6	24.0	30.1	25.0	25.3
517	22.0	22.6	26.1	24.6	25.1	25.6	26.9	27.1	27.0	27.3	27.4	28.0
518	20.7	23.4	25.1	24.1	24.0	24.9	29.4	26.7	28.3	27.6	26.9	29.6
519	24.8	26.3	26.3	26.3	25.6	39.0	26.3	25.7	28.0	27.3	27.0	27.4
520	23.5	24.3	27.0	29.0	28.1	27.3	27.7	28.0	27.7	26.7	27.1	28.0
521	28.5	26.1	26.0	26.7	27.4	26.1	27.0	25.7	26.4	29.1	27.6	29.3
522	30.7	25.0	22.9	25.1	23.6	26.7	26.4	26.4	27.0	26.9	27.7	29.7
523	26.5	25.9	26.7	30.9	27.9	30.0	28.6	28.6	28.7	28.9	30.0	31.4
524	23.3	22.3	23.0	25.1	26.4	26.7	27.6	27.7	28.0	27.6	28.4	30.1
525	24.3	25.9	24.9	29.0	25.3	23.4	25.1	27.7	29.1	26.4	26.9	26.4
MEAN	24.3	24.5	25.3	26.6	25.8	26.1	27.1	26.8	27.6	27.8	27.8	28.8
S.D.	2.36	1.47	1.68	1.91	1.96	3.84	2.25	1.98	1.77	1.89	1.83	1.88
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
501	28.0	24.0	25.4	25.1	27.3	25.9	24.7	27.6	27.4	28.1	29.6	24.1
502	28.9	25.6	24.9	32.7	27.9	27.1	24.9	29.4	29.4	26.1	26.6	22.6
503	27.4	28.1	25.9	26.3	29.1	22.3	22.1	24.7	25.9	28.4	25.4	23.3
504	24.9	24.1	25.6	25.7	23.7	25.0	24.3	24.1	24.0	26.4	26.0	24.1
505	28.1	25.7	25.3	25.6	25.9	25.7	25.7	26.3	27.7	28.1	29.6	22.7
506	30.3	27.4	26.7	26.1	28.7	28.3	26.1	28.1	28.6	27.3	29.9	25.9
507	28.7	24.1	25.7	28.0	29.0	28.3	25.1	26.7	27.0	27.7	29.6	26.3
508	28.0	24.7	27.6	25.4	29.9	25.9	25.1	28.3	27.9	27.6	28.9	25.9
509	24.9	22.0	23.0	21.1	23.7	23.6	23.4	23.9	26.1	25.6	25.9	21.4
510	25.9	24.9	25.0	25.7	25.0	24.1	23.6	25.1	25.9	26.4	26.1	25.3
511	31.7	28.4	27.7	28.4	27.9	27.1	27.4	28.1	29.0	28.7	27.3	27.3
512	30.7	27.4	28.7	27.9	27.7	28.0	29.3	30.6	30.1	31.0	30.7	27.1
513	30.9	27.4	28.3	25.4	26.3	25.9	26.1	27.7	27.1	29.6	29.9	25.9
514	29.4	25.6	27.7	28.0	31.9	30.3	28.4	28.1	27.9	27.7	28.6	26.9
515	31.4	27.1	29.3	29.0	29.1	30.0	21.7	26.3	32.4	33.4	32.1	30.0
516	24.3	21.0	22.7	21.1	22.9	23.0	21.1	23.3	24.0	24.4	24.9	22.9
517	26.1	24.6	31.0	24.1	27.0	24.4	24.3	25.1	25.7	24.7	25.4	25.4
518	37.4	26.4	26.4	28.9	28.7	28.3	26.7	27.0	28.0	28.0	27.6	25.1
519	27.3	26.3	25.0	24.7	24.7	19.7	24.0	25.6	25.9	25.4	27.0	23.9
520	27.0	25.3	25.4	23.4	26.3	21.7	24.4	25.9	27.1	27.1	27.4	26.3
521	31.7	28.3	28.1	31.1	29.0	29.6	26.1	30.3	29.1	29.7	29.9	28.9
522	31.4	30.3	27.1	31.6	27.3	27.4	25.9	25.3	26.1	28.9	27.9	27.6
523	31.9	29.7	29.1	29.1	27.6	27.3	27.9	27.6	29.4	27.7	27.7	29.4
524	31.0	28.0	25.9	25.6	25.3	24.7	22.0	22.9	24.7	27.3	26.7	25.7
525	26.7	25.0	20.9	26.0	27.7	27.7	26.6	28.0	25.4	27.1	27.6	27.6
MEAN	29.0	26.1	26.3	26.6	27.2	26.1	25.1	26.6	27.3	27.7	27.9	25.7
S.D.	2.95	2.22	2.24	2.88	2.14	2.68	2.09	2.06	1.99	1.95	1.88	2.20
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-M SEX: MALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
501	24.1	25.0	27.5
502	23.9	25.9	31.2
503	25.7	23.9	22.5
504	24.1	22.9	25.2
505	23.6	27.1	28.2
506	26.4	27.9	24.5
507	27.0	26.9	26.7
508	27.3	27.4	28.3
509	21.1	23.4	22.7
510	22.4	23.3	25.7
511	26.7	28.4	30.2
512	26.3	30.0	31.2
513	25.7	25.3	26.5
514	25.6	26.6	29.3
515	30.7	29.3	31.7
516	22.9	23.4	25.2
517	25.1	24.0	23.7
518	24.7	27.3	30.2
519	24.7	25.3	26.7
520	26.1	26.7	30.8
521	26.1	28.0	--
522	26.6	26.0	--
523	28.4	28.3	--
524	26.9	24.1	--
525	27.1	29.1	--
MEAN	25.6	26.2	27.4
S.D.	2.02	2.09	2.92
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
551	21.8	19.1	20.3	19.1	20.0	17.1	21.6	20.3	21.9	22.6	23.1	23.4
552	23.2	20.7	18.3	19.7	18.4	19.4	19.7	19.9	20.6	19.4	22.1	22.4
553	22.8	19.7	19.7	20.6	18.6	17.6	19.7	19.4	20.7	22.9	18.7	21.9
554	21.3	22.4	21.6	22.4	22.6	21.4	23.6	24.9	23.4	22.4	24.0	27.1
555	23.3	20.3	19.4	15.9	16.9	13.0	16.6	16.7	15.0	14.1	19.0	20.7
556	24.8	24.3	19.7	20.3	21.0	17.9	20.3	20.7	19.9	20.6	21.1	20.9
557	23.3	21.0	20.3	21.4	21.1	21.1	24.4	25.1	26.9	24.9	26.3	25.7
558	23.8	20.6	20.7	21.6	20.9	17.3	17.3	12.4	10.3	8.1	10.4	22.1
559	24.7	23.0	20.3	21.3	21.0	21.1	24.7	22.1	22.6	22.1	24.0	24.1
560	21.2	20.1	17.3	17.1	17.9	20.1	19.0	21.3	19.1	17.1	19.0	17.0
561	23.0	21.0	21.6	20.3	21.0	20.0	22.9	22.6	22.0	22.0	22.0	25.6
562	22.8	22.7	22.4	19.7	22.1	21.9	22.7	23.3	23.1	21.9	23.0	24.1
563	25.3	23.3	22.0	20.4	20.7	22.6	25.7	26.1	24.1	24.9	23.9	26.0
564	22.0	20.7	18.7	18.4	19.1	18.6	21.0	21.6	18.9	20.1	21.1	22.4
565	25.5	25.3	22.0	20.6	22.0	22.3	24.3	23.6	25.0	24.1	25.1	23.9
566	23.3	21.4	19.4	18.7	18.4	18.9	22.6	21.7	20.0	21.1	21.4	20.9
567	24.0	25.6	20.6	19.7	19.0	20.6	23.1	24.0	21.9	22.0	21.4	25.6
568	27.0	21.4	18.1	17.0	17.4	17.3	18.3	17.4	17.6	11.9	5.1	12.7
569	29.2	24.9	20.0	22.1	12.6	23.7	22.1	26.6	23.6	24.0	24.0	26.0
570	23.2	23.0	22.1	22.9	22.9	21.3	24.9	26.0	26.4	25.7	28.0	29.3
571	25.7	25.3	22.6	24.7	24.3	25.6	26.7	24.9	24.3	24.9	26.9	12.4
572	23.8	25.6	23.6	22.3	23.7	23.3	21.4	23.4	22.4	22.4	23.4	25.6
573	22.3	21.4	21.9	22.0	22.3	21.9	21.1	24.0	23.4	23.9	25.1	23.6
574	27.2	27.7	23.9	19.3	19.3	22.0	23.3	27.4	22.7	22.7	24.7	25.6
575	20.3	21.6	21.0	20.0	19.6	20.6	26.6	24.6	23.7	22.0	23.0	24.1
MEAN	23.8	22.5	20.7	20.3	20.1	20.3	22.1	22.4	21.6	21.1	21.8	22.9
S.D.	2.05	2.25	1.68	1.99	2.51	2.66	2.74	3.44	3.56	4.22	4.90	4.00
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
551	24.0	21.0	20.6	19.9	23.9	23.7	23.9	23.9	23.6	24.6	21.4	21.0
552	24.0	19.7	19.7	19.7	21.4	21.6	20.1	20.9	22.0	27.4	19.9	22.0
553	20.6	15.4	19.1	18.3	23.1	22.4	19.0	18.1	18.7	21.0	20.1	18.7
554	24.0	18.9	22.1	21.3	25.9	25.7	22.7	24.0	24.4	26.6	24.7	23.0
555	19.1	16.0	17.6	16.7	18.4	16.7	20.7	4.0	17.6	20.1	21.6	22.6
556	21.4	18.4	19.7	21.4	21.0	21.0	20.9	20.4	21.4	25.3	22.1	21.4
557	28.3	22.6	26.0	20.9	25.9	24.0	26.3	25.4	26.1	28.0	27.6	23.1
558	25.9	20.7	20.3	19.0	22.0	20.1	18.6	16.1	c	c	c	c
559	23.1	21.1	22.3	20.9	24.4	23.3	23.0	22.3	23.0	25.1	19.9	21.3
560	20.1	15.4	16.9	17.3	18.1	19.9	17.9	18.9	16.4	20.3	19.0	17.9
561	22.4	20.4	29.4	25.7	22.9	22.9	23.4	23.0	23.7	29.3	24.3	21.4
562	25.7	17.9	20.7	28.9	21.7	21.7	21.6	22.1	25.1	24.1	24.4	23.6
563	24.7	21.7	24.9	20.6	26.4	26.4	24.1	23.7	26.4	32.9	26.9	23.3
564	21.6	20.1	20.7	25.6	19.9	22.0	20.4	22.3	21.6	23.1	23.4	20.0
565	25.1	22.0	24.9	23.4	24.1	25.6	23.0	24.6	24.6	28.0	21.7	22.4
566	23.9	18.7	17.6	19.0	21.7	15.6	16.6	23.6	21.0	22.7	22.3	18.0
567	25.0	19.7	24.7	25.6	23.6	23.4	21.6	21.0	23.7	27.0	24.7	20.9
568	26.4	21.0	19.7	20.4	19.7	17.7	18.3	18.3	16.0	17.7	22.9	17.6
569	23.7	23.4	23.7	25.6	25.9	24.7	23.9	24.1	21.7	29.6	26.7	22.7
570	29.9	24.4	26.6	25.9	29.0	24.1	25.4	28.1	27.4	29.9	31.3	25.7
571	30.6	30.4	29.0	26.9	26.1	27.4	25.7	26.4	27.3	29.3	29.3	26.7
572	24.3	24.0	24.9	23.7	27.3	25.9	21.7	24.3	25.1	27.0	26.4	21.6
573	24.6	24.1	23.7	22.1	25.4	25.1	23.3	25.1	25.3	27.6	27.1	24.9
574	23.9	24.1	24.7	25.0	26.0	25.1	23.7	23.1	25.4	28.1	28.9	24.6
575	23.4	21.1	23.0	21.0	23.6	23.9	23.4	21.9	18.0	23.0	25.4	23.1
MEAN	24.2	20.9	22.5	22.2	23.5	22.8	22.0	21.8	22.7	25.7	24.3	22.0
S.D.	2.72	3.27	3.41	3.24	2.82	3.01	2.55	4.61	3.36	3.68	3.30	2.38
N	25	25	25	25	25	25	25	25	24	24	24	24

--: Data Unavailable c: Animal Found Dead

[a]Calculated daily food consumption for successive periods

SIX MONTH ORAL TOXICITY STUDY OF
WR238605 SUCCINATE IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 4-M SEX: MALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
551	22.9	24.9	26.3
552	21.7	24.6	23.8
553	18.0	21.1	23.0
554	22.4	23.3	24.8
555	18.3	18.6	27.2
556	22.3	22.9	23.7
557	23.7	25.4	28.2
558	c	c	c
559	22.1	23.9	25.0
560	19.4	19.1	19.8
561	22.9	22.6	24.8
562	24.7	19.6	24.5
563	22.6	25.0	29.7
564	21.9	22.0	23.5
565	13.6	11.1	28.2
566	19.9	20.6	24.5
567	21.9	23.9	26.0
568	20.4	20.7	22.7
569	21.0	24.9	30.5
570	27.4	29.3	33.3
571	25.0	26.7	--
572	22.4	25.6	--
573	23.1	24.3	--
574	25.6	25.7	--
575	21.0	22.0	--
MEAN	21.8	22.8	25.8
S.D.	2.80	3.58	3.17
N	24	24	19

--: Data Unavailable c: Animal Found Dead

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
426	22.2	20.9	19.0	18.6	17.1	17.0	18.1	18.3	20.1	19.3	19.6	24.0
427	27.0	18.9	20.0	34.0	22.1	16.1	18.4	20.9	20.4	20.7	19.3	26.6
428	19.0	18.0	18.6	18.7	17.6	17.7	16.9	18.6	19.6	19.9	18.7	23.9
429	18.0	22.6	19.3	20.3	16.7	16.1	17.4	18.6	19.6	20.3	20.0	23.4
430	17.2	19.0	18.6	19.9	18.7	18.6	21.6	20.6	21.9	21.9	19.7	25.9
431	32.3	21.6	19.7	19.3	16.6	15.0	17.6	17.6	19.4	18.1	17.6	18.7
432	18.8	18.1	16.9	17.9	19.1	24.7	17.6	19.1	20.0	19.4	19.1	22.4
433	18.0	23.1	17.4	18.9	18.7	16.7	19.4	19.6	19.3	21.0	21.7	20.0
434	16.2	17.7	16.6	16.6	14.6	15.1	16.1	18.4	19.1	18.0	18.7	18.3
435	22.3	21.4	18.1	19.9	20.1	16.4	17.4	19.9	21.6	19.9	20.1	20.4
436	24.7	20.1	22.6	22.1	19.7	27.7	19.1	23.6	22.3	21.4	20.0	22.3
437	18.2	17.3	17.4	17.3	17.1	15.4	15.7	18.3	19.3	20.0	18.3	17.7
438	16.0	15.3	16.1	16.0	15.4	17.1	15.6	15.3	17.6	19.7	20.3	20.7
439	18.5	18.9	16.7	17.1	17.1	16.3	16.7	17.9	18.0	18.3	17.4	18.7
440	14.5	15.9	16.0	17.6	17.1	16.7	17.1	16.6	15.6	17.0	15.4	14.7
441	48.5	24.4	27.9	21.4	21.3	20.9	--	34.7	29.6	27.6	29.1	43.7
442	18.2	20.4	19.0	16.9	18.3	18.4	24.6	18.1	20.9	19.7	18.1	19.0
443	14.8	15.9	15.3	16.9	14.4	17.4	14.9	15.7	17.6	16.9	16.3	17.3
444	19.8	19.3	17.6	22.0	16.9	18.0	18.0	18.0	20.4	20.3	17.0	18.1
445	14.7	14.9	14.7	16.6	15.3	14.3	15.0	16.0	17.4	17.0	16.6	17.0
446	16.5	16.7	16.7	18.1	15.6	18.3	17.0	18.3	20.1	17.4	17.0	19.1
447	20.0	15.6	17.6	18.0	16.1	16.6	17.9	19.7	18.7	19.4	19.1	19.9
448	17.8	15.4	15.9	16.6	15.3	16.0	16.7	15.7	16.3	16.1	17.1	17.4
449	25.5	17.3	17.3	18.0	20.1	22.9	18.0	18.3	18.0	18.0	18.0	22.3
450	15.5	15.6	17.9	16.0	17.0	16.4	17.3	16.3	18.3	16.6	17.7	19.0
MEAN	20.6	18.6	18.1	19.0	17.5	17.8	17.7	19.0	19.6	19.4	18.9	21.2
S.D.	7.21	2.69	2.65	3.59	2.05	3.14	2.07	3.77	2.65	2.34	2.59	5.52
N	25	25	25	25	25	25	24	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
426	19.4	16.4	17.9	16.1	20.7	20.9	22.3	20.0	18.6	17.7	17.6	10.7
427	18.7	20.6	16.4	16.1	21.1	21.0	19.3	22.9	21.3	22.0	20.3	15.0
428	19.4	19.0	20.3	19.9	14.1	17.0	18.1	18.7	19.3	22.9	22.0	13.7
429	19.6	24.3	21.9	18.6	18.7	18.1	18.7	19.1	18.3	20.0	16.6	14.4
430	20.9	22.9	18.6	16.6	20.4	19.4	19.3	19.0	19.3	21.0	21.0	16.7
431	18.7	16.0	14.7	13.7	16.1	18.9	18.3	18.3	18.3	18.4	17.6	12.9
432	22.1	17.7	16.9	17.7	19.3	21.0	19.1	22.1	19.3	20.4	19.6	15.4
433	21.3	19.6	18.0	18.3	20.6	22.3	22.1	21.9	17.6	22.4	20.7	18.9
434	20.1	16.1	14.1	14.0	18.0	17.7	16.9	16.3	17.1	16.7	15.4	13.9
435	19.7	18.0	18.0	14.0	19.7	22.3	20.6	19.7	21.0	21.3	19.3	14.1
436	19.7	19.1	16.3	18.6	20.4	21.9	22.1	22.1	24.7	25.6	25.0	22.3
437	19.9	17.1	15.6	14.4	19.3	19.6	17.9	18.7	18.4	18.7	17.0	13.0
438	23.6	19.6	19.4	17.1	19.7	19.0	19.9	20.3	20.6	20.3	20.6	17.9
439	20.7	18.3	16.4	16.7	19.1	17.7	17.6	18.0	17.1	18.6	18.9	14.3
440	20.1	15.6	15.7	17.7	18.0	17.0	15.9	16.3	16.0	16.6	15.0	14.6
441	35.7	45.9	35.3	40.3	37.9	26.3	20.7	28.0	26.7	33.9	39.3	28.9
442	20.7	21.3	16.7	17.6	21.4	18.6	18.1	19.7	17.7	18.0	17.6	14.3
443	17.6	13.9	13.6	12.6	15.1	16.0	15.1	15.3	16.6	15.6	15.3	11.1
444	18.9	14.0	17.6	22.4	10.7	21.0	19.7	18.1	15.9	17.1	16.7	15.6
445	17.9	16.6	15.0	14.4	15.4	16.4	16.3	15.7	16.7	17.4	17.0	15.6
446	20.9	20.3	16.7	19.6	18.0	18.4	18.1	31.6	23.6	18.9	17.7	14.4
447	20.3	20.3	18.9	16.9	16.1	17.7	17.0	18.1	14.0	16.4	20.7	16.7
448	17.0	16.3	15.0	14.9	15.9	17.1	16.4	15.6	15.6	16.0	15.0	15.0
449	22.4	19.4	17.4	18.7	19.3	19.4	18.3	16.6	17.7	21.3	19.7	19.7
450	20.1	15.4	19.4	18.1	18.4	19.3	20.4	19.6	22.3	21.4	21.1	19.9
MEAN	20.6	19.3	17.8	17.8	18.9	19.4	18.7	19.7	18.9	19.9	19.5	16.0
S.D.	3.47	6.11	4.14	5.21	4.69	2.33	1.95	3.74	3.00	3.83	4.81	3.81
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
426	12.7	19.6	25.2
427	16.7	19.4	22.8
428	16.0	17.3	23.8
429	15.7	18.1	21.8
430	17.6	20.3	21.5
431	14.3	17.0	19.5
432	18.0	20.7	22.7
433	19.4	21.3	24.0
434	15.4	17.9	17.7
435	17.3	20.7	21.3
436	23.7	24.6	22.2
437	16.9	19.0	18.7
438	19.1	20.1	19.2
439	16.7	18.0	18.3
440	16.1	19.0	20.3
441	33.6	29.0	31.8
442	16.9	19.1	18.2
443	12.7	13.6	16.8
444	15.7	16.7	17.7
445	15.9	15.6	17.7
446	17.0	19.4	--
447	14.9	14.6	--
448	15.0	16.0	--
449	13.0	16.9	--
450	18.6	20.4	--
MEAN	17.2	19.0	21.1
S.D.	4.14	3.14	3.53
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
476	25.0	19.6	18.3	19.1	20.1	18.3	22.1	21.1	21.7	24.7	20.6	23.3
477	16.8	17.1	16.3	17.6	16.4	16.0	24.4	18.3	18.3	17.3	17.4	21.6
478	14.8	15.3	14.4	15.9	15.1	15.9	17.9	16.0	17.0	15.7	16.1	17.9
479	22.3	18.4	19.0	18.3	18.7	18.0	21.0	20.7	21.0	19.4	18.9	22.0
480	19.0	19.4	16.6	18.1	18.1	16.4	19.7	18.6	19.3	20.6	19.1	23.0
481	18.0	18.6	18.6	17.9	19.6	20.1	22.0	20.3	23.0	23.1	24.9	26.0
482	21.7	15.3	14.1	15.0	16.9	13.7	14.7	15.3	16.1	15.4	14.9	16.7
483	18.0	14.1	15.1	15.6	15.3	16.0	17.1	17.6	17.7	16.3	17.7	17.0
484	17.2	16.0	15.6	16.6	16.9	15.3	18.1	16.9	17.6	17.6	17.0	18.7
485	16.8	18.6	21.1	15.1	14.6	15.0	17.7	17.0	17.9	16.4	17.1	18.1
486	19.0	18.6	16.9	17.0	16.0	15.1	17.0	15.3	16.9	15.3	15.1	18.3
487	24.5	19.4	19.3	19.7	19.7	17.1	19.6	20.7	20.9	19.9	20.4	21.9
488	19.8	17.0	18.0	18.4	18.0	16.4	19.6	21.6	21.0	20.0	21.1	21.3
489	18.5	16.3	16.6	17.7	17.1	16.1	18.0	17.0	19.6	17.6	17.7	19.3
490	17.0	18.1	17.9	17.0	16.7	15.7	19.1	19.3	20.4	22.9	20.7	22.3
491	24.7	17.7	20.4	19.0	18.4	17.3	20.1	20.4	22.4	16.7	16.6	18.7
492	17.3	18.3	17.3	18.9	18.1	18.0	20.6	23.7	20.6	19.6	18.1	24.6
493	20.3	20.0	19.0	30.3	17.4	17.3	20.1	19.9	18.7	18.9	18.9	20.4
494	17.0	17.4	16.6	17.0	19.1	19.4	17.9	17.3	17.9	19.7	16.6	24.4
495	18.3	16.1	16.9	17.9	17.9	16.3	18.6	18.9	19.6	18.9	18.6	18.7
496	18.0	18.7	20.6	21.3	20.7	18.7	20.4	22.9	24.9	23.4	18.6	21.1
497	19.8	18.4	19.0	19.3	19.0	17.7	19.3	19.0	20.4	18.9	20.3	19.7
498	24.8	21.3	20.7	23.6	20.3	18.9	20.0	18.7	19.6	19.1	20.9	22.0
499	17.7	17.1	17.1	18.1	19.0	18.1	18.9	18.6	18.3	19.7	19.9	20.6
500	18.0	16.7	16.0	16.7	16.7	16.4	19.9	20.1	19.7	20.6	17.3	21.1
MEAN	19.4	17.7	17.7	18.4	17.8	16.9	19.4	19.0	19.6	19.1	18.6	20.7
S.D.	2.87	1.67	1.94	3.10	1.66	1.53	1.95	2.18	2.08	2.55	2.22	2.44
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods
[b]Baseline is day -6

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5(mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
476	21.6	19.1	19.3	16.6	21.9	22.0	21.9	21.0	19.3	22.3	--	--
477	17.9	17.1	15.7	18.3	20.0	18.6	18.3	18.1	18.9	18.6	17.9	18.9
478	16.4	14.6	14.6	17.0	17.7	17.4	16.7	17.3	17.1	16.7	15.7	15.0
479	22.3	20.4	18.0	18.0	20.7	21.6	18.0	19.9	21.9	19.6	17.7	15.7
480	20.9	17.0	17.1	20.3	21.1	22.3	19.0	19.4	19.1	19.4	16.6	16.6
481	24.7	22.3	17.7	28.1	23.4	23.3	23.0	22.3	22.0	24.1	24.3	22.7
482	14.7	15.3	14.1	19.1	13.7	14.6	15.0	14.3	14.4	15.1	--	--
483	18.7	15.9	17.3	19.3	17.1	16.9	17.9	18.3	19.3	19.1	19.0	18.9
484	17.0	15.6	14.4	13.9	17.4	17.0	18.1	18.0	16.9	17.3	17.0	11.3
485	18.4	16.1	15.0	15.7	18.0	16.1	17.1	16.4	17.6	17.4	15.1	16.7
486	18.1	15.0	15.4	16.3	16.1	17.9	19.0	17.6	18.1	19.1	16.7	17.9
487	20.9	17.3	19.3	18.7	21.0	18.7	19.1	20.3	19.7	19.9	19.3	17.4
488	21.0	17.9	16.9	19.0	22.0	22.1	21.3	21.9	22.4	22.3	18.1	16.0
489	18.1	16.4	17.3	16.0	17.9	18.4	17.0	20.1	18.1	18.9	16.4	14.7
490	21.7	19.9	19.7	19.4	20.7	21.0	18.3	20.9	21.7	21.6	20.4	18.3
491	18.6	17.3	16.1	17.3	20.0	19.1	17.6	19.1	17.9	18.9	16.0	14.0
492	21.7	18.7	18.4	21.9	21.6	18.3	17.3	19.0	21.0	21.4	23.6	19.3
493	18.4	18.0	16.7	17.0	19.1	18.7	17.3	17.3	19.3	18.9	17.0	17.1
494	22.3	28.9	16.6	19.0	17.7	18.7	16.7	19.1	18.3	19.0	19.7	14.4
495	19.0	19.0	16.6	17.3	20.0	19.4	18.4	17.1	19.3	19.3	18.4	16.9
496	21.3	21.4	18.7	19.7	20.9	20.1	17.4	19.6	19.4	18.3	21.4	18.7
497	20.4	20.6	17.6	18.7	18.6	19.9	18.9	19.9	19.6	21.4	22.0	19.6
498	23.1	24.7	18.1	19.1	20.9	19.7	18.6	20.0	18.6	20.6	17.3	18.6
499	21.3	20.6	18.3	19.6	18.9	18.1	19.1	17.7	18.6	20.4	19.3	20.0
500	18.9	21.6	17.6	--	17.4	18.1	17.0	18.4	18.9	20.3	19.3	16.9
MEAN	19.9	18.8	17.1	18.6	19.4	19.1	18.3	18.9	19.1	19.6	18.6	17.2
S.D.	2.32	3.30	1.56	2.67	2.20	2.08	1.72	1.80	1.78	1.95	2.44	2.42
N	25	25	25	24	25	25	25	25	25	25	23	23

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 2-F SEX: FEMALE
DOSE: 0.5 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
476	16.4	20.7	22.7
477	17.4	19.1	19.3
478	15.9	19.0	18.0
479	18.0	20.1	23.8
480	18.3	22.7	22.2
481	19.9	22.7	24.7
482	7.6	13.7	16.2
483	17.1	18.6	17.8
484	16.3	18.1	18.5
485	18.0	17.9	18.5
486	18.9	17.4	19.0
487	18.7	20.1	24.3
488	14.9	20.4	24.7
489	15.7	19.0	18.0
490	18.9	20.4	21.8
491	15.7	17.7	20.0
492	19.9	19.3	26.3
493	18.0	18.7	19.3
494	17.6	17.3	23.8
495	17.4	19.1	20.0
496	20.3	20.7	--
497	19.9	20.0	--
498	19.1	18.4	--
499	18.3	17.3	--
500	18.3	16.7	--
MEAN	17.5	19.0	20.9
S.D.	2.52	1.90	2.92
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 1[b]	DAY 8	DAY 15	DAY 22	DAY 29	DAY 36	DAY 43	DAY 50	DAY 57	DAY 64	DAY 71	DAY 78
526	18.3	17.7	20.4	21.9	20.4	19.3	20.7	22.4	22.3	24.1	22.3	21.9
527	19.2	16.0	18.1	26.9	16.7	17.4	16.6	18.3	17.0	16.7	18.4	18.3
528	15.8	16.1	16.9	16.7	17.6	16.1	18.7	19.0	17.0	17.9	16.3	18.0
529	18.5	16.4	17.4	18.1	18.6	17.7	18.3	18.6	18.4	18.1	18.6	17.7
530	18.2	17.0	17.6	17.6	17.7	16.3	17.4	18.6	19.4	19.7	18.3	18.4
531	14.8	16.1	17.3	17.4	16.1	16.4	17.1	18.3	18.7	20.1	18.1	21.6
532	20.8	24.0	20.3	20.6	21.0	16.3	20.1	22.9	22.9	21.3	20.4	22.7
533	18.3	17.3	18.1	19.1	20.0	17.1	19.7	21.6	21.9	21.4	21.1	20.0
534	18.0	18.1	18.6	20.3	19.3	17.4	20.7	21.9	21.4	22.9	21.4	22.0
535	17.2	15.7	17.1	18.9	15.1	27.7	16.6	17.4	17.3	16.6	16.1	17.4
536	27.3	20.6	17.9	16.7	17.4	20.9	18.9	18.9	20.0	19.7	15.7	17.6
537	16.8	17.3	17.9	17.6	17.7	19.6	20.4	21.4	17.4	18.4	19.9	21.6
538	18.2	29.9	37.7	32.9	26.3	27.9	24.4	30.0	23.3	22.9	25.0	30.3
539	17.8	17.3	17.1	18.9	18.3	17.7	21.1	16.6	19.9	19.6	17.6	20.9
540	17.8	17.9	18.4	18.4	18.6	17.3	19.6	21.4	21.1	20.0	18.9	21.3
541	16.2	16.6	16.1	17.4	15.9	15.0	17.0	18.1	17.7	17.3	16.7	20.4
542	23.0	15.9	16.6	23.6	17.4	16.4	21.4	18.7	19.9	20.3	17.7	22.6
543	17.8	16.6	19.7	18.9	18.4	17.7	20.4	18.7	20.7	19.3	20.0	20.9
544	20.0	16.1	17.7	18.7	18.6	18.3	18.1	21.0	20.0	18.9	19.1	21.6
545	16.3	16.6	15.9	16.7	16.3	15.1	19.3	17.4	18.1	18.1	18.0	20.6
546	17.0	17.1	18.3	20.4	20.3	18.4	20.7	20.7	21.7	22.1	20.3	21.6
547	17.8	16.3	15.7	17.6	16.4	15.1	16.6	16.6	16.6	16.3	17.1	16.7
548	17.0	18.0	16.6	18.9	17.0	30.6	20.7	17.4	19.7	19.3	18.0	19.1
549	18.2	16.6	17.0	17.0	17.3	16.9	18.1	17.1	18.1	17.3	17.4	22.6
550	17.2	17.9	16.0	19.6	18.6	15.4	18.3	18.4	18.4	17.3	17.7	19.1
MEAN	18.3	17.8	18.4	19.6	18.3	18.6	19.2	19.7	19.6	19.4	18.8	20.6
S.D.	2.49	3.06	4.21	3.62	2.24	4.12	1.89	2.86	1.97	2.12	2.13	2.73
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a] Calculated daily food consumption for successive periods
[b] Baseline is day -6

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
526	23.6	17.7	16.7	17.7	19.3	19.9	20.0	20.9	19.6	19.9	20.0	16.7
527	21.1	19.6	18.9	19.3	21.6	16.9	17.9	18.1	18.3	22.7	19.3	17.6
528	20.9	15.9	13.4	14.9	18.6	16.9	16.7	18.6	16.6	18.9	17.6	13.1
529	18.4	17.3	16.4	17.0	17.9	18.0	17.3	18.1	16.9	17.6	17.4	13.3
530	20.6	20.1	16.6	18.7	19.9	18.3	18.4	20.9	19.7	20.7	19.9	18.1
531	21.6	25.4	27.0	22.7	32.3	17.9	18.1	19.6	32.6	33.7	26.4	28.7
532	23.1	17.6	16.1	19.4	20.3	23.7	22.1	25.0	23.9	22.7	23.3	20.4
533	18.6	17.3	19.0	15.9	18.7	21.4	21.7	20.1	20.4	21.0	19.0	15.7
534	21.1	16.7	15.9	16.6	18.7	19.1	18.7	19.0	19.0	20.9	18.9	16.7
535	17.7	15.4	17.0	16.0	18.4	18.7	16.6	18.1	17.0	19.1	17.1	16.7
536	18.3	19.6	17.3	18.0	23.0	22.3	20.9	22.0	20.6	22.7	20.1	14.6
537	18.1	17.7	18.4	17.3	19.4	20.4	18.1	19.7	18.3	20.6	20.6	16.7
538	22.3	31.6	19.9	25.0	25.1	22.1	20.1	25.0	23.1	28.0	23.9	18.1
539	20.3	18.3	15.3	16.9	18.6	18.4	18.7	18.1	18.9	21.9	21.7	13.4
540	21.1	17.0	15.0	14.9	19.7	19.6	21.9	23.0	22.0	23.9	21.7	18.6
541	19.1	18.7	17.3	20.6	19.4	18.7	17.0	17.6	22.9	22.4	18.4	15.6
542	20.0	17.3	17.7	16.6	20.4	21.1	21.1	22.3	20.4	24.7	23.1	15.9
543	25.7	17.7	17.9	17.7	20.1	21.6	19.6	18.6	22.9	22.6	23.1	19.3
544	20.6	22.9	16.3	21.1	24.6	26.4	22.9	24.4	22.6	30.7	21.3	21.6
545	19.1	16.9	16.9	19.4	18.7	19.3	18.4	18.3	19.1	10.7	19.7	16.0
546	21.3	18.3	19.1	14.3	18.3	23.9	23.6	22.9	23.6	27.6	24.1	22.1
547	17.3	16.1	17.0	19.6	16.0	15.7	16.6	17.6	17.7	17.9	16.0	15.4
548	20.7	19.1	17.9	19.6	21.4	22.7	19.0	16.1	19.9	18.1	18.4	18.9
549	17.3	19.6	16.6	20.7	17.4	18.1	16.6	17.1	19.4	18.4	18.0	17.9
550	19.7	18.3	17.0	17.6	17.9	19.3	18.4	19.3	20.3	21.4	18.4	19.1
MEAN	20.3	18.9	17.5	18.3	20.2	20.0	19.2	20.0	20.6	22.0	20.3	17.6
S.D.	2.05	3.41	2.44	2.52	3.28	2.53	2.09	2.55	3.29	4.63	2.58	3.31
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 3-F SEX: FEMALE
DOSE: 2.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
526	18.0	20.4	20.7
527	18.1	19.0	22.8
528	15.3	15.3	19.3
529	15.7	16.1	18.5
530	17.7	19.1	21.2
531	24.6	24.3	30.8
532	19.0	19.4	23.3
533	16.0	19.1	22.8
534	16.3	19.4	20.3
535	17.6	18.7	20.7
536	17.9	22.6	25.8
537	18.1	21.6	21.8
538	20.0	20.3	27.5
539	17.6	20.0	22.8
540	18.4	19.7	23.7
541	18.4	18.1	25.7
542	21.9	16.6	19.8
543	20.0	22.4	23.0
544	20.3	20.1	28.2
545	15.3	16.9	23.3
546	19.3	22.3	--
547	14.0	15.9	--
548	20.4	25.3	--
549	17.1	17.4	--
550	19.6	20.1	--
MEAN	18.3	19.6	23.1
S.D.	2.29	2.53	3.17
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) [a]

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 85	DAY 92	DAY 99	DAY 106	DAY 113	DAY 120	DAY 127	DAY 134	DAY 141	DAY 148	DAY 155	DAY 162
576	20.3	16.3	17.4	16.3	16.4	17.6	16.9	17.6	17.6	18.1	18.0	17.0
577	17.4	15.3	15.0	15.3	16.6	15.7	16.4	16.0	16.9	17.0	15.9	14.6
578	18.6	15.1	16.9	21.1	19.9	18.6	15.4	15.4	15.7	17.6	20.7	15.7
579	19.4	20.9	14.0	15.6	21.0	20.6	16.4	10.6	18.6	22.4	17.1	15.9
580	17.3	14.9	15.7	14.9	18.0	16.3	16.3	14.7	11.7	16.3	18.0	14.7
581	13.1	13.1	15.1	14.3	15.3	14.6	15.3	15.7	13.7	21.1	18.7	17.1
582	17.7	10.7	16.0	14.0	16.6	15.6	15.0	15.6	16.7	15.9	17.0	14.7
583	20.4	14.7	16.9	15.4	17.4	17.6	18.6	18.1	19.7	19.9	18.4	15.9
584	16.3	14.7	16.4	15.1	17.9	17.7	16.0	16.7	16.4	18.4	16.7	13.6
585	15.9	14.7	16.3	17.9	17.3	16.1	16.0	17.1	15.3	18.0	15.6	16.6
586	17.3	16.3	14.7	14.9	17.1	17.3	16.4	16.1	15.9	18.0	17.0	14.1
587	19.4	16.3	15.4	16.0	21.1	17.3	17.0	20.1	19.7	21.9	17.0	19.9
588	17.6	12.9	13.7	13.0	16.3	14.6	14.4	15.9	14.7	17.3	13.7	12.6
589	18.7	13.9	16.6	16.7	18.3	18.3	16.6	17.4	17.7	19.3	19.6	15.9
590	17.0	12.9	15.4	12.3	18.6	15.7	15.3	16.1	12.0	18.1	17.6	15.0
591	19.4	19.0	18.0	16.0	21.6	26.1	16.6	15.7	17.7	22.7	19.9	18.7
592	26.1	13.7	13.4	15.6	16.6	14.7	16.4	15.3	14.1	17.7	13.7	13.3
593	16.6	13.1	13.6	16.1	17.4	20.7	14.9	15.4	15.1	30.1	15.1	15.3
594	28.9	15.1	15.4	15.1	15.6	15.1	15.1	15.9	18.3	16.9	17.3	15.0
595	15.7	12.6	13.4	14.1	16.0	15.4	14.6	14.6	14.4	16.3	15.3	14.6
596	17.9	12.7	17.1	16.9	17.6	17.4	14.6	17.7	16.6	19.1	16.7	16.3
597	16.9	16.9	14.6	19.0	15.6	15.3	12.9	15.9	14.7	21.3	16.6	13.4
598	22.6	16.1	16.0	19.7	21.0	25.4	17.7	25.0	24.3	36.7	21.9	18.1
599	19.1	17.9	15.4	16.9	17.0	18.3	16.9	16.6	17.0	19.6	18.7	17.3
600	18.3	16.9	17.9	17.9	17.6	19.1	18.0	20.0	18.7	20.3	20.4	19.0
MEAN	18.7	15.1	15.6	16.0	17.8	17.6	16.0	16.6	16.5	20.0	17.5	15.8
S.D.	3.25	2.25	1.37	2.01	1.83	2.99	1.26	2.52	2.67	4.57	2.05	1.87
N	25	25	25	25	25	25	25	25	25	25	25	25

--: Data Unavailable

[a] Calculated daily food consumption for successive periods

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)[a]

STUDY: 152 GROUP: 4-F SEX: FEMALE
DOSE: 9.0 (mg base/kg/day)

ANIMAL #	DAY 169	DAY 176	DAY 182
576	18.3	20.1	21.5
577	15.1	16.3	17.3
578	17.3	18.6	18.3
579	16.6	17.3	23.8
580	15.3	16.1	20.5
581	17.4	13.4	17.0
582	14.4	16.4	18.7
583	17.1	17.3	20.5
584	15.3	16.9	19.8
585	15.9	18.6	23.8
586	16.3	18.3	20.7
587	17.7	18.9	18.8
588	14.3	15.4	17.7
589	17.7	17.7	23.3
590	17.3	17.9	18.3
591	17.3	16.9	23.8
592	16.1	19.1	18.3
593	14.6	16.3	24.8
594	15.7	17.9	18.8
595	12.6	14.4	15.8
596	16.0	19.7	--
597	13.4	15.0	--
598	21.3	21.3	--
599	14.4	16.1	--
600	17.7	19.3	--
MEAN	16.2	17.4	20.1
S.D.	1.82	1.86	2.64
N	25	25	20

--: Data Unavailable

[a]Calculated daily food consumption for successive periods

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Clinical Chemistry Test Directory

STUDY: UIC-15B

NO.	ABBR. / UNITS	DESCRIPTION / PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT--- MALE	---LOWER LIMIT--- FEMALE	---UPPER LIMIT--- MALE	---UPPER LIMIT--- FEMALE
1.	ALT IU/L	Alanine Aminotransferase Integer	NO			30	30	70	70
2.	SDH IU/L	Sorbitol Dehydrogenase 0.0	NO			10	10	30	30
3.	TP g/dL	Total Protein 0.0	NO			6.0	6.0	9.5	9.5
4.	ALB g/dL	Albumin 0.0	NO			3.4	3.4	5.6	5.6
5.	TBA umol/L	Total Bile Acids 0.0	NO			25.0	25.0	75.0	75.0
6.	ALKP IU/L	Alkaline Phosphatase Integer	NO			60	40	500	250
7.	LDH IU/L	Lactate Dehydrogenase Integer	NO			100	100	400	400
8.	CK IU/L	Creatine Kinase Integer	NO			100	100	400	400
9.	BUN mg/dL	Blood Urea Nitrogen 0.0	NO			12.0	12.0	22.0	22.0
10.	CREAT mg/dL	Creatinine 0.00	NO			0.40	0.40	0.80	0.80
11.	NA mEq/L	Sodium Integer	NO			140	140	148	148
12.	K mEq/L	Potassium 0.00	NO			5.00	5.00	7.00	7.00
13.	CL mEq/L	Chloride Integer	NO			95	95	115	115
14.	CA mg/dL	Calcium 0.0	NO			9.0	9.0	12.0	12.0
15.	IP mg/dL	Inorganic Phosphorus 0.0	NO			5.5	5.5	11.0	11.0

(REPORT CONTINUED)

DRAFT

Clinical Chemistry Test Directory

STUDY: UIC-15B

NO.	ABBR. UNITS	DESCRIPTION PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT--- MALE	FEMALE	---UPPER LIMIT--- MALE	FEMALE
16.	GLU	Glucose							
	mg/dL	Integer	NO			80	80	175	175
17.	GLOB	Globulin							
	g/dL	0.0	Operand A - Operand B	TP	ALB	2.5	2.5	5.0	5.0
18.	A/G	A/G Ratio							
	-	0.00	Operand A / Operand B	ALB	GLOB	0.75	0.75	1.50	1.50

(END OF REPORT)

UIC/TRL - CLINICAL CHEMISTRY DRAFT

HISTORICAL DATABASE REPORT

		ALB	ALKP	ALT	AST	BUN	CA	CHOL	CK
RAT CD Male									
control data1	MEAN	4.0	304	59	121	16.7	11.2	57	46
	SD	0.33	101.3	15.4	44.7	2.82	0.59	16.1	104.9
	N	140	140	140	45	140	140	80	175
RAT CD Female									
control data1	MEAN	4.3	222	61	140	17.8	11.2	60	41
	SD	0.46	92.0	14.5	67.8	3.14	0.57	11.8	93.9
	N	140	140	140	45	140	140	80	175
RAT CD Both									
control data1	MEAN	4.1	263	60	130	17.2	11.2	59	43
	SD	0.42	105.0	14.9	57.9	3.03	0.58	14.2	99.4
	N	280	280	280	90	280	280	160	350
RAT CD Male									
control data2	MEAN	4.1	213	58	91	16.9	11.1	67	86
	SD	0.34	78.4	16.4	15.3	3.06	0.50	18.0	218.6
	N	80	80	80	40	80	80	60	100
RAT CD Female									
control data2	MEAN	4.6	137	71	103	17.2	11.0	68	95
	SD	0.39	65.7	31.4	25.5	3.35	0.60	15.1	236.0
	N	60	60	60	20	60	60	40	80
RAT CD Both									
control data2	MEAN	4.3	181	64	95	17.0	11.0	68	90
	SD	0.43	82.2	24.7	19.8	3.18	0.54	16.8	225.9
	N	140	140	140	60	140	140	100	180

control data1-40-120 days

control data2-120-300 days

LABCAT CC4.32

HISTORICAL DATABASE REPORT

		CL	CREAT	GLU	IP	K	LDH	NA	SDH
RAT CD Male									
control data1	MEAN	111	0.50	159	10.1	5.95	168	144	14.5
	SD	6.3	0.060	36.9	1.11	0.503	134.5	1.7	5.76
	N	140	120	140	140	140	35	140	70
RAT CD Female									
control data1	MEAN	112	0.56	157	9.2	5.71	179	144	14.9
	SD	6.9	0.079	38.9	1.41	0.567	155.1	4.7	5.30
	N	140	120	140	140	140	35	140	70
RAT CD Both									
control data1	MEAN	111	0.53	158	9.6	5.83	174	144	14.7
	SD	6.6	0.076	37.9	1.35	0.549	144.2	3.5	5.52
	N	280	240	280	280	280	70	280	140
RAT CD Male									
control data2	MEAN	108	0.53	164	8.8	5.90	495	145	15.9
	SD	4.9	0.069	38.8	1.13	0.499	433.0	1.6	7.68
	N	80	70	80	80	80	20	80	40
RAT CD Female									
control data2	MEAN	107	0.59	147	7.9	5.56	463	145	13.3
	SD	6.4	0.080	30.4	1.15	0.493	231.3	1.8	4.84
	N	60	60	60	60	60	20	60	38
RAT CD Both									
control data2	MEAN	108	0.56	157	8.4	5.76	479	145	14.7
	SD	5.6	0.080	36.3	1.22	0.524	343.0	1.7	6.54
	N	140	130	140	140	140	40	140	78

control data1-40-120 days

control data2-120-300 days

LABCAT CC4.32

HISTORICAL DATABASE REPORT

		TBA	TBILI	TP	TRIG
RAT CD Male					
control data1	MEAN	40.9	0.11	7.7	129
	SD	24.58	0.026	0.65	49.5
	N	90	25	140	5
RAT CD Female					
control data1	MEAN	34.6	0.17	7.8	70
	SD	31.60	0.093	0.65	38.7
	N	90	25	140	5
RAT CD Both					
control data1	MEAN	37.7	0.14	7.7	100
	SD	28.41	0.074	0.65	52.3
	N	180	50	280	10
RAT CD Male					
control data2	MEAN	45.6	0.11	7.9	--
	SD	24.49	0.023	0.59	--
	N	40	40	80	--
RAT CD Female					
control data2	MEAN	51.0	0.11	8.4	--
	SD	38.70	0.018	0.92	--
	N	40	20	60	--
RAT CD Both					
control data2	MEAN	48.3	0.11	8.1	--
	SD	32.29	0.021	0.80	--
	N	80	60	140	--

(--)-Data Unavailable
control data1-40-120 days
control data2-120-300 days

LABCAT CC4.32

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALT

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	57	62	58
402	39	64	94
403	55	70	70
404	47	54	73
405	63	56	71
406	51	52	63
407	68	60	69
408	44	102	111
409	49	70	76
410	56	61	68
MEAN	53	65	75
SD	8.7	14.3	15.7
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	65	70	81
452	45	46	47
453	49	57	44
454	49	66	193
455	40	41	52
456	60	70	82
457	66	86	91
458	45	54	70
459	43	68	70
460	62	64	77
MEAN	52	62	81
SD	9.8	13.1	42.5
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALT

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	52	69	72
502	57	58	63
503	47	55	80
504	42	55	43
505	46	48	45
506	50	52	67
507	55	64	53
508	65	80	73
509	53	65	87
510	62	57	65
MEAN	53	60	65
SD	7.2	9.4	14.4
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	46	69	138
552	40	113	111
553	56	63	111
554	56	81	79
555	43	73	70
556	51	102	119
557	38	50	60
558	48	62	--
559	45	59	45
560	52	96	84
561	--	--	69
MEAN	48	77	89
SD	6.3	20.7	29.7
N	10	10	10

(--) - Data Unavailable

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: SOH

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	27.4	20.8	12.6
402	23.1	7.5	7.1
403	12.2	17.4	10.8
404	25.2	30.2	11.5
405	7.3	13.4	18.8
406	5.2	44.2	13.2
407	15.0	8.3	17.2
408	22.6	36.6	15.0
409	10.8	19.2	18.2
410	6.3	3.1	5.7
MEAN	15.5	20.1	13.0
SD	8.40	13.31	4.44
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	10.5	11.9	23.1
452	24.7	9.3	26.4
453	37.2	10.6	15.8
454	18.0	17.7	21.7
455	18.1	5.4	5.2
456	19.1	17.5	21.4
457	20.7	20.8	19.3
458	5.4	18.5	5.4
459	13.5	24.7	12.1
460	19.6	27.8	9.3
MEAN	18.7	16.4	16.0
SD	8.53	7.08	7.60
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: SDH

SEX: MALE
UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	4.6	35.6	7.8
502	15.7	20.3	4.5
503	6.5	18.0	19.1
504	36.0	9.6	12.8
505	28.4	7.2	6.9
506	13.2	24.5	16.9
507	27.1	24.5	23.5
508	6.9	11.6	10.3
509	15.0	18.3	17.5
510	9.4	12.5	4.9
MEAN	16.3	18.2	12.4
SD	10.71	8.55	6.57
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	20.0	19.7	7.0
552	7.0	18.8	19.9
553	16.2	7.9	17.9
554	16.8	25.0	30.3
555	29.6	18.3	6.4
556	23.7	11.2	15.9
557	24.1	19.3	24.4
558	18.6	6.2	--
559	17.0	20.7	13.7
560	17.0	19.7	12.9
561	--	--	9.6
MEAN	19.0	16.7	15.8
SD	6.02	6.10	7.62
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Protein

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	7.7	8.6	6.8
402	8.4	8.3	7.1
403	8.2	9.4	7.5
404	7.8	7.5	7.2
405	6.0	8.8	8.2
406	8.0	8.5	8.2
407	8.4	8.8	7.3
408	6.8	7.8	7.8
409	7.6	7.8	8.5
410	8.4	7.8	7.3
MEAN	7.7	8.3	7.6
SD	0.78	0.60	0.56
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	6.8	7.8	7.3
452	8.0	7.5	7.7
453	7.5	7.8	6.4
454	8.6	7.7	6.4
455	7.6	7.5	7.4
456	7.9	7.7	8.0
457	7.[illegible]	8.7	8.3
458	7.8	8.1	7.3
459	8.3	7.9	7.5
460	8.0	8.3	7.0
MEAN	7.8	7.9	7.3
SD	0.48	0.37	0.61
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Protein

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	7.8	8.4	8.2
502	7.8	7.0	8.2
503	8.0	8.3	6.9
504	7.5	8.3	7.5
505	8.1	7.3	7.8
506	7.4	7.6	7.9
507	7.4	7.6	7.5
508	8.3	8.7	7.7
509	6.9	8.5	7.3
510	7.7	8.1	7.0
MEAN	7.7	8.0	7.6
SD	0.41	0.57	0.45
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	7.4	6.9	7.4
552	7.3	8.1	6.8
553	8.5	7.5	7.8
554	8.2	7.7	7.2
555	7.8	8.2	6.7
556	8.0	7.7	6.8
557	7.9	7.9	6.7
558	7.4	8.0	--
559	8.4	8.7	7.9
560	8.4	8.3	7.7
561	--	--	7.6
MEAN	7.9	7.9	7.3
SD	0.45	0.49	0.48
N	10	10	10

(--) - Data Unavailable

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Albumin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	4.0	4.9	4.5
402	4.0	4.2	4.0
403	4.2	4.8	4.4
404	4.0	3.7	4.5
405	3.3	4.5	4.2
406	4.1	4.2	3.9
407	4.6	4.6	4.5
408	3.5	4.2	3.8
409	4.0	3.9	3.9
410	4.1	3.9	4.4
MEAN	4.0	4.3	4.2
SD	0.36	0.40	0.28
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	3.7	4.2	4.1
452	3.8	3.9	3.6
453	3.6	3.8	3.9
454	4.3	4.0	4.1
455	4.0	4.1	4.3
456	3.9	4.1	4.0
457	3.8	4.4	3.7
458	4.0	4.4	4.1
459	4.3	3.9	3.8
460	4.0	4.3	4.3
MEAN	3.9	4.1	4.0
SD	0.23	0.21	0.24
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Albumin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	3.9	4.7	4.3
502	4.0	3.8	4.2
503	3.9	4.2	4.5
504	3.9	4.6	3.8
505	4.0	3.7	3.9
506	3.8	3.9	3.7
507	4.3	3.9	3.9
508	4.6	4.3	4.0
509	4.2	4.6	4.5
510	3.9	4.3	4.5
MEAN	4.1	4.2	4.1
SD	0.25	0.36	0.31
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	3.9	3.9	3.8
552	3.9	4.5	4.3
553	4.3	4.1	4.1
554	4.2	4.3	3.9
555	4.2	4.4	4.3
556	4.0	4.3	4.1
557	4.2	3.9	4.3
558	4.3	4.5	--
559	4.2	4.7	4.3
560	4.0	4.3	4.0
561	--	--	3.8
MEAN	4.1	4.3	4.1
SD	0.15	0.26	0.21
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Globulin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLOB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	3.7	3.7	2.3
402	4.4	4.1	3.1
403	4.0	4.6	3.1
404	3.8	3.8	2.7
405	2.7	4.3	4.0
406	3.9	4.3	4.3
407	3.8	4.2	2.8
408	3.3	3.6	4.0
409	3.6	3.9	4.6
410	4.3	3.9	2.9
MEAN	3.8	4.0	3.4
SD	0.49	0.31	0.78
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	3.1	3.6	3.2
452	4.2	3.6	4.1
453	3.9	4.0	2.5
454	4.3	3.7	2.3
455	3.6	3.4	3.1
456	4.0	3.6	4.0
457	3.9	4.3	4.6
458	3.8	3.7	3.2
459	4.0	4.0	3.7
460	4.0	4.0	2.7
MEAN	3.9	3.8	3.3
SD	0.34	0.27	0.75
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Globulin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLOB

SEX: MALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	3.9	3.7	3.9
502	3.8	3.2	4.0
503	4.1	4.1	2.4
504	3.6	3.7	3.7
505	4.1	3.6	3.9
506	3.6	3.7	4.2
507	3.1	3.7	3.6
508	3.7	4.4	3.7
509	2.7	3.9	2.8
510	3.8	3.8	2.5
MEAN	3.6	3.8	3.5
SD	0.44	0.32	0.65
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	3.5	3.0	3.6
552	3.4	3.6	2.5
553	4.2	3.4	3.7
554	4.0	3.4	3.3
555	3.6	3.8	2.4
556	4.0	3.4	2.7
557	3.7	4.0	2.4
558	3.1	3.5	--
559	4.2	4.0	3.6
560	4.4	4.0	3.7
561	--	--	3.8
MEAN	3.8	3.6	3.2
SD	0.41	0.33	0.60
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: A/G

SEX: MALE

UNITS: -

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	1.08	1.32	1.96
402	0.91	1.02	1.29
403	1.05	1.04	1.42
404	1.05	0.97	1.67
405	1.22	1.05	1.05
406	1.05	0.98	0.91
407	1.21	1.10	1.61
408	1.06	1.17	0.95
409	1.11	1.00	0.85
410	0.95	1.00	1.52
MEAN	1.07	1.07	1.32
SD	0.097	0.108	0.375
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	1.19	1.17	1.28
452	0.90	1.08	0.88
453	0.92	0.95	1.56
454	1.00	1.08	1.78
455	1.11	1.21	1.39
456	0.98	1.14	1.00
457	0.97	1.02	0.80
458	1.05	1.19	1.28
459	1.08	0.98	1.03
460	1.00	1.08	1.59
MEAN	1.02	1.09	1.26
SD	0.089	0.088	0.327
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: UIC-158
STUDY NO: 152
ABBR: A/G

SEX: MALE

UNITS: -

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	1.00	1.27	1.10
502	1.05	1.19	1.05
503	0.95	1.02	1.88
504	1.08	1.24	1.03
505	0.98	1.03	1.00
506	1.06	1.05	0.88
507	1.39	1.05	1.08
508	1.24	0.98	1.08
509	1.56	1.18	1.61
510	1.03	1.13	1.80
MEAN	1.13	1.11	1.25
SD	0.200	0.101	0.365
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	1.11	1.30	1.06
552	1.15	1.25	1.72
553	1.02	1.21	1.11
554	1.05	1.26	1.18
555	1.17	1.16	1.79
556	1.00	1.26	1.52
557	1.14	0.98	1.79
558	1.39	1.29	--
559	1.00	1.18	1.19
560	0.91	1.08	1.08
561	--	--	1.00
MEAN	1.09	1.20	1.34
SD	0.132	0.101	0.324
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Bile Acids

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: MALE

UNITS: umol/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	19.5	22.6	20.4
402	23.8	68.8	89.0
403	20.1	39.9	39.0
404	23.2	58.7	35.8
405	45.8	44.1	140.6
406	23.2	23.4	66.6
407	22.9	22.7	34.5
408	23.6	73.9	68.9
409	23.8	62.1	64.1
410	21.0	27.8	38.9
MEAN	24.7	44.4	59.8
SD	7.58	20.18	35.22
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	102.9	50.7	48.5
452	38.6	38.8	67.8
453	29.0	24.8	16.4
454	22.7	23.7	32.7
455	31.4	53.4	38.4
456	21.2	43.9	61.1
457	22.9	41.9	51.5
458	32.1	28.3	30.4
459	18.9	110.5	83.0
460	21.6	47.1	52.4
MEAN	34.1	46.3	48.2
SD	24.94	24.88	19.59
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Bile Acids

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: MALE

UNITS: umol/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	19.9	111.0	89.1
502	16.8	77.0	57.0
503	22.1	49.2	122.9
504	26.2	60.8	24.2
505	54.5	69.4	26.8
506	22.6	26.7	86.4
507	24.5	103.2	58.4
508	27.3	53.5	37.6
509	44.3	42.8	33.5
510	80.0	79.2	66.7
MEAN	33.8	67.3	60.3
SD	20.01	26.35	31.87
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	50.9	69.0	116.1
552	27.6	60.7	156.9
553	17.8	39.0	128.0
554	32.7	36.7	72.8
555	24.2	113.4	44.7
556	52.1	84.6	95.1
557	20.9	43.7	42.0
558	40.9	90.7	--
559	31.1	43.2	102.3
560	31.9	40.8	72.5
561	--	--	119.5
MEAN	33.0	62.2	95.0
SD	11.72	26.53	37.05
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alkaline Phosphatase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALKP

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	456	313	232
402	312	192	166
403	499	335	313
404	316	200	182
405	339	250	223
406	328	168	121
407	282	148	146
408	264	167	118
409	331	205	193
410	555	383	343
MEAN	368	236	204
SD	98.7	80.9	76.0
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	424	334	269
452	336	205	154
453	296	196	70
454	329	200	198
455	318	192	160
456	354	238	137
457	380	224	238
458	287	178	169
459	319	189	136
460	361	261	202
MEAN	340	222	173
SD	41.0	46.8	56.5
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alkaline Phosphatase

STUDY IO: UIC-158 SEX: MALE
STUDY NO: 152
ABBR: ALKP UNITS: IU/L

Animal IO	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	314	201	134
502	349	215	168
503	227	142	134
504	256	147	78
505	524	366	330
506	258	177	125
507	347	195	156
508	554	400	334
509	289	163	176
510	517	353	279
MEAN	364	236	191
SD	122.7	98.0	90.1
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	219	193	170
552	404	311	305
553	312	224	200
554	529	299	272
555	285	165	152
556	354	268	242
557	328	190	197
558	221	177	--
559	369	226	194
560	226	166	125
561	--	--	170
MEAN	325	222	203
SD	96.8	54.0	55.5
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Lactate Dehydrogenase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: LDH

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	157	262	573
402	225	248	586
403	165	319	349
404	113	167	506
405	558	659	403
406	70	156	133
407	66	639	230
408	167	220	959
409	56	214	158
410	129	1845	1266
MEAN	171	473	516
SD	146.3	515.2	359.7
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	383	533	146
452	71	373	149
453	236	418	189
454	42	255	425
455	159	1177	526
456	193	414	237
457	96	175	211
458	166	278	696
459	73	204	467
460	211	300	1168
MEAN	163	413	421
SD	101.5	289.8	321.1
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Lactate Dehydrogenase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: LDH

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	50	236	449
502	119	252	555
503	97	318	239
504	175	501	325
505	155	571	736
506	485	214	288
507	80	137	188
508	95	483	366
509	54	258	166
510	454	356	741
MEAN	176	333	405
SD	159.6	142.3	210.9
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	335	518	549
552	245	620	503
553	133	498	484
554	76	176	225
555	170	426	1072
556	84	482	617
557	141	336	307
558	79	880	--
559	399	323	252
560	217	344	312
561	--	--	277
MEAN	188	460	460
SD	111.1	193.4	255.3
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatine Kinase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CK

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	256	119	181
402	273	415	276
403	99	127	219
404	360	342	1012
405	661	181	163
406	44	131	326
407	153	201	387
408	163	129	814
409	164	831	336
410	250	644	1304
MEAN	242	312	502
SD	173.4	249.1	397.4
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	856	178	60
452	71	930	87
453	182	203	138
454	55	373	169
455	401	983	179
456	270	218	642
457	221	91	1094
458	131	274	350
459	64	1119	210
460	790	192	846
MEAN	304	456	378
SD	293.8	392.0	358.6
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatine Kinase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CK

SEX: MALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	88	225	999
502	69	812	200
503	88	137	99
504	207	141	124
505	78	604	339
506	459	125	107
507	83	516	140
508	85	1021	139
509	162	130	97
510	382	98	1084
MEAN	170	381	333
SD	140.2	335.6	380.8
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	646	208	1841
552	99	122	171
553	105	308	1791
554	77	81	384
555	61	135	286
556	90	639	461
557	108	212	102
558	63	233	--
559	307	177	139
560	109	141	309
561	--	--	577
MEAN	167	226	606
SD	182.7	159.0	654.3
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: BUN

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	21.9	22.1	20.1
402	16.3	26.4	20.1
403	18.5	24.2	18.6
404	18.6	17.3	17.3
405	17.5	23.3	14.9
406	16.9	16.8	15.1
407	19.6	23.9	18.2
408	16.9	21.5	15.3
409	17.7	18.3	22.5
410	19.5	16.1	18.5
MEAN	18.3	21.0	18.1
SD	1.67	3.61	2.48
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	17.5	17.1	13.2
452	15.4	15.0	17.4
453	16.5	14.7	8.2
454	18.1	14.9	15.2
455	17.3	17.1	16.8
456	18.?	18.0	15.4
457	19.1	23.6	20.7
458	17.7	14.5	14.6
459	14.0	16.7	14.7
460	19.2	18.5	18.7
MEAN	17.3	17.0	15.5
SD	1.62	2.73	3.38
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: BUN

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	16.9	22.3	18.4
502	16.7	15.9	15.8
503	16.1	20.4	19.3
504	17.2	19.2	13.4
505	16.6	18.2	15.2
506	18.0	13.6	16.4
507	19.3	14.2	15.0
508	14.4	18.3	16.1
509	16.5	17.1	13.1
510	18.0	21.4	15.0
MEAN	17.0	18.1	15.8
SD	1.31	2.91	1.95
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	14.8	12.7	12.8
552	16.0	20.4	15.6
553	17.8	15.7	17.8
554	12.9	17.4	13.3
555	19.5	16.6	17.9
556	16.5	15.5	12.8
557	15.2	11.7	12.6
558	19.2	16.1	--
559	14.6	14.4	12.9
560	11.8	13.1	12.5
561	--	--	12.1
MEAN	15.8	15.4	14.0
SD	2.52	2.54	2.23
N	10	10	10

(--) - Data Unavailable

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatinine

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CREAT

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	0.60	0.59	0.58
402	0.46	0.64	0.64
403	0.54	0.59	0.68
404	0.50	0.51	0.61
405	0.59	0.54	0.55
406	0.47	0.51	0.54
407	0.62	0.59	0.60
408	0.64	0.73	0.56
409	0.48	0.54	0.61
410	0.48	0.50	0.65
MEAN	0.54	0.57	0.60
SD	0.069	0.071	0.046
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	0.57	0.50	0.54
452	0.54	0.52	0.69
453	0.61	0.51	0.61
454	0.54	0.53	0.58
455	0.49	0.46	0.56
456	0.48	0.49	0.59
457	0.51	0.58	0.53
458	0.52	0.52	0.53
459	0.55	0.61	0.54
460	0.54	0.49	0.56
MEAN	0.56	0.52	0.57
SD	0.094	0.044	0.049
N	10	10	10

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatinine

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CREAT

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	0.54	0.75	0.62
502	0.46	0.59	0.54
503	0.54	0.63	0.88
504	0.53	0.55	0.53
505	0.49	0.49	0.56
506	0.51	0.48	0.54
507	0.52	0.60	0.64
508	0.61	0.61	0.60
509	0.48	0.56	0.62
510	0.54	0.52	0.63
MEAN	0.52	0.58	0.62
SD	0.042	0.079	0.102
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	0.93	0.51	0.61
552	0.55	0.60	0.61
553	0.60	0.55	0.64
554	0.56	0.55	0.54
555	0.61	0.62	0.60
556	0.53	0.69	0.61
557	0.53	0.50	0.52
558	0.59	0.55	--
559	0.54	0.56	0.52
560	0.48	0.57	0.57
561	--	--	0.60
MEAN	0.59	0.57	0.58
SD	0.125	0.055	0.042
N	10	10	10

(--) - Data Unavailable

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sodium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NA

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	152	145	147
402	143	143	148
403	143	146	147
404	142	144	148
405	148	145	145
406	143	146	148
407	146	145	148
408	141	146	145
409	144	147	145
410	141	144	145
MEAN	144	145	147
SD	3.5	1.2	1.4
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	149	145	148
452	154	145	146
453	151	146	148
454	145	145	144
455	144	142	146
456	144	144	146
457	145	147	148
458	145	147	146
459	146	145	145
460	146	146	147
MEAN	147	145	146
SD	3.3	1.5	1.3
N	10	10	10

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sodium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NA

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	144	146	146
502	145	146	147
503	146	145	147
504	143	146	145
505	144	143	142
506	151	147	148
507	146	145	144
508	145	144	145
509	145	147	149
510	144	144	145
MEAN	145	145	146
SD	2.2	1.3	2.0
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	149	143	146
552	150	141	144
553	145	144	144
554	147	145	144
555	148	145	144
556	154	145	145
557	146	146	144
558	153	145	--
559	144	145	142
560	143	144	146
561	--	--	145
MEAN	148	144	144
SD	3.7	1.4	1.2
N	10	10	10

(--) - Data Unavailable

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Potassium

STUDY ID: UIC-158
STUDY NO: 152
ABBR: K

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	6.98	5.73	5.78
402	6.10	5.38	5.85
403	6.30	5.95	6.17
404	6.29	7.01	6.01
405	6.38	5.87	6.27
406	6.07	6.21	5.25
407	6.54	6.34	6.28
408	5.14	5.47	5.73
409	5.79	5.73	5.28
410	6.45	6.42	6.26
MEAN	6.20	6.01	5.89
SD	0.489	0.493	0.387
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	6.17	6.10	5.92
452	5.80	6.25	5.51
453	6.90	5.94	5.20
454	5.79	5.97	5.90
455	5.79	5.57	5.73
456	5.76	5.83	5.68
457	7.06	5.67	6.12
458	6.20	6.51	6.22
459	6.80	4.54	5.61
460	5.52	6.41	6.11
MEAN	6.18	5.88	5.80
SD	0.552	0.559	0.316
N	10	10	10

 DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Potassium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: K

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	4.98	4.65	6.27
502	5.85	6.09	6.23
503	6.32	6.03	5.47
504	5.49	5.77	5.92
505	5.92	6.21	6.17
506	6.13	6.46	5.09
507	5.92	5.55	5.34
508	4.83	5.12	5.77
509	5.49	5.78	5.86
510	5.73	5.79	6.25
MEAN	5.67	5.75	5.84
SD	0.476	0.533	0.418
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	6.65	6.68	5.74
552	5.65	5.85	5.47
553	6.34	6.28	5.31
554	6.01	4.96	5.52
555	6.62	5.92	5.86
556	7.57	6.01	5.68
557	6.23	5.97	5.90
558	6.59	5.78	--
559	6.11	6.26	5.85
560	6.21	5.78	5.57
561	--	--	5.14
MEAN	6.40	5.95	5.60
SD	0.515	0.446	0.251
N	10	10	10

(--) - Data Unavailable

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Chloride

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CL

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	105	111	103
402	105	109	101
403	105	108	103
404	107	104	101
405	103	110	107
406	106	98	102
407	110	108	99
408	103	109	103
409	101	104	108
410	107	96	104
MEAN	105	106	103
SD	2.5	5.1	2.7
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	102	97	97
452	100	100	108
453	106	99	108
454	104	102	103
455	102	101	102
456	107	97	102
457	102	110	105
458	114	94	99
459	101	102	106
460	103	97	101
MEAN	104	100	103
SD	4.1	4.4	3.7
N	10	10	10

 DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Chloride

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CL

SEX: MALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	112	114	107
502	105	100	104
503	104	109	106
504	104	108	108
505	106	100	104
506	106	97	108
507	106	101	110
508	110	110	103
509	109	110	100
510	103	109	103
MEAN	107	106	105
SD	2.9	5.7	3.0
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	104	101	116
552	106	112	103
553	102	100	104
554	102	112	110
555	103	109	102
556	104	115	103
557	103	102	102
558	107	109	--
559	108	111	104
560	108	115	105
561	--	--	107
MEAN	105	109	106
SD	2.4	5.6	4.4
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Calcium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CA

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	11.7	10.3	11.5
402	11.1	10.7	11.3
403	11.1	11.3	12.5
404	11.3	11.4	11.6
405	12.3	11.0	11.7
406	11.3	10.9	11.1
407	11.6	10.5	11.8
408	10.7	10.7	10.8
409	10.8	11.4	11.4
410	10.8	10.4	11.1
MEAN	11.3	10.9	11.5
SD	0.49	0.41	0.47
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	12.2	10.8	11.9
452	11.1	10.6	11.9
453	10.7	10.4	11.7
454	11.0	10.6	11.3
455	11.2	10.6	11.6
456	11.5	11.3	11.8
457	11.5	10.9	11.5
458	10.9	11.1	11.3
459	11.2	11.3	11.3
460	12.2	11.3	12.2
MEAN	11.4	10.9	11.7
SD	0.51	0.34	0.31
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Calcium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CA

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	11.2	11.3	11.4
502	10.7	10.8	11.2
503	10.9	11.3	12.3
504	10.7	10.8	11.0
505	11.1	10.9	11.3
506	11.0	10.5	11.5
507	11.6	11.2	11.8
508	11.1	10.6	11.8
509	11.7	10.8	11.6
510	11.4	10.0	11.6
MEAN	11.1	10.8	11.6
SD	0.34	0.40	0.37
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	10.6	10.2	11.7
552	10.9	10.2	11.5
553	11.6	10.5	11.4
554	11.1	10.6	10.7
555	10.9	10.4	11.2
556	11.6	10.3	11.4
557	11.4	10.8	11.5
558	10.9	10.4	--
559	11.0	10.9	11.2
560	11.1	10.6	10.8
561	--	--	11.4
MEAN	11.1	10.5	11.3
SD	0.33	0.24	0.32
N	10	10	10

(--) - Data Unavailable

 DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	9.6	7.5	8.1
402	9.0	9.8	10.2
403	10.0	7.2	7.7
404	8.9	8.0	8.8
405	9.5	7.7	9.5
406	9.8	5.9	7.0
407	9.6	7.6	8.7
408	9.9	8.4	8.3
409	9.0	8.0	9.0
410	10.8	7.6	8.6
MEAN	9.6	7.8	8.6
SD	0.57	0.98	0.90
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	9.6	7.3	8.3
452	8.0	7.4	10.5
453	9.6	7.6	8.3
454	10.0	6.8	8.1
455	9.7	7.8	8.8
456	9.0	5.9	7.4
457	9.0	8.2	8.8
458	9.7	7.3	9.3
459	9.7	8.6	6.6
460	9.5	7.4	8.9
MEAN	9.4	7.4	8.5
SD	0.58	0.74	1.06
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	9.9	8.2	8.3
502	9.2	7.5	7.1
503	9.8	7.9	11.3
504	9.5	7.3	7.8
505	10.2	8.2	8.0
506	10.5	7.8	8.4
507	9.0	8.3	10.7
508	9.5	8.5	9.2
509	8.7	8.7	7.9
510	9.7	7.8	9.1
MEAN	9.6	8.0	8.8
SD	0.54	0.44	1.33
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	8.3	7.5	8.4
552	8.2	9.0	9.3
553	8.4	6.7	10.0
554	9.3	7.2	7.5
555	10.3	8.0	8.4
556	8.4	9.6	9.1
557	10.6	7.1	8.4
558	8.7	8.8	--
559	9.2	8.5	7.9
560	10.1	8.2	6.9
561	--	--	8.0
MEAN	9.2	8.1	8.4
SD	0.90	0.93	0.90
N	10	10	10

(--) - Data Unavailable

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Glucose

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1 M:0 mg base/kg/day			
401	134	156	157
402	168	268	277
403	163	147	180
404	146	176	188
405	160	139	193
406	138	115	135
407	141	143	175
408	265	254	170
409	129	167	257
410	165	131	184
MEAN	161	170	192
SD	39.1	51.3	43.4
N	10	10	10
GROUP: 2-M:0.5 mg base/kg/day			
451	149	118	147
452	141	117	280
453	147	109	233
454	136	120	110
455	144	140	148
456	131	122	228
457	140	191	188
458	137	118	130
459	154	260	183
460	170	136	196
MEAN	145	143	184
SD	11.1	47.3	52.5
N	10	10	10

 DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Glucose

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: MALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-M:2.0 mg base/kg/day			
501	185	236	186
502	133	177	123
503	146	147	248
504	141	134	142
505	147	133	142
506	157	142	267
507	120	197	263
508	168	184	158
509	125	163	146
510	190	132	188
MEAN	151	165	186
SD	23.8	34.2	54.3
N	10	10	10
GROUP: 4-M:9.0 mg base/kg/day			
551	160	111	161
552	126	140	174
553	135	110	219
554	134	137	136
555	128	139	165
556	122	176	163
557	140	112	145
558	135	138	--
559	121	140	138
560	144	134	106
561	--	--	201
MEAN	135	134	161
SD	11.7	19.6	32.6
N	10	10	10

(--) - Data Unavailable

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: ALT

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	42	47	87
427	58	61	225
428	57	80	95
429	45	53	65
430	64	71	76
431	55	63	83
432	50	80	144
433	42	55	70
434	50	83	117
435	49	50	168
MEAN	51	64	113
SD	7.3	13.4	51.6
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	48	74	128
477	49	69	103
478	60	49	45
479	38	58	59
480	55	49	283
481	39	57	33
482	38	52	86
483	46	63	60
484	57	61	123
485	51	68	64
MEAN	48	60	98
SD	8.4	8.6	72.3
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALT

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	51	70	108
527	49	71	80
528	53	66	66
529	49	50	132
530	51	57	99
531	48	87	45
532	54	63	93
533	44	72	251
534	49	82	243
535	43	57	54
MEAN	49	68	117
SD	3.5	11.4	73.2
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	47	41	99
577	57	53	60
578	51	65	156
579	78	97	96
580	54	71	75
581	54	79	71
582	64	82	86
583	66	77	67
584	52	74	70
585	51	66	111
MEAN	57	71	89
SD	9.3	15.6	28.6
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: SDH

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	6.9	6.5	0.0
427	18.9	19.0	13.1
428	12.9	14.8	15.7
429	12.9	7.1	6.5
430	16.5	14.1	11.6
431	17.3	8.3	14.2
432	15.2	16.5	5.0
433	16.3	12.3	15.8
434	14.3	9.7	5.5
435	18.1	13.7	0.0
MEAN	14.9	12.2	8.7
SD	3.48	4.18	6.12
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	11.4	15.7	9.3
477	16.1	15.7	5.8
478	15.8	11.4	10.2
479	16.6	18.3	11.1
480	15.3	9.1	11.5
481	15.4	7.7	7.4
482	14.8	6.8	0.0
483	12.9	9.6	5.3
484	15.5	28.6	13.6
485	13.8	8.4	13.2
MEAN	14.8	13.1	8.7
SD	1.60	6.69	4.19
N	10	10	10

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: SDH

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	15.9	33.0	3.9
527	19.0	22.5	0.0
528	20.4	14.5	12.5
529	10.8	6.5	7.4
530	11.3	29.2	9.9
531	10.3	14.6	4.3
532	26.9	18.6	15.8
533	16.8	16.9	0.0
534	17.0	20.7	11.2
535	4.0	10.2	4.9
MEAN	15.2	18.7	7.0
SD	6.40	8.11	5.30
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	19.0	16.5	0.0
577	22.1	19.5	6.2
578	15.5	17.5	0.0
579	21.8	19.0	4.3
580	16.9	19.2	8.0
581	18.9	20.1	13.2
582	18.2	15.2	0.0
583	15.2	12.1	10.1
584	21.6	18.2	0.9
585	18.4	17.0	15.1
MEAN	18.8	17.4	5.8
SD	2.49	2.40	5.70
N	10	10	10

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Protein

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	7.3	6.8	9.2
427	7.7	7.9	10.0
428	7.2	7.3	9.4
429	6.8	7.7	9.4
430	8.1	8.8	9.1
431	6.9	7.7	9.4
432	7.1	6.8	9.3
433	6.9	7.7	10.3
434	7.5	8.5	11.7
435	7.5	8.1	10.8
MEAN	7.3	7.7	9.9
SD	0.41	0.65	0.85
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	6.7	8.0	9.2
477	6.9	8.4	9.5
478	7.4	7.7	10.0
479	7.5	8.4	8.6
480	8.3	8.1	9.4
481	7.2	9.2	9.6
482	6.3	7.4	8.4
483	6.9	7.9	8.7
484	7.5	7.3	9.3
485	7.6	8.0	8.8
MEAN	7.2	8.0	9.2
SD	0.56	0.55	0.51
N	10	10	10

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Protein

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TP

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	7.3	7.5	9.5
527	7.0	7.5	9.2
528	7.7	8.1	9.8
529	6.8	7.7	10.2
530	7.1	6.9	9.5
531	7.8	9.3	9.9
532	8.0	8.2	11.1
533	7.5	8.1	9.7
534	6.9	7.0	9.9
535	7.4	7.0	9.2
MEAN	7.4	7.7	9.8
SD	0.40	0.73	0.56
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	6.8	6.9	8.2
577	7.7	8.7	8.9
578	7.0	8.5	10.0
579	7.8	8.0	9.7
580	7.0	7.2	9.1
581	7.1	7.6	8.3
582	7.3	6.7	9.5
583	6.8	7.3	9.3
584	7.9	7.8	9.1
585	7.0	7.9	8.7
MEAN	7.2	7.7	9.1
SD	0.41	0.65	0.58
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Albumin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	4.1	4.2	4.2
427	4.3	4.5	4.4
428	3.9	4.4	4.7
429	4.1	4.6	4.7
430	4.6	5.1	4.5
431	3.7	4.2	4.4
432	3.8	4.4	4.8
433	3.9	4.7	5.1
434	3.9	5.0	4.7
435	4.4	4.5	5.0
MEAN	4.1	4.6	4.7
SD	0.29	0.30	0.28
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	3.8	4.4	4.3
477	3.5	4.4	4.5
478	4.1	4.3	5.0
479	4.2	4.7	4.7
480	4.3	4.4	4.7
481	4.0	5.5	4.5
482	3.6	4.1	4.4
483	3.9	4.6	4.4
484	4.3	4.5	4.9
485	4.2	5.0	4.8
MEAN	4.0	4.6	4.6
SD	0.28	0.40	0.23
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Albumin

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	4.2	4.6	4.9
527	3.9	5.0	4.6
528	4.3	4.7	4.4
529	3.6	4.1	5.0
530	3.8	3.9	4.7
531	4.2	5.3	4.9
532	4.4	4.4	4.9
533	4.2	4.6	4.5
534	3.8	4.1	4.8
535	4.1	4.3	4.6
MEAN	4.1	4.5	4.7
SD	0.26	0.43	0.20
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	3.6	4.2	4.2
577	4.3	5.1	4.6
578	3.7	4.6	5.1
579	4.4	4.5	4.6
580	4.0	4.5	4.7
581	3.7	4.0	4.3
582	3.9	4.0	4.8
583	3.8	4.5	5.1
584	4.3	4.7	4.9
585	3.9	4.3	4.4
MEAN	4.0	4.4	4.7
SD	0.28	0.33	0.31
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Globulin

STUDY ID: UIC-158
STUDY NO: 152
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	3.2	2.6	5.0
427	3.4	3.4	5.6
428	3.3	2.9	4.7
429	2.7	3.1	4.7
430	3.5	3.7	4.6
431	3.2	3.5	5.0
432	3.3	2.4	4.5
433	3.0	3.0	5.2
434	3.6	3.5	7.0
435	3.1	3.6	5.8
MEAN	3.2	3.2	5.2
SD	0.26	0.44	0.76
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	2.9	3.6	4.9
477	3.4	4.0	5.0
478	3.3	3.4	5.0
479	3.3	3.7	3.9
480	4.0	3.7	4.7
481	3.?	3.7	5.1
482	2.7	3.3	4.0
483	3.0	3.3	4.3
484	3.2	2.8	4.4
485	3.4	3.0	4.0
MEAN	3.2	3.5	4.5
SD	0.35	0.36	0.47
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Globulin

STUDY ID: UIC-158
STUDY NO: 152
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	3.1	2.9	4.6
527	3.1	2.5	4.6
528	3.4	3.4	5.4
529	3.2	3.6	5.2
530	3.3	3.0	4.8
531	3.6	4.0	5.0
532	3.6	3.8	6.2
533	3.3	3.5	5.2
534	3.1	2.9	5.1
535	3.3	2.7	4.6
MEAN	3.3	3.2	5.1
SD	0.19	0.50	0.49
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	3.2	2.7	4.0
577	3.4	3.6	4.3
578	3.3	3.9	4.9
579	3.4	3.5	5.1
580	3.0	2.7	4.4
581	3.4	3.6	4.0
582	3.4	2.7	4.7
583	3.0	2.8	4.2
584	3.6	3.1	4.2
585	3.1	3.6	4.3
MEAN	3.3	3.2	4.4
SD	0.20	0.47	0.37
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: UIC-158
STUDY NO: 152
ABBR: A/G

SEX: FEMALE
UNITS: -

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	1.28	1.62	0.84
427	1.26	1.32	0.79
428	1.18	1.52	1.00
429	1.52	1.48	1.00
430	1.31	1.38	0.98
431	1.16	1.20	0.88
432	1.15	1.83	1.07
433	1.30	1.57	0.98
434	1.08	1.43	0.67
435	1.42	1.25	0.86
MEAN	1.27	1.46	0.91
SD	0.133	0.188	0.121
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	1.31	1.22	0.88
477	1.03	1.10	0.90
478	1.24	1.26	1.00
479	1.27	1.27	1.21
480	1.08	1.19	1.00
481	1.25	1.49	0.88
482	1.33	1.24	1.10
483	1.30	1.39	1.02
484	1.34	1.61	1.11
485	1.24	1.67	1.20
MEAN	1.24	1.34	1.03
SD	0.104	0.189	0.123
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: UIC-158
STUDY NO: 152
ABBR: A/G

SEX: FEMALE

UNITS: -

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	1.35	1.59	1.07
527	1.26	2.00	1.00
528	1.26	1.38	0.81
529	1.13	1.14	0.96
530	1.15	1.30	0.98
531	1.17	1.33	0.98
532	1.22	1.16	0.79
533	1.27	1.31	0.87
534	1.23	1.41	0.94
535	1.24	1.59	1.00
MEAN	1.23	1.42	0.94
SD	0.065	0.253	0.089
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	1.13	1.56	1.05
577	1.26	1.42	1.07
578	1.12	1.18	1.04
579	1.29	1.29	0.90
580	1.33	1.67	1.07
581	1.09	1.11	1.08
582	1.15	1.48	1.02
583	1.27	1.61	1.21
584	1.19	1.52	1.17
585	1.26	1.19	1.02
MEAN	1.21	1.40	1.06
SD	0.083	0.198	0.085
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Bile Acids

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: FEMALE

UNITS: umol/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	26.0	35.1	78.5
427	13.2	27.4	124.3
428	36.4	47.2	38.0
429	21.9	42.3	151.5
430	19.9	24.6	94.3
431	22.1	34.4	59.3
432	18.9	39.3	83.5
433	59.8	128.3	84.5
434	20.2	29.0	47.6
435	17.3	43.8	177.3
MEAN	25.6	45.1	93.9
SD	13.51	30.14	44.84
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	19.0	30.7	41.8
477	27.6	97.6	73.2
478	16.1	40.2	96.1
479	19.3	31.5	82.7
480	20.2	23.7	156.4
481	24.5	43.1	45.1
482	18.6	52.8	65.7
483	20.0	46.8	64.5
484	21.0	277.8	81.9
485	40.8	222.2	115.7
MEAN	22.7	86.6	82.3
SD	7.13	89.41	34.15
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Total Bile Acids

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: TBA

SEX: FEMALE

UNITS: umol/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	71.2	93.8	62.0
527	16.2	58.3	121.3
528	30.9	46.6	53.4
529	19.0	69.6	44.9
530	23.4	21.2	115.4
531	35.1	87.3	84.4
532	24.3	35.4	50.2
533	21.0	36.3	75.4
534	15.7	56.8	54.8
535	37.7	91.7	163.1
MEAN	29.5	59.7	82.5
SD	16.51	25.49	38.92
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	31.5	33.4	159.6
577	22.6	145.4	82.4
578	55.9	102.8	596.7
579	71.7	63.6	221.0
580	27.0	127.0	47.3
581	37.3	101.0	130.5
582	12.5	26.9	85.7
583	38.5	101.5	66.4
584	52.5	87.2	79.6
585	18.9	112.9	69.4
MEAN	36.8	90.2	153.9
SD	18.47	38.40	164.18
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alkaline Phosphatase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: ALKP

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	167	105	118
427	237	147	111
428	168	105	86
429	232	126	121
430	301	189	205
431	191	113	77
432	217	119	86
433	234	149	106
434	153	115	102
435	233	112	89
MEAN	213	128	110
SD	44.4	26.5	36.5
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	201	129	79
477	312	232	175
478	206	112	99
479	136	100	74
480	260	111	82
481	147	114	105
482	228	351	78
483	299	180	134
484	224	124	89
485	355	308	225
MEAN	237	176	114
SD	70.5	90.7	50.0
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Alkaline Phosphatase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: ALKP

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	212	84	85
527	511	344	382
528	147	103	73
529	195	155	133
530	155	107	88
531	134	90	59
532	367	229	179
533	236	145	137
534	268	120	125
535	193	134	103
MEAN	242	151	136
SD	116.7	79.6	93.3
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	162	86	106
577	255	168	129
578	204	122	122
579	437	277	258
580	153	90	111
581	314	224	176
582	175	104	99
583	309	267	237
584	395	249	209
585	191	119	84
MEAN	260	171	153
SD	100.6	76.5	62.3
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Lactate Dehydrogenase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: LOH

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	810	853	505
427	223	187	1103
428	374	318	366
429	108	460	318
430	154	292	250
431	209	555	242
432	181	391	505
433	123	453	273
434	113	639	513
435	230	287	756
MEAN	253	444	483
SD	211.0	197.3	270.4
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	407	138	839
477	336	722	356
478	265	367	487
479	62	152	437
480	343	471	1042
481	188	815	293
482	100	388	442
483	215	544	755
484	180	249	544
485	302	727	302
MEAN	240	457	550
SD	110.8	242.7	249.7
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Lactate Dehydrogenase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: LDH

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	315	164	662
527	170	187	592
528	637	322	127
529	518	703	510
530	466	344	378
531	529	403	484
532	113	156	149
533	169	328	968
534	131	207	455
535	872	386	534
MEAN	392	320	486
SD	254.2	163.4	243.2
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	64	340	417
577	229	212	248
578	228	311	999
579	244	402	539
580	356	290	300
581	119	217	267
582	137	852	522
583	212	521	596
584	127	280	432
585	109	327	545
MEAN	183	375	487
SD	86.7	190.0	218.5
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatine Kinase

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CK

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	645	318	201
427	126	206	763
428	176	154	670
429	105	159	127
430	340	589	138
431	182	297	103
432	135	1687	291
433	89	373	141
434	127	310	230
435	188	179	317
MEAN	211	427	298
SD	167.9	461.4	232.5
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	214	114	387
477	178	386	120
478	140	182	293
479	63	109	341
480	196	489	206
481	156	298	109
482	80	1890	1446
483	150	321	384
484	131	375	287
485	163	726	1212
MEAN	147	489	479
SD	47.2	525.6	462.0
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatine Kinase

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CK

SEX: FEMALE

UNITS: IU/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	350	216	237
527	119	831	1818
528	273	159	187
529	337	346	468
530	212	336	136
531	212	166	366
532	99	181	71
533	103	648	2834
534	82	577	142
535	808	619	267
MEAN	260	408	653
SD	216.3	242.1	921.2
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	131	173	170
577	233	134	604
578	152	513	2514
579	130	119	156
580	233	400	432
581	92	176	126
582	116	384	276
583	126	250	326
584	111	120	548
585	163	131	736
MEAN	149	240	589
SD	48.7	142.1	707.0
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: UIC-158
STUDY NO: 152
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	18.4	15.3	23.1
427	16.5	14.8	17.7
428	19.9	19.1	19.6
429	20.8	14.5	17.1
430	17.5	19.6	18.9
431	19.0	14.6	17.5
432	17.5	18.4	17.7
433	18.6	15.8	16.3
434	16.1	23.0	19.5
435	19.6	12.4	20.1
MEAN	18.4	16.8	18.8
SD	1.50	3.18	1.96
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	18.3	21.3	15.0
477	15.9	13.3	19.2
478	19.9	16.3	20.2
479	16.4	15.7	15.9
480	16.4	15.8	18.1
481	16.[illegible]	15.2	14.7
482	19.4	21.2	20.5
483	20.6	16.7	19.3
484	20.4	23.0	18.4
485	19.3	24.8	20.1
MEAN	18.3	18.3	18.1
SD	1.85	3.89	2.18
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	22.2	21.7	21.7
527	17.6	18.1	19.5
528	21.9	21.5	18.1
529	18.1	18.4	21.2
530	17.8	18.8	20.0
531	20.4	16.6	17.6
532	17.9	15.1	15.0
533	19.9	19.4	17.8
534	18.6	17.0	16.6
535	20.4	21.5	20.0
MEAN	19.5	18.8	18.8
SD	1.72	2.26	2.10
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	18.4	14.2	18.5
577	19.3	13.5	15.5
578	14.9	13.0	16.7
579	17.1	14.3	18.3
580	15.7	19.0	15.5
581	18.1	12.4	15.4
582	19.9	20.5	16.7
583	14.6	18.2	15.9
584	22.4	14.7	13.0
585	19.3	16.0	13.9
MEAN	18.0	15.6	15.9
SD	2.44	2.76	1.72
N	10	10	10

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatinine

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CREAT

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	0.59	0.57	0.81
427	0.57	0.52	0.67
428	0.53	0.57	0.63
429	0.53	0.50	0.54
430	0.52	0.59	0.64
431	0.53	0.54	0.67
432	0.59	0.80	0.68
433	0.51	0.64	0.46
434	0.55	0.67	0.65
435	0.55	0.57	0.73
MEAN	0.55	0.60	0.65
SD	0.028	0.088	0.096
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	0.57	0.31	0.65
477	0.48	0.52	0.60
478	0.55	0.55	0.63
479	0.57	0.54	0.61
480	0.61	0.58	0.72
481	0.49	0.48	0.69
482	0.61	0.62	0.70
483	0.53	0.58	0.62
484	0.61	0.71	0.53
485	0.55	0.63	0.75
MEAN	0.56	0.55	0.65
SD	0.047	0.107	0.066
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Creatinine

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CREAT

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	0.64	0.73	0.66
527	0.56	0.70	0.69
528	0.61	0.63	0.71
529	0.50	0.56	0.73
530	0.64	0.55	0.60
531	0.53	0.52	0.57
532	0.59	0.61	0.66
533	0.55	0.61	0.79
534	0.62	0.74	0.68
535	0.50	0.62	0.62
MEAN	0.57	0.63	0.67
SD	0.054	0.075	0.065
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	0.61	0.65	0.73
577	0.59	0.53	0.68
578	0.54	0.54	0.79
579	0.58	0.59	0.54
580	0.54	0.46	0.61
581	0.57	0.57	0.59
582	0.58	0.56	0.59
583	0.59	0.73	0.65
584	0.57	0.53	0.58
585	0.55	0.55	0.51
MEAN	0.57	0.57	0.63
SD	0.023	0.074	0.086
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sodium

STUDY ID: UIC-158
STUDY NO: 152
ABBR: NA

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	144	143	147
427	145	146	146
428	143	145	143
429	145	143	143
430	145	144	145
431	144	144	147
432	144	148	145
433	143	144	143
434	146	147	149
435	142	144	147
MEAN	144	145	146
SD	1.2	1.7	2.1
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	142	146	145
477	142	142	146
478	143	145	146
479	146	145	145
480	145	147	147
481	144	145	147
482	144	146	150
483	144	144	144
484	144	143	146
485	145	146	147
MEAN	144	145	146
SD	1.3	1.5	1.6
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Sodium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: NA

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	143	144	145
527	145	147	146
528	143	146	148
529	144	143	146
530	142	144	143
531	142	147	145
532	146	151	147
533	142	148	147
534	144	142	147
535	147	149	147
MEAN	144	146	146
SD	1.8	2.8	1.4
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	144	144	145
577	144	142	144
578	144	146	148
579	144	146	144
580	144	144	145
581	145	146	144
582	144	138	144
583	141	144	144
584	144	144	144
585	143	144	144
MEAN	144	144	145
SD	1.1	2.4	1.3
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Potassium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: K

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	5.50	5.89	5.37
427	5.64	5.40	6.21
428	5.81	6.24	6.33
429	5.46	5.54	6.20
430	5.08	5.73	5.68
431	5.10	5.93	4.34
432	5.71	5.54	4.68
433	5.36	5.97	5.70
434	5.60	6.67	6.12
435	5.42	5.15	5.50
MEAN	5.47	5.81	5.61
SD	0.241	0.438	0.671
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	5.44	5.01	5.08
477	5.83	5.64	6.44
478	5.22	5.61	5.68
479	5.35	5.72	5.09
480	5.04	5.67	5.02
481	5.16	5.90	5.51
482	5.58	5.58	6.06
483	5.35	5.14	5.62
484	5.71	4.64	5.70
485	5.89	5.61	5.57
MEAN	5.46	5.45	5.58
SD	0.288	0.391	0.448
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Potassium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: K

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	5.27	4.92	6.04
527	5.38	5.01	5.42
528	6.35	5.90	4.86
529	5.82	5.45	5.82
530	5.66	6.03	6.06
531	5.99	5.84	5.24
532	5.82	5.85	6.12
533	5.16	5.69	5.32
534	5.24	4.76	5.28
535	6.19	5.29	4.96
MEAN	5.69	5.47	5.51
SD	0.417	0.457	0.465
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	5.04	5.32	5.08
577	6.02	5.23	5.90
578	5.77	5.54	5.39
579	5.43	5.67	6.05
580	5.75	5.48	5.59
581	5.53	5.92	5.72
582	5.85	5.80	6.07
583	5.79	5.55	6.28
584	5.55	5.36	5.19
585	5.58	5.49	6.10
MEAN	5.63	5.54	5.74
SD	0.272	0.214	0.413
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Chloride

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	107	101	106
427	109	100	109
428	108	102	102
429	102	101	97
430	100	102	101
431	103	97	108
432	101	99	104
433	102	94	102
434	98	99	107
435	105	99	108
MEAN	104	99	104
SD	3.6	2.5	3.9
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	105	105	100
477	102	99	101
478	105	100	101
479	97	97	104
480	108	100	103
481	101	98	104
482	103	103	105
483	105	99	102
484	110	105	103
485	101	100	102
MEAN	104	101	103
SD	3.7	2.8	1.6
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Chloride

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	107	103	102
527	108	101	104
528	104	104	105
529	102	101	102
530	108	106	103
531	104	97	97
532	103	102	107
533	104	99	118
534	99	104	104
535	107	106	105
MEAN	105	102	105
SD	2.9	2.9	5.4
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	101	104	103
577	107	97	104
578	102	101	105
579	103	103	103
580	110	105	100
581	100	103	104
582	106	101	100
583	103	104	101
584	107	97	101
585	103	102	100
MEAN	104	102	102
SD	3.2	2.8	1.9
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Calcium

STUDY ID: UIC-158
STUDY NO: 152
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	10.6	11.0	11.0
427	10.4	10.3	11.1
428	11.1	10.8	10.9
429	10.3	10.4	10.7
430	11.0	11.1	11.5
431	10.3	10.7	10.9
432	11.0	11.0	10.9
433	11.0	11.0	11.6
434	10.8	12.7	10.9
435	11.1	10.9	11.5
MEAN	10.8	11.0	11.1
SD	0.33	0.66	0.32
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	10.4	11.2	10.7
477	10.6	10.9	10.8
478	10.9	10.4	11.3
479	11.1	11.2	11.0
480	10.9	10.3	11.0
481	10.8	11.8	11.0
482	10.6	10.4	11.2
483	10.7	10.5	10.5
484	11.1	11.0	11.3
485	11.0	11.8	11.6
MEAN	10.8	11.0	11.0
SD	0.23	0.56	0.32
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Calcium

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	10.9	11.5	11.5
527	10.3	11.4	10.8
528	11.5	11.5	10.7
529	10.8	10.7	10.7
530	11.1	10.7	11.0
531	10.9	11.3	10.8
532	11.5	12.1	11.1
533	11.2	11.3	10.9
534	10.7	11.0	11.0
535	10.4	10.6	10.8
MEAN	10.9	11.2	10.9
SD	0.41	0.47	0.24
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	11.0	10.5	11.0
577	11.1	11.1	11.1
578	10.6	11.1	11.7
579	11.1	11.1	10.9
580	11.5	11.3	10.7
581	10.2	11.6	10.8
582	10.8	10.8	10.9
583	10.5	11.6	10.8
584	11.1	11.0	10.6
585	11.0	10.9	10.7
MEAN	10.9	11.1	10.9
SD	0.37	0.34	0.31
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	7.3	7.9	8.8
427	9.0	6.9	10.6
428	9.3	8.1	8.8
429	6.9	7.2	9.2
430	7.1	7.0	8.3
431	7.6	7.3	9.4
432	7.1	10.1	10.3
433	8.4	9.0	9.3
434	7.0	8.9	7.8
435	8.2	7.0	9.3
MEAN	7.8	7.9	9.2
SD	0.88	1.08	0.84
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	7.9	8.1	7.5
477	7.8	7.8	8.2
478	8.0	6.9	8.7
479	7.3	7.3	8.4
480	8.4	7.4	9.9
481	7.7	7.5	7.7
482	7.6	7.5	9.8
483	7.9	6.6	8.0
484	9.2	8.6	7.4
485	8.0	9.0	10.7
MEAN	8.0	7.7	8.6
SD	0.52	0.73	1.13
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	9.5	8.1	9.7
527	7.4	7.6	9.0
528	9.6	8.4	11.3
529	7.4	8.4	8.2
530	9.0	7.3	8.4
531	8.8	7.8	7.9
532	7.6	9.1	9.3
533	8.2	8.1	10.1
534	7.0	8.3	7.6
535	9.2	8.8	9.1
MEAN	8.4	8.2	9.1
SD	0.97	0.54	1.12
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	8.6	7.7	9.0
577	8.3	7.4	10.5
578	7.4	7.2	10.5
579	8.8	8.0	9.3
580	9.2	9.3	8.7
581	7.1	7.9	8.3
582	8.4	7.4	7.6
583	8.3	10.2	8.7
584	8.1	7.6	8.8
585	8.7	7.7	8.5
MEAN	8.3	8.0	9.0
SD	0.63	0.96	0.91
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Glucose

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 1-F:0 mg base/kg/day			
426	166	154	196
427	149	124	156
428	141	129	115
429	114	129	131
430	127	116	132
431	131	114	182
432	112	199	180
433	112	188	131
434	116	150	114
435	119	118	194
MEAN	129	142	153
SD	18.2	30.3	32.5
N	10	10	10
GROUP: 2-F:0.5 mg base/kg/day			
476	132	162	127
477	116	123	110
478	136	128	117
479	120	140	131
480	149	143	187
481	147	148	135
482	114	126	120
483	138	135	141
484	155	204	138
485	121	135	185
MEAN	133	144	139
SD	14.7	23.9	26.5
N	10	10	10

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP
TEST: Glucose

STUDY ID: UIC-15B
STUDY NO: 152
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

Animal ID	Week 4	Week 13	Week 26
GROUP: 3-F:2.0 mg base/kg/day			
526	183	261	193
527	141	193	144
528	132	130	216
529	126	145	105
530	195	133	151
531	141	120	136
532	129	168	130
533	121	146	202
534	141	204	112
535	149	157	184
MEAN	146	166	157
SD	24.4	43.0	38.9
N	10	10	10
GROUP: 4-F:9.0 mg base/kg/day			
576	191	152	173
577	145	113	201
578	123	118	154
579	131	116	127
580	166	163	127
581	116	142	151
582	124	139	112
583	131	266	104
584	123	120	111
585	144	136	113
MEAN	139	147	137
SD	23.3	45.1	31.7
N	10	10	10