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(Attn: TSCA Section 8(e) Coordinator)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Oxirane, 2,2'-[1,4-phenylenebis(oxymethylene)]bis-
CASRN 2425-01-6
28-Day Dietary Toxicity Study in Fischer 344 Rats

Dear Sir/Madam:

On January 28, 2004, we submitted a letter for the above substance. Since the submission, we learned the final report is available.

Please find enclosed two copies of the above study; one includes Confidential Business Information and the other copy is for the public file.

Questions may be addressed to the undersigned.

Sincerely,

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Enclosures (2)

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STUDY TITLE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

Data Requirement

OECD Guideline 407

Author(s)

Study Completion Date

19 December 2003

Contact Phone

Sponsor

Performing Laboratory

Laboratory Project Study ID

021018

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

Compound: HQDGE

Title: HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

All phases of this study were conducted in compliance with the following Good Laboratory Practice Standards:

Organisation for Economic Co-Operation and Development (OECD)
OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 1. OECD Principles on Good Laboratory Practice (as revised in 1997) ENV/MC/CHEM(98)17

US Environmental Protection Agency-TSCA GLPS
Title 40 CFR, Part 792-Toxic Substance Control Act (TSCA); Good Laboratory Practice Standards, Final Rule

Exception: the test material was not characterized, assayed for purity or checked for structural conformation.

QUALITY ASSURANCE STATEMENT

Compound: HQDGE

Title: HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

This study was examined for conformance with Good Laboratory Practices as published by the USEPA (TSCA) and OECD. The final report was determined to be an accurate reflection of the data obtained. The dates of Quality Assurance activities on this study are listed below.

Study Initiation Date: 10 January 2003

TYPE OF AUDIT:	DATE OF AUDIT:	DATE FINDINGS REPORTED TO STUDY DIRECTOR/MANAGEMENT:
Final protocol	20 January 2003	29 January 2003
Study conduct	20 February 2003	21 February 2003
Protocol, data, and draft report	30 July 2003 – 15 August 2003	09 September 2003
Final report	The date of the signature below is the date of the final report audit.	

The final report accurately reflects the raw data of the study.

SIGNATURE PAGE

Compound: HQDGE

Title: HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

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SUMMARY

Hydroquinone diglycidyl ether (HQDGE) was administered in the diet to Fischer 344 rats at targeted doses of 0, 10, 100 or 1000 mg HQDGE/kg body weight/day (mg/kg/day) to evaluate systemic toxicity. The 1000 mg/kg/day group was humanely euthanized at five days due to decreases in body weight by day 4 of 21% and 16% in males and females, respectively, and concomitant clinical moribundity. One week after initiation of the study, additional rats from the same shipment were placed on study at a dose of 200 mg/kg/day. Except as noted at 1000 mg/kg/day, all rats (10/sex/group) were maintained on study for at least 28 days. Separate statistical analyses of the data derived from the 200 mg/kg/day group was conducted due to the staggered start.

At study termination, body weight gains at 200 mg/kg/day were 9% and 34% of the respective male and female control values. At 100 mg/kg/day, body weight gains were 88% and 87% of the respective male and female control values, effects mostly related to irritation and poor palatability. Average feed consumption was markedly decreased at 200 mg/kg/day (54% and 67% of respective male and female control values). At 100 mg/kg/day, feed consumption was 89% and 91% of the respective male and female controls. For diets targeted to provide 0, 10, 100, 200, or 1000 mg/kg/day HQDGE, test material intake was 0, 11.1, 109.7, 183.9, and 249 mg/kg/day for males and 0, 10.6, 106.7, 192, or 277 mg/kg/day for females, respectively.

At 200 mg/kg/day, treatment-related dehydration, thinness, and decreased fecal output occurred that mostly subsided by the end of the study. Functional tests, which included a sensory evaluation, rectal temperature, grip performance, and motor activity assessment, were conducted pre-exposure and during the last week of the treatment. Forelimb grip performance was significantly higher for the 200 mg/kg/day versus control group at pre-treatment, likely because of an age difference (51 vs. 41 days old, respectively) and the associated differences in weight and strength. Forelimb grip performance was reduced following treatment, a change that was likely secondary to the significant body weight gain decrements in this group.

The only treatment-related gross pathological effect was a thickening of the nonglandular stomach mucosa in the majority of males and females given 100 or 200 mg/kg/day. Treatment-related histopathologic effects in animals given 100 or 200 mg/kg/day consisted of: 1) epithelial hyperplasia, hyperkeratosis, ulceration (mainly in the 200 mg/kg/day group) and chronic active inflammation of the nonglandular stomach

mucosa, 2) hyperplasia of mucous neck cells of the pylorus of the glandular stomach mucosa, and 3) diffuse epithelial hyperplasia of the duodenal mucosa in males and in females (200 mg/kg/day only). Histopathologic changes in animals given 200 mg/kg/day that were interpreted to be secondary to stress, irritation of the stomach and duodenum, or to poor nutrition/decreased feed consumption and body weights, consisted of: 1) hypertrophy of the zona fasciculata of adrenal glands (males), 2) hypertrophy of the acinar cells of the submandibular salivary glands (some males affected at 100 mg/kg/day), 3) atrophy of thymus (males), uterus, cervix, vagina, mesenteric adipose tissue, dermal adipose tissue, hair follicles and sebaceous glands of skin, 4) decreased amounts of secretory material in the coagulating glands, seminal vesicles and prostate, and 5) hypocellularity of the bone marrow.

Increases in absolute and relative adrenal weights and decreases in absolute and relative thymus weights for males in the 200 mg/kg/day group were interpreted to be related to stress and gastrointestinal tract irritation. These effects corresponded with hypertrophy and vacuolization of the adrenal cortex and very slight thymic atrophy, respectively, effects typically associated with stress. Statistically identified differences in the absolute and/or relative weights of the heart, kidneys, liver, brain, testes, or epididymis at either 100 (males) or 200 mg/kg/day (males and females) were considered secondary to decreases in body weight.

Statistically identified changes in sodium, chloride, and potassium for males and/or females at 100 and/or 200 mg/kg/day, decreases in calcium at all dose levels, decreases in total protein at 100 mg/kg/day, or decreases in creatinine at 100 and 200 mg/kg/day were not considered treatment-related because values for these parameters were either within historical control ranges, there were no dose response trends, and/or they were minimal. Statistically identified differences in several clinical pathology parameters were attributed to stress resulting from the irritation of the gastrointestinal tract. These included: a decrease in alkaline phosphatase (ALP) at 100 and 200 mg/kg/day, slightly lower glucose for males given 200 mg/kg/day, elevated cholesterol levels of males given 200 mg/kg/day that was likely related to hypertrophy of the adrenal fasciculata cells and/or decreased body weight. In addition, there was a dose-dependent decrease in urine volume for male and female rats at 100 and 200 mg/kg/day that was attributed, by inference, to decreased water consumption, and an increase in urine specific gravity at 100 and 200 mg/kg/day that was reflective of the decrease in urine volume. There was a trend of increased urinary protein for male and female rats that was reflective of the dose-dependent

decrease in urine volume. There was a trend of increased urinary ketone bodies with increasing dose of test article for both male and female that may have reflected a more concentrated urine, a decreased feed consumption with concomitant increased utilization of lipid reserves, or both. Urinary bilirubin was slightly elevated with increasing dose of test article in male and female rats, however, this was considered a secondary consequence of decreased urinary volume and higher specific gravity.

A statistically identified decrease in hematocrit (HCT) for all dose levels and decrease in hemoglobin at 200 mg/kg/day were not considered treatment-related as values were within historical control limits for these parameters. Other changes interpreted to be a stress response and/or consistent with inflammation in the stomach or changes in the adrenals included statistically identified increase in white blood cell (WBC) counts for female rats given 200 mg/kg/day, and a shift in the differential leukocyte count for males given 200 mg/kg/day consisting of an increase in percent neutrophils (from 18.9% to 27.1%) and a decrease in percent lymphocytes (from 75.5% to 68.5%) for controls versus treated rats, respectively.

Under the conditions of this study, the no-observed-effect level (NOEL) for male and female Fischer 344 rats after four weeks dietary administration of HQDGE was identified as the targeted dose of 10 mg/kg/day.

INTRODUCTION

Previous Toxicity Information

The acute oral and dermal LD_{50} of HQDGE were both greater than 2000 mg/kg in female Fischer 344 rats .

Purpose

The purpose of this study was to evaluate the potential toxicity of HQDGE in rats following dietary administration for at least 28 days.

Test Guidelines

This study was designed to fulfill the following requirements:

OECD Organisation for Economic Co-operation and Development, *Guidelines for Testing of Chemicals*. Guideline Number 407 (Repeated Dose 28-day Oral Toxicity Study in Rodents), 27 July 1995.

Quality Assurance

The study conduct, data, protocol, protocol changes/revisions, and final report were inspected by the Quality Assurance Unit,

Archiving

The data, protocol, protocol changes/revisions, and final report are archived at

TEST MATERIAL INFORMATION

Test Material Name

Hydroquinone Diglycidyl Ether

Chemical Name

2,2'[1,4-phenylenebis(oxymethylene)]bis-Oxirane

Synonyms

HQDGE

Supplier, City, State (lot number)

Purity/Characterization (method of analysis and reference)

HQDGE, lot #QC251974M1, has a purity of 81.6% with four impurities at concentrations greater than 1% identified by electrospray liquid chromatography-mass spectroscopy and gas chromatography-mass spectrometry

Characteristics

Appearance (physical state, color)

Solid (powder); off-white

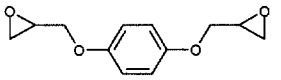
Molecular Formula

$C_{12}H_{14}O_4$

Molecular Weight

222.24 atomic mass units

Chemical Structure



Vehicle

LabDiet® Certified Rodent Diet Meal #5002 (PMI Nutrition International, St. Louis, Missouri)

TEST SPECIES AND HUSBANDRY

Species and Sex

Rats (male and female)

Strain and Justification

Fischer 344 rats were selected because of their general acceptance and suitability for toxicity testing, availability of historical background data, and the reliability of the commercial supplier.

Supplier and Location

Charles River Laboratories, Inc. (Raleigh, North Carolina)

Age at Study Start

Animals were 6-7 weeks old at the start of the study.

Physical and Acclimation

Each animal was evaluated by a trained toxicology technician, under the direct supervision of a lab veterinarian, to determine the general health status and acceptability for study purposes upon arrival at the laboratory[1]. The animals were housed 2-3 per cage in stainless steel cages, in rooms designed to maintain adequate conditions (temperature, humidity, and photocycle), and acclimated to the laboratory for at least one week prior to the start of the study.

Housing

Animals were housed one per cage in stainless steel cages in rooms designed to maintain adequate conditions (temperature, humidity, and photocycle). A 12-hour light/dark photocycle was maintained with lights on at 6:00 a.m. and off at 6:00 p.m. Room air was exchanged approximately 12-15 times/hour. Cages had wire-mesh floors and were suspended above absorbent cage papers. Cages contained feed crocks and pressure activated, nipple-type watering systems. Room temperature was recorded daily. The relative humidity ranged from 48.6 to 51.6%, while the room temperature ranged from 21.8 to 22.0°C. These values were within the laboratory recommended range of study room humidity and temperature for rats of 40-70% and 22 ± 1°C, respectively.

Randomization and Identification

Animals were stratified by pre-exposure body weight and then randomly assigned to treatment groups using a computer program. Animals placed on study were uniquely identified via subcutaneously implanted transponders (BioMedic Data Systems, Seaford, Delaware) which were correlated to unique alphanumeric identification numbers.

Text Table 1. Animal Identification Numbers

Dose Level (mg/kg/day)	Males	Females
0	7682 – 7691	7722 – 7731
10	7692 – 7701	7732 – 7741
100	7702 – 7711	7742 – 7751
200	81 – 90	91 – 99
1000	7712 – 7721	7752 – 7761

[1] Fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

Feed and Water

Animals were provided LabDiet® Certified Rodent Diet #5002 (PMI Nutrition International, St. Louis, Missouri) in meal form. Feed and municipal water was provided *ad libitum*. Analyses of the feed were performed by PMI Nutrition International to confirm the diet provided adequate nutrition and to quantify the levels of selected contaminants (Appendix Table 35). Drinking water obtained from the municipal water source was periodically analyzed for chemical parameters and biological contaminants by the municipal water department (Appendix Table 36). In addition, specific analyses for chemical contaminants were conducted at periodic intervals by an independent testing facility (Appendix Table 37). Copies of these analyses are maintained at

There were no contaminates detected in the feed or water at levels that adversely affected this study.

Animal Welfare

In response to the Final Rules amending the U.S. Animal Welfare Act promulgated by the U.S. Department of Agriculture effective October 30, 1989, the Animal Care and Use Activities (ACUA) required for the conduct of this study were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). The IACUC determined that the proposed Activities were in full accordance with these Final Rules. The IACUC assigned File No. Subchronic/Chronic Tox 01, DCO 01, Neuro Tox 01 and Animal ID 01 to these Animal Care and Use Activities.

STUDY DESIGN

Experimental Design and Critical Dates

Four groups of ten male and ten female Fischer 344 rats were fed diets formulated to contain 0, 10, or 100 mg HQDGE/kg body weight/day (mg/kg/day) for at least 28 days to evaluate the potential for systemic toxicity. Initially, the study also consisted of a group of ten male and ten female Fischer 344 rats targeted to receive 1000 mg HQDGE/kg/day, however, this group was euthanized for humane reasons related to body weight loss after five days. In an effort to obtain dose-response information for a dose between 100 and 1000 mg/kg/day, a group of ten male and nine female rats that were additional animals from the original study shipment were placed on study at 200 mg/kg/day. These animals were placed on study one week after dosing had been initiated for all other animals and were maintained on study for at least 28 days. At in-life termination, rats in the 200-mg/kg/day group were approximately one week older than the other rats due to the staggering of study start.

Cage-side clinical observations, detailed clinical observations, ophthalmologic examinations, functional testing, body weights, feed consumption, hematology, clinical chemistry, urinalysis, organ weights, gross necropsy, and histopathologic examination of tissues were conducted. Test material administration for all animals given 0, 10, 100, or 1000 mg/kg/day began on 27 January 2003. Test material administration for all animals given 200 mg/kg/day began on 03 February 2003. Male and female rats given 0, 10, or 100 mg/kg/day were necropsied on 25 February 2003 and 26 February 2003, respectively (test days 30 and 31, respectively). Male and female rats given 200 mg/kg/day were necropsied on 4 March 2003 (test day 30). All animals given 1000 mg/kg/day were euthanized (no necropsy conducted) for humane reasons on 31 January 2003 (test day 5).

Route, Method of Administration, Frequency, Duration and Justification

Possible routes of human exposure to HQDGE would be dermal, inhalation, or oral as a result of swallowing dust being cleared from the nasopharynx by mucocilliary clearance after inhalation. Thus, administration of the test material to rats via the diet represented an appropriate means of exposure. Furthermore, the oral route of administration is specified as the preferred route of administration in OECD guideline number 407.

Dose Levels and Justification

The high-dose level of 1000 mg/kg/day represented the limit test, as specified by several regulatory agencies, for this type and duration of study. The remaining dose levels were expected to provide dose-response data for any treatment-related effect(s) observed in the high-dose group and to help define a potential no-observed-effect level (NOEL). The acute toxicity data on HQDGE (*i.e.*, LD_{50}>2000 mg/kg) did not indicate a dose lower than the limit dose specified in OECD 407.

Dose Preparation and Analysis

Diets were prepared by serially diluting a concentrated test material-feed mixture (premix) with ground feed. Premixes were mixed weekly throughout the study. Diets were prepared weekly based upon the most recent body weight and feed consumption data. Initial concentrations of test material in the diet were calculated from historical body weight and feed consumption data.

Analysis

Homogeneity

The homogeneity of the low-dose female and the high-dose female test material-feed mixtures were determined prior to the start of the study.

Stability

Stability of HQDGE in rodent diet was evaluated at 8, 12, and 28 days from initial mixing at concentrations of 5, 0.5, 0.05, 0.005, and 0.0005% (w/w). Stability of the 10% concentration was also determined out to 36 days. Due to degradation at the 0.005% level by day 12 (79.1% of day 0), the diets mixed for this study were only considered stable for 8 days post mixing, hence diets were mixed weekly throughout the study.

Concentration Verification

Analyses of all dose levels, plus control and premix, were determined prior to the study start. The method for analyzing the test material in feed was a solvent extraction method followed by analysis using gas chromatography-mass spectrometry (GC-MS) and solvent standards incorporating an internal standard.

Retainer Samples

Reference samples (one/sex/dose/mix and premix) were retained and stored in sealed vials in a manner consistent with the sample retention policy of the laboratory.

In-Life Observations

Twice each day a cage-side examination was conducted and to the extent possible the following parameters were evaluated: skin, fur, mucous membranes, respiration, nervous system function (including tremors and convulsions), animal behavior, moribundity, mortality, and the availability of feed and water.

Detailed Clinical Observations

Detailed clinical observations (DCO) were conducted pre-exposure and weekly throughout the study. The DCO was conducted on all animals, at approximately the same time on each examination day according to an established format (Table 1). The examination included cage-side, hand-held, and open-field observations that were recorded categorically or using explicitly defined scales (scored) as outlined in Appendix A.

Cage-Side Observations

A cage-side (general) clinical examination was conducted once a day, preferably at the same time each day, usually in the morning. This examination was performed with the animals in their cages and was designed to: 1) detect significant clinical abnormalities that are clearly visible upon a limited examination, and 2) to monitor the general health of the animals. Significant clinical abnormalities that could have been observed included, but

were not limited to: activity, repetitive behavior, vocalization, incoordination/lameness, injury, neuromuscular function (convulsion, fasciculation, tremor, twitches), altered respiration, blue/pale skin and mucous membranes, severe eye injury (rupture), fecal consistency, and fecal/urinary quantity. At least twice daily, usually at the beginning and end of each day, all animals were also observed for morbidity and mortality, and the availability of feed/water.

Functional Tests

The functional tests included a sensory evaluation, rectal temperature, grip performance, and motor activity. Functional tests were conducted pre-exposure and during the last week of the treatment period.

Sensory Evaluation

The sensory evaluation included a test for nociception (responsiveness to tail pinch) and for startle response (responsiveness to sharp noise). The evaluation was conducted in a small clear plastic box. Details of the methods for each test and specific definition of the ranks can be found in Appendix A.

Rectal Temperature

Rectal temperature was measured by carefully placing a rectal thermistor (Physitemp RET-2, T-type) approximately 4 cm into the rectum for about 15-20 seconds. Temperature was then recorded. The thermistor was validated at 37°C before and after the study. The instrument was re-calibrated if the validation temperature recordings differ from the reference thermometer by more than ± 0.5°C.

Grip Performance

Hind-limb grip performance was tested according to the procedure described by Briefly, the observer placed the animal's forelegs on a bench and the hind-feet were set on a horizontal screen attached to an electronic strain gauge (Chatillon, Greensboro, North Carolina). The observer then smoothly but firmly pulled backward on the tail until the animal's grip on the screen was broken (Appendix B). An electronic strain gauge reading was used to record the animal's resistance to the pull in grams. The averages of three trials were used for statistical analysis. Forelimb grip performance was similarly tested. In this application, a bench was not used, and the animal was placed so that the forefeet are on the screen and the hind-feet were suspended approximately 10 cm above the smooth horizontal plastic surface.

Instrument Validation

A standard 500 g weight attached to a fine-gauge wire was suspended from the load cell (weight was measured from the load cell in grams). A 1% tolerance (*i.e.*, 500 ± 5 grams) was acceptable and was checked just before and just after testing.

Motor Activity

An automated system was used for motor activity (MA) data collection (Appendix C). No entry into the MA test room was allowed during the testing period. For the Fischer 344 rat strain, each test session consisted of six 8-minute epochs, totaling 48 minutes of testing per animal per test session. This duration was chosen based on the results of a validation study indicating that performance of control animals approached an asymptote in 30-40 minutes in Fischer 344 rats . Activity counts for each epoch were recorded.

Motor Activity Cage Calibration

Cages were calibrated prior to testing each day. Calibration was performed with a rod attached to a rotary motor that breaks the infrared beam at a constant speed. The duration of each beam break was calculated to ensure equivalence across chambers.

Motor Activity Cage

Allocation: the rats were allocated to the motor activity cages in such a way that counterbalancing of treatment groups and sexes across cages and test times was maximized.

Ophthalmology

The eyes of all animals were examined by a veterinarian pre-exposure and prior to termination using indirect ophthalmoscopy. One drop of 0.5% tropicamide ophthalmic solution was instilled in each eye to produce mydriasis prior to the indirect ophthalmic examinations. Eyes were also examined by a prosector during necropsy through a moistened glass slide pressed to the animal's cornea.

Body Weights/Body Weight Gains

All rats were weighed during the pre-exposure period, twice during the first week, and at least weekly during the remainder of the study. Body weight gains were calculated for each interval between collection of body weight data.

Feed Consumption

Feed consumption data were collected pre-exposure, twice during the first week and at least weekly thereafter for all animals. Feed containers were weighed at the start and end of a measurement cycle and consumption was calculated using the following equation:

$$\text{Feed consumption (g/day)} = \frac{\text{(initial weight of feed container - final weight of feed container)}}{\text{\# of days in measurement cycle}}$$

Test Material Intake

The actual test material intake (TMI) was calculated using test material feed concentrations, body weights, and feed consumption in the following equation:

$$TMI = \frac{\left(\text{feed consumption}\left(\frac{g}{day}\right) * (1000\,mg/g) * \frac{(\%\text{ of test material in feed})}{100}\right)}{\left(\frac{\text{current BW[g]} + \text{previous BW[g]}}{2}\right)_{1000\,g/kg}}$$

Clinical Pathology

Blood samples were collected from the orbital sinus of all fasted animals, anesthetized with CO_2, at the scheduled necropsy. Blood samples were not obtained from the 1000 mg/kg/day animals that were euthanized on day 5 of the study.

Hematology

Sample Preparation

Blood samples to evaluate a complete blood count were mixed with ethylenediamine-tetraacetic acid (EDTA). Blood smears were prepared, stained with Wright-Giemsa stain and archived for potential future evaluation if warranted. Hematologic parameters were assayed using a Technicon H•1E Hematology Analyzer (Bayer Corporation, Tarrytown, New York).

Assays

Hematocrit (HCT)
Hemoglobin (HGB) concentrations
Red blood cell (RBC) counts
Total white blood cell (WBC) counts
Platelet (PLAT) counts
Differential WBC counts
RBC indices: mean corpuscular hemoglobin (MCH)
mean corpuscular volumes (MCV)
mean corpuscular hemoglobin concentrations (MCHC)

Coagulation

Sample Preparation

Blood samples to evaluate coagulation were collected in sodium citrate tubes, centrifuged and plasma collected and assayed using an ACL9000 (Instrumentation Laboratory, Lexington, Massachusetts).

Assay

Prothrombin time (PT)

Clinical Chemistry

Sample Preparation

Blood samples were collected in glass tubes and sera were separated from cells as soon as possible following blood collection. Serum parameters were measured using a Hitachi 914 Clinical Chemistry Analyzer (Boehringer-Mannheim, Indianapolis, Indiana).

Enzyme Activities of:

Alkaline phosphatase (ALP)
Alanine aminotransferase (ALT)
Aspartate aminotransferase (AST)

Concentrations of:

Albumin (ALB)
Cholesterol (CHOL)
Creatinine (CREA)
Electrolytes (Na, K, PHOS, Cl and Ca)
Glucose (GLUC)
Total bilirubin (TBIL)
Total protein (TP)
Urea nitrogen (UN)

Urinalysis

Urine was obtained from all surviving non-fasted rats the week prior to necropsy. Animals were housed in metabolism cages and the urine collected overnight (approximately 16 hours).

Assays

Color, appearance and specific gravity (refractometer), and urine volume

Semiquantitative analysis (Multistix® Reagent Strips, Bayer Corporation, Elkhardt, Indiana on the Clinitek 200+) of:

pH
Bilirubin
Glucose
Protein
Ketones
Blood
Urobilinogen

Urine was also collected by manual compression of the bladder prior to the necropsy for characterization of the microsediment using a pooled sample from each dose group/sex.

Anatomic Pathology

Necropsy

Fasted rodents submitted alive for necropsy were anesthetized by the inhalation of CO_2, weighed, and blood samples were obtained from the orbital sinus. Their tracheas were exposed and clamped, and the animals were euthanized by decapitation.

A complete necropsy was conducted on all animals by a veterinary pathologist assisted by a team of trained individuals. The necropsy included an examination of the external tissues and all orifices. The head was removed, the cranial cavity opened and the brain, pituitary and adjacent cervical tissues were examined. The eyes were examined *in situ* by application of a moistened glass slide to each cornea. The skin was reflected from the carcass, the thoracic and abdominal cavities were opened and the viscera examined. All visceral tissues were dissected from the carcass, re-examined and selected tissues were incised. The nasal cavity was flushed via the nasopharyngeal duct and the lungs were distended to an approximately normal inspiratory volume with neutral, phosphate-buffered 10% formalin using a hand-held syringe and blunt needle.

The brain, liver, kidneys, heart, adrenals, testes, epididymides, thymus, and spleen were trimmed and weighed immediately. The ratios of organ weight to terminal body weight or brain weight were calculated.

Representative samples of tissues listed in Table 2 were collected and preserved in neutral, phosphate-buffered 10% formalin. Transponders were removed and placed in jars with the saved tissues.

Histopathology

The number of sections from all preserved tissues listed in Table 2 were processed by standard histologic procedures from the control- and 200 mg/kg/day group animals. Paraffin embedded tissues were sectioned approximately 6 µm thick, stained with hematoxylin and eosin and examined by a veterinary pathologist using a light microscope. The following tissues from the remaining groups were processed and histopathologically examined: relevant gross lesions and target organs. Selected histopathologic findings were graded to reflect the severity of specific lesions to evaluate: 1) the contribution of a specific lesion to the health status of an animal, 2) exacerbation of common naturally occurring lesions as a result of the test material, and 3) dose-response relationships for treatment-related effects. Very slight and slight grades were for conditions that were altered from the normal textbook appearance of an organ/tissue, but were of minimal severity and usually with less than 25% involvement of the parenchyma. This type of change would neither be expected to significantly affect the function of the specific organ/tissue nor would it have a significant effect on the overall health of the animal. A moderate grade was used for conditions that were of sufficient severity and/or extent (up to 50% of the parenchyma) that the function of the organ/tissue may have been adversely affected, but not to the point of organ failure. The health status of the animal may or may not have been affected, depending on the organ/tissue involved, but generally lesions graded as moderate would not be life threatening. A severe grade would have been used for conditions that were extensive enough to cause significant organ/tissue dysfunction or failure. This degree of change in a critical organ/tissue may have been life threatening.

STATISTICS

Means and standard deviations were calculated for all continuous data. All parameters examined statistically, with the exception of feed consumption, which is addressed below, were first tested for equality of variance using Bartlett's test (alpha = 0.01; Winer, 1971). If the results from Bartlett's test were significant, then the data for the parameter may have been subjected to a transformation to obtain equality of the variances. The transformations that were examined were the common log, the inverse, and the square root, in that order. The data were reviewed and an appropriate form of the data was selected. The selected form of the data was then subjected to the appropriate parametric analysis as described below. Removing outlying data point(s)

farthest from the mean and rerunning the Bartlett's for any given transformation was also considered. The method of identifying outliers is discussed below.

In-life body weights were evaluated using a repeated measures (RM) analysis of variance (ANOVA), the multivariate approach, for time (the repeated factor), sex, and dose (Winer, 1971). In the RM-ANOVA, differences between the groups were primarily detected by the time-dose interaction.

The first examination in the RM-ANOVA was of the time-sex-dose interaction. If significant at alpha = 0.02, the analysis was repeated separately for each sex without examining the results of other factors. The time-dose interaction was examined next. If the time-dose interaction was statistically significant at alpha = 0.05, linear contrasts tested the time-dose interaction for the comparisons of each dose group to the control group. A Bonferroni correction was applied to the alpha level to compensate for the multiple comparisons with the control group (Miller, 1966). This correction controls the experiment-wise error rate. The corrected comparison-wise error rate of alpha = 0.02 was reported so direct comparison could be made to the Pillai's Trace p-values generated.

Terminal body weight, organ weight (absolute and relative, epididymides and testes), urine specific gravity, hematologic parameters (excluding RBC indices and differential WBC counts), coagulation and clinical chemistry parameters were evaluated using a two-way ANOVA (Steel and Torrie, 1960) with the factors of sex and dose. Differences between the groups were primarily detected by the dose factor. For these parameters the first examination was whether the sex-dose interaction was significant at alpha = 0.05; if it was, a one-way ANOVA was done separately for each sex. Comparisons of individual dose groups to the control group were made with Dunnett's test only when a statistically significant dose effect existed at alpha = 0.05. Dunnett's test corrects for multiple comparisons to the control and the experiment-wise error rate of alpha = 0.05 was reported (Winer, 1971).

Results for epididymides and testes weight (absolute and relative) were analyzed using a one-way ANOVA. If significant dose effects (alpha = 0.05) were determined in the one-way ANOVA, then separate doses were compared to controls using Dunnett's test.

Feed consumption data were evaluated by Bartlett's test for equality of variances at alpha = 0.01. Exploratory data analysis was performed by a parametric ANOVA and if significant at alpha = 0.05, was followed by Dunnett's test at alpha = 0.05, experiment-wise error. Outliers were identified by a sequential test at alpha = 0.02

(Grubbs, 1969), but were routinely excluded only from feed consumption. Other outliers may have been excluded only for documented scientifically sound reasons. Descriptive statistics only (means and standard deviations) were reported for body weight gains, RBC indices, and differential WBC counts.

DCO incidence scores for ranked observations and sensory evaluations were statistically analyzed by a z-test of proportions comparing each treated group to the control group at alpha = 0.05 (Bruning and Kintz, 1987). Data collected at different time points were analyzed separately.

Rectal temperature and grip performance data were analyzed by a factorial analysis of covariance (ANCOVA) with the factors of sex and treatment and the covariate of the pre-exposure time point measure of the variable (Steel and Torrie, 1960). The first examination in the ANCOVA was for the treatment-by-pre-exposure measure interaction. If this was significant at alpha = 0.05, an ANOVA was run separately for the pre-exposure time point and the study time point. The second examination for ANCOVA was to determine whether the sex-by-treatment interaction was significant at alpha = 0.05; if it was, a one-way ANCOVA was done separately for each sex. If there was a significant treatment effect (alpha = 0.05), then least squares means were generated and a t-test done to compare the individual dose groups to the control group. The comparison-wise error rate was set to alpha = 0.02 to correct for multiple comparisons to the control.

Motor activity counts were reported as their square roots to minimize problems of heterogeneity of variance and departure from normality that commonly occur from treatment (Pryor *et al.*, 1983). Thus, the motor activity data were not subjected to any other transforms. Motor activity data were analyzed by a factorial repeated-measure design, the multivariate approach, with factors of sex and treatment and the repeated factor of time. Motor activity also had the repeated factor of epoch (within time) in the model. The inclusion of pre-exposure data in the analysis made relevant only the analyses that included factors of both treatment and time. The primary interactions examined at alpha = 0.05 were treatment-by-time-by-sex, treatment-by-time, and treatment-by-time-by-epoch. In the repeated-measure ANOVA with a pre-exposure time point, the treatment-by-time interaction assessed the true effect of treatment (Bonate, 2000) whereas the treatment-by-time-by-epoch reflected the effects of the test compound on the distribution of motor activity over time. The statistical significance of the treatment-by-time-by sex interaction was examined first. If significant, the

analysis was repeated separately for each sex. The treatment-by-time interaction and the treatment-by-time-by epoch interaction were examined. If either was significant, linear contrasts were calculated to determine which treatment groups were different from the control group. The comparison-wise error rate was set to alpha = 0.02 to correct for multiple comparisons to the control. The Pillai's Trace p-values were used.

The type-I error rate (alpha) per comparison was set to 0.05 for all primary planned analyses. To reduce the rate of false declarations, subsequent analyses (e.g., contrasts after MANOVA or ANOVA) were conducted at alpha = 0.02 following a significant primary analysis. If the study director felt it appropriate to perform further analyses even after a statistically non-significant primary analysis, these analyses were conducted at alpha = 0.01. This overall approach is consistent with the recommendations proposed by Tukey *et al.* (1985), Mantel (1980), and by the EPA (1991). The probability values were reported without correction.

Because numerous measurements were statistically compared in the same group of animals, the overall false positive rate (Type I errors) was greater than the nominal alpha levels. Therefore, the final toxicologic interpretation of the data considered other factors, such as dose-response relationships, biological plausibility and consistency, and historical control values.

RESULTS AND DISCUSSION

Analytical Chemistry

The homogeneity of HQDGE in rodent feed was determined prior to study start for the 10 and 1000 mg/kg/day male test diets, the lowest and highest concentrations used in the study (Table 3). The test material was determined to be distributed homogeneously throughout the diet, with relative standard deviations for all diets sampled between 5.79% and 7.9%.

HQDGE was stable in the diet for 8 days at concentrations ranging from 0.0005% to 10% (Table 4).

Concentrations of all dose levels, including premix and control, were determined prior to the start of the study (Table 5). Concentrations of HQDGE in the diet ranged from 95.0-107% of the targeted concentrations, indicating an acceptable agreement between actual and target levels. No test material was found in the control diet.

Mortality

There were no spontaneous deaths during this study. All rats survived the 4-week dosing period, except the 1000 mg/kg/day dose level animals, which were humanely euthanized on day 5 of the study due to significant body weight decrements and the interpretation that the maximum tolerated dose had been exceeded.

Detailed Clinical Observations

Detailed clinical observations are summarized in Tables 6 and 7. Individual DCO and daily cage-side observations are reported in Appendix Tables 1 and 2. All males and females in the 1000 mg/kg/day dose level had decreased fecal production on study days 2 through 5. They were also thin, with an ungroomed appearance on day 5, at which point they were humanely euthanized. Treatment-related observations of dehydration, thinness, and decrease of fecal output were observed in males and female given 200 mg/kg/day. These observations mostly subsided by the end of the study.

On days 8 and 9, red perioral soiling occurred in 3 males given 200 mg/kg/day. Red perinasal soiling occurred on days 8 and 9 in 1 male given 200 mg/kg/day, and on day 22 in 1 male and 1 female given 200 mg/kg/day. One female given 200 mg/kg/day exhibited an increased pupil size in both eyes on study days 15, 22, and 29. Due to a lack of histopathological correlation, and that only 1 out of 9 animals in the group had this observation, it is not considered a treatment-related effect. Single occurrences of red periocular soiling were observed throughout the study in males given 100 or 200 mg/kg/day and females given 0 or 10 mg/kg/day and were considered not-treatment related since they were sporadic and occurred in controls. Additional observations considered not-related to treatment included single occurrences of eyes cloudy, enlarge/protruding, malocclusion, and reddened earflaps.

Functional Tests

For clarity, data analysis is divided into two sections: first, data from 0, 10, and 100 mg/kg/day; then, data from 0 and 200 mg/kg/day. This approach is followed below for rectal temperature, grip performance, and motor activity.

Sensory Evaluation

Sensory evaluation data are summarized in Tables 8 and 9; and individual data are reported in Appendix Tables 3 and 4. Examinations performed on males and females at termination revealed no treatment-related findings.

Rectal Temperature

Rectal temperature data are presented in Figure 5, summarized in Tables 10 and 11; individual data are reported in Appendix Tables 5 and 6.

0, 10, and 100 mg/kg/day

Neither treatment (p=0.8132) nor the treatment-by-sex interaction (p=0.4985) were statistically significant, indicating that, overall, treatment did not affect rectal temperature and, when sexes were separately considered, the data did not show any treatment effect on rectal temperature in either males or females.

0 and 200 mg/kg/day

Neither treatment (p=0.1337) nor the treatment-by-sex interaction (p=0.8991) were statistically significant, indicating that, overall, treatment did not affect rectal temperature and, when sexes were separately considered, the data did not show any treatment effect on rectal temperature in either males or females.

Grip Performance

Grip performance data are presented in Figures 6 and 7, summarized in Tables 12-15; individual data are reported in Appendix tables 7-10.

0, 10, and 100 mg/kg/day

Neither treatment (p=0.9537) nor the treatment-by-sex interaction (p=0.0963) were statistically significant for hindlimb grip performance, indicating that, overall, treatment did not affect hindlimb grip performance and, when sexes were separately considered, the data did not show any treatment effect on hindlimb grip performance in either males or females.

Similarly, effects on forelimb grip performance were not significant for treatment (p=0.1567) or the treatment-by-sex interaction (p=0.5492).

0 and 200 mg/kg/day

Neither treatment (p=0.2564) nor the treatment-by-sex interaction (p=0.6270) were statistically significant for hindlimb grip performance, indicating that, overall, treatment did not affect hindlimb grip performance and, when sexes were separately considered, the data did not show any treatment effect on hindlimb grip performance in either males or females.

Because the baseline-by-treatment interaction was significant in the analysis of covariance of forelimb grip performance (p=0.0130), the two time periods were analyzed separately by analyses of variance, as per protocol.

1. Under *baseline* conditions (*i.e.*, before treatment), there was a significant "treatment" effect (p=0.0001) and "treatment"-by-sex interaction (p=0.0087) for forelimb grip performance. Examination of the data indicates that, both in males and females (but to a greater extent in males), forelimb grip performance was higher in the high-dose vs. control group. This observation is most likely related to the fact that the high-dose group rats were older than the controls (51 vs. 41 days old, respectively), and therefore, heavier. This age/body weight difference before treatment started is reflected here in greater grip performance in the high-dose group.
2. Under *treatment* conditions (*i.e.*, week 4 of study), there was a significant treatment effect (p=0.0004) and a non-significant treatment-by-sex interaction (p=0.9780) for forelimb grip performance. Examination of the data shows that grip performance was reduced under treatment conditions in the high-dose group compared to the control group.

It is concluded that forelimb grip performance is reduced under treatment conditions in males and females given 200 mg/kg/day compared to the control group.

Motor Activity

Motor activity data are presented in Figures 8-10, summarized in Tables 16-19; individual data are reported in Appendix Tables 11-14.

0, 10, and 100 mg/kg/day

Neither treatment-by-time (p=0.4082) nor the treatment-by-time-by-sex interaction (p=0.4543) were statistically significant for motor activity, indicating that, overall, treatment did not affect motor activity and, when sexes were separately considered, the data did not show any treatment effect on motor activity in either males or females. Furthermore, the treatment-by-time-by-epoch (p=0.4247) indicates that treatment did not differentially affect the within-session distribution of the motor activity counts at either time interval.

0 and 200 mg/kg/day

Neither treatment-by-time (p=0.2018) nor the treatment-by-time-by-sex interaction (p=0.1159) were statistically significant for motor activity, indicating that, overall, treatment did not affect motor activity and, when sexes were separately considered, the data did not show any treatment effect on motor activity in either males or females. Furthermore, the treatment-by-time-by-epoch (p=0.3962) indicates that treatment did not differentially affect the within-session distribution of the motor activity counts at either time interval.

Ophthalmology

Ophthalmology results are summarized in Tables 20 and 21, and individual data are reported in Appendix Tables 15 and 16. Examinations performed on all animals prior to the study and at termination revealed no treatment-related findings. Pale fundus, cloudy cornea, periocular soiling, and microphthalmia were noted in multiple dose groups, both male and female, but at a low incidence and not in a treatment-related manner.

Body Weights/Body Weight Gains

Mean body weight and body weight gain data for male and female rats are presented in Figures 1-4, summarized in Tables 22 and 23. Individual data are reported in Appendix Tables 17 and 18 and statistical analysis of body weight is presented in Table 48 and 49. Male rats given 1000 mg/kg/day lost an average of 27 grams body weight by Day 4 (21% of day 1 weight), while female rats given 1000 mg/kg/day lost an average of 16.2 grams body weight by Day 4 (16% of day 1 weight). Male rats given 200 mg/kg/day gained an average of 10.7 grams over the 4-week study, which was 9% of what the male control group gained over four weeks on study. This difference was statistically identified as lower than control. Female rats given 200 mg/kg/day gained an average of 18.6 grams over the 4-week study, which was 34% of what the female control group gained over four weeks on study. This difference was statistically identified as lower than control. In males and females given 100 mg/kg/day, body weight gain was 88% and 87% of control, respectively, differences that were statistically identified. Males and females given 10 mg/kg/day had body weight gains of 105% and 90% of controls, respectively. These differences were not statistically different from control.

Feed Consumption

Mean feed consumption data for male and female rats are summarized in Tables 24 - 27, and individual data are reported in Appendix Tables 19 - 22. Group mean feed consumption values for males and females given 1000 mg/kg/day at day 4 of study were 17% and 21% of controls, respectively. Week 1-3 group mean feed consumption values for males given 200 mg/kg/day averaged 55% of week 2-4 control values. Week 1-3 group mean feed consumption values for females given 200 mg/kg/day averaged 68% of week 2-4 control values. Mean feed consumption values for males and females given 100 mg/kg/day averaged 89% and 91% of controls, while mean feed consumption values for males and females given 10 mg/kg/day averaged 100% and 96% of their respective controls. Statistical analysis identified a slightly lower but significant group mean average, compared to controls, for males throughout the entire study, and females given 100 mg/kg/day during days 1-18 of the study.

Test Material Intake

Test material intake for male and female rats is presented in Tables 28 and 29. The average test material intake for males given diets targeted to provide 0, 10, 100, or 200 mg/kg/day HQDGE was 0, 11.1, 109.7, and 154.7 mg/kg/day, respectively. The average intake for females given diets targeted to provide 0, 10, 100, or 200 mg/kg/day HQDGE was 0, 10.55, 106.7, and 161 mg/kg/day, respectively. Male and female rats given 1000 mg/kg/day had day 4 test material intake values of 249 and 277 mg/kg/day, respectively, after which the animals were terminated for humane reasons.

Clinical Pathology

Hematology

Hematology data for male and female rats are summarized in Tables 32-35, and individual data are reported in Appendix Tables 23-26. Statistical analysis of hematology parameters is presented in Tables 46 and 47. Hematology parameters that were statistically identified and/or considered affected by HQGDE are summarized in Text Tables 2 and 3.

A decrease in hematocrit (HCT) was statistically identified for all test article-treated groups, however, this decrease was not considered treatment-related as it fell within historical control limits for this parameter. There was a statistically identified decrease in red blood cell count (RBC) for males at the low dose, however, this decrease was not

considered treatment-related because it was minimal and because there was no dose response trend. There was a statistically identified decrease in hemoglobin at the high dose, however, this decrease was not considered treatment-related as it fell within historical control limits for this parameter. There was a statistically identified increase in white blood cell (WBC) counts for female rats given 200 mg/kg/day. This increase was considered treatment-related but likely may have been a secondary consequence of stress. There were no significant changes in monocyte, eosinophil, or basophil counts for male or female rats. There was a shift in the differential leukocyte count for males given 200 mg/kg/day consisting of an increase in percent neutrophils (from 18.9% to 27.1%) and a decrease in percent lymphocytes (from 75.5% to 68.5%) for controls versus treated rats, respectively. This shift is interpreted to be a stress response and is consistent with the inflammation that occurred in the stomach and changes identified in the adrenals of male rats at this dose level. There were no significant changes in any of the other hematologic parameters for male or female rats.

Text Table 2. Hematologic Effects of F344 Rats Given HQDGE – Males

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
Hgb (g/dl)	15.4	14.9-16.4	15.1	15.3	15.1*
RBC (E6/UL)	8.3	8.20-9.1	8.07*	8.14	8.42
Hematocrit (%)	44.3	42.7-46.6	43.1*	43.7*	42.8*
Neutrophils (%)	18.9	17.1-21.5	17.5	17.6	**27.1**
Lymphocytes (%)	75.5	71.6-78.1	77.6	78.1	**68.5**

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment related, but secondary to stress.
[1]Historical controls group mean range from thirteen, 28-day dietary studies done since 1998.

Text Table 3. Hematologic Effects of F344 Rats Given HQDGE – Females

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
Hgb (g/dl)	14.9	14.0-16.0	14.9	14.7	14.5*
Hematocrit (%)	41.4	38.4-44.8	41.2*	40.5*	40.1*
WBC X10E3/ccmm	6.44	4.23-8.02	7.46	7.16	**9.24***

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment related, but secondary to stress.
[1]Historical controls group mean range from ten, 28-day dietary studies done since 1998.

Prothrombin Time

Prothrombin time (PT) data for male and female rats are summarized in Tables 30 and 31, and individual data are reported in Appendix Tables 23 and 24. Statistical analysis of prothrombin time is presented in Tables 46 and 47. There were no test article mediated effects for PT.

Clinical Chemistry

Clinical chemistry data for male and female rats are summarized in Tables 36-39, and individual data are reported in Appendix Tables 27-30. Statistical analysis of clinical chemistry parameters is presented in Tables 46 and 47. Clinical chemistry parameters that were statistically identified and/or considered affected by HQGDE are summarized in Text Tables 4 and 5.

There was not a statistically identified change in phosphorus. There was a statistically identified slight increase in sodium levels at 200 mg/kg/day, however, the values were within the historical control range for this parameter and the increase was not considered treatment-related. There was a statistically identified slight increase in chloride levels at 100 mg/kg/day for females only, however, the increase was not considered treatment-related because the increase was below the historical control range for this parameter and because there was no dose response. There was a statistically identified increase in potassium levels at 200 mg/kg/day, however, the values were within the historical control range for this parameter and the increase was not considered treatment-related. Calcium levels of all treated dose levels were decreased compared to control values and were statistically identified, however, the decreases were not considered treatment-related because they were minimal, were within the historical control range for this parameter, and there was not a clear dose response trend across dosages.

There were no changes considered treatment-related for serum transaminases (ALT and AST), urea nitrogen, total protein, albumin, total bilirubin, or creatinine. There was a statistically identified decrease in total protein at the 100 mg/kg/day level, however, this was not considered treatment-related because the change was small and there was no dose-response trend. There was a statistically identified decrease in creatinine at the 100 mg/kg/day and 200 mg/kg/day dose levels, however, these were not considered treatment-related because the changes were small (there was no change for females from control values).

Male and female rats given 100 and 200 mg/kg/day had significantly lower alkaline phosphatase (ALP) activities than the controls. This decrease was considered treatment-related as the magnitude of the decline appeared to be dose-dependent. Nevertheless, the decline in ALP was likely a consequence of test article-induced effects that occurred either in the bone marrow secondary to decreased feed consumption with concomitantly decreased growth, or in the gastrointestinal tract (as this is a primary source of blood-derived ALP). Regardless, the decrease in ALP is interpreted as being not toxicologically meaningful.

Glucose levels of males given 200 mg/kg/day were slightly lower than the controls but were statistically identified as different from controls. This decrease was considered test article-related but likely secondary to the decreased feed consumption that occurred for this group (approximately 56.5% of control for the last data collection interval).

Cholesterol levels of male rats given 200 mg/kg/day were elevated compared to control values and were statistically identified. This elevation was considered test article-related but secondary to stress effects with concomitant disruption of adrenal cholesterol homeostasis as suggested by hypertrophy of the adrenal fasciculata cells that occurred in high dose male rats.

Text Table 4. Clinical Chemistry Effects of F-344 Rats Given HQDGE – Males

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
ALP (u/l)	196	135-236	190	**175***	**111***
GLU (mg/dl)	109	93-173	111	106	**86***
TP (g/dl)	6.3	6.0-7.5	6.2	6.2*	6.2
CHOL (mg/dl)	40	41-52	39	43*	**74***
CREAT (mg/dl)	0.4	0.4-0.8	0.3	0.3*	0.3*
Calcium (mg/dl)	12.4	9.3-14.0	12.1*	12.2*	11.6*
Sodium (mmol/l)	149	144-169	149	149	150*
Potassium (mmol/l)	5.7	4.2-6.8	5.7	5.7	6.5*

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment related.
[1]Historical controls group mean range from thirteen, 28-day dietary studies done since 1998, except for cholesterol which included fourteen, 28-day dietary studies done since 1998.

Text Table 5. Clinical Chemistry Effects of F-344 Rats Given HQDGE – Females

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
ALP (u/l)	155	121-179	152	**142***	**124***
TP (g/dl)	6.1	5.4-6.8	5.9	5.8*	5.9
CREAT (mg/dl)	0.3	0.4-0.7	0.3	0.3*	0.3*
Calcium (mg/dl)	11.9	9.5-13.1	11.7*	11.4*	11.5*
Sodium (mmol/l)	149	142-167	149	149	150*
Potassium (mmol/l)	6.6	4.5-6.9	6.4	6.2	6.8*
Chloride (mmol/l)	100	102-123	100	101*	100

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment related.
[1]Historical controls group mean range from ten, 28-day dietary studies done since 1998.

Urinalysis

Urinalysis data for male and female rats are summarized in Tables 40-43, and individual data are reported in Appendix Tables 31 and 32. Statistical analysis of urinalysis parameters is presented in Tables 46 and 47. Urinalysis parameters that were statistically identified and/or considered affected by HQGDE are summarized in Text Tables 6 and 7. There were no treatment-related changes observed in male and female rats for urinary color, appearance, pH, glucose, blood, or urobilinogen.

There was a dose-dependent decrease in urine volume for male and female rats. This was statistically identified at 100 and 200 mg/kg/day. The decrease was considered treatment-related but likely a consequence of decreased feed intake secondary to gastric irritation and, by inference, concomitantly decreased water intake.

There was a dose-dependent increase in urine specific gravity for male and female rats. This was statistically identified at 100 mg/kg/day and 200 mg/kg/day. The increase was considered treatment-related but reflective of the dose-dependent decrease in urine volume.

There was a trend of increased urinary protein with increasing dose of test article for male and female rats across all dose levels. This increase was considered treatment-related but reflective of more concentrated urine secondary to decreased feed consumption and, therefore, likely decreased water consumption.

There was a trend of increased urinary ketone bodies with increasing dose of test article for both male and female rats in the 100 and 200 mg/kg/day dose groups. This increase was considered treatment-related but likely reflective of more concentrated urine, of decreased feed consumption with concomitant increased utilization of lipid reserves, or both.

Urinary bilirubin was slightly elevated with increasing dose of test article in male and female rats. Since urinary urobilinogen and blood bilirubin levels were not elevated with increasing dose of test article, and since there was no remarkable indication of an anemia, the increase in urinary bilirubin is considered a secondary consequence of decreased urinary volume and higher specific gravity with increasing test article dose.

Text Table 6. Urinalysis – Males

	Dose (mg/kg/day)				
Parameter	0	Historical[1,2]	10	100	200
Volume (ml)	5.6	4.6	4.4	**3.1***	**2.0***
Specific Gravity	1.064	1.043-1.069	1.072	**1.085***	**1.085***
Protein (Trace)	1	NA	0	0	0
Protein (+)	5	NA	2	2	4
Protein (++)	4	NA	8	8	6
Ketones (Neg)	1	NA	0	0	0
Ketones (Trace)	6	NA	7	4	3
Ketones (+)	3	NA	3	6	7
Bilirubin (Neg)	10	NA	8	2	3
Bilirubin (+)	0	NA	2	8	7

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
NA = Not applicable.
Bold type indicates the effects judged to be treatment related.
[1]Historical control group mean for urine volume from one 28-day dietary study done since 1998.
[2]Historical controls group mean range for specific gravity from fourteen, 28-day dietary studies done since 1998.

Text Table 7. Urinalysis – Females

	Dose (mg/kg/day)				
Parameter	0	Historical[1,2]	10	100	200
Volume (ml)	4.0	2.8	3.6	**2.2***	**1.2***
Specific Gravity	1.061	1.016-1.079	1.062	**1.080***	**1.096***
Protein (Neg)	2	NA	0	0	0
Protein (Trace)	1	NA	3	0	0
Protein (+)	7	NA	6	7	4
Protein (++)	0	NA	1	3	4
Protein (+++)	0	NA	0	0	1
Ketones (Neg)	4	NA	4	0	0
Ketones (Trace)	6	NA	6	10	5
Ketones (+)	0	NA	0	0	4
Bilirubin (Neg)	6	NA	7	1	1
Bilirubin (+)	4	NA	3	9	7
Bilirubin (++)	0	NA	0	0	1

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
NA = Not applicable.
Bold type indicates the effects judged to be treatment related.
[1]Historical control group mean for urine volume from one 28-day dietary study done since 1998.
[2]Historical controls group mean range for specific gravity from ten, 28-day dietary studies done since 1998.

Anatomic Pathology

Organ Weights

Terminal body and organ weight data for male and female rats are summarized in Tables 44 and 45, and individual data are reported in Appendix Tables 33 and 34. Statistical analysis of organ weights is presented in Tables 46 and 47. Organ weights that were statistically identified and/or considered affected by HQGDE are summarized in Text Tables 8 and 9.

At 200 mg/kg/day, males gained 9% and females gained 34% of their respective controls over four weeks on study. Males given 100 or 10 mg/kg/day had body weight gains of 88% and 105% of controls, respectively. Females given 100 or 10 mg/kg/day had body weight gains of 87% and 90% of controls, respectively.

The only organ weight changes that were considered treatment-related were statistically identified increases in the absolute and relative adrenal weights and decreases in the absolute and relative thymus weights for males in the 200 mg/kg/day group. The alterations in adrenal gland and thymus weights were interpreted to be

secondary to stress, and corresponded with hypertrophy and vacuolization of the adrenal cortex and with very slight thymic atrophy, respectively.

Other statistically identified differences that occurred in a number of absolute or relative organ weights at either 100 (males) or 200 mg/kg/day (males and females) were considered secondary to decreases in body weight with a relatively differential impact of this decrease on the systemic organs. This included changes in the absolute and/or relative weights of the heart, kidneys, liver, brain, or epididymis. There were no histopathologic correlates for these other organ weight alterations.

Text Table 8. Body and Organ Weight Effects – Males

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
Final Body Weight (g)	225.5	210.3-239.9	231.9	**211.4***	**162.8***
Adrenals (g)	0.041	0.035-0.050	0.039	0.039	**0.050***
Rel. Adrenals (g/100)	0.018	0.016-0.023	0.017	0.018	**0.030***
Heart (g)	0.850	0.701-0.868	0.882	0.799*	0.577*
Rel. Heart (g/100)	0.377	0.310-0.405	0.381	0.378	0.354*
Kidneys (g)	1.908	1.535-1.881	2.012*	1.907	1.578*
Rel. Kidneys (g/100)	0.846	0.688-0.878	0.867	0.902*	0.969*
Liver (g)	7.531	6.627-7.874	7.767	7.340	5.476*
Rel. Liver (g/100)	3.336	3.061-3.554	3.347	3.473*	3.360
Brain (g)	1.858	1.79-1.862	1.862	1.853	1.775*
Rel. Brain (g/100)	0.826	0.75-0.868	0.804	0.877*	1.094*
Spleen (g)	0.523	0.473-0.549	0.553*	0.513	0.414*
Rel. Spleen (g/100)	0.232	0.214-0.256	0.238	0.243*	0.255*
Thymus (g)	0.333	0.252-0.378	0.352	0.342	**0.197***
Rel. Thymus (g/100)	0.148	0.108-0.177	0.152	0.162	**0.121***
Testes (g)	2.931	2.777-2.966	2.937	2.900	2.879
Rel Testes (g/100)	1.301	1.197-1.345	1.268	1.372*	1.770*
Epididymis (g)	0.584	0.617-0.713	0.586	0.564	0.579
Rel Epididymis (g/100)	0.259	0.274-0.298	0.252	0.267	0.355*

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment-related and/or secondary to stress.
[1]Historical controls group mean range from ten, 28-day dietary studies done since 1998, except that epididymide value ranges were from only seven studies.

Text Table 9. Body and Organ Weight Effects – Females

	Dose (mg/kg/day)				
Parameter	0	Historical[1]	10	100	200
Final Body Weight (g)	144.0	134.6-145.8	139.5	137.5	124.5*
Adrenals (g)	0.050	0.043-0.057	0.046	0.047	0.039*
Rel. Adrenals (g/100)	0.035	0.030-0.039	0.033	0.034	0.031*
Heart (g)	0.535	0.486-0.571	0.523	0.511*	0.454*
Rel. Heart (g/100)	0.373	0.357-0.419	0.375	0.371	0.366*
Kidneys (g)	1.200	0.972-1.259	1.179	1.208	1.145
Rel. Kidneys (g/100)	0.835	0.723-0.922	0.845	0.878*	0.920
Liver (g)	4.521	4.010-4.556	4.278	4.421	3.841*
Rel. Liver (g/100)	3.142	2.922-3.335	3.066	3.216*	3.081
Brain (g)	1.717	1.642-1.766	1.718	1.705	1.697
Rel. Brain (g/100)	1.195	1.205-1.255	1.232	1.241	1.373*
Spleen (g)	0.401	0.343-0.409	0.384	0.396	0.358*
Rel. Spleen (g/100)	0.278	0.251-0.297	0.275	0.288*	0.288*

*Statistically Different from Control Mean by Dunnett's Test, Alpha = 0.05.
Bold type indicates the effects judged to be treatment related.
[1]Historical controls group mean range from nine, 28-day dietary studies done since 1998.
* =Statistically different from control mean by Dunnett's test, alpha = 0.05

Gross Pathology

The gross pathologic observations are summarized in Table 44, and individual data are reported in Appendix Table 38. Treatment-related gross pathological findings were confined to the stomach and consisted of: 1) diffuse thickening of the nonglandular mucosa of the stomach in all males and all females given 200 mg/kg/day, and 2) focal or multifocal thickening of the nonglandular mucosa of the stomach in 9 out of 10 males and 9 out of 10 females given 100 mg/kg/day. The stomach mucosa of all males and all females given 10 mg/kg/day were grossly within normal limits. All other gross observations were interpreted to be spontaneous changes unassociated with the exposure to HQDGE.

Histopathology

Histopathologic observations are summarized in Table 45, and individual data are reported in Appendix Table 38. Histopathologic changes associated with exposure to HQDGE are summarized in Text Table 10.

Text Table 10. Treatment-Related Histopathologic Effects

Sex	Males				Females			
Targeted Dose (mg/kg/day)	0	10	100	200	0	10	100	200
Number of animals examined	10	10	10	10	10	10	10	9
STOMACH: Hyperplasia, hyperkeratosis, nonglandular mucosa diffuse *moderate*	0	0	0	**10**	0	0	0	**9**
STOMACH: Hyperplasia, hyperkeratosis, nonglandular mucosa, multifocal *very slight*	0	0	**2**	0	0	0	**1**	0
slight	0	0	**8**	0	0	0	**6**	0
moderate	0	0	0	0	0	0	**3**	0
STOMACH: Inflammation, chronic active, nonglandular mucosa, *very slight*	0	0	**2**	0	0	0	**2**	**1**
slight	0	0	**6**	**1**	0	0	**6**	**6**
moderate	0	0	0	**9**	0	0	0	**2**
STOMACH: Ulcer, non glandular mucosa	0	0	0	**9**	0	0	**1**	**6**
STOMACH: Hyperplasia, mucous neck cell, pylorus, *very slight*	0	0	**10**	0	0	0	**10**	**1**
slight	0	0	0	**10**	0	0	0	**8**
STOMACH; Necrosis, individual cell, glandular, pylorus, multifocal, *very slight*	0	0	**10**	**2**	0	0	**10**	**9**
slight	0	0	0	**8**	0	0	0	0
STOMACH; Dilatation, glandular lumen, pylorus, multifocal, *very slight*	0	0	**8**	**3**	0	0	**8**	**4**
slight	0	0	0	**6**	0	0	0	0
DUODENUM: Hyperplasia, epithelium, mucosa, diffuse, *very slight*	0	0	**5**	**1**	0	0	0	**6**
slight	0	0	0	**9**	0	0	0	0
DUODENUM: Dilatation, crypt, multifocal, *very slight*	0	0	**3**	**1**	0	0	**4**	**6**
DUODENUM: Necrosis, individual cell, crypt, multifocal, *very slight*	0	0	**4**	**10**	0	0	**6**	**7**
MESENTERIC LYMPH NODE: Sinus histiocytosis, increased *slight*	0	0*	0	**7**	0	0	0	**3**
moderate	0	0*	0	**3**	0	0	0	**1**
SALIVARY GLAND: Hypertrophy, acinus, diffuse, *very slight*	0	0	**5**	0	0	0	0	0
slight	0	0	0	**10**	0	0	0	**9**
ADRENAL GLAND; Hypertrophy, zona fasciculata, bilateral, *very slight*	0	0	0	**10**	0	NE	NE	0
BONE MARROW: Hypocellularity, all cell lines, diffuse *very slight*	0	0	0	0	2	0	0	**7**
slight	0	0	0	**1**	0	0	0	**1**
moderate	0	0	0	**9**	0	0	0	0
THYMUS: Atrophy, *very slight*	0	0	0	**7**	0	NE	NE	0
SKIN: Atrophy, hair follicle, sebaceous gland diffuse, *slight*	0	0	0	**1**	0	0	0	**5**
moderate	0	0	0	**9**	0	0	0	0
SKIN: Atrophy, adipose tissue, dermis, diffuse *slight*	0	0	0	**1**	0	0	0	**2**
moderate	0	0	0	**9**	0	0	0	0
MESENTERIC TISSUE: Atrophy, adipose tissue, *slight*	0	0*	0	**10**	0	0	0	**6**
COAGULATING GLAND, SEMINAL VESICLE & PROSTATE: Decreased secretory material *very slight*	0	0	0	**1**	--	--	--	--
Slight	0	0	0	**9**	--	--	--	--
UTERUS: Atrophy, endometrium, myometrium, *slight*	--	--	--	--	0	0	0	**9**
CERVIX: Atrophy, *very slight*	--	--	--	--	0	0	0	**4**
slight	--	--	--	--	0	0	0	**1**
VAGINA: Atrophy *very slight*	--	--	--	--	0	0	0	**1**
slight	--	--	--	--	0	0	0	**6**

Bold type indicates the effects judged to be treatment-related.
*Only 9 mesenteric nodes/mesenteric tissues were examined in this group.
NE: Not examined.

Treatment-related histopathologic effects were noted in numerous organs and tissues, including the stomach, duodenum, submandibular salivary gland, mesenteric lymph nodes, bone marrow, adrenal gland, skin, thymus, mesenteric adipose tissue, coagulating glands, prostate, seminal vesicles, uterus, cervix, and vagina.

The stomach and the duodenum were considered the primary target organs. Treatment-related histopathologic changes in the stomach of males and females given 200 mg/kg/day consisted of moderate diffuse epithelial hyperplasia, hyperkeratosis, ulceration and slight to moderate chronic active inflammation of the nonglandular mucosa. Males and females given 100 mg/kg/day had very slight, slight or moderate multifocal epithelial hyperplasia and hyperkeratosis with very slight to slight chronic active inflammation and occasional ulceration (female, 1 out of 10) of the nonglandular mucosa of the stomach. In the glandular region of the stomach, there was slight or very slight hyperplasia of the mucous neck cells of the pyloric mucosa in most males and females given 200 or 100 mg/kg/day, respectively. Other associated treatment-related changes in the stomach were very slight to slight or very slight multifocal dilatation and individual cell necrosis of the pyloric gastric glands in males given ≥ 100 mg/kg/day and in females given ≥ 100 mg/kg/day, respectively. Treatment-related histopathologic changes in the duodenum consisted of very slight to slight or very slight diffuse epithelial hyperplasia of the mucosa in males given ≥ 100 mg/kg/day and in females given 200 mg/kg/day, respectively. Other associated treatment-related changes in the duodenum consisted of very slight multifocal dilatation and individual cell necrosis of the crypts in males and females given ≥ 100 mg/kg/day. In all males and in some females given 200 mg/kg/day, there was a slight to moderate increase in the degree of sinus histiocytosis (increased numbers of histiocytes/macrophages in the lymph node sinuses) of the mesenteric lymph nodes over that seen in the controls. This increase in sinus histiocytosis was attributed to be a consequence to the ongoing ulceration and chronic active inflammation of the nonglandular stomach mucosa. The effects on the stomach and duodenum were interpreted to be due to the direct irritant/toxic effects of HQDGE. Males and females given 10 mg/kg/day had no treatment-related changes in the stomach or duodenum.

Treatment-related histopathologic changes in males and females given 200 mg/kg/day that were interpreted to be secondary to stress, irritation to the stomach and duodenum, or poor nutrition/decreased feed consumption and body weights, consisted of: very slight hypertrophy of the zona fasciculata of the adrenal glands (males only), very slight thymic atrophy (males only), slight atrophy of the mesenteric adipose tissue, slight to moderate

diffuse atrophy of the dermal adipose tissue and slight to moderate diffuse atrophy of hair follicles and sebaceous glands of the skin, very slight to slight atrophy of the cervix and vagina, slight atrophy of the uterus, very slight to slight decrease in the amounts of secretory material in the coagulating glands, seminal vesicles and prostate, very slight, slight or moderate hypocellularity of all cell lines in the bone marrow, and slight hypertrophy of the acinar cells of the submandibular salivary gland. Very slight hypertrophy of the acinar cells of the submandibular salivary gland was seen in some males given 100 mg/kg/day . Hypertrophy of the salivary gland acinar cells of rats and mice has been shown to be mediated through an adrenergic mechanism (Chan and Mahler, 1992).

Histopathological changes other than those previously discussed were interpreted to be spontaneous alterations, unassociated with exposure to HQDGE.

CONCLUSIONS

Under the conditions of this study, the no-observed-effect level (NOEL) for male and female Fischer 344 rats after four weeks dietary administration of HQDGE was identified as the targeted dose of 10 mg/kg/day.

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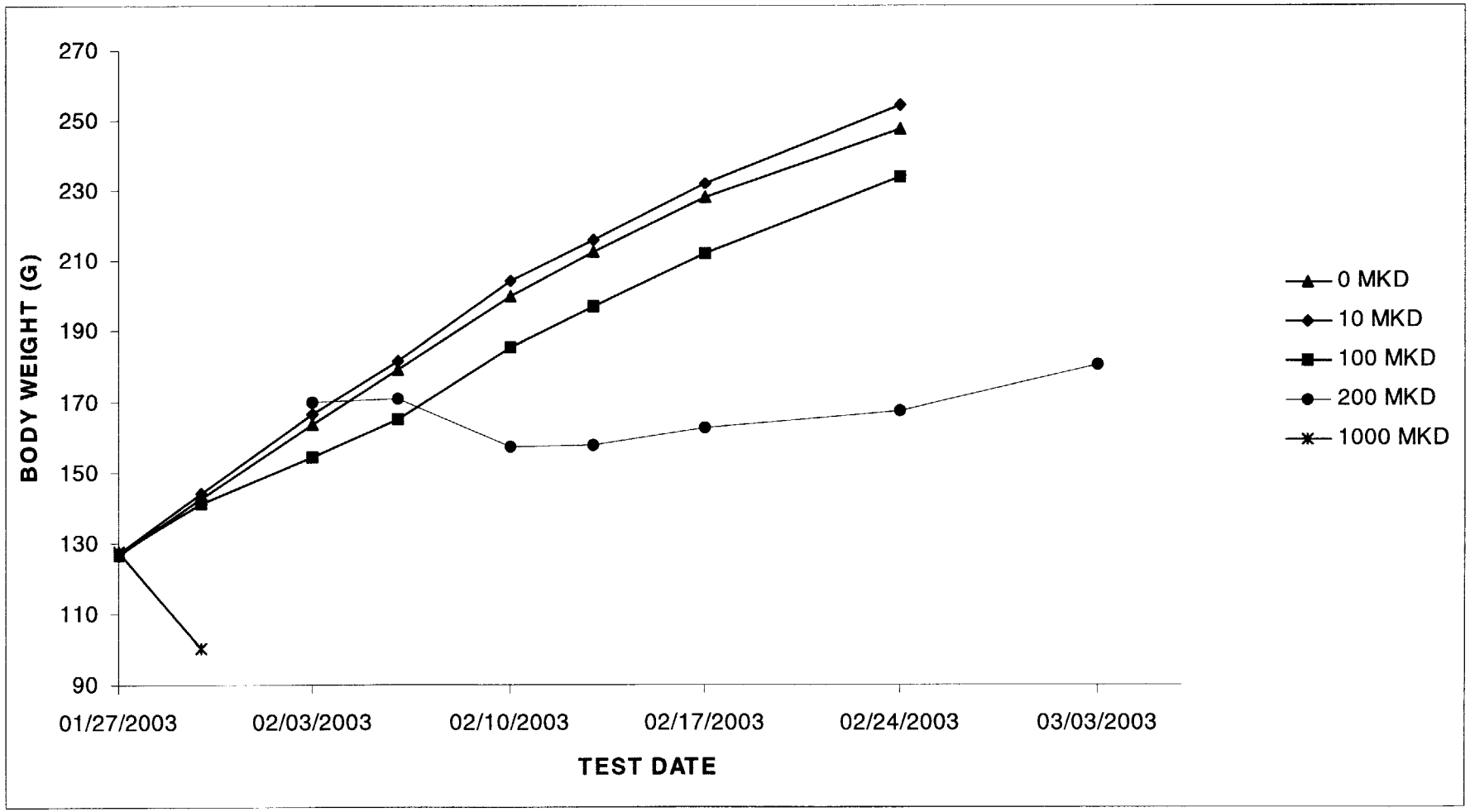
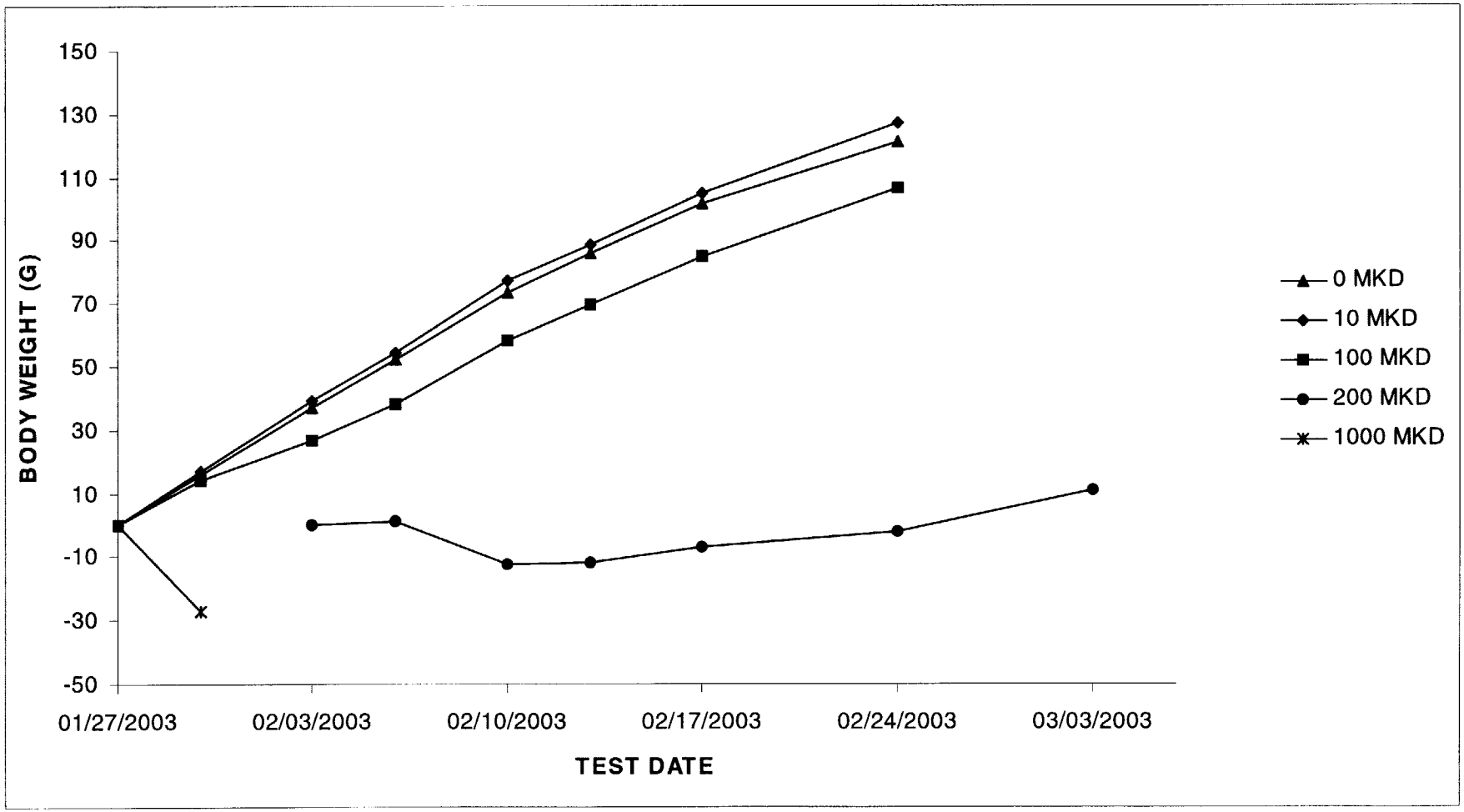
HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

FIGURE 1. Body Weights – Males



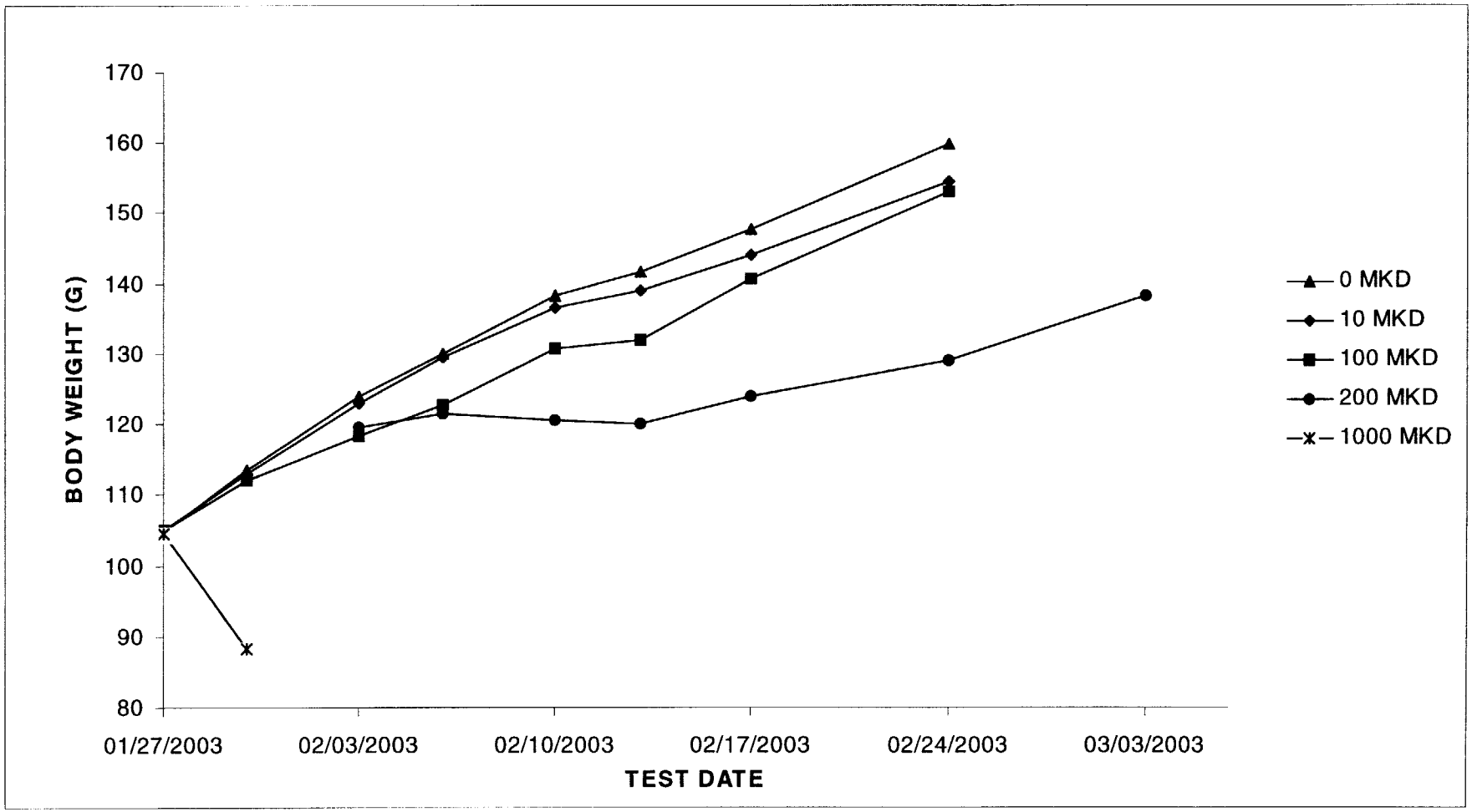
HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

FIGURE 2. Cumulative Body Weight Gains – Males



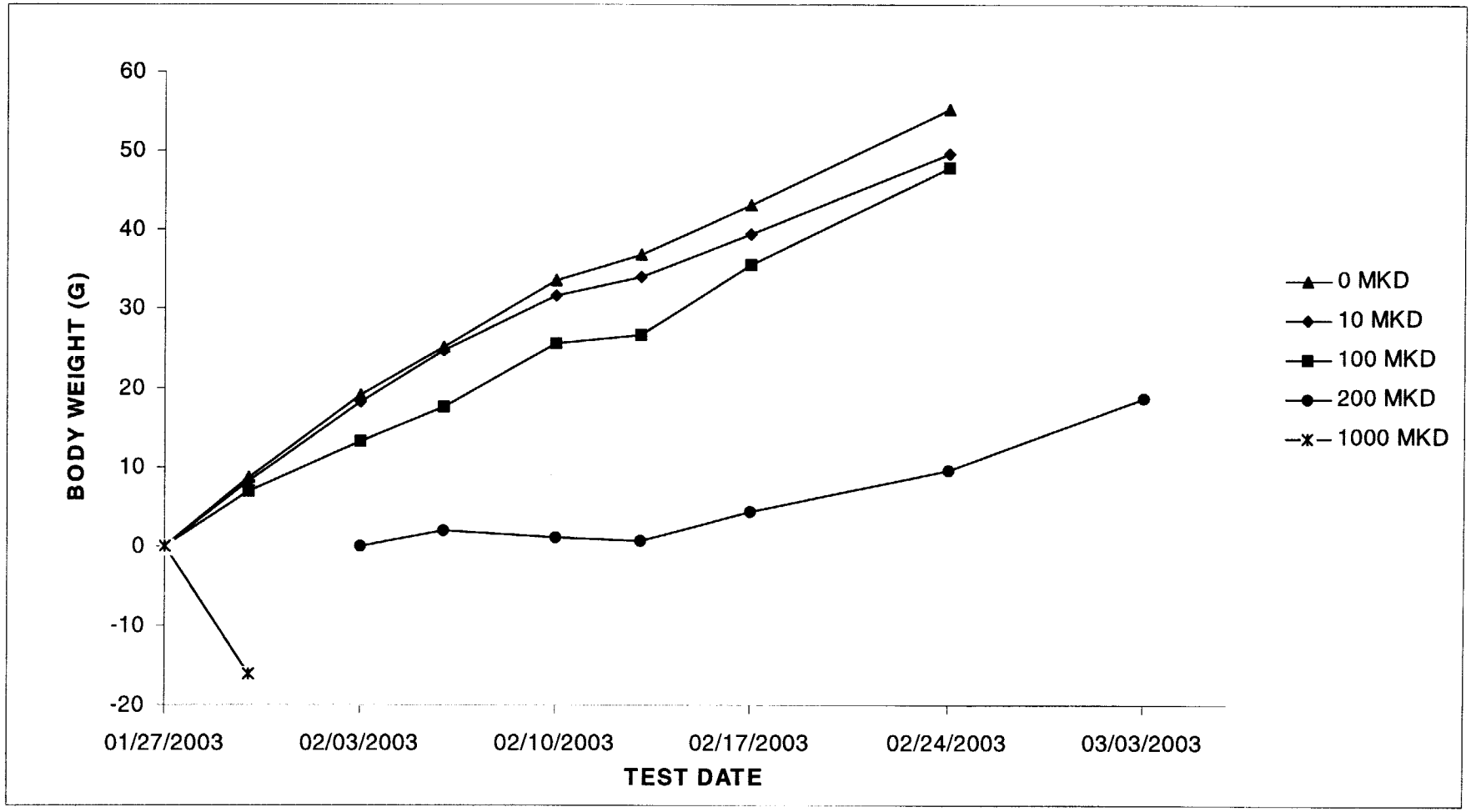
HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

FIGURE 3. Body Weights – Females



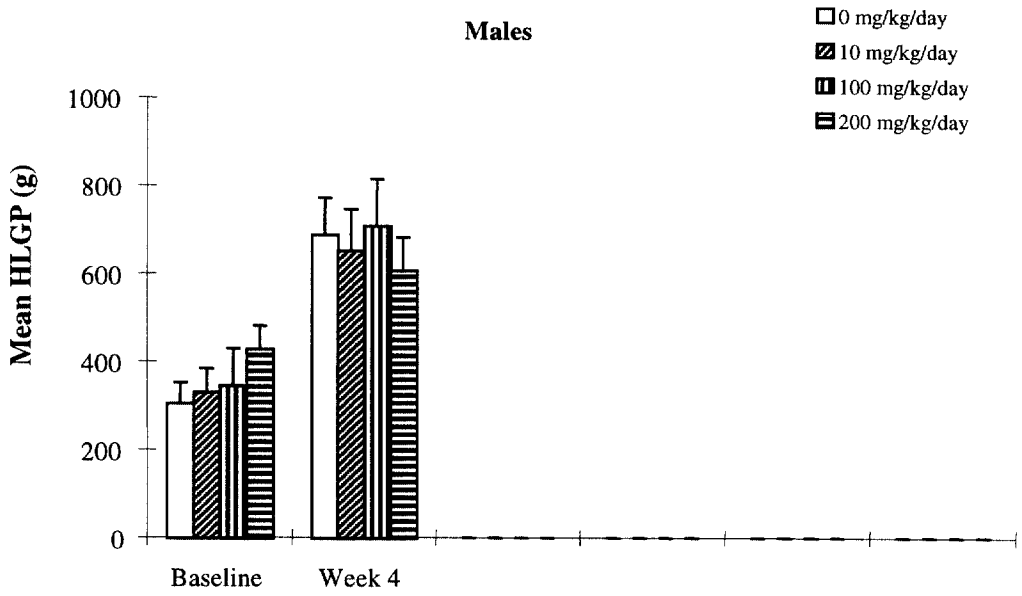
HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

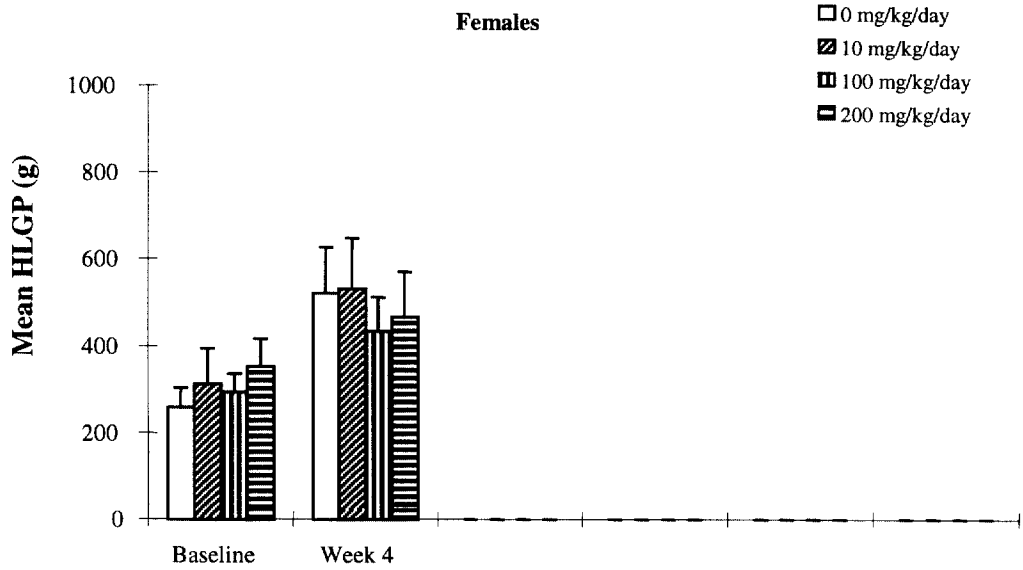
FIGURE 4. Cumulative Body Weight Gains – Females



HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

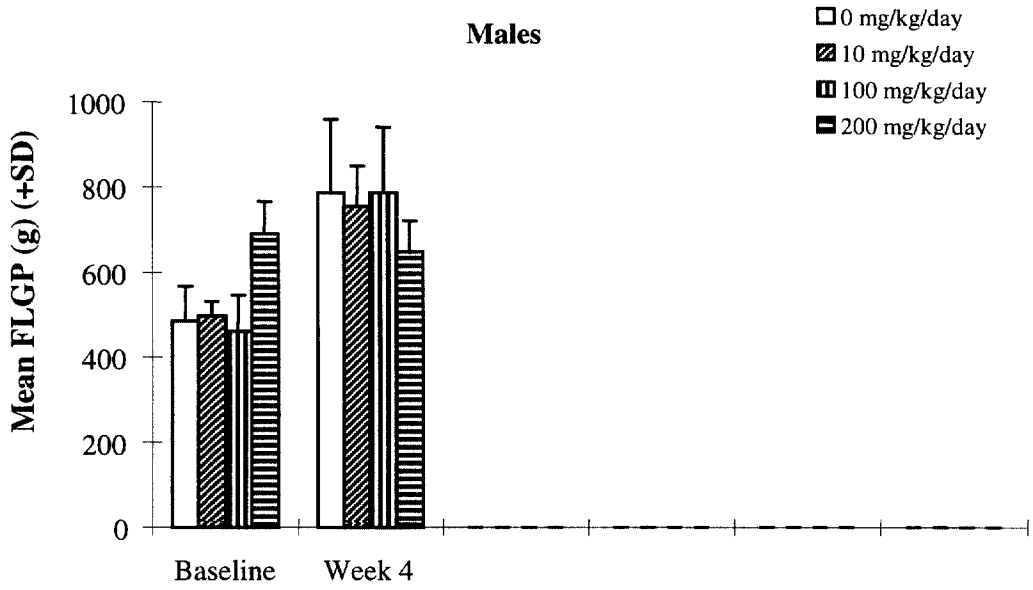
FIGURE 6. Hindlimb Grip Performance (G)

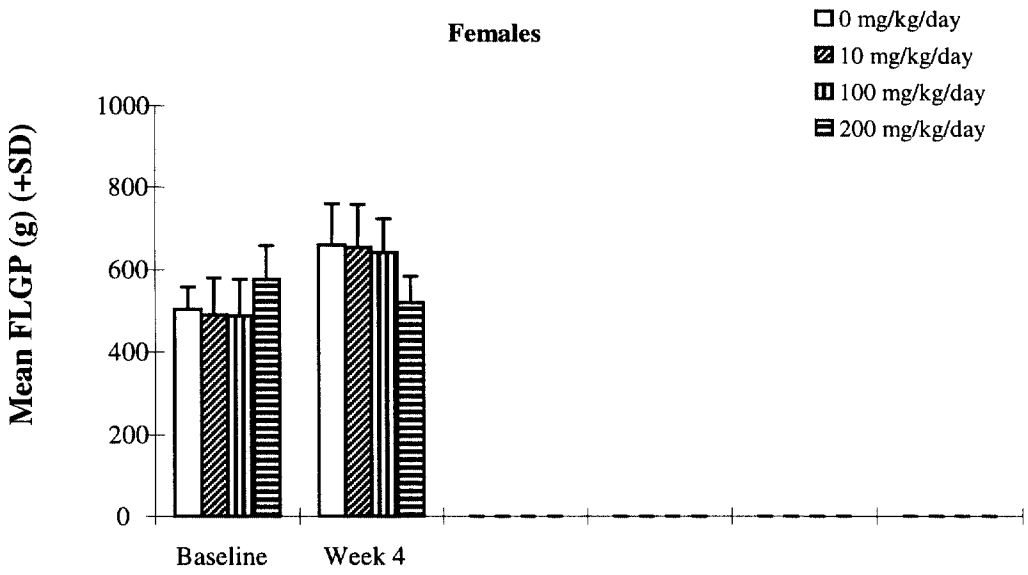




HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

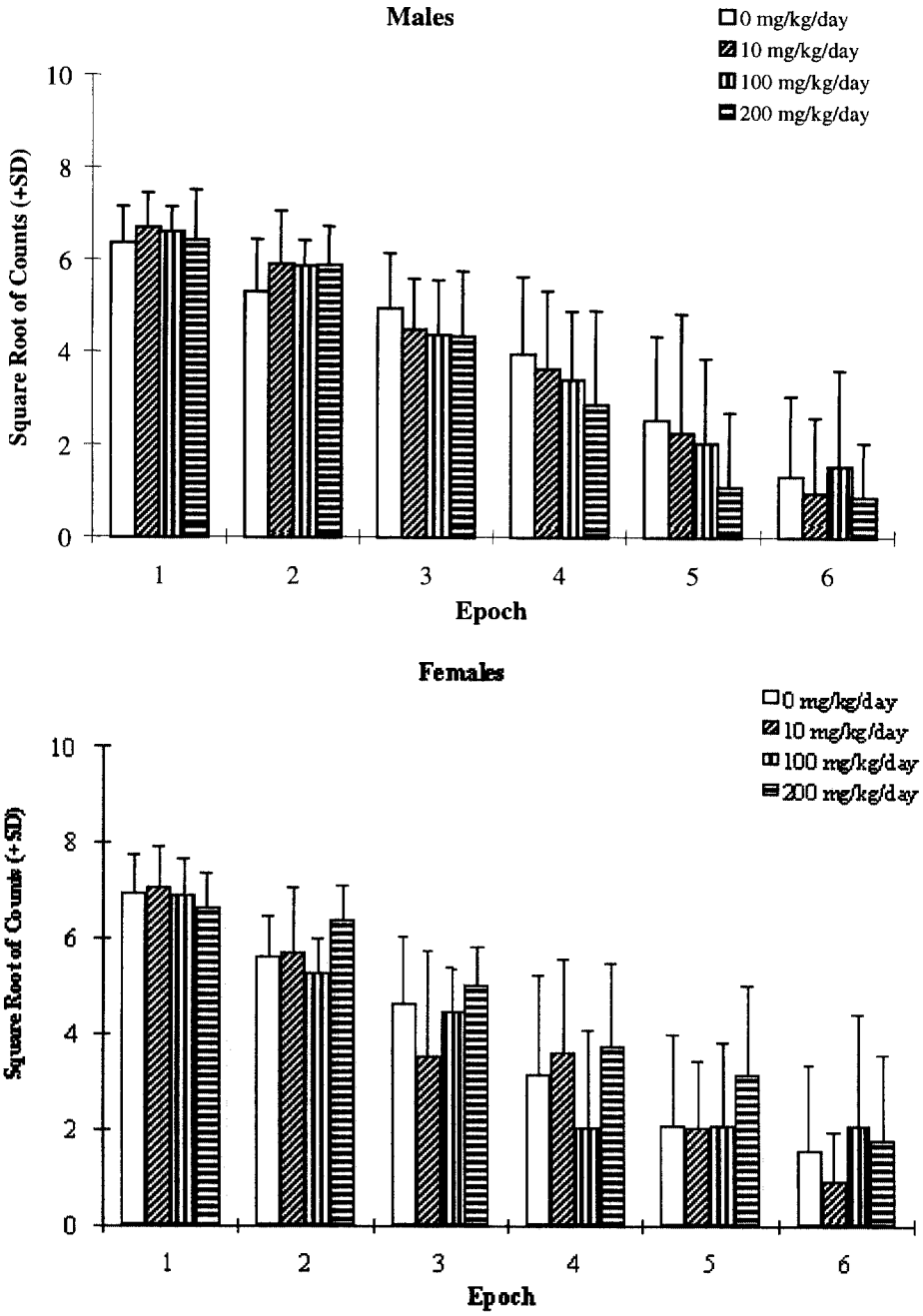
FIGURE 7. Forelimb Grip Performance (G)





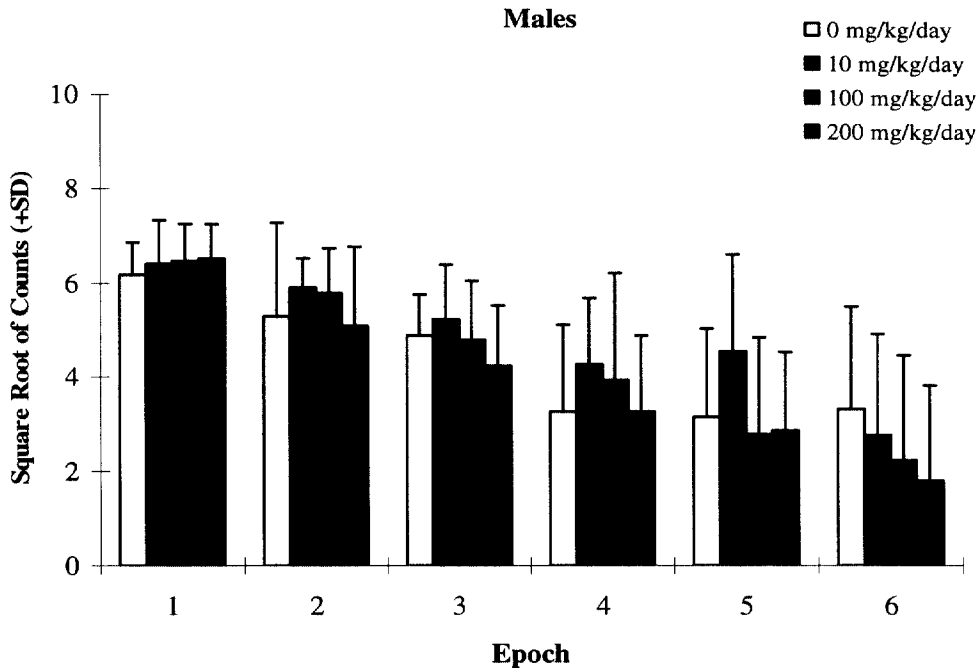
HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

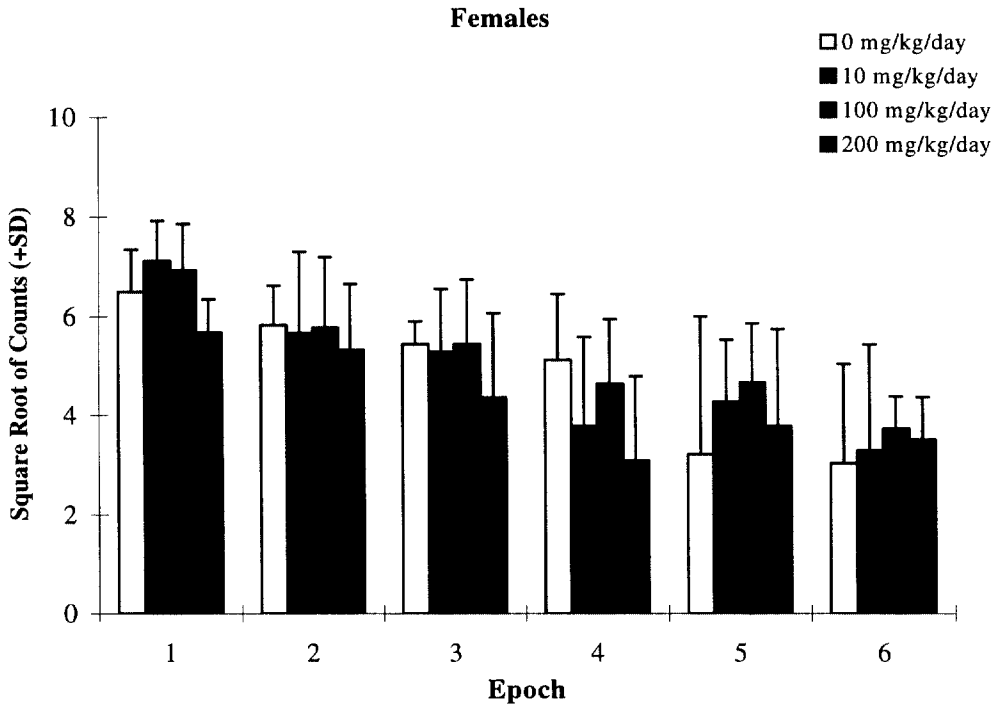
FIGURE 8. Motor Activity Epoch Data – Baseline



HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

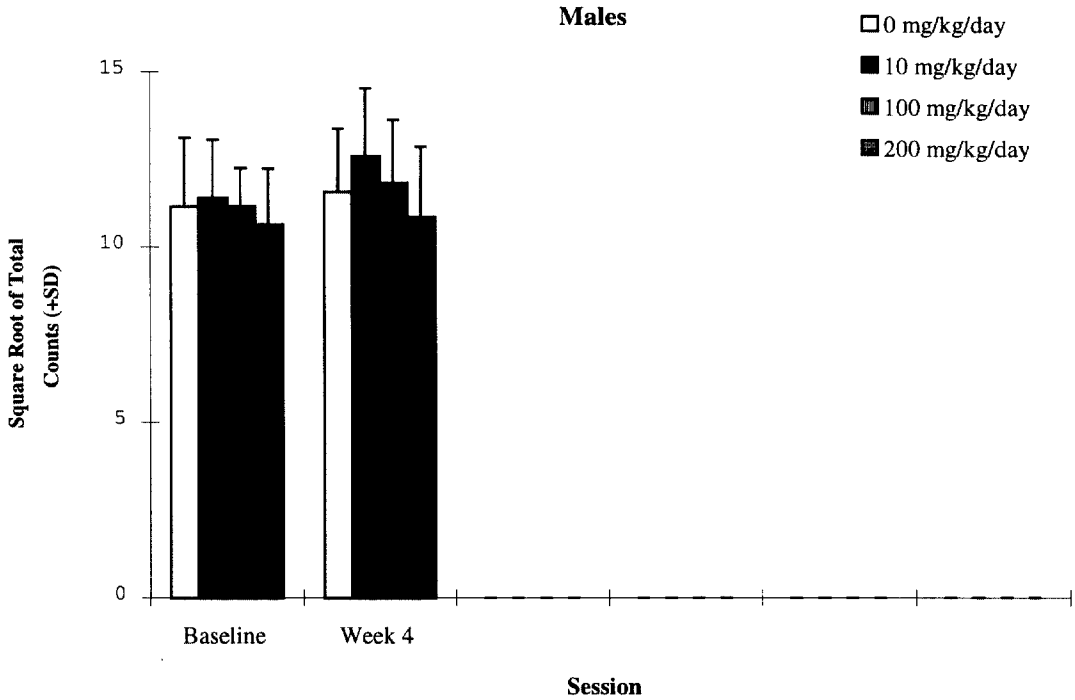
FIGURE 9. Motor Activity Epoch Data – Week 4





HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

FIGURE 10. Motor Activity Epoch Data – Total Counts Data



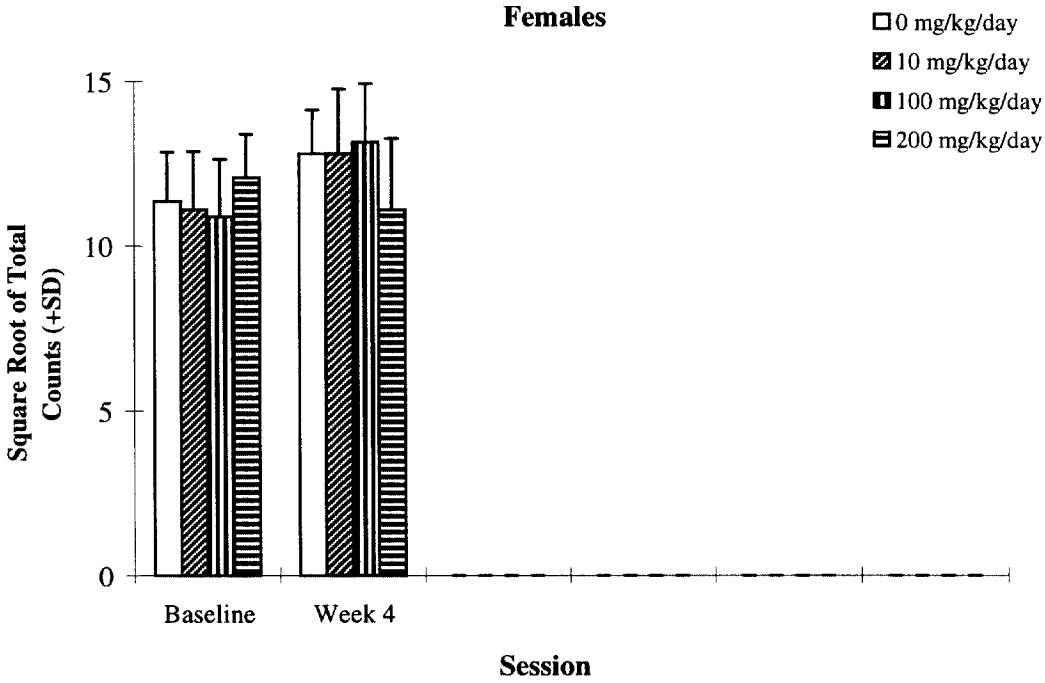


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TABLE 1. DCO Parameters, Functional Tests and Mode of Recording

Cage-side Observations	Recorded As
Abnormal movements or behavior	See Categorical
Resistance to removal from cage	Score

Hand-held Observations	Recorded As
Palpebral closure	Score
Lacrimation (non-colored periocular wetness)	Score
Pupil size	Score
Salivation (non-colored perioral wetness)	Score
Muscle tone	Score
Extensor-thrust response	Score
Reactivity to handling	Score

Open-field Observations	Recorded As
Responsiveness to touch	Score
Gait evaluation	Score

Categorical Observations (anytime during the DCO)	Recorded As
Abnormal behavior	Description
Abnormalities of the eye	Description
Abnormal urine or feces	Description
Abnormalities of the gastrointestinal (GI) tract	Description
Injury	Description
Missing extremity	Description
Abnormal muscle movements	Description
Palpable mass/swellings	Description
Abnormal posture	Description
Abnormalities of the reproductive system	Description
Abnormal respiration	Description
Abnormal skin or hair-coat/mucous membranes	Description
Excessive soiling	Description
General abnormalities	Description

Functional Tests	Recorded As
Motor activity	Square root of beam breaks
Grip performance	Grams
Rectal temperature	°C
Sensory evaluation	
Responsiveness to sharp noise	Rank
Responsiveness to tail pinch	Rank

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TABLE 2. Tissues Collected and Preserved at Necropsy

ADRENALS (2)
AORTA (1)
AUDITORY SEBACEOUS GLANDS (0)
BONE (1) (INCLUDING JOINT)(1)
BONE MARROW (1)
BRAIN (CEREBRUM, BRAINSTEM, CEREBELLUM) (3)
CECUM (1)
CERVIX (1)
COAGULATING GLANDS (2)
COLON (1)
CRANIAL NERVE - OPTIC (2)
DUODENUM (1)
EPIDIDYMIDES (2)
ESOPHAGUS (1)
EYES (2)
GROSS LESIONS (1)
HEART (1)
ILEUM (1)
JEJUNUM (1)
KIDNEYS (2)
LACRIMAL/HARDERIAN GLANDS (2)
LARYNX (1)
LIVER (3)
LUNGS (5)
MAMMARY GLAND - FEMALES ONLY(1)
MEDIASTINAL LYMPH NODE (1)
MEDIASTINAL TISSUES (1)
MESENTERIC LYMPH NODE (1)
MESENTERIC TISSUES (1)
NASAL TISSUES/PHARYNX (2)
ORAL TISSUES (2)
OVARIES (2)
OVIDUCTS (2)
PANCREAS (1)
PARATHYROID GLANDS (1)
PERIPHERAL NERVE - TIBIAL(1)
PITUITARY (1)
PROSTATE (1)
RECTUM (1)
SALIVARY GLANDS (1)
SEMINAL VESICLES (2)
SKELETAL MUSCLE (1)
SKIN AND SUBCUTIS (1)
SPINAL CORD (CERVICAL, THORACIC, LUMBAR) (3)
SPLEEN (1)
STOMACH (1)
TESTES (2)
THYMUS (1)
THYROID GLAND (1)
TONGUE (0)
TRACHEA (1)
URINARY BLADDER (1)
UTERUS (4)
VAGINA (1)

The number in parenthesis represents the minimum number of sections examined histopathologically.

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TABLE 3. Homogeneity of Test Material in Vehicle

Dose Level	Sample I.D.*	Observed Conc. (%w/w)	Relative Standard Deviation
10 mg/kg/day- Male	A	0.0111	
	B	0.0121	
	C	0.0109	
	D	0.0108	
	E	0.0124	
	F	0.0117	5.79%
1000 mg/kg/day- Male	A	1.14	
	B	1.31	
	C	1.07	
	D	1.12	
	E	1.08	
	F	1.09	7.90%

mg/kg/day = mg of test material per kg of bodyweight per day
Data were obtained from ACL Reports which are Dow Internal Reports
*Samples A-F taken from six separate locatoins of diet/test material r

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 4. Stability in Test Material

ACL Report #	2003-6		2003-6		2003-6		2003-6		2003-6	
Date of Analysis	**12/5/02**		**12/13/02**		**12/17/02**		**1/2/03**		**1/13/03**	
	Observed Conc	% of	Observed Conc	% of	Observed Conc	% of	Observed Conc	% of	Observed Conc	% of
Dose Level	(%)	Initial Value	(%)	Initial Value	(%)	Initial Value	(%)	Initial Value	(%)	Initial Value
0.0005%	0.000452	NA	0.000462	102	0.000436	96.5	0.000294	65.0	NA	NA
0.005%	0.00499	NA	0.00466	93.4	0.00378	75.8	0.00370	74.1	NA	NA
0.05%	0.0464	NA	0.0468	101	0.0459	98.9	0.0372	80.2	NA	NA
0.5%	0.519	NA	0.483	93.1	0.497	95.8	0.463	89.2	NA	NA
10% Premix	10.04	NA	9.79	97.5	10.16	102	9.70	96.6	9.62	96.6

Data were obtained from ACL Reports which are Dow Internal Reports
NA not analyzed

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TABLE 5. Concentration of Test Material in Vehicle

	ACL Report #: 2003-14 Date Mixed: 1/26/2003		
Dose Level (mg/kg/day)	Target Concentration (%)	Actual Concentration (%)	% of Target
0	0.0	<LLQ	NA
10- male	0.011	0.0115	105%
100- male	0.107	0.107	100%
1000- male	1.090	1.14	105%
10- female	0.0111	0.0114	103%
100- female	0.110	0.118	107%
1000- female	1.070	1.08	101%
10 % Premix	10.000	9.91	99%

<LLQ = below lower limit of quantitation of 0.000093 %(w/w)

ACL Report #: Date Mixed:	2003-17 2/3/03		
Dose Level (mg/kg/day)	Target Concentration (%)	Actual Concentration (%)	% of Target
2 % Premix	2.000	1.9	95%
200- male	0.222	0.212	95.5%
200- female	0.186	0.178	95.7%

<LLQ = below lower limit of quantitation of 0.00249 %(w/w)

NA = Not applicable
mg/kg/day = mg of test material per kg bodyweight per day
Data were obtained from ACL Reports which are Dow Internal Reports.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 6. Summary of Scored DCO Observations

SEX	MALES					FEMALES				
DOSE (MKD)	0	10	100	200	1000	0	10	100	200	1000
	Number of Animals with Observation									
Pupil Size - Bilateral, Increased[@]										
Day 15	0	0	0	0	*	0	0	0	1	*
Day 22	0	0	0	0	*	0	0	0	1	*
Day 29	0	0	0	0	*	0	0	0	1	*
Examinations (Number Animals Within Normal Limits / Number Animals Examined)										
Day 1	10/10	10/10	10/10	10/10	10/10	10/10	10/10	10/10	9/9	10/10
Day 8	10/10	10/10	10/10	10/10	*	10/10	10/10	10/10	9/9	*
Day 15	10/10	10/10	10/10	10/10	*	10/10	10/10	10/10	8/9	*
Day 22	10/10	10/10	10/10	10/10	*	10/10	10/10	10/10	8/9	*
Day 29	10/10	10/10	10/10	10/10	*	10/10	10/10	10/10	8/9	*

Days presented are examination days when the specified observations were reported.

There were no statistically significant differences from controls by *z*-test of proportions, alpha = 0.05.

*All 1000 mkd animals euthanized on Day 5 of study.

[@] This parameter was statistically analyzed.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 7. Summary of Categorical DCO Observations

SEX	MALES					FEMALES				
DOSE (MKD)	0	10	100	200	1000	0	10	100	200	1000
	Number of Animals with Observation									
Disposition, Removed										
Day 5	-	-	-	-	10	-	-	-	-	10
Eyes, Cloudy										
Day 15	0	0	1	0	*	0	0	0	1	*
Day 22	0	0	1	0	*	0	0	0	1	*
Day 29	0	0	1	0	*	0	1	0	1	*
Eyes, Enlarged or Protruding										
Day 15	0	0	1	0	*	0	0	0	0	*
Day 22	0	0	1	0	*	0	0	0	0	*
Day 29	0	0	1	0	*	0	0	0	0	*
Feces, Abnormal Quantity, Decreased										
Day 2@	-	-	-	-	10	-	-	-	-	10
Day 3@	-	-	-	-	10	-	-	-	-	10
Day 4@	-	-	-	-	10	-	-	-	-	10
Day 5@	-	-	-	-	10	-	-	-	-	10
Day 8	0	0	0	1	*	0	0	0	0	*
Day 9@	-	-	-	10	*	-	-	-	2	*
Day 10@	-	-	-	10	*	-	-	-	2	*
Day 17@	-	-	-	2	*	-	-	-	1	*
Gastrointestinal Tract, Maloccluded Incisors, Not Clipped										
Day 22	0	0	0	0	*	0	0	1	0	*
Day 29	0	0	0	0	*	0	0	1	0	*

Days presented are examination days when the specified observations were reported.

-- These animals not observed on this date.

* All 1000 mg/kg/day animals euthanized on Day 5.

@ This observation was documented during a cageside exam.

There were no statistically significant differences from controls by z-test of proportions, alpha = 0.05.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 7. Summary of Categorical DCO Observations (continued)

SEX	MALES					FEMALES				
DOSE (MKD)	0	10	100	200	1000	0	10	100	200	1000
	Number of Animals with Observation									
Miscellaneous, Thin										
Day 5@	-	-	-	-	10	-	-	-	-	10
Day 8	0	0	0	2	*	0	0	0	0	*
Day 9@	-	-	-	7	*	-	-	-	2	*
Day 10@	-	-	-	7	*	-	-	-	0	*
Day 15	0	0	0	2	*	0	0	0	1	*
Day 17@	-	-	-	1	*	-	-	-	0	*
Day 22	0	0	0	1	*	0	0	0	1	*
Day 29	0	0	0	0	*	0	0	0	1	*
Skin/Fur/Mucous Membranes, Dehydrated										
Day 8	0	0	0	2	*	0	0	0	0	*
Day 9@	-	-	-	3	*	-	-	-	0	*
Day 10@	-	-	-	2	*	-	-	-	0	*
Day 15	0	0	0	1	*	0	0	0	0	*
Day 17	-	-	-	1	*	-	-	-	0	*
Skin/Fur/Mucous Membranes, Reddened, Multifocal										
Day 29	0	0	0	0	*	0	1	0	0	*
Skin/Fur/Mucous Membranes, Ungroomed Appearance										
Day 5@	-	-	-	-	10	-	-	-	-	10

Days presented are examination days when the specified observations were reported.

-- These animals not observed on this date.

* All 1000 mg/kg/day animals euthanized on Day 5.

@ This observation was documented during a cageside exam.

There were no statistically-significant differences from controls by z-test of proportions, alpha = 0.05.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 7. Summary of Categorical DCO Observations (continued)

SEX	MALES					FEMALES				
DOSE (MKD)	0	10	100	200	1000	0	10	100	200	1000
	Number of Animals with Observation									
Soiling, Perinasal, Red										
Day 8	0	0	0	1	*	0	0	0	0	*
Day 9@	-	-	-	1	*	-	-	-	0	*
Day 22	0	0	0	1	*	0	0	0	1	*
Soiling, Periocular, Red										
Day 8	0	0	0	0	*	1	1	0	0	*
Day 15	0	0	0	0	*	1	0	0	0	*
Day 22	0	0	0	1	*	0	0	0	0	*
Day 29	0	0	1	1	*	1	0	0	0	*
Soiling, Perioral, Red										
Day 8	0	0	0	3	*	0	0	0	0	*
Day 9@	-	-	-	3	*	-	-	-	0	*
Examinations (Number Animals Within Normal Limits / Number Animals Examined)										
Day 1	10/10	10/10	10/10	10/10	10/10	10/10	10/10	10/10	9/9	10/10
Day 2@	-	-	-	-	0/10	-	-	-	-	0/10
Day 3@	-	-	-	-	0/10	-	-	-	-	0/10
Day 4@	-	-	-	-	0/10	-	-	-	-	0/10
Day 5@	-	-	-	-	0/10	-	-	-	-	0/10
Day 8	10/10	10/10	10/10	7/10	*	9/10	9/10	10/10	9/9	*
Day 9@	-	-	-	0/10	*	-	-	-	0/4	*
Day 10@	-	-	-	0/10	*	-	-	-	0/2	*

Days presented are examination days when the specified observations were reported.

-- These animals not observed on this date.

* All 1000 mg/kg/day animals euthanized on Day 5.

@ This observation was documented during a cageside exam.

There were no statistically-significant differences from controls by z-test of proportions, alpha = 0.05.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 7. Summary of Categorical DCO Observations (continued)

SEX	MALES					FEMALES				
DOSE (MKD)	0	10	100	200	1000	0	10	100	200	1000
	Number of Animals with Observation									
Examinations (Number Animals Within Normal Limits / Number Animals Examined) (continued)										
Day 15	10/10	10/10	9/10	8/10	*	9/10	10/10	10/10	8/9	*
Day 17@	-	-	-	0/2	*	-	-	-	0/1	*
Day 22	10/10	10/10	9/10	7/10	*	10/10	10/10	9/10	8/9	*
Day 29	10/10	10/10	8/10	9/10	*	9/10	8/10	9/10	8/9	*

Days presented are examination days when the specified observations were reported.

-- These animals not observed on this date.

* All 1000 mg/kg/day animals euthanized on Day 5.

@ This observation was documented during a cageside exam.

There were no statistically-significant differences from controls by z-test of proportions, alpha = 0.05.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 8. Sensory Evaluation Summary – Baseline

SEX:	MALES				FEMALES			
DOSE (MKD):	0.0	10	100	200	0.0	10	100	200
NUMBER OF ANIMALS OBSERVED:	10	10	10	10	10	10	10	9
Scored Observations								
Responsiveness to Tail Pinch, Moderate	10	10	10	10	10	10	10	9
Responsiveness to Sharp Noise, Moderate	10	10	10	10	10	10	10	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 9. Sensory Evaluation Summary – Week 4

SEX:	MALES				FEMALES			
DOSE (MKD):	0.0	10	100	200	0.0	10	100	200
NUMBER OF ANIMALS OBSERVED:	10	10	10	10	10	10	10	9
Scored Observations								
Responsiveness to Tail Pinch, Moderate	10	10	10	10	10	10	10	9
Responsiveness to Sharp Noise, Moderate	10	10	10	10	10	10	10	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 10. Rectal Temperature (°C) – ANCOVA

Sources of Variation 0,10 and 100 mg/kg/day	P values (n = 60)
Treatment x Sex	0.4985[1]
Treatment	0.8132[2]

Sources of Variation 0 and 200 mg/kg/day	P values (n = 39)
Treatment x Sex	0.8991[1]
Treatment	0.1337[2]

[1] A nonsignificant p value for the Treatment x Sex interaction indicates that treatment effects (or lack thereof) were not different between males and females.
[2] A nonsignificant p value for Treatment indicates that, taken together, males and females were not affected by treatment.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 11. Rectal Temperature (C) – Descriptive Statistics

Males		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	38.71	38.66	38.75	38.27
	S.D.	0.35	0.46	0.42	0.40
	N	10	10	10	10
Week 4	Mean	37.99	38.50	38.14	37.91
	S.D.	0.79	0.55	0.57	0.38
	N	10	10	10	10

Females		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	38.91	38.95	38.99	38.86
	S.D.	0.38	0.45	0.37	0.59
	N	10	10	10	9
Week 4	Mean	38.97	39.13	38.97	38.78
	S.D.	0.49	0.60	0.76	0.47
	N	10	10	10	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 12. Hindlimb Grip Performance (G) – ANCOVA

Sources of Variation 0,10 and 100 mg/kg/day	P values (n = 60)
Treatment x Sex	0.0963[1]
Treatment	0.9537[2]

Sources of Variation 0 and 200 mg/kg/day	P values (n = 39)
Treatment x Sex	0.6270[1]
Treatment	0.2564[2]

[1] A nonsignificant p value for the Treatment x Sex interaction indicates that treatment effects (or lack thereof) were not different between males and females.

[2] A nonsignificant p value for Treatment indicates that, taken together, males and females were not affected by treatment.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 13. Hindlimb Grip Performance (G) – Descriptive Statistics

Males		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	304.47	330.63	344.26	427.20
	S.D.	47.87	53.80	85.33	52.51
	N	10	10	10	10
Week 4	Mean	685.68	651.57	706.52	605.92
	S.D.	85.13	93.23	106.86	75.86
	N	10	10	10	10

Females		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	257.74	311.47	293.13	351.68
	S.D.	45.08	81.46	41.79	63.15
	N	10	10	10	9
Week 4	Mean	520.66	531.11	433.13	466.54
	S.D.	105.91	116.52	78.54	103.59
	N	10	10	10	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 14. Forelimb Grip Performance (G) – ANCOVA / ANOVA

ANCOVA - Sources of Variation 0,10 and 100 mg/kg/day	P values (n = 60)
Treatment x Sex	0.5492[1]
Treatment	0.1567[2]

ANOVA - Sources of Variation 0 and 200 mg/kg/day	P values (n = 39)
Baseline	
Treatment x Sex	0.0087[3]
Treatment	0.0001[4]
Treatment (Males)	0.0001[4]
Treatment (Females)	0.0344[4]
Post Exposure	
Treatment x Sex	0.9780[1]
Treatment	0.0004[4]

[1] This non-significant p value for the Treatment x Sex interaction indicates that treatment effects (or lack thereof) were not different between males and females.

[2] This non-significant p value for Treatment indicates that, taken together, males and females were not affected by treatment.

[3] This significant p value for the treatment x Sex interaction indicates that treatment differentially affected males and females.

[4] This significant p value for treatment indicates the presence of a treatment effect.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 15. Forelimb Grip Performance (G) – Descriptive Statistics

Males		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	484.71	496.52	459.95	689.63
	S.D.	82.14	34.47	86.41	75.36
	N	10	10	10	10
Week 4	Mean	786.70	754.39	787.30	648.24
	S.D.	171.79	94.18	153.29	72.83
	N	10	10	10	10

Females		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	503.32	490.24	487.26	576.09
	S.D.	54.94	89.67	89.28	81.71
	N	10	10	10	9
Week 4	Mean	659.29	653.43	641.70	518.84
	S.D.	99.69	103.64	80.72	65.05
	N	10	10	10	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 16. Motor Activity – Repeated – Measure ANOVA

Sources of Variation 0,10 and 100 mg/kg/day	P values (n = 60)
Treatment x Time x Sex	0.4543[1]
Treatment x Time	0.4082[2]
Treatment x Time x Epoch	0.4247[3]

Sources of Variation 0 and 200 mg/kg/day	P values (n = 39)
Treatment x Time x Sex	0.1159[1]
Treatment x Time	0.2018[2]
Treatment x Time x Epoch	0.3962[3]

[1] This non-significant p value for the interaction Treatment x Time x Sex indicates that treatment effects were not different between males and females at either time interval.
[2] This non-significant p value for the interaction Treatment x Time indicates that, taken together, neither males nor females were affected by treatment at either time interval.
[3] This non-significant p value for the interaction Treatment x Time x Epoch indicates that treatment did not differentially affect the within session distribution of counts at either time interval.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 17. Square Root of Motor Activity Counts by Epoch – Descriptive Statistics (Baseline)

Baseline Males		Periods 1	2	3	4	5	6
0 mg/kg/day	Mean	6.36	5.30	4.94	3.95	2.53	1.31
	S.D.	0.79	1.13	1.20	1.68	1.80	1.73
	N	10	10	10	10	10	10
10 mg/kg/day	Mean	6.68	5.90	4.47	3.62	2.26	0.95
	S.D.	0.77	1.16	1.11	1.70	2.56	1.63
	N	10	10	10	10	10	10
100 mg/kg/day	Mean	6.60	5.86	4.35	3.39	2.03	1.53
	S.D.	0.54	0.55	1.20	1.49	1.82	2.07
	N	10	10	10	10	10	10
200 mg/kg/day	Mean	6.41	5.88	4.32	2.86	1.08	0.86
	S.D.	1.10	0.84	1.43	2.03	1.61	1.18
	N	10	10	10	10	10	10
Females							
0 mg/kg/day	Mean	6.93	5.61	4.62	3.14	2.07	1.58
	S.D.	0.83	0.88	1.43	2.10	1.92	1.79
	N	10	10	10	10	10	10
10 mg/kg/day	Mean	7.06	5.70	3.55	3.63	2.02	0.91
	S.D.	0.84	1.36	2.19	1.93	1.43	1.04
	N	10	10	10	10	10	10
100 mg/kg/day	Mean	6.89	5.27	4.45	2.04	2.10	2.08
	S.D.	0.80	0.75	0.94	2.06	1.72	2.33
	N	10	10	10	10	10	10
200 mg/kg/day	Mean	6.62	6.40	5.02	3.75	3.12	1.77
	S.D.	0.74	0.70	0.81	1.76	1.92	1.79
	N	9	9	9	9	9	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 18. Square Root of Motor Activity Counts by Epoch – Descriptive Statistics (Week 4)

Week 4 Males		Epochs 1	2	3	4	5	6
0 mg/kg/day	Mean	6.18	5.29	4.88	3.27	3.15	3.33
	S.D.	0.68	1.98	0.87	1.84	1.88	2.17
	N	10	10	10	10	10	10
10 mg/kg/day	Mean	6.41	5.90	5.22	4.27	4.54	2.77
	S.D.	0.92	0.63	1.17	1.41	2.06	2.14
	N	10	10	10	10	10	10
100 mg/kg/day	Mean	6.47	5.79	4.79	3.94	2.79	2.23
	S.D.	0.78	0.94	1.26	2.27	2.06	2.24
	N	10	10	10	10	10	10
200 mg/kg/day	Mean	6.51	5.09	4.24	3.27	2.86	1.81
	S.D.	0.73	1.68	1.28	1.61	1.67	2.01
	N	10	10	10	10	10	10
Females							
0 mg/kg/day	Mean	6.50	5.83	5.45	5.13	3.22	3.03
	S.D.	0.84	0.79	0.46	1.33	2.79	2.01
	N	10	10	10	10	10	10
10 mg/kg/day	Mean	7.11	5.67	5.29	3.79	4.28	3.29
	S.D.	0.81	1.63	1.26	1.80	1.26	2.16
	N	10	10	10	10	10	10
100 mg/kg/day	Mean	6.93	5.78	5.45	4.64	4.66	3.73
	S.D.	0.93	1.41	1.29	1.31	1.20	0.66
	N	10	10	10	10	10	10
200 mg/kg/day	Mean	5.68	5.33	4.36	3.08	3.79	3.51
	S.D.	0.67	1.32	1.71	1.71	1.97	0.87
	N	9	9	9	9	9	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 19. Square Root of Motor Activity Counts – Descriptive Statistics

Males		Dose Group (mg/kg/day) 0	10	100	200
Baseline	Mean	11.15	11.39	11.15	10.63
	S.D.	1.95	1.67	1.09	1.59
	N	10	10	10	10
Week 4	Mean	11.56	12.58	11.81	10.85
	S.D.	1.81	1.95	1.82	2.00
	N	10	10	10	10
Females					
Baseline	Mean	11.35	11.09	10.89	12.07
	S.D.	1.50	1.77	1.74	1.31
	N	10	10	10	9
Week 4	Mean	12.80	12.79	13.14	11.09
	S.D.	1.32	1.98	1.80	2.17
	N	10	10	10	9

S.D. = standard deviation
N = sample size

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 20. Ophthalmic Observations Summary – Pre-exposure

STUDY DAY: -14

SEX:	MALES	FEMALES
DOSE (MKD):	200	200
NUMBER OF ANIMALS OBSERVED:	10	9
Eyes		
Within Normal Limits	7	6
Dilation Incomplete	2	0
Cloudy Cornea	1	0
Periocular Soiling	0	1
Microphthalmia	0	2

Data are the number of animals with the specified observation.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 20. Ophthalmic Observations Summary – Pre-exposure (continued)

STUDY DAY: -7

SEX:	MALES				FEMALES			
DOSE (MKD):	0.0	10	100	1000	0.0	10	100	1000
NUMBER OF ANIMALS OBSERVED:	10	10	10	10	10	10	10	10
Eyes								
Within Normal Limits	10	10	10	10	10	10	10	10

Data are the number of animals with the specified observation.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 21. Ophthalmic Observations Summary – Terminal

STUDY DAY: 29

SEX:	MALES				FEMALES			
DOSE (MKD):	0.0	10	100	200	0.0	10	100	200
NUMBER OF ANIMALS OBSERVED:	10	10	10	10	10	10	10	9
Eyes								
Within Normal Limits	7	8	6	8	9	9	7	8
Pale Fundus	1	1	2	1	1	1	3	0
Cloudy Cornea	1	1	3	1	0	0	1	0
Periocular Soiling	1	0	1	1	0	0	0	0
Microphthalmia	0	0	0	0	0	0	0	1

Data are the number of animals with the specified observation.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 22. Body Weight/Body Weight Gains Summary (G) – Males

DOSE MKD		DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
0	MEAN	126.6	142.4	15.8&	163.7	37.1&	179.0	52.3&	200.1	73.5&	212.7	86.0&	228.1	101.5&
	S.D.	5.8	6.8	1.7	8.5	3.8	9.2	4.8	9.5	5.2	10.0	6.4	9.5	5.6
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	MEAN	127.2	144.1	16.9&	166.4	39.2&	181.7	54.5&	204.2	77.0&	215.8	88.6&	232.0	104.8&
	S.D.	5.2	7.3	2.5	9.5	5.6	11.2	7.8	12.2	8.8	11.4	8.2	11.0	7.8
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
100	MEAN	127.2	141.3	14.1&	154.0	26.8&	165.0	37.8&	185.2	58.0&	196.8	69.6&	211.9	84.7&
	S.D.	4.4	4.7	2.0	5.4	2.3	5.7	2.4	5.5	2.6	5.2	2.9	5.4	2.6
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	MEAN	169.6	170.6	1.0&	157.2	-12.4&	157.6	-12.1&	162.7	-7.0&	===	===	167.5	-2.1&
	S.D.	11.0	12.2	4.4	18.5	13.3	17.6	12.8	15.8	10.7	===	===	13.9	7.4
	N=	10	10	10	10	10	10	10	10	10	0	0	10	10
1000	MEAN	127.5	100.4	-27.0&	===	===	===	===	===	===	===	===	===	===
	S.D.	7.8	4.6	4.4	===	===	===	===	===	===	===	===	===	===
	N=	10	10	10	0	0	0	0	0	0	0	0	0	0

& INDICATES NO STATISTICAL COMPARISON OF MEANS.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 22. Body Weight/Body Weight Gains Summary (G) – Males (continued)

DOSE MKD		DAYS ON TEST 1	29	GAIN
0	MEAN	126.6	247.6	121.0&
	S.D.	5.8	11.4	7.6
	N=	10	10	10
10	MEAN	127.2	254.3	127.1&
	S.D.	5.2	12.0	8.2
	N=	10	10	10
100	MEAN	127.2	233.8	106.6&
	S.D.	4.4	5.4	3.2
	N=	10	10	10
200	MEAN	169.6	180.3	10.7&
	S.D.	11.0	13.7	6.7
	N=	10	10	10
1000	MEAN	127.5	===	===
	S.D.	7.8	===	===
	N=	10	0	0

& INDICATES NO STATISTICAL COMPARISON OF MEANS.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 23. Body Weight/Body Weight Gains Summary (G) – Females

DOSE MKD		DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
0	MEAN	104.8	113.4	8.7&	123.8	19.1&	130.0	25.2&	138.3	33.5&	141.7	36.9&	147.8	43.0&
	S.D.	4.3	4.4	1.7	4.8	2.1	6.1	3.1	7.1	4.5	6.9	4.6	7.9	5.9
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	MEAN	104.9	113.1	8.2&	123.0	18.2&	129.5	24.7&	136.6	31.7&	138.9	34.0&	144.1	39.3&
	S.D.	4.2	3.5	1.1	5.1	1.6	5.4	1.8	5.0	2.0	5.8	3.2	7.1	3.7
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
100	MEAN	105.1	112.0	6.8&	118.3	13.1&	122.7	17.5&	130.7	25.5&	131.8	26.7&	140.7	35.6&
	S.D.	3.6	3.8	1.1	3.4	1.7	3.3	2.1	4.0	3.6	4.0	3.2	4.2	3.5
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	MEAN	119.6	121.4	1.8&	120.6	1.0&	120.1	0.5&	123.8	4.2&	===	===	129.0	9.4&
	S.D.	8.8	8.7	1.2	8.0	2.8	10.3	4.0	9.9	3.2	===	===	12.0	6.0
	N=	9	9	9	9	9	9	9	9	9	0	0	9	9
1000	MEAN	104.5	88.3	-16.2&	===	===	===	===	===	===	===	===	===	===
	S.D.	2.6	2.2	1.1	===	===	===	===	===	===	===	===	===	===
	N=	10	10	10	0	0	0	0	0	0	0	0	0	0

& INDICATES NO STATISTICAL COMPARISON OF MEANS.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 23. Body Weight/Body Weight Gains Summary (G) – Females (continued)

DOSE MKD		DAYS ON TEST 1	29	GAIN
0	MEAN	104.8	159.9	55.2&
	S.D.	4.3	9.5	7.1
	N=	10	10	10
10	MEAN	104.9	154.4	49.5&
	S.D.	4.2	5.4	2.6
	N=	10	10	10
100	MEAN	105.1	152.9	47.8&
	S.D.	3.6	5.2	4.2
	N=	10	10	10
200	MEAN	119.6	138.2	18.6&
	S.D.	8.8	15.3	8.7
	N=	9	9	9
1000	MEAN	104.5	===	===
	S.D.	2.6	===	===
	N=	10	0	0

& INDICATES NO STATISTICAL COMPARISON OF MEANS.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 24. Feed Consumption (G/Day) Summary – Males (0, 10 and 100 mg/kg/day)

DOSE MKD		DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
0	MEAN	15.0	15.6	16.7	17.5	17.8	18.2	18.4
	S.D.	0.8	0.7	1.0	0.8	0.8	0.8	1.1
	N=	10	10	9	9	10	10	10
10	MEAN	15.2	15.6	16.8	17.7	17.5	18.2	18.2
	S.D.	1.0	1.3	1.4	1.3	1.1	0.9	0.9
	N=	10	10	10	10	10	10	10
100	MEAN	14.0*	13.1*	13.9*	15.8*	15.8*	16.9*	17.1*
	S.D.	0.7	0.8	0.8	0.6	0.9	0.8	0.7
	N=	10	10	10	10	10	10	10
1000	MEAN	2.6*	===	===	===	===	===	===
	S.D.	0.6	===	===	===	===	===	===
	N=	10	0	0	0	0	0	0

* STATISTICALLY DIFFERENT FROM CONTROL MEAN BY DUNNETT'S TEST, ALPHA=0.05.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 25. Feed Consumption (G/Day) Summary – Males (200 mg/kg/day)

DOSE MKD		DAYS ON TEST 1-4	4-8	8-11	11-15	15-22	22-29
200	MEAN	12.0	7.8	8.6	11.0	9.4	10.4
	S.D.	1.8	2.4	1.5	1.0	0.7	0.8
	N=	10	10	9	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 26. Feed Consumption (G/Day) Summary – Females (0, 10, 100 mg/kg/day)

DOSE MKD		DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
0	MEAN	12.0	12.3	12.8	12.9	12.4	12.9	12.3
	S.D.	0.6	0.7	0.7	0.8	0.8	0.8	0.8
	N=	10	10	10	10	10	10	10
10	MEAN	11.8	12.0	12.3	12.2*	11.8	12.6	11.7
	S.D.	0.3	0.6	0.6	0.5	0.9	0.7	0.5
	N=	10	10	10	10	10	10	10
100	MEAN	11.1*	10.6*	10.8*	11.8*	10.7*	13.1	12.0
	S.D.	0.3	0.3	0.7	0.6	0.4	0.2	0.5
	N=	10	10	10	10	10	9	10
1000	MEAN	2.5*	===	===	===	===	===	===
	S.D.	0.4	===	===	===	===	===	===
	N=	10	0	0	0	0	0	0

* STATISTICALLY DIFFERENT FROM CONTROL MEAN BY DUNNETT'S TEST, ALPHA=0.05.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 27. Feed Consumption (G/Day) Summary – Females (200 mg/kg/day)

DOSE MKD		DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	15-22	18-22	22-29
200	MEAN	9.5	8.4	7.2	9.2	===	8.6	===	9.1
	S.D.	0.7	0.7	1.0	0.6	===	0.9	===	0.9
	N=	9	9	9	9	0	9	0	9

=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 28. Test Material Intake Summary – Males

DOSE	0 MKD		10 MKD		100 MKD		200 MKD			1000 MKD	
Day	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)		Conc. (ppm)	Intake (mkd)
1-4	0	0	11	12.4	107	112.0	222	156.5		1091	248.9
4-8	0	0	11	11.1	107	95.3	222	105.6		-	-
8-11	0	0	12	11.8	126	109.9	287	157.0		-	-
11-15	0	0	12	11.2	126	113.8	287	197.3		-	-
15-18	0	0	13	10.9	139	114.6	369	-		-	-
18-22	0	0	13	10.6	139	114.5	369	210.0	*	-	-
22-29	0	0	14	10.5	143	109.8	320	191.5		-	-
Avg.	0	0	12.6	11.1	128.8	109.7	299.5	154.7		1091	248.9
±SD	0	0	1.1	0.67	14.7	6.79	61.0	38.24			

*Values represents days 15-22.
– 1000 mkd group euthanized at Day 5

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 29. Test Material Intake Summary – Females

DOSE	0 MKD		10 MKD		100 MKD		200 MKD		1000 MKD	
Day	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)	Conc. (ppm)	Intake (mkd)
1-4	0	0	11	12.0	110	112.4	185	145.5	1067	276.7
4-8	0	0	11	11.3	110	101.2	185	128.2	-	-
8-11	0	0	11	11.0	116	104.4	265	158.6	-	-
11-15	0	0	11	10.4	116	108.4	265	200.0	-	-
15-18	0	0	12	10.1	124	100.9	330	-	-	-
18-22	0	0	12	10.5	124	119.0	330	224.6 *	-	-
22-29	0	0	12	9.6	126	102.8	290	197.7	-	-
Avg.	0	0	11.6	10.55	119	106.7	268	161	1067	277
±SD	0	0	0.46	0.78	6.59	6.7	60.60	37.2		

*Values represents days 15-22.
– 1000 mkd group euthanized at Day 5

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 30. Prothrombin Time Summary – Males

DOSE (MKD)		PT SECONDS
0	MEAN	11.7
	S.D.	0.4
	N=	10
10	MEAN	11.9
	S.D.	0.8
	N=	10
100	MEAN	11.9
	S.D.	0.5
	N=	10
200	MEAN	12.7
	S.D.	0.4
	N=	10

PT = PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 31. Prothrombin Time Summary – Females

DOSE (MKD)		PT SECONDS
0	MEAN	11.8
	S.D.	0.4
	N=	10
10	MEAN	12.0
	S.D.	0.4
	N=	10
100	MEAN	12.0
	S.D.	0.3
	N=	10
200	MEAN	12.7
	S.D.	0.4
	N=	9

PT = PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 32. Hematology Summary – Males

DOSE (MKD)		WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
0	MEAN	9.69	8.30	15.4	44.3	53.4&	18.5&	34.7&	766
	S.D.	1.23	0.21	0.3	1.0	0.4	0.2	0.3	39
	N=	10	10	10	10	10	10	10	10
10	MEAN	9.53	8.07	15.1	43.1	53.4&	18.7&	35.0&	761
	S.D.	1.22	0.16	0.3	0.8	0.5	0.2	0.4	31
	N=	10	10	10	10	10	10	10	10
100	MEAN	9.63	8.14	15.3	43.7	53.6&	18.8&	35.0&	771
	S.D.	1.46	0.15	0.2	0.7	0.5	0.2	0.2	30
	N=	10	10	10	10	10	10	10	10
200	MEAN	9.21	8.42	15.1	42.8	50.8&	17.9&	35.3&	785
	S.D.	2.23	0.32	0.5	1.4	0.5	0.2	0.3	67
	N=	10	10	10	10	10	10	10	10

& = INDICATES NO STATISTICAL COMPARISON OF MEANS.
WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 33. Hematology Summary – Females

DOSE (MKD)		WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
0	MEAN	6.44	7.83	14.9	41.4	52.9&	19.1&	36.0&	772
	S.D.	1.91	0.19	0.3	0.9	0.6	0.2	0.6	34
	N=	10	10	10	10	10	10	10	10
10	MEAN	7.46	7.86	14.9	41.2	52.4&	19.0&	36.2&	772
	S.D.	1.73	0.25	0.4	1.4	0.5	0.2	0.5	61
	N=	10	10	10	10	10	10	10	10
100	MEAN	7.16	7.67	14.7	40.5	52.8&	19.1&	36.2&	811
	S.D.	1.10	0.12	0.2	0.7	0.4	0.2	0.5	46
	N=	10	10	10	10	10	10	10	10
200	MEAN	9.24	7.89	14.5	40.1	50.9&	18.4&	36.1&	744
	S.D.	2.41	0.31	0.4	1.5	0.7	0.3	0.5	62
	N=	9	9	9	9	9	9	9	9

& = INDICATES NO STATISTICAL COMPARISON OF MEANS.
WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 34. Differential WBC Summary – Males

DOSE (MKD)		NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
0	MEAN	18.9	75.5	2.1	0.7	0.6	2.2
	S.D.	2.2	2.3	0.3	0.3	0.2	0.5
	N=	10	10	10	10	10	10
10	MEAN	17.5	77.6	2.1	0.6	0.5	1.8
	S.D.	2.1	2.5	0.4	0.2	0.1	0.4
	N=	10	10	10	10	10	10
100	MEAN	17.6	78.1	1.8	0.6	0.5	1.5
	S.D.	3.2	3.7	0.3	0.2	0.2	0.2
	N=	10	10	10	10	10	10
200	MEAN	27.1	68.5	1.9	0.9	0.4	1.2
	S.D.	5.6	6.0	0.3	0.2	0.2	0.5
	N=	10	10	10	10	10	10

NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE: ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS
AUTOMATIC DIFFERENTIAL COUNTING

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 35. Differential WBC Summary – Females

DOSE (MKD)		NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
0	MEAN	18.7	76.5	2.0	1.2	0.3	1.2
	S.D.	5.1	5.1	0.4	0.4	0.2	0.3
	N=	10	10	10	10	10	10
10	MEAN	17.7	77.6	2.0	1.0	0.4	1.3
	S.D.	2.9	3.4	0.5	0.3	0.2	0.4
	N=	10	10	10	10	10	10
100	MEAN	17.5	78.3	1.5	0.9	0.4	1.3
	S.D.	3.7	3.9	0.2	0.2	0.2	0.4
	N=	10	10	10	10	10	10
200	MEAN	18.0	78.3	1.5	0.9	0.3	1.1
	S.D.	3.8	4.2	0.3	0.3	0.1	0.2
	N=	9	9	9	9	9	9

NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE: ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 36. Clinical Chemistry Summary – Males

DOSE (MKD)		UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
0	MEAN	15	44	196	91	109	6.3	3.4	40	0.1	0.4
	S.D.	2	4	13	8	15	0.2	0.1	4	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
10	MEAN	15	40	190	85	111	6.2	3.3	39	0.1	0.3
	S.D.	1	4	11	9	12	0.2	0.1	2	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
100	MEAN	15	40	175	81	106	6.2	3.3	43	0.1	0.3
	S.D.	1	4	11	8	10	0.1	0.0	3	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10
200	MEAN	15	55	111	101	86	6.2	3.3	74	0.1	0.3
	S.D.	1	32	8	36	17	0.3	0.1	7	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10

UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 37. Clinical Chemistry Summary – Females

DOSE (MKD)		UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
0	MEAN	16	41	155	105	90	6.1	3.2	76	0.1	0.3
	S.D.	2	16	14	28	10	0.3	0.1	8	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
10	MEAN	16	39	152	102	85	5.9	3.2	70	0.1	0.3
	S.D.	1	9	8	19	11	0.2	0.1	4	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
100	MEAN	16	35	142	94	86	5.8	3.2	73	0.1	0.3
	S.D.	2	2	12	9	8	0.2	0.1	4	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10
200	MEAN	16	51	124	112	91	5.9	3.2	70	0.1	0.3
	S.D.	1	26	7	32	8	0.3	0.1	9	0.0	0.0
	N=	9	9	9	9	9	9	9	9	9	9

UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 38. Electrolytes Summary – Males

DOSE (MKD)		CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
0	MEAN	12.4	12.9	149	5.7	97
	S.D.	0.3	0.4	1	0.3	1
	N=	10	10	10	10	10
10	MEAN	12.1	12.7	149	5.7	97
	S.D.	0.3	0.4	1	0.2	1
	N=	10	10	10	10	10
100	MEAN	12.2	13.0	149	5.7	97
	S.D.	0.2	0.5	1	0.3	1
	N=	10	10	10	10	10
200	MEAN	11.6	12.4	150	6.5	98
	S.D.	0.3	0.9	1	0.5	1
	N=	10	10	10	10	10

CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 39. Electrolytes Summary – Females

DOSE (MKD)		CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
0	MEAN	11.9	12.7	149	6.6	100
	S.D.	0.4	1.5	1	0.9	1
	N=	10	10	10	10	10
10	MEAN	11.7	12.2	149	6.4	100
	S.D.	0.3	1.1	1	0.5	1
	N=	10	10	10	10	10
100	MEAN	11.4	12.2	149	6.2	101
	S.D.	0.3	1.0	1	0.3	1
	N=	10	10	10	10	10
200	MEAN	11.5	12.7	150	6.8	100
	S.D.	0.4	1.1	1	0.9	1
	N=	9	9	9	9	9

CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 40. Urinalysis Summary – Males

DOSE (MKD)		URINE VOL (ML)	SPECIFIC GRAVITY	Color	Appear	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
0	MEAN	5.6	1.064	YELLOW (10)	SL. CL (10)	6.5 (1)	TRC (1)	NEG (10)	NEG (1)	NEG (10)	NEG (9)	<=1 (10)
	S.D.	3.3	0.013			7.0 (9)	+ (5)		TRC (6)		++ (1)	
	N=	10	10				++ (4)		+ (3)			
10	MEAN	4.4	1.072	YELLOW (10)	SL. CL (10)	6.5 (4)	+ (2)	NEG (10)	TRC (7)	NEG (8)	NEG (9)	<=1 (10)
	S.D.	0.8	0.008			7.0 (6)	++ (8)		+ (3)	+ (2)	++ (1)	
	N=	10	10									
100	MEAN	3.1	1.085	YELLOW (10)	SL. CL (10)	6.0 (1)	+ (2)	NEG (10)	TRC (4)	NEG (2)	NEG (8)	<=1 (10)
	S.D.	0.8	0.008			6.5 (8)	++ (8)		+ (6)	+ (8)	+ (1)	
	N=	10	10			7.0 (1)					++ (1)	
200	MEAN	2.0	1.085	YELLOW (10)	SL. CL (10)	6.5 (2)	+ (4)	NEG (10)	TRC (3)	NEG (3)	NEG (9)	<=1 (10)
	S.D.	0.7	0.021			7.0 (3)	++ (6)		+ (7)	+ (7)	+ (1)	
	N=	10	10			7.5 (4)						
						8.5 (1)						

URINE VOLUME AND SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS.
ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE.
THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF
ANIMALS IN THE DOSE GROUP DUE TO INSUFFICIENT QUANTITY OF SAMPLE OR EXCLUSION OF ANIMAL(S) FROM ANALYSIS
UROBILINOGEN IS MEASURED IN EU/DL=EHRLICH UNITS/DECILITER
NEG=NEGATIVE TRC=TRACE SL. CL=SLIGHTLY CLOUDY
+ = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE EU/DL=EHRLICH UNITS/DECILITER

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 41. Urinalysis Summary – Females

DOSE (MKD)		URINE VOL (ML)	SPECIFIC GRAVITY	Color	Appear	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
0	MEAN	4.0	1.061	YELLOW (10)	SL. CL (10)	6.0 (1)	NEG (2)	NEG (10)	NEG (4)	NEG (6)	NEG (8)	<=1 (10)
	S.D.	2.0	0.018			6.5 (2)	TRC (1)		TRC (6)	+ (4)	+ (2)	
	N=	10	10			7.0 (5)	+ (7)					
						7.5 (2)						
10	MEAN	3.6	1.062	YELLOW (10)	SL. CL (10)	6.0 (1)	TRC (3)	NEG (10)	NEG (4)	NEG (7)	NEG (7)	<=1 (10)
	S.D.	0.8	0.013			6.5 (2)	+ (6)		TRC (6)	+ (3)	+ (2)	
	N=	10	10			7.0 (2)	++ (1)				++ (1)	
						7.5 (3)						
						8.5 (2)						
100	MEAN	2.2	1.080	YELLOW (10)	SL. CL (10)	6.0 (1)	+ (7)	NEG (10)	TRC (10)	NEG (1)	NEG (6)	<=1 (10)
	S.D.	0.8	0.012			6.5 (5)	++ (3)			+ (9)	+ (3)	
	N=	10	10			7.0 (4)					++ (1)	
200	MEAN	1.2	1.096	YELLOW (9)	SL. CL (9)	6.0 (1)	+ (4)	NEG (9)	TRC (5)	NEG (1)	NEG (7)	<=1 (9)
	S.D.	0.8	0.020			7.0 (4)	++ (4)		+ (4)	+ (7)	++ (2)	
	N=	9	9			7.5 (1)	+++ (1)			++ (1)		
						8.0 (1)						
						8.5 (2)						

URINE VOLUME AND SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS.
ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE.
THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF
ANIMALS IN THE DOSE GROUP DUE TO INSUFFICIENT QUANTITY OF SAMPLE OR EXCLUSION OF ANIMAL(S) FROM ANALYSIS
UROBILINOGEN IS MEASURED IN EU/DL=EHRLICH UNITS/DECILITER
NEG=NEGATIVE TRC=TRACE SL.CL=SLIGHTLY CLOUDY
+ = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 42. Urine Microscopic – Males

DOSE (MKD)	WBC /HPF	RBC /HPF	CASTS /LPF	CRYSTALS /LPF	EPI /LPF	BACTERIA /HPF	YEAST /HPF	MUCUS /LPF	MICROSCOPIC COMMENTS
0	OCC			URATE PRESENT CA OXAL PRESENT					
10	OCC			URATE PRESENT CA OXAL PRESENT					
100	OCC			URATE PRESENT CA OXAL PRESENT	OCC				
200	OCC			URATE PRESENT CA OXAL PRESENT	OCC				

DATA ARE POOLED SAMPLES FOR EACH DOSE GROUP

AM PHOS=AMORPHOUS PHOSPHATES	EPI=EPITHELIAL	URIC=URIC ACID	CRS=COARSE GRANULAR CASTS
CA CARB=CALCIUM CARBONATE	GRAN=GRANULAR	URATE=AMORPHOUS URATES	FINE=FINE GRANULAR CASTS
CA OXAL=CALCIUM OXALATE	HYLN=HYALINE	OCC=OCCASIONAL	/HPF=PER HIGH POWER FIELD
TR PHOS=TRIPLE PHOSPHATES	SULF=SULFONAMIDE	TNTC=TOO NUMEROUS TO COUNT	/LPF=PER LOW POWER FIELD

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 43. Urine Microscopic – Females

DOSE (MKD)	WBC /HPF	RBC /HPF	CASTS /LPF	CRYSTALS /LPF	EPI /LPF	BACTERIA /HPF	YEAST /HPF	MUCUS /LPF	MICROSCOPIC COMMENTS
0	OCC			URATE PRESENT CA OXAL PRESENT	OCC				
10	OCC			URATE PRESENT CA OXAL PRESENT					
100	OCC			URATE PRESENT CA OXAL PRESENT					
200	1-4			URATE PRESENT CA OXAL PRESENT	1-4				

DATA ARE POOLED SAMPLES FOR EACH DOSE GROUP

AM PHOS=AMORPHOUS PHOSPHATES
CA CARB=CALCIUM CARBONATE
CA OXAL=CALCIUM OXALATE
TR PHOS=TRIPLE PHOSPHATES

EPI=EPITHELIAL
GRAN=GRANULAR
HYLN=HYALINE
SULF=SULFONAMIDE

URIC=URIC ACID
URATE=AMORPHOUS URATES
OCC=OCCASIONAL
TNTC=TOO NUMEROUS TO COUNT

CRS=COARSE GRANULAR CASTS
FINE=FINE GRANULAR CASTS
/HPF=PER HIGH POWER FIELD
/LPF=PER LOW POWER FIELD

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 44. Organ and Organ/Body Weights Summary – Males

DOSE MKD		FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
0	MEAN	225.5	0.041	0.018	0.850	0.377	1.908	0.846	7.531	3.336	1.858	0.826	0.523	0.232
	S.D.	9.5	0.010	0.005	0.060	0.015	0.091	0.018	0.651	0.176	0.029	0.044	0.022	0.012
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	MEAN	231.9	0.039	0.017	0.882	0.381	2.012	0.867	7.767	3.347	1.862	0.804	0.553	0.238
	S.D.	9.8	0.002	0.001	0.055	0.019	0.095	0.017	0.479	0.076	0.034	0.030	0.020	0.006
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
100	MEAN	211.4	0.039	0.018	0.799	0.378	1.907	0.902	7.340	3.473	1.853	0.877	0.513	0.243
	S.D.	5.5	0.008	0.004	0.044	0.019	0.094	0.031	0.267	0.099	0.019	0.025	0.019	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	MEAN	162.8	0.050	0.030	0.577	0.354	1.578	0.969	5.476	3.360	1.775	1.094	0.414	0.255
	S.D.	11.6	0.009	0.004	0.039	0.011	0.125	0.020	0.505	0.099	0.034	0.066	0.015	0.012
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 44. Organ and Organ/Body Weights Summary – Males (continued)

DOSE MKD		FINAL BODY WT. (G)	TESTES (G)	TESTES (G/100)	THYMUS (G)	THYMUS (G/100)	EPIDIDYMIDES (G)	EPIDIDYMIDES (G/100)
0	MEAN	225.5	2.931	1.301	0.333	0.148	0.584	0.259
	S.D.	9.5	0.086	0.033	0.041	0.017	0.043	0.012
	N=	10	10	10	10	10	10	10
10	MEAN	231.9	2.937	1.268	0.352	0.152	0.586	0.252
	S.D.	9.8	0.073	0.039	0.027	0.015	0.047	0.013
	N=	10	10	10	10	10	10	10
100	MEAN	211.4	2.900	1.372	0.342	0.162	0.564	0.267
	S.D.	5.5	0.069	0.037	0.020	0.008	0.038	0.018
	N=	10	10	10	10	10	10	10
200	MEAN	162.8	2.879	1.770	0.197	0.121	0.579	0.355
	S.D.	11.6	0.199	0.072	0.022	0.009	0.071	0.022
	N=	10	10	10	10	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 45. Organ and Organ/Body Weights Summary – Females

DOSE MKD		FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
0	MEAN	144.0	0.050	0.035	0.535	0.372	1.200	0.835	4.521	3.142	1.717	1.195	0.401	0.278
	S.D.	7.6	0.003	0.002	0.022	0.011	0.040	0.030	0.199	0.094	0.047	0.056	0.037	0.015
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	MEAN	139.5	0.046	0.033	0.523	0.375	1.179	0.845	4.278	3.066	1.718	1.232	0.384	0.275
	S.D.	5.7	0.007	0.004	0.013	0.013	0.066	0.026	0.221	0.108	0.053	0.050	0.018	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
100	MEAN	137.5	0.047	0.034	0.511	0.371	1.208	0.878	4.421	3.216	1.705	1.241	0.396	0.288
	S.D.	3.7	0.003	0.002	0.027	0.014	0.064	0.034	0.233	0.152	0.049	0.049	0.023	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	MEAN	124.5	0.039	0.031	0.454	0.366	1.145	0.920	3.841	3.081	1.697	1.373	0.358	0.288
	S.D.	12.8	0.006	0.003	0.034	0.018	0.121	0.022	0.474	0.114	0.049	0.109	0.040	0.018
	N=	9	9	9	9	9	9	9	9	9	9	9	9	9

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TABLE 45. Organ and Organ/Body Weights Summary – Females (continued)

DOSE MKD		FINAL BODY WT. (G)	THYMUS (G)	THYMUS (G/100)
0	MEAN	144.0	0.289	0.200
	S.D.	7.6	0.039	0.019
	N=	10	10	10
10	MEAN	139.5	0.289	0.207
	S.D.	5.7	0.025	0.021
	N=	10	10	10
100	MEAN	137.5	0.288	0.209
	S.D.	3.7	0.021	0.014
	N=	10	10	10
200	MEAN	124.5	0.259	0.209
	S.D.	12.8	0.027	0.015
	N=	9	9	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations

Removal Reasons: All of those SELECTED

	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
ADRENAL GLANDS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
AORTA;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
AUDITORY SEBACEOUS GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
BONE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
BONE - JOINT;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
BONE MARROW;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
BRAIN;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
CECUM;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
CERVIX;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
CERVIX; (continued)								
No Visible Lesions	-	-	-	-	10	10	10	9
COAGULATING GLAND;								
Submitted	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
No Visible Lesions	10	10	10	10	-	-	-	-
COLON;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
CRANIAL NERVE - OPTIC;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	8
Absent; bilateral	0	0	0	0	0	0	0	1
KIDNEYS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
DUODENUM;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
EPIDIDYMIDES;								
Submitted	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
No Visible Lesions	10	10	10	10	-	-	-	-
ESOPHAGUS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
EYE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
EYE; (continued)								
No Visible Lesions	10	10	7	10	10	9	10	9
Cloudy; right; cornea	0	0	2	0	0	1	0	0
Cloudy; bilateral; cornea	0	0	1	0	0	0	0	0
GENERAL;								
Submitted	(1)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
No Visible Lesions	1	0	0	0	0	0	0	0
HEART;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
ILEUM;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
JEJUNUM;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
LACRIMAL/HARDERIAN GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
LARYNX;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
LIVER;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	9	7
Focus; pale; papillary process	0	0	0	0	0	0	1	0
Hernia; left medial lobe	0	0	0	0	0	0	0	1

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
LIVER; (continued)								
Hernia; right medial lobe	0	0	0	0	0	0	0	1
LUNG;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
LYMPH NODE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
MAMMARY GLAND;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
No Visible Lesions	-	-	-	-	10	10	10	9
MEDIASTINAL TISSUE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
MESENTERIC TISSUE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
NASAL TISSUE - PHARYNX;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
ORAL TISSUE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
OVARIES;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
No Visible Lesions	-	-	-	-	10	10	10	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
OVIDUCT;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
No Visible Lesions	-	-	-	-	10	10	10	9
PANCREAS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
PARATHYROID GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
PERIPHERAL NERVE - TIBIAL;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
PITUITARY GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
PROSTATE;								
Submitted	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
No Visible Lesions	10	10	10	10	-	-	-	-
RECTUM;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
SALIVARY GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
SEMINAL VESICLES;								
Submitted	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
SEMINAL VESICLES; (continued)								
No Visible Lesions	10	10	10	10	-	-	-	-
SKELETAL MUSCLE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
SKIN AND SUBCUTIS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
SPINAL CORD;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
SPLEEN;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
STOMACH;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	1	0	10	10	1	0
Thickened; nonglandular mucosa; focal	0	0	2	0	0	0	5	0
Thickened; nonglandular mucosa; multifocal	0	0	7	0	0	0	4	0
Thickened; nonglandular mucosa; diffuse	0	0	0	10	0	0	0	9
TESTES;								
Submitted	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
No Visible Lesions	10	10	10	10	-	-	-	-
THYMUS;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 46. Gross Pathological Observations (continued)

Removal Reasons: All of those SELECTED	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
THYROID GLAND;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
TONGUE;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
TRACHEA;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
URINARY BLADDER;								
Submitted	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
No Visible Lesions	10	10	10	10	10	10	10	9
UTERUS;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
No Visible Lesions	-	-	-	-	10	10	10	9
VAGINA;								
Submitted	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
No Visible Lesions	-	-	-	-	10	10	10	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations

Observations: Neo-Plastic and Non Neo-Plastic

Removal Reasons: All of those SELECTED

	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
ADRENAL GLANDS;								
Examined	(10)	(10)	(10)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	10	10	0	10	0	0	9
Hypertrophy; zona fasciculata; bilateral	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)
very slight	0	0	0	10	0	0	0	0
AORTA;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
BONE;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
BONE - JOINT;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
BONE MARROW;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	10	10	0	8	10	10	1
Hypocellularity; all cell lines; diffuse	(0)	(0)	(0)	(10)	(2)	(0)	(0)	(8)
very slight	0	0	0	0	2	0	0	7
slight	0	0	0	1	0	0	0	1
moderate	0	0	0	9	0	0	0	0
BRAIN;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	8	0	0	9	9	0	0	9
Degeneration; axonal; optic tract; unilateral; multifocal	(2)	(0)	(0)	(1)	(1)	(0)	(0)	(0)
very slight	2	0	0	1	1	0	0	0
CECUM;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
CECUM; (continued)								
Within Normal Limits	10	0	0	10	10	0	0	9
CERVIX;								
Examined	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
Within Normal Limits	-	-	-	-	10	10	10	4
Atrophy	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(5)
very slight	-	-	-	-	0	0	0	4
slight	-	-	-	-	0	0	0	1
COAGULATING GLAND;								
Examined	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
Within Normal Limits	10	10	10	0	-	-	-	-
Decreased Secretory Material; bilateral	(0)	(0)	(0)	(10)	(-)	(-)	(-)	(-)
very slight	0	0	0	1	-	-	-	-
slight	0	0	0	9	-	-	-	-
COLON;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
CRANIAL NERVE - OPTIC;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	8	0	0	9	9	0	0	8
Aplasia; bilateral	0	0	0	0	0	0	0	1
Degeneration; axonal; unilateral; multifocal	(2)	(0)	(0)	(1)	(1)	(0)	(0)	(0)
very slight	2	0	0	0	0	0	0	0
slight	0	0	0	1	1	0	0	0
DUODENUM;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	10	2	0	10	10	4	0
Dilatation; crypt; multifocal	(0)	(0)	(3)	(1)	(0)	(0)	(4)	(6)
very slight	0	0	3	1	0	0	4	6

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
DUODENUM; (continued)								
Hyperplasia; epithelium; mucosa; diffuse	(0)	(0)	(5)	(10)	(0)	(0)	(0)	(6)
very slight	0	0	5	1	0	0	0	6
slight	0	0	0	9	0	0	0	0
Necrosis; individual cell; crypt; epithelium; multifocal	(0)	(0)	(4)	(10)	(0)	(0)	(6)	(7)
very slight	0	0	4	10	0	0	6	7
EPIDIDYMIDES;								
Examined	(10)	(0)	(0)	(10)	(-)	(-)	(-)	(-)
Within Normal Limits	10	0	0	10	-	-	-	-
ESOPHAGUS;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
EYE;								
Examined	(10)	(0)	(3)	(10)	(10)	(1)	(0)	(9)
Within Normal Limits	1	0	1	5	5	0	0	4
Atrophy; retina; unilateral	(2)	(0)	(0)	(1)	(0)	(1)	(0)	(0)
very slight	2	0	0	0	0	1	0	0
moderate	0	0	0	1	0	0	0	0
Atrophy; retina; bilateral	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)
moderate	0	0	0	0	0	0	0	1
Inflammation; subacute; cornea; focal	(0)	(0)	(1)	(0)	(0)	(0)	(0)	(0)
very slight	0	0	1	0	0	0	0	0
Mineralization; cornea; unilateral; focal	(0)	(0)	(1)	(0)	(0)	(0)	(0)	(0)
very slight	0	0	1	0	0	0	0	0
Mineralization; cornea; unilateral; multifocal	(5)	(0)	(0)	(3)	(3)	(1)	(0)	(4)
very slight	5	0	0	3	3	1	0	4
Mineralization; cornea; bilateral; multifocal	(2)	(0)	(0)	(2)	(2)	(0)	(0)	(1)
very slight	2	0	0	2	2	0	0	1
HEART;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic

Removal Reasons: All of those SELECTED

	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
HEART; (continued)								
Within Normal Limits	8	0	0	6	9	0	0	7
Degeneration; with or without inflammation; myocardium; focal	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
very slight	0	0	0	1	0	0	0	0
Degeneration; with or without inflammation; myocardium; multifocal	(2)	(0)	(0)	(3)	(1)	(0)	(0)	(2)
very slight	2	0	0	3	1	0	0	1
slight	0	0	0	0	0	0	0	1
ILEUM;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
JEJUNUM;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
KIDNEYS;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	6	0	0	8	7	0	0	9
Degeneration; with regeneration; tubule; focal	(4)	(0)	(0)	(1)	(3)	(0)	(0)	(0)
very slight	4	0	0	1	3	0	0	0
Degeneration; with regeneration; tubule; multifocal	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
very slight	0	0	0	1	0	0	0	0
LACRIMAL/HARDERIAN GLAND;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
LARYNX;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
LIVER;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(1)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic

Removal Reasons: All of those SELECTED

	MALES				FEMALES			
	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
LIVER; (continued)								
Within Normal Limits	6	0	0	5	7	0	1	7
Aggregates Of Macrophages - Histiocytes	(3)	(0)	(0)	(2)	(3)	(0)	(0)	(0)
very slight	3	0	0	2	3	0	0	0
Aggregates Of Macrophages - Histiocytes; adjacent to necrotic or degenerative hepato-cytes	(1)	(0)	(0)	(3)	(0)	(0)	(0)	(0)
very slight	1	0	0	3	0	0	0	0
Architecture Altered Secondary To Diaphragmatic Hernia	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)
very slight	0	0	0	0	0	0	0	2
LUNG;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
LYMPH NODE - MEDIASTINAL;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
LYMPH NODE - MESENTERIC;								
Examined	(10)	(9)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	9	10	0	10	10	10	5
Not Examined: MISSING	0	1	0	0	0	0	0	0
Sinus Histiocytosis; increased	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)
slight	0	0	0	7	0	0	0	3
moderate	0	0	0	3	0	0	0	1
MAMMARY GLAND;								
Examined	(-)	(-)	(-)	(-)	(10)	(0)	(0)	(9)
Within Normal Limits	-	-	-	-	10	0	0	9
MEDIASTINAL TISSUE;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
MESENTERIC TISSUE;								
Examined	(10)	(9)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	9	10	0	10	10	10	3
Not Examined: MISSING	0	1	0	0	0	0	0	0
Atrophy; adipose tissue	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(6)
slight	0	0	0	10	0	0	0	6
NASAL TISSUE - PHARYNX;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	9	10	0	0	9
Inflammation; chronic active; respiratory epithelium; multifocal	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
very slight	0	0	0	1	0	0	0	0
ORAL TISSUE;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	8
Inflammation; chronic active; periodontal tissue; focal	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)
slight	0	0	0	0	0	0	0	1
OVARIES;								
Examined	(-)	(-)	(-)	(-)	(10)	(0)	(0)	(9)
Within Normal Limits	-	-	-	-	10	0	0	9
OVIDUCT;								
Examined	(-)	(-)	(-)	(-)	(10)	(0)	(0)	(9)
Within Normal Limits	-	-	-	-	10	0	0	9
PANCREAS;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
PARATHYROID GLAND;								
Examined	(10)	(0)	(0)	(9)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	9	10	0	0	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
PARATHYROID GLAND; (continued)								
Not Examined: MISSING	0	0	0	1	0	0	0	0
PERIPHERAL NERVE - TIBIAL;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
PITUITARY GLAND;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
PROSTATE;								
Examined	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
Within Normal Limits	9	9	9	0	-	-	-	-
Decreased Secretory Material	(0)	(0)	(0)	(10)	(-)	(-)	(-)	(-)
very slight	0	0	0	1	-	-	-	-
slight	0	0	0	9	-	-	-	-
Inflammation; subacute to chronic; focal	(1)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
very slight	1	0	0	0	-	-	-	-
Inflammation; subacute to chronic; multifocal	(0)	(1)	(1)	(4)	(-)	(-)	(-)	(-)
very slight	0	1	1	2	-	-	-	-
slight	0	0	0	2	-	-	-	-
RECTUM;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
SALIVARY GLAND;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	10	5	0	10	10	10	0
Hypertrophy; acinus; diffuse	(0)	(0)	(5)	(10)	(0)	(0)	(0)	(9)
very slight	0	0	5	0	0	0	0	0
slight	0	0	0	10	0	0	0	9

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
SEMINAL VESICLES;								
Examined	(10)	(10)	(10)	(10)	(-)	(-)	(-)	(-)
Within Normal Limits	10	10	10	0	-	-	-	-
Decreased Secretory Material; bilateral	(0)	(0)	(0)	(10)	(-)	(-)	(-)	(-)
very slight	0	0	0	1	-	-	-	-
slight	0	0	0	9	-	-	-	-
SKELETAL MUSCLE;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
SKIN AND SUBCUTIS;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	10	10	0	10	10	10	2
Atrophy; adipose tissue; dermis; diffuse	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(2)
slight	0	0	0	1	0	0	0	2
moderate	0	0	0	9	0	0	0	0
Atrophy; hair follicle; sebaceous gland; diffuse	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(7)
slight	0	0	0	1	0	0	0	5
moderate	0	0	0	8	0	0	0	2
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
SPLEEN;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
STOMACH;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
Within Normal Limits	10	10	0	0	10	9	0	0
Dilatation; glandular; glandular mucosa; focal	(0)	(0)	(0)	(0)	(0)	(1)	(0)	(0)
slight	0	0	0	0	0	1	0	0

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
STOMACH; (continued)								
Dilatation; glandular lumen; pylorus; multifocal	(0)	(0)	(8)	(9)	(0)	(0)	(8)	(4)
very slight	0	0	8	3	0	0	8	4
slight	0	0	0	6	0	0	0	0
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)
very slight	0	0	2	0	0	0	1	0
slight	0	0	8	0	0	0	6	0
moderate	0	0	0	0	0	0	3	0
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(9)
moderate	0	0	0	10	0	0	0	9
Hyperplasia; epithelium; nonglandular mucosa; multifocal	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)
very slight	0	0	2	0	0	0	1	0
slight	0	0	8	0	0	0	6	0
moderate	0	0	0	0	0	0	3	0
Hyperplasia; epithelium; nonglandular mucosa; diffuse	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(9)
moderate	0	0	0	10	0	0	0	9
Hyperplasia; pylorus; neck mucous cell	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(9)
very slight	0	0	10	0	0	0	10	1
slight	0	0	0	10	0	0	0	8
Inflammation; chronic active; nonglandular mucosa	(0)	(0)	(8)	(10)	(0)	(0)	(8)	(9)
very slight	0	0	2	0	0	0	2	1
slight	0	0	6	1	0	0	6	6
moderate	0	0	0	9	0	0	0	2
Necrosis; individual cell; glandular; pylorus; multifocal	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(9)
very slight	0	0	10	2	0	0	10	9
slight	0	0	0	8	0	0	0	0
Ulcer; nonglandular mucosa	0	0	0	9	0	0	1	6
TESTES;								
Examined	(10)	(0)	(0)	(10)	(-)	(-)	(-)	(-)
Within Normal Limits	10	0	0	10	-	-	-	-
THYMUS;								
Examined	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 47. Histopathological Observations (continued)

Observations: Neo-Plastic and Non Neo-Plastic	MALES				FEMALES			
Removal Reasons: All of those SELECTED	0.0 mkd	10 mkd	100 mkd	200 mkd	0.0 mkd	10 mkd	100 mkd	200 mkd
Number of Animals on Study :	10	10	10	10	10	10	10	9
Number of Animals Completed:	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)
THYMUS; (continued)								
Within Normal Limits	10	10	10	3	10	10	10	9
Atrophy	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)
very slight	0	0	0	7	0	0	0	0
THYROID GLAND;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
TRACHEA;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
URINARY BLADDER;								
Examined	(10)	(0)	(0)	(10)	(10)	(0)	(0)	(9)
Within Normal Limits	10	0	0	10	10	0	0	9
UTERUS;								
Examined	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
Within Normal Limits	-	-	-	-	10	10	10	0
Atrophy; endometrium; myometrium	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(9)
slight	-	-	-	-	0	0	0	9
VAGINA;								
Examined	(-)	(-)	(-)	(-)	(10)	(10)	(10)	(9)
Within Normal Limits	-	-	-	-	10	10	10	2
Atrophy	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(7)
very slight	-	-	-	-	0	0	0	1
slight	-	-	-	-	0	0	0	6

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data)

ORGAN WEIGHT PARAMETERS

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
TERMINAL BODY WEIGHT	DOSE	BOTH SEXES	0.0001	---	---	---
	SEX*DOSE		0.0008#	---	---	---
	DOSE	FEMALES ONLY	0.0566	---	---	---
	DOSE	MALES ONLY	0.0001#	6.450	-14.090*	8.8307
ADRENAL WEIGHT	DOSE	BOTH SEXES	0.3220	---	---	---
	SEX*DOSE		0.8001	---	---	---
RELATIVE ADRENAL WEIGHT	DOSE	BOTH SEXES	0.4059	---	---	---
	SEX*DOSE		0.8846	---	---	---
HEART WEIGHT	DOSE	BOTH SEXES	0.0008*	0.0035	-0.0235*	0.0166
	SEX*DOSE		0.0743	---	---	---
RELATIVE HEART WEIGHT	DOSE	BOTH SEXES	0.7119	---	---	---
	SEX*DOSE		0.9881	---	---	---
KIDNEY WEIGHT	DOSE	BOTH SEXES	0.1901	---	---	---
	SEX*DOSE		0.0139#	---	---	---
	DOSE	FEMALES ONLY	0.5070	---	---	---
	DOSE	MALES ONLY	0.0275#	0.1033*	-0.0013	0.0976
RELATIVE KIDNEY WEIGHT	DOSE	BOTH SEXES	0.0001#	0.0156	0.0497*	0.0192
	SEX*DOSE		0.7440	---	---	---
LIVER WEIGHT	DOSE	BOTH SEXES	0.4623	---	---	---
	SEX*DOSE		0.0258#	---	---	---
	DOSE	FEMALES ONLY	0.0559	---	---	---
	DOSE	MALES ONLY	0.1765	---	---	---
RELATIVE LIVER WEIGHT	DOSE	BOTH SEXES	0.0022#	-0.0323	0.1052*	0.0881
	SEX*DOSE		0.5152	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test from Analysis Performed on Data) (continued)

ORGAN WEIGHT PARAMETERS (CONT)

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
BRAIN WEIGHT	DOSE	BOTH SEXES	0.7010	---	---	---
	SEX*DOSE		0.9661	---	---	---
RELATIVE BRAIN WEIGHT	DOSE	BOTH SEXES	0.0017	---	---	---
	SEX*DOSE		0.0414#	---	---	---
	DOSE	FEMALES ONLY	0.1249	---	---	---
	DOSE	MALES ONLY	0.0001#	-0.0220	0.0516*	0.0353
SPLEEN WEIGHT	DOSE	BOTH SEXES	0.2016	---	---	---
	SEX*DOSE		0.0017#	---	---	---
	DOSE	FEMALES ONLY	0.3708	---	---	---
	DOSE	MALES ONLY	0.0004#	0.0301*	-0.0100	0.0213
RELATIVE SPLEEN WEIGHT	DOSE	BOTH SEXES	0.0112#	0.0019	0.0104*	0.0081
	SEX*DOSE		0.3639	---	---	---
TESTICULAR WEIGHT	DOSE	MALE ONLY	0.5117	---	---	---
RELATIVE TESTICULAR WEIGHT	DOSE	MALE ONLY	0.0001#	-0.0332	0.0715*	0.038
THYMUS WEIGHT	DOSE	BOTH SEXES	0.6218	---	---	---
	SEX*DOSE		0.5887	---	---	---
RELATIVE THYMUS WEIGHT	DOSE	BOTH SEXES	0.0909	---	---	---
	SEX*DOSE		0.7467	---	---	---
EPIDIDYMIDES WEIGHT	DOSE	FEMALE ONLY	0.4424	---	---	---
RELATIVE EPIDIDYMIDES WEIGHT	DOSE	FEMALE ONLY	0.1089	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test from Analysis Performed on Data) (continued)

CLINICAL CHEMISTRIES

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
UREA NITROGEN	DOSE	BOTH SEXES	0.5150	---	---	---
	SEX*DOSE		0.8684	---	---	---
ALANINE AMINOTRANSFERASE	DOSE	BOTH SEXES	0.1967	---	---	---
	SEX*DOSE		0.5030	---	---	---
ALKALINE PHOSPHATASE	DOSE	BOTH SEXES	0.0001#	-4.200	-16.600*	8.3661
	SEX*DOSE		0.5485	---	---	---
ASPARTATE AMINOTRANSFERASE	DOSE	BOTH SEXES	0.0974	---	---	---
	SEX*DOSE		0.6473	---	---	---
GLUCOSE	DOSE	BOTH SEXES	0.6120	---	---	---
	SEX*DOSE		0.5756	---	---	---
TOTAL PROTEIN	DOSE	BOTH SEXES	0.0029#	-0.1250	-0.2150*	0.1356
	SEX*DOSE		0.2407	---	---	---
ALBUMIN	DOSE	BOTH SEXES	0.2210	---	---	---
	SEX*DOSE		0.1681	---	---	---
CHOLESTEROL	DOSE	BOTH SEXES	0.0189	---	---	---
	SEX*DOSE		0.0437#	---	---	---
	DOSE	FEMALES ONLY	0.0714	---	---	---
	DOSE	MALES ONLY	0.0186#	-0.0042	0.0365*	0.0344
TOTAL BILIRUBIN	DOSE	BOTH SEXES	0.3468	---	---	---
	SEX*DOSE		0.3468	---	---	---
CREATININE	DOSE	BOTH SEXES	0.0074#	-0.0350	-0.0500*	0.0355
	SEX*DOSE		0.6231	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test from Analysis Performed on Data) (continued)

ELECTROLYTES

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
CALCIUM	DOSE	BOTH SEXES	0.0052#	-0.2450*	-0.3150*	0.2204
	SEX*DOSE		0.1902	---	---	---
PHOSPHORUS	DOSE	BOTH SEXES	0.5507	---	---	---
	SEX*DOSE		0.5848	---	---	---
SODIUM	DOSE	BOTH SEXES	0.7485	---	---	---
	SEX*DOSE		0.6015	---	---	---
POTASSIUM	DOSE	BOTH SEXES	0.5695	---	---	---
	SEX*DOSE		0.5990	---	---	---
CHLORIDE	DOSE	BOTH SEXES	0.2238	---	---	---
	SEX*DOSE		0.0320#	---	---	---
	DOSE	FEMALES ONLY	0.0460#	0.4000	1.3000*	1.1813
	DOSE	MALES ONLY	0.3754	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test from Analysis Performed on Data) (continued)

HEMATOLOGIC AND COAGULATION PARAMETERS

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
WHITE BLOOD CELL	DOSE	BOTH SEXES	0.6283	---	---	---
	SEX*DOSE		0.4428	---	---	---
RED BLOOD CELL COUNT	DOSE	BOTH SEXES	0.0332	---	---	---
	SEX*DOSE		0.0488#	---	---	---
	DOSE	FEMALES ONLY	0.0940	---	---	---
	DOSE	MALES ONLY	0.0217#	-0.2290*	-0.1560	0.1834
HEMOGLOBIN	DOSE	BOTH SEXES	0.1597	---	---	---
	SEX*DOSE		0.0571	---	---	---
HEMATOCRIT	DOSE	BOTH SEXES	0.0185#	-0.7400*	-0.7700*	0.6757
	SEX*DOSE		0.0939	---	---	---
PLATELET COUNT	DOSE	BOTH SEXES	0.1243	---	---	---
	SEX*DOSE		0.3827	---	---	---
PROTHROMBIN TIME	DOSE	BOTH SEXES	0.5150	---	---	---
	SEX*DOSE		0.8684	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 48. Difference Between Control and Dose Means (Dunnett's Test from Analysis Performed on Data) (continued)

URINE SPECIFIC GRAVITY

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE DIFFERENCE	100 DOSE DIFFERENCE	MINIMUM SIGNIFICANT DIFFERENCE
URINE VOLUME	DOSE	BOTH SEXES	0.0001#	0.004	0.020*	0.009
	SEX*DOSE		0.6805	---	---	---
SPECIFIC GRAVITY	DOSE	BOTH SEXES	0.0001#	-0.0476	-0.2426*	0.1045
	SEX*DOSE		0.7000	---	---	---

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* DUNNETT'S TEST STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups)

ORGAN WEIGHT PARAMETERS

	FACTOR	SEX	P-VALUE
TERMINAL BODY WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0008*
	DOSE	MALES ONLY	0.0001*
LOG OF ADRENAL WEIGHT	DOSE	BOTH SEXES	0.5154
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0001*
	DOSE	MALES ONLY	0.0253*
RELATIVE ADRENAL WEIGHT	DOSE	BOTH SEXES	0.0016
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0056*
	DOSE	MALES ONLY	0.0001*
HEART WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0001*
	DOSE	MALES ONLY	0.0001*
RELATIVE HEART WEIGHT	DOSE	BOTH SEXES	0.0037*
	SEX*DOSE		0.0637
KIDNEY WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.1927
	DOSE	MALES ONLY	0.0001*
RELATIVE KIDNEY WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0174#
	DOSE	FEMALES ONLY	0.0001*
	DOSE	MALES ONLY	0.0001*
LIVER WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0007*
	DOSE	MALES ONLY	0.0001*

INTERACTION STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

ORGAN WEIGHTS (CONT)

	FACTOR	SEX	P-VALUE
RELATIVE LIVER WEIGHT	DOSE	BOTH SEXES	0.6528
	SEX*DOSE		0.2993
BRAIN WEIGHT	DOSE	BOTH SEXES	0.0003
	SEX*DOSE		0.0204#
	DOSE	FEMALES ONLY	0.3735
	DOSE	MALES ONLY	0.0001*
RELATIVE BRAIN WEIGHT	DOSE	BOTH SEXES	0.0001*
	SEX*DOSE		0.0576
SPLEEN WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0015#
	DOSE	FEMALES ONLY	0.0289*
	DOSE	MALES ONLY	0.0001*
RELATIVE SPLEEN WEIGHT	DOSE	BOTH SEXES	0.0011*
	SEX*DOSE		0.1892
TESTICULAR WEIGHT	DOSE	MALE	0.6774
RELATIVE TESTICULAR WEIGHT	DOSE	MALE	0.0001*
THYMUS WEIGHT	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0700
	DOSE	MALES ONLY	0.0001*
RELATIVE THYMUS WEIGHT	DOSE	BOTH SEXES	0.0759
	SEX*DOSE		0.0011#
	DOSE	FEMALES ONLY	0.2973
	DOSE	MALES ONLY	0.0003*
EPIDIDYMIDES WEIGHT	DOSE	MALE	0.7593
RELATIVE EPIDIDYMIDES WEIGHT	DOSE	MALE	0.0001*

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

```
#    INTERACTION STATISTICALLY IDENTIFIED AT ALPHA = 0.05
*    ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
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HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

CLINICAL CHEMISTRIES

	FACTOR	SEX	P-VALUE
UREA NITROGEN	DOSE	BOTH SEXES	0.9715
	SEX*DOSE		0.8585
LOG OF ALANINE AMINOTRANSFERASE	DOSE	BOTH SEXES	0.1953
	SEX*DOSE		0.4534
ALKALINE PHOSPHATASE	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.0001*
	DOSE	MALES ONLY	0.0001*
LOG OF ASPARTATE AMINOTRANSFERASE	DOSE	BOTH SEXES	0.4269
	SEX*DOSE		0.9563
GLUCOSE	DOSE	BOTH SEXES	0.0112
	SEX*DOSE		0.0058#
	DOSE	FEMALES ONLY	0.7950
	DOSE	MALES ONLY	0.0040*
TOTAL PROTEIN	DOSE	BOTH SEXES	0.0791
	SEX*DOSE		0.5749
ALBUMIN	DOSE	BOTH SEXES	0.1341
	SEX*DOSE		0.2167
CHOLESTEROL	DOSE	BOTH SEXES	0.0001
	SEX*DOSE		0.0001#
	DOSE	FEMALES ONLY	0.1424
	DOSE	MALES ONLY	0.0001*
TOTAL BILIRUBIN	DOSE	BOTH SEXES	0.1535
	SEX*DOSE		0.1535
CREATININE	DOSE	BOTH SEXES	0.0002*
	SEX*DOSE		0.9402

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

```
#   INTERACTION STATISTICALLY IDENTIFIED AT ALPHA = 0.05
*   ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
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HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

ELECTROLYTES

	FACTOR	SEX	P-VALUE
CALCIUM	DOSE	BOTH SEXES	0.0001*
	SEX*DOSE		0.1619
PHOSPHORUS	DOSE	BOTH SEXES	0.5144
	SEX*DOSE		0.4542
SODIUM DOSE	BOTH SEXES		0.0016*
	SEX*DOSE		0.6795
LOG OF POTASSIUM	DOSE	BOTH SEXES	0.0142*
	SEX*DOSE		0.1412
CHLORIDE	DOSE	BOTH SEXES	0.2321
	SEX*DOSE		0.2209

* ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

HEMATOLOGIC AND COAGULATION PARAMETERS

	FACTOR	SEX	P-VALUE
WHITE BLOOD CELL	DOSE	BOTH SEXES	0.0767
	SEX*DOSE		0.0145#
	DOSE	FEMALES ONLY	0.0118*
	DOSE	MALES ONLY	0.5620
RED BLOOD CELL COUNT	DOSE	BOTH SEXES	0.2875
	SEX*DOSE		0.7037
HEMOGLOBIN	DOSE	BOTH SEXES	0.0154*
	SEX*DOSE		0.5223
HEMATOCRIT	DOSE	BOTH SEXES	0.0009*
	SEX*DOSE		0.7587
PLATELET COUNT	DOSE	BOTH SEXES	0.8007
	SEX*DOSE		0.1712
PROTHROMBIN TIME	DOSE	BOTH SEXES	0.9715
	SEX*DOSE		0.8585

INTERACTION STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 49. Difference Between Control and Dose Means (Dunnett's Test From Analysis Performed on Data from the 0 and 200 Dose Groups) (continued)

URINE SPECIFIC GRAVITY

	FACTOR	SEX	P-VALUE
LOG OF URINE VOLUME	DOSE	BOTH SEXES	0.0001*
	SEX*DOSE		0.3832
SPECIFIC GRAVITY	DOSE	BOTH SEXES	0.0001*
	SEX*DOSE		0.2417

* ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 50. P-Value Table (Bonferroni Adjustment Applied) From Analysis Performed on Data

IN-LIFE BODY WEIGHTS

	FACTOR	SEX	ALL DOSES P-VALUE	10 DOSE P-VALUE	100 DOSE P-VALUE
IN-LIFE BODY WEIGHTS	TIME*DOSE	BOTH SEXES	0.0001	---	---
	TIME*SEX*DOSE		0.0070+	---	---
	TIME*DOSE	FEMALES ONLY	0.0001#	0.1791	0.0001*
	TIME"*DOSE	MALES ONLY	0.0002#	0.2229	0.0001*

--- ANALYSIS NOT PERFORMED
ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.05
* CONTRAST STATISTICALLY IDENTIFIED AT BONFERRONI CORRECTED ALPHA = 0.02
+ ANOVA STATISTICALLY IDENTIFIED AT ALPHA = 0.02

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

TABLE 51. P-Value Table (Bonferroni Adjustment Applied) From Analysis Performed on Data From the 0 and 200 Dose Groups

IN-LIFE BODY WEIGHTS

	FACTOR	SEX	P-VALUE
SQUARE ROOT OF IN-LIFE BODY WEIGHTS	TIME*DOSE	BOTH SEXES	0.0001
	TIME*SEX*DOSE		0.0001+
	TIME*DOSE	FEMALES ONLY	0.0001*
	TIME*DOSE	MALES ONLY	0.0001*

* ANOVA STATISTICALLY IDENTIFIED AT BONFERRONI CORRECTED ALPHA = 0.02
\+ INTERACTION STATISTICALLY IDENTIFIED AT ALPHA = 0.02

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 1. Detailed Clinical Observations – Males

Animal Dose	Number	Day Observed First	Last	Observation/Comment
0.0 mkd				
	7682	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7683	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7684	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7685	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7686	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7687	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7688	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7689	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7690	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7691	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
10 mkd				
	7692	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7693	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7694	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 1. Detailed Clinical Observations – Males (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
10 mkd				
	7695	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7696	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7697	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7698	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7699	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7700	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7701	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
100 mkd				
	7702	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7703	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7704	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7705	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7706	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 1. Detailed Clinical Observations – Males (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
100 mkd				
	7707	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7708	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7709	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7710	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7711	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
200 mkd				
	81	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	82	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	83	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	84	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	85	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	86	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	87	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	88	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 1. Detailed Clinical Observations – Males (continued)

Animal Dose	Number	Day Observed First	Last	Observation/Comment
200 mkd				
	89	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	90	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
1000 mkd				
	7712	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7713	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7714	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7715	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7716	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7717	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7718	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7719	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7720	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7721	1	1	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 2. Detailed Clinical Observations – Females

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7722	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7723	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7724	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7725	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7726	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7727	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7728	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7729	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7730	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7731	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
10 mkd				
	7732	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7733	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 2. Detailed Clinical Observations – Females (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
10 mkd				
	7734	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7735	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7736	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7737	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7738	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7739	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7740	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7741	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
100 mkd				
	7742	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7743	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7744	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7745	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 2. Detailed Clinical Observations – Females (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
100 mkd				
	7746	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7747	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7748	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7749	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7750	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7751	1	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
200 mkd				
	91	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	92	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	93	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	94	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	95	1	8	No Remarkable Observations
		15	29	DCO, Pupil Size - Bilateral, Increased
		30	30	Disposition, Scheduled Necropsy
	96	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 2. Detailed Clinical Observations – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
200 mkd				
	97	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	98	1	29	No Remarkable Observations
	98	30	30	Disposition, Scheduled Necropsy
	99	1	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
1000 mkd				
	7752	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7753	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7754	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7755	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7756	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7757	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7758	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7759	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7760	1	1	No Remarkable Observations
		5	5	Disposition, Removed
	7761	1	1	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Sensory Evaluation – Males

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7682	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7683	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7684	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7685	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7686	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7687	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7688	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7689	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7690	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7691	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Sensory Evaluation – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
10 mkd				
	7692	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7693	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7694	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7695	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7696	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7697	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7698	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7699	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Sensory Evaluation – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
10 mkd				
	7700	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7701	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
100 mkd				
	7702	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7703	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7704	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7705	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7706	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7707	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7708	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Sensory Evaluation – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
100 mkd				
	7709	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7710	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7711	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
200 mkd				
	81	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	82	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	83	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	84	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	85	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Sensory Evaluation – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
200 mkd				
	86	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	87	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	88	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	89	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	90	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 4. Sensory Evaluation – Females

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7722	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7723	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7724	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7725	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7726	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7727	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7728	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7729	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7730	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7731	-4	25	Responsiveness to Tail Pinch (nociception), Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 4. Sensory Evaluation – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7731	-4	25	Responsiveness to Sharp Noise, Moderate
10 mkd				
	7732	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7733	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7734	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7735	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7736	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7737	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7738	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7739	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 4. Sensory Evaluation – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
10 mkd				
	7740	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7741	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
100 mkd				
	7742	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7743	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7744	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7745	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7746	-5	24	Responsiveness to Tail Pinch (nociception), Moderate
		-5	24	Responsiveness to Sharp Noise, Moderate
	7747	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7748	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 4. Sensory Evaluation – Females (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
100 mkd				
	7749	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7750	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
	7751	-4	25	Responsiveness to Tail Pinch (nociception), Moderate
		-4	25	Responsiveness to Sharp Noise, Moderate
200 mkd				
	91	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	92	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	93	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	94	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	95	-2	24	Responsiveness to Tail Pinch (nociception), Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 4. Sensory Evaluation – Females (continued)

Dose	Animal Number	Day Observed First	Last	Observation/Comment
200 mkd				
	95	-2	24	Responsiveness to Sharp Noise, Moderate
	96	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	97	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	98	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate
	99	-2	24	Responsiveness to Tail Pinch (nociception), Moderate
		-2	24	Responsiveness to Sharp Noise, Moderate

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 5. Individual Animal Rectal Temperature (°C) Data – Males

Sex, Dose	Animal ID	Baseline	Treated
Male,0 mg/kg/day	7682	38.0	37.5
	7683	38.8	36.9
	7684	38.4	38.8
	7685	38.9	38.5
	7686	39.0	38.2
	7687	39.0	37.4
	7688	38.8	39.1
	7689	38.3	37.9
	7690	38.9	36.9
	7691	39.0	38.7
Male,10 mg/kg/day	7692	39.0	38.8
	7693	38.9	39.1
	7694	38.6	39.0
	7695	37.6	38.1
	7696	38.1	38.1
	7697	38.7	39.0
	7698	39.1	39.1
	7699	38.9	37.6
	7700	38.8	38.1
	7701	38.9	38.1
Male,100 mg/kg/day	7702	37.6	38.5
	7703	39.0	37.6
	7704	38.7	36.9
	7705	38.6	38.0
	7706	38.9	38.6
	7707	39.0	38.7
	7708	39.0	38.3
	7709	38.9	38.2
	7710	38.9	37.9
	7711	38.9	38.7
Male,200 mg/kg/day	81	37.5	38.5
	82	38.1	37.8
	83	38.2	38.3
	84	38.2	37.7
	85	38.8	37.6
	86	38.9	38.0
	87	38.5	37.4
	88	38.3	38.4
	89	38.2	37.8
	90	38.0	37.6

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 6. Individual Animal Rectal Temperature (°C) Data – Females

Sex, Dose	Animal ID	Baseline	Treated
Female,0 mg/kg/day	7722	39.2	39.3
	7723	39.2	39.6
	7724	38.7	38.6
	7725	38.3	38.8
	7726	39.0	39.1
	7727	39.3	39.1
	7728	39.3	39.3
	7729	38.3	37.9
	7730	38.8	38.7
	7731	39.0	39.3
Female,10 mg/kg/day	7732	39.0	39.2
	7733	39.3	39.6
	7734	39.2	39.6
	7735	37.9	37.6
	7736	39.4	39.3
	7737	38.9	39.4
	7738	39.0	39.4
	7739	39.1	39.4
	7740	38.5	38.7
	7741	39.2	39.1
Female,100 mg/kg/day	7742	38.9	39.0
	7743	39.6	39.5
	7744	38.3	39.1
	7745	38.9	38.3
	7746	39.2	39.6
	7747	39.1	39.1
	7748	39.2	39.4
	7749	39.0	39.0
	7750	38.5	37.1
	7751	39.2	39.6
Female,200 mg/kg/day	91	38.0	38.4
	92	38.9	39.4
	93	38.3	39.0
	94	38.9	38.6
	95	39.2	37.8
	96	39.3	38.8
	97	39.5	39.1
	98	39.5	39.1
	99	38.1	38.8

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 7. Individual Animal Hindlimb Grip Performance (G) Data – Males

Baseline	Animal ID	HGP Trial 1	HGP Trial 2	HGP Trial 3	Ave HGP
Male,0 mg/kg/day	7682	276	246	354	292.0
	7683	331	229	335	298.3
	7684	269	329	254	284.0
	7685	257	306	281	281.3
	7686	319	249	310	292.7
	7687	201	316	196	237.7
	7688	509	331	410	416.7
	7689	382	262	270	304.7
	7690	310	254	300	288.0
	7691	306	403	339	349.3
Male,10 mg/kg/day	7692	296	374	293	321.0
	7693	359	337	384	360.0
	7694	309	222	278	269.7
	7695	286	310	355	317.0
	7696	315	302	230	282.3
	7697	271	245	279	265.0
	7698	273	327	376	325.3
	7699	406	286	372	354.7
	7700	340	321	446	369.0
	7701	366	357	604	442.3
Male,100 mg/kg/day	7702	181	329	193	234.3
	7703	310	441	360	370.3
	7704	256	267	330	284.3
	7705	351	292	275	306.0
	7706	200	176	322	232.7
	7707	460	570	496	508.7
	7708	331	326	310	322.3
	7709	443	433	319	398.3
	7710	386	421	392	399.7
	7711	242	438	478	386.0
Male,200 mg/kg/day	81	494	356	376	408.7
	82	379	500	365	414.7
	83	367	667	346	460.0
	84	395	253	352	333.3
	85	446	457	429	444.0
	86	378	425	549	450.7
	87	515	437	609	520.3
	88	329	304	451	361.3
	89	379	393	582	451.3

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 3. Individual Animal Rectal Temperature (C) Data (continued)

90	387	394	502	427.7

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 7. Individual Animal Hindlimb Grip Performance (G) Data – Males (continued)

Week 4	Animal ID	HGP Trial 1	HGP Trial 2	HGP Trial 3	Ave HGP
Male,0 mg/kg/day	7682	623	781	758	720.7
	7683	614	451	458	507.7
	7684	586	465	790	613.7
	7685	566	789	700	685.0
	7686	695	741	820	752.0
	7687	733	700	682	705.0
	7688	589	664	1029	760.7
	7689	830	809	695	778.0
	7690	500	683	634	605.7
	7691	738	703	744	728.3
Male,10 mg/kg/day	7692	672	707	783	720.7
	7693	800	866	546	737.3
	7694	648	403	417	489.3
	7695	506	807	659	657.3
	7696	509	534	709	584.0
	7697	569	525	423	505.7
	7698	580	920	689	729.7
	7699	602	730	785	705.7
	7700	675	759	565	666.3
	7701	736	636	787	719.7
Male,100 mg/kg/day	7702	864	607	608	693.0
	7703	691	673	560	641.3
	7704	685	612	594	630.3
	7705	678	662	622	654.0
	7706	703	546	631	626.7
	7707	596	994	645	745.0
	7708	752	735	698	728.3
	7709	439	635	757	610.3
	7710	887	951	1066	968.0
	7711	752	714	839	768.3
Male,200 mg/kg/day	81	747	852	465	688.0
	82	767	439	588	598.0
	83	783	588	938	769.7
	84	510	729	370	536.3
	85	748	586	530	621.3
	86	533	461	576	523.3
	87	792	526	488	602.0
	88	708	452	589	583.0
	89	458	598	535	530.3
	90	782	497	543	607.3

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 8. Individual Animal Hindlimb Grip Performance (G) Data – Females

Baseline	Animal ID	HGP Trial 1	HGP Trial 2	HGP Trial 3	Ave HGP
Female,0 mg/kg/day	7722	336	313	296	315.0
	7723	242	233	209	228.0
	7724	270	300	283	284.3
	7725	270	277	205	250.7
	7726	282	239	272	264.3
	7727	309	181	226	238.7
	7728	288	220	244	250.7
	7729	357	239	414	336.7
	7730	199	211	271	227.0
	7731	209	176	161	182.0
Female,10 mg/kg/day	7732	251	344	349	314.7
	7733	480	351	264	365.0
	7734	404	474	637	505.0
	7735	207	206	193	202.0
	7736	251	227	284	254.0
	7737	286	275	401	320.7
	7738	313	296	270	293.0
	7739	245	322	322	296.3
	7740	378	282	274	311.3
	7741	251	255	252	252.7
Female,100 mg/kg/day	7742	250	319	270	279.7
	7743	246	423	276	315.0
	7744	290	345	397	344.0
	7745	408	240	183	277.0
	7746	227	238	208	224.3
	7747	362	265	305	310.7
	7748	245	198	281	241.3
	7749	330	339	400	356.3
	7750	262	295	364	307.0
	7751	298	220	310	276.0
Female,200 mg/kg/day	91	393	358	285	345.3
	92	602	336	423	453.7
	93	317	412	368	365.7
	94	447	274	301	340.7
	95	234	412	308	318.0
	96	246	345	239	276.7
	97	318	448	309	358.3
	98	275	258	273	268.7
	99	441	457	416	438.0

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 8. Individual Animal Hindlimb Grip Performance (G) Data – Females (continued)

Week 4	Animal ID	HGP Trial 1	HGP Trial 2	HGP Trial 3	Ave HGP
Female,0 mg/kg/day	7722	865	597	515	659.0
	7723	434	272	348	351.3
	7724	516	447	529	497.3
	7725	448	617	773	612.7
	7726	345	672	375	464.0
	7727	328	356	462	382.0
	7728	542	670	443	551.7
	7729	416	519	529	488.0
	7730	705	599	674	659.3
	7731	607	569	448	541.3
Female,10 mg/kg/day	7732	627	495	506	542.7
	7733	451	388	463	434.0
	7734	588	401	655	548.0
	7735	330	600	545	491.7
	7736	617	420	436	491.0
	7737	389	400	440	409.7
	7738	815	726	885	808.7
	7739	411	490	686	529.0
	7740	619	600	645	621.3
	7741	465	444	396	435.0
Female,100 mg/kg/day	7742	599	694	385	559.3
	7743	510	407	323	413.3
	7744	271	439	490	400.0
	7745	361	580	441	460.7
	7746	366	315	348	343.0
	7747	198	339	458	331.7
	7748	287	499	315	367.0
	7749	467	420	401	429.3
	7750	583	576	467	542.0
	7751	447	446	562	485.0
Female,200 mg/kg/day	91	440	286	294	340.0
	92	654	383	722	586.3
	93	474	784	361	539.7
	94	570	603	529	567.3
	95	320	440	454	404.7
	96	331	256	452	346.3
	97	664	636	429	576.3
	98	355	390	360	368.3
	99	420	498	492	470.0

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 9. Individual Animal Forelimb Grip Performance (G) Data – Males

Baseline	Animal ID	FGP Trial 1	FGP Trial 2	FGP Trial 3	Ave FGP
Male,0 mg/kg/day	7682	637	458	225	440.0
	7683	571	414	399	461.3
	7684	268	410	374	350.7
	7685	321	409	437	389.0
	7686	598	482	227	435.7
	7687	566	397	569	510.7
	7688	613	618	586	605.7
	7689	587	529	542	552.7
	7690	653	533	476	554.0
	7691	717	462	463	547.3
Male,10 mg/kg/day	7692	515	517	556	529.3
	7693	681	374	467	507.3
	7694	453	533	398	461.3
	7695	563	356	560	493.0
	7696	526	525	509	520.0
	7697	491	540	471	500.7
	7698	593	435	487	505.0
	7699	315	613	315	414.3
	7700	553	413	586	517.3
	7701	626	514	411	517.0
Male,100 mg/kg/day	7702	294	397	413	368.0
	7703	513	290	388	397.0
	7704	484	492	438	471.3
	7705	540	432	324	432.0
	7706	222	480	190	297.3
	7707	597	483	559	546.3
	7708	567	452	550	523.0
	7709	601	492	330	474.3
	7710	560	515	485	520.0
	7711	451	540	720	570.3
Male,200 mg/kg/day	81	409	717	717	614.3
	82	619	688	839	715.3
	83	814	738	689	747.0
	84	888	674	781	781.0
	85	654	696	739	696.3
	86	529	396	713	546.0
	87	874	566	554	664.7
	88	803	777	576	718.7
	89	719	601	583	634.3
	90	769	699	868	778.7

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 9. Individual Animal Forelimb Grip Performance (G) Data – Males (continued)

Week 4	Animal ID	FGP Trial 1	FGP Trial 2	FGP Trial 3	Ave FGP
Male,0 mg/kg/day	7682	750	987	650	795.7
	7683	742	592	723	685.7
	7684	721	459	527	569.0
	7685	739	506	410	551.7
	7686	864	746	856	822.0
	7687	994	653	493	713.3
	7688	1089	761	1067	972.3
	7689	1072	1116	1089	1092.3
	7690	910	1008	831	916.3
	7691	897	734	615	748.7
Male,10 mg/kg/day	7692	933	947	740	873.3
	7693	984	863	769	872.0
	7694	806	765	853	808.0
	7695	706	487	900	697.7
	7696	874	589	671	711.3
	7697	843	601	807	750.3
	7698	731	497	923	717.0
	7699	487	624	547	552.7
	7700	771	898	717	795.3
	7701	811	831	657	766.3
Male,100 mg/kg/day	7702	812	1038	943	931.0
	7703	617	606	589	604.0
	7704	742	377	730	616.3
	7705	831	765	951	849.0
	7706	697	576	599	624.0
	7707	952	736	740	809.3
	7708	678	1069	1108	951.7
	7709	976	515	609	700.0
	7710	908	1093	1103	1034.7
	7711	878	561	820	753.0
Male,200 mg/kg/day	81	507	635	789	643.7
	82	807	764	713	761.3
	83	735	540	773	682.7
	84	583	778	796	719.0
	85	262	677	731	556.7
	86	882	443	593	639.3
	87	608	609	571	596.0
	88	536	820	287	547.7
	89	370	670	791	610.3

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 5. Individual Animal Forelimb Grip Performance (G) Data (continued)

90	882	750	545	725.7

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 10. Individual Animal Forelimb Grip Performance (G) Data – Females

Baseline	Animal ID	FGP Trial 1	FGP Trial 2	FGP Trial 3	Ave FGP
Female,0 mg/kg/day	7722	515	615	375	501.7
	7723	330	631	313	424.7
	7724	547	490	517	518.0
	7725	721	520	369	536.7
	7726	495	583	652	576.7
	7727	543	505	578	542.0
	7728	507	486	587	526.7
	7729	433	379	418	410.0
	7730	496	351	523	456.7
	7731	546	546	528	540.0
Female,10mg/kg/day	7732	363	433	562	452.7
	7733	329	416	367	370.7
	7734	655	599	547	600.3
	7735	330	471	281	360.7
	7736	611	623	596	610.0
	7737	372	524	460	452.0
	7738	635	487	619	580.3
	7739	491	521	479	497.0
	7740	609	507	483	533.0
	7741	511	450	376	445.7
Female,100mg/kg/day	7742	415	440	367	407.3
	7743	526	441	375	447.3
	7744	577	605	468	550.0
	7745	749	501	427	559.0
	7746	471	414	311	398.7
	7747	497	457	397	450.3
	7748	601	367	359	442.3
	7749	745	631	621	665.7
	7750	542	248	412	400.7
	7751	534	481	639	551.3
Female,200mg/kg/day	91	499	414	598	503.7
	92	724	667	558	649.7
	93	631	670	525	608.7
	94	732	692	583	669.0
	95	599	673	769	680.3
	96	659	372	631	554.0
	97	473	516	349	446.0
	98	553	452	518	507.7
	99	767	444	486	565.7

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 5. Individual Animal Forelimb Grip Performance (G) Data (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 10. Individual Animal Forelimb Grip Performance (G) Data – Females (continued)

Week 4	Animal ID	FGP Trial 1	FGP Trial 2	FGP Trial 3	Ave FGP
Female,0 mg/kg/day	7722	690	643	403	578.7
	7723	597	691	788	692.0
	7724	707	485	692	628.0
	7725	685	494	312	497.0
	7726	879	703	912	831.3
	7727	913	659	640	737.3
	7728	853	680	706	746.3
	7729	650	492	518	553.3
	7730	623	664	696	661.0
	7731	695	579	730	668.0
Female,10mg/kg/day	7732	605	628	589	607.3
	7733	692	540	608	613.3
	7734	666	545	667	626.0
	7735	591	482	423	498.7
	7736	777	547	887	737.0
	7737	773	329	485	529.0
	7738	798	766	812	792.0
	7739	844	488	870	734.0
	7740	1030	785	549	788.0
	7741	640	505	682	609.0
Female,100mg/kg/day	7742	731	422	337	496.7
	7743	572	684	643	633.0
	7744	657	472	914	681.0
	7745	871	487	655	671.0
	7746	753	466	597	605.3
	7747	799	646	927	790.7
	7748	734	481	485	566.7
	7749	824	679	643	715.3
	7750	629	706	583	639.3
	7751	519	653	682	618.0
Female,200mg/kg/day	91	409	595	530	511.3
	92	515	558	401	491.3
	93	488	531	601	540.0
	94	596	632	328	518.7
	95	527	553	576	552.0
	96	465	418	608	497.0
	97	737	256	218	403.7
	98	725	659	570	651.3
	99	588	358	567	504.3

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 11. Square Root of Individual Motor Activity Counts by Epoch – Males

Baseline Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Males,0 mg/kg/day	7682	5.00	2.65	2.65	3.74	2.24	0.00	7.62
	7683	6.86	4.80	6.71	5.66	2.83	0.00	12.45
	7684	6.16	6.48	4.69	2.65	1.41	4.00	11.27
	7685	6.48	4.58	4.47	1.41	0.00	0.00	9.22
	7686	5.48	5.74	4.24	4.12	4.12	3.00	11.14
	7687	6.63	6.16	5.20	5.10	2.24	0.00	11.83
	7688	6.78	4.90	5.66	3.32	5.20	0.00	11.83
	7689	5.66	5.66	4.00	1.73	0.00	0.00	9.11
	7690	6.93	6.16	5.39	5.48	4.80	3.61	13.45
	7691	7.62	5.83	6.40	6.24	2.45	2.45	13.56
Males,10 mg/kg/day	7692	5.48	4.12	2.45	0.00	4.36	0.00	8.49
	7693	6.48	4.24	3.46	4.36	0.00	0.00	9.54
	7694	6.16	6.78	4.58	3.00	4.58	2.83	11.96
	7695	5.66	6.00	4.80	6.56	4.24	0.00	12.33
	7696	7.21	6.24	4.58	4.24	7.00	2.24	13.56
	7697	6.63	4.80	3.61	2.24	1.41	0.00	9.33
	7698	6.93	6.63	5.39	4.36	0.00	0.00	11.83
	7699	6.78	6.56	6.40	3.32	1.00	4.47	12.73
	7700	7.87	5.92	5.20	4.00	0.00	0.00	11.83
	7701	7.55	7.68	4.24	4.12	0.00	0.00	12.29
Males,100 mg/kg/day	7702	6.86	5.48	6.16	5.10	3.16	0.00	12.29
	7703	6.78	6.93	5.29	1.00	0.00	0.00	11.09
	7704	5.83	6.00	3.32	4.12	4.24	3.61	11.36
	7705	5.74	5.83	4.69	4.36	0.00	0.00	10.39
	7706	6.32	5.57	4.00	4.00	0.00	0.00	10.15
	7707	6.24	6.16	3.87	4.47	3.61	0.00	11.18
	7708	6.93	5.10	4.58	2.24	2.45	4.12	11.09
	7709	7.14	5.48	4.00	4.47	2.83	5.10	12.29
	7710	7.35	6.48	5.57	3.16	4.00	2.45	12.61
	7711	6.78	5.57	2.00	1.00	0.00	0.00	9.06
Males,200 mg/kg/day	81	7.00	5.74	6.32	2.83	3.32	0.00	11.87
	82	7.48	5.29	5.57	4.12	1.41	0.00	11.58
	83	5.92	5.74	1.41	0.00	0.00	0.00	8.37
	84	8.43	7.28	5.20	5.00	4.36	1.41	14.04
	85	5.92	5.66	3.00	5.57	0.00	0.00	10.34
	86	6.08	6.24	4.24	1.00	0.00	0.00	9.75
	87	5.57	4.12	5.29	0.00	0.00	2.45	9.06
	88	6.86	6.32	3.74	2.00	0.00	1.73	10.39
	89	6.32	6.63	3.74	4.00	0.00	0.00	10.68

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 11. Square Root of Individual Motor Activity Counts by Epoch – Males (continued)

	90	4.47	5.74	4.69	4.12	1.73	3.00	10.20

Week 4 Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Males,0 mg/kg/day	7682	5.00	0.00	3.87	0.00	3.46	0.00	7.21
	7683	6.48	6.24	4.00	4.36	4.00	4.24	12.25
	7684	6.08	5.74	5.10	3.46	4.58	3.32	11.83
	7685	5.48	5.48	6.00	3.74	0.00	0.00	10.49
	7686	6.63	5.00	4.12	3.00	5.39	6.93	13.11
	7687	5.74	6.71	4.36	0.00	0.00	4.36	10.77
	7688	5.83	5.00	4.80	4.36	3.87	3.16	11.22
	7689	6.86	6.86	6.40	3.74	2.00	4.69	13.23
	7690	6.48	5.29	5.57	5.10	4.58	4.58	13.00
	7691	7.21	6.56	4.58	4.90	3.61	2.00	12.53
Males,10 mg/kg/day	7692	5.83	5.74	5.57	2.65	3.61	6.00	12.41
	7693	7.21	6.24	5.66	5.83	5.20	4.12	14.18
	7694	4.36	4.69	2.45	2.24	4.00	0.00	8.25
	7695	6.16	5.83	4.36	3.74	0.00	2.65	10.58
	7696	7.00	6.32	5.92	5.39	3.46	1.00	12.88
	7697	6.86	5.66	5.66	3.00	4.12	0.00	11.70
	7698	7.28	5.48	4.47	4.58	5.00	5.48	13.38
	7699	6.40	6.63	5.92	6.24	6.00	3.32	14.35
	7700	5.74	6.86	5.74	3.61	7.42	3.74	13.96
	7701	7.21	5.57	6.48	5.39	6.56	1.41	14.11
Males,100 mg/kg/day	7702	6.32	5.66	2.65	0.00	3.16	4.00	10.25
	7703	5.48	4.90	4.24	1.73	3.87	4.69	10.58
	7704	6.93	6.24	6.56	5.20	3.74	0.00	13.08
	7705	5.66	5.48	4.47	5.20	1.73	0.00	10.58
	7706	6.86	6.00	5.00	4.00	0.00	0.00	11.14
	7707	5.74	4.69	5.92	7.21	1.00	5.74	13.27
	7708	5.83	4.80	4.36	1.41	0.00	2.00	9.06
	7709	7.62	7.87	5.83	4.69	6.24	4.12	15.23
	7710	6.71	6.24	5.74	3.74	4.69	0.00	12.37
	7711	7.55	6.00	3.16	6.24	3.46	1.73	12.53
Males,200 mg/kg/day	81	7.94	6.93	4.69	4.80	4.36	3.61	13.71
	82	6.93	7.55	5.74	4.24	2.45	0.00	12.73
	83	6.63	3.87	2.45	4.36	4.00	3.00	10.44
	84	6.08	5.83	5.10	2.24	3.00	3.32	11.05
	85	5.48	1.73	2.00	3.46	0.00	0.00	7.00
	86	6.63	5.29	5.00	3.00	4.24	5.20	12.29
	87	6.48	3.61	4.80	0.00	3.74	0.00	9.59
	88	7.14	5.66	5.10	4.36	4.36	0.00	12.12

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 11. Square Root of Individual Motor Activity Counts by Epoch – Males (continued)

89	5.57	5.00	4.47	1.41	0.00	0.00	8.83
90	6.24	5.39	3.00	4.80	2.45	3.00	10.72

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 12. Square Root of Individual Motor Activity Counts by Epoch -- Females

Baseline Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Females,0 mg/kg/day	7722	5.48	5.74	4.36	3.61	3.32	2.65	10.63
	7723	6.93	5.39	4.36	4.47	0.00	0.00	10.77
	7724	7.07	6.86	5.29	2.83	2.65	0.00	11.83
	7725	7.00	4.58	5.48	1.00	0.00	0.00	10.05
	7726	8.77	6.32	6.63	2.00	0.00	0.00	12.85
	7727	6.63	6.56	4.69	4.90	4.47	0.00	12.37
	7728	7.35	5.83	6.48	5.48	3.87	2.83	13.53
	7729	7.14	5.92	3.61	6.08	4.36	2.00	12.61
	7730	6.48	4.69	3.32	1.00	2.00	4.36	9.95
	7731	6.48	4.24	2.00	0.00	0.00	4.00	8.94
Females,10 mg/kg/day	7732	6.48	5.10	0.00	0.00	0.00	2.65	8.66
	7733	8.00	5.83	3.00	4.58	4.12	2.00	12.21
	7734	6.56	3.74	3.61	6.56	1.00	0.00	10.68
	7735	7.28	4.36	0.00	3.32	2.24	0.00	9.38
	7736	7.07	5.29	2.83	4.24	2.83	0.00	10.58
	7737	8.06	7.28	6.00	6.00	2.00	2.00	14.07
	7738	6.32	5.48	5.39	2.65	4.00	1.41	11.14
	7739	5.57	6.08	3.61	3.32	1.73	0.00	9.75
	7740	7.21	5.39	5.57	1.73	0.00	0.00	10.72
	7741	8.06	8.49	5.48	3.87	2.24	1.00	13.71
Females,100 mg/kg/day	7742	6.56	4.90	4.24	0.00	0.00	0.00	9.22
	7743	7.14	4.47	4.80	3.16	3.74	3.16	11.31
	7744	7.87	5.92	5.39	3.00	2.65	0.00	11.92
	7745	7.48	5.48	5.10	1.00	1.00	0.00	10.68
	7746	7.62	6.48	4.36	3.46	4.24	5.57	13.42
	7747	5.74	6.24	5.66	5.20	4.00	1.00	12.17
	7748	5.48	4.24	3.87	0.00	0.00	0.00	7.94
	7749	7.55	5.20	5.10	4.58	3.16	3.87	12.49
	7750	6.86	5.00	2.83	0.00	2.24	5.74	10.86
	7751	6.63	4.80	3.16	0.00	0.00	1.41	8.89
Females,200 mg/kg/day	91	6.63	6.48	4.00	5.00	1.73	4.12	12.12
	92	7.21	6.32	6.32	4.24	5.39	0.00	13.38
	93	5.74	6.56	4.58	0.00	2.24	0.00	10.1
	94	6.48	5.92	4.36	5.48	0.00	0.00	11.22
	95	5.74	5.20	5.66	4.47	4.69	4.00	12.25
	96	6.56	6.48	4.80	3.74	1.41	2.00	11.31
	97	7.00	7.68	6.08	5.48	5.48	3.00	14.63
	98	6.16	7.00	4.90	2.65	4.12	2.83	11.96
	99	8.06	5.92	4.47	2.65	3.00	0.00	11.66

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 11. Square Root of Individual Motor Activity Counts by Epoch – Males (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 12. Square Root of Individual Motor Activity Counts by Epoch – Females (continued)

Week 4

Sex, Dose	Animal ID	1	2	3	4	5	6	Total
Females,0 mg/kg/day	7722	6.63	6.32	4.58	4.47	5.00	4.12	12.92
	7723	4.47	5.66	5.92	4.00	0.00	2.24	10.39
	7724	7.68	6.86	5.66	4.12	1.00	0.00	12.49
	7725	6.32	6.24	5.83	3.00	0.00	1.73	11.18
	7726	6.24	6.63	5.29	5.48	4.36	3.16	13.04
	7727	6.56	5.83	6.00	5.66	3.16	5.00	13.42
	7728	6.93	4.47	4.90	7.48	7.35	4.80	15.00
	7729	6.24	4.90	5.39	5.39	5.29	5.74	13.49
	7730	7.07	5.10	5.29	6.78	0.00	0.00	12.25
	7731	6.86	6.24	5.66	4.90	6.08	3.46	13.82
Females,10 mg/kg/day	7732	6.24	6.32	2.45	0.00	5.00	2.00	10.68
	7733	5.48	5.20	4.47	2.45	2.45	4.24	10.34
	7734	6.93	2.00	4.80	3.32	3.87	0.00	10.05
	7735	7.87	5.74	5.66	3.32	3.32	0.00	12.21
	7736	7.28	4.69	6.63	3.00	4.12	4.80	12.96
	7737	7.00	7.94	6.08	4.69	3.32	2.83	13.78
	7738	7.28	6.16	5.10	5.00	5.48	3.61	13.60
	7739	7.00	5.66	6.71	4.24	5.10	4.24	13.71
	7740	7.68	7.55	4.90	5.83	3.46	4.24	14.28
	7741	8.31	5.48	6.08	6.08	6.63	6.93	16.28
Females,100 mg/kg/day	7742	5.57	4.47	4.00	2.24	3.00	3.32	9.59
	7743	7.00	5.00	6.00	6.00	4.90	3.61	13.53
	7744	8.31	8.12	6.93	4.90	6.16	4.00	16.16
	7745	7.62	6.32	7.28	5.48	4.47	2.65	14.42
	7746	7.81	8.31	4.47	4.00	4.47	4.12	14.25
	7747	6.00	5.66	5.29	4.69	6.16	3.74	13.04
	7748	5.83	4.90	3.74	3.46	4.47	4.69	11.22
	7749	7.42	4.90	5.57	3.74	5.29	4.69	13.19
	7750	7.35	4.47	4.36	6.63	2.45	3.16	12.37
	7751	6.40	5.66	6.86	5.29	5.20	3.32	13.64
Females,200 mg/kg/day	91	4.58	5.10	4.24	3.74	6.63	3.00	11.49
	92	5.29	4.00	5.20	5.39	4.69	5.00	12.12
	93	6.24	5.74	4.69	2.00	5.20	3.00	11.58
	94	6.78	5.83	4.24	2.65	2.00	3.46	11.00
	95	5.39	3.16	1.73	0.00	0.00	2.00	6.78
	96	6.08	6.08	5.10	3.74	4.00	4.36	12.21
	97	5.10	5.48	2.00	1.41	2.65	3.16	8.89
	98	6.00	7.81	7.42	4.58	4.80	3.61	14.46
	99	5.66	4.80	4.58	4.24	4.12	4.00	11.27

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HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 13. Untransformed Individual Motor Activity Counts – Males

Baseline Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Males, 0 mg/kg/day	7682	25	7	7	14	5	0	58
	7683	47	23	45	32	8	0	155
	7684	38	42	22	7	2	16	127
	7685	42	21	20	2	0	0	85
	7686	30	33	18	17	17	9	124
	7687	44	38	27	26	5	0	140
	7688	46	24	32	11	27	0	140
	7689	32	32	16	3	0	0	83
	7690	48	38	29	30	23	13	181
	7691	58	34	41	39	6	6	184
Males,10 mg/kg/day	7692	30	17	6	0	19	0	72
	7693	42	18	12	19	0	0	91
	7694	38	46	21	9	21	8	143
	7695	32	36	23	43	18	0	152
	7696	52	39	21	18	49	5	184
	7697	44	23	13	5	2	0	87
	7698	48	44	29	19	0	0	140
	7699	46	43	41	11	1	20	162
	7700	62	35	27	16	0	0	140
	7701	57	59	18	17	0	0	151
Males, 100 mg/kg/day	7702	47	30	38	26	10	0	151
	7703	46	48	28	1	0	0	123
	7704	34	36	11	17	18	13	129
	7705	33	34	22	19	0	0	108
	7706	40	31	16	16	0	0	103
	7707	39	38	15	20	13	0	125
	7708	48	26	21	5	6	17	123
	7709	51	30	16	20	8	26	151
	7710	54	42	31	10	16	6	159
	7711	46	31	4	1	0	0	82
Males, 200 mg/kg/day	81	49	33	40	8	11	0	141
	82	56	28	31	17	2	0	134
	83	35	33	2	0	0	0	70
	84	71	53	27	25	19	2	197
	85	35	32	9	31	0	0	107
	86	37	39	18	1	0	0	95
	87	31	17	28	0	0	6	82
	88	47	40	14	4	0	3	108
	89	40	44	14	16	0	0	114
	90	20	33	22	17	3	9	104

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 13. Untransformed Individual Motor Activity Counts – Males (continued)

Week 4 Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Males, 0 mg/kg/day	7682	25	0	15	0	12	0	52
	7683	42	39	16	19	16	18	150
	7684	37	33	26	12	21	11	140
	7685	30	30	36	14	0	0	110
	7686	44	25	17	9	29	48	172
	7687	33	45	19	0	0	19	116
	7688	34	25	23	19	15	10	126
	7689	47	47	41	14	4	22	175
	7690	42	28	31	26	21	21	169
	7691	52	43	21	24	13	4	157
Males,10 mg/kg/day	7692	34	33	31	7	13	36	154
	7693	52	39	32	34	27	17	201
	7694	19	22	6	5	16	0	68
	7695	38	34	19	14	0	7	112
	7696	49	40	35	29	12	1	166
	7697	47	32	32	9	17	0	137
	7698	53	30	20	21	25	30	179
	7699	41	44	35	39	36	11	206
	7700	33	47	33	13	55	14	195
	7701	52	31	42	29	43	2	199
Males, 100 mg/kg/day	7702	40	32	7	0	10	16	105
	7703	30	24	18	3	15	22	112
	7704	48	39	43	27	14	0	171
	7705	32	30	20	27	3	0	112
	7706	47	36	25	16	0	0	124
	7707	33	22	35	52	1	33	176
	7708	34	23	19	2	0	4	82
	7709	58	62	34	22	39	17	232
	7710	45	39	33	14	22	0	153
	7711	57	36	10	39	12	3	157
Males, 200 mg/kg/day	81	63	48	22	23	19	13	188
	82	48	57	33	18	6	0	162
	83	44	15	6	19	16	9	109
	84	37	34	26	5	9	11	122
	85	30	3	4	12	0	0	49
	86	44	28	25	9	18	27	151
	87	42	13	23	0	14	0	92
	88	51	32	26	19	19	0	147
	89	31	25	20	2	0	0	78
	90	39	29	9	23	6	9	115

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APPENDIX TABLE 14. Untransformed Individual Motor Activity Counts – Females

Baseline Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Females,0 mg/kg/day	7722	30	33	19	13	11	7	113
	7723	48	29	19	20	0	0	116
	7724	50	47	28	8	7	0	140
	7725	49	21	30	1	0	0	101
	7726	77	40	44	4	0	0	165
	7727	44	43	22	24	20	0	153
	7728	54	34	42	30	15	8	183
	7729	51	35	13	37	19	4	159
	7730	42	22	11	1	4	19	99
	7731	42	18	4	0	0	16	80
Females,10 mg/kg/day	7732	42	26	0	0	0	7	75
	7733	64	34	9	21	17	4	149
	7734	43	14	13	43	1	0	114
	7735	53	19	0	11	5	0	88
	7736	50	28	8	18	8	0	112
	7737	65	53	36	36	4	4	198
	7738	40	30	29	7	16	2	124
	7739	31	37	13	11	3	0	95
	7740	52	29	31	3	0	0	115
	7741	65	72	30	15	5	1	188
Females,100 mg/kg/day	7742	43	24	18	0	0	0	85
	7743	51	20	23	10	14	10	128
	7744	62	35	29	9	7	0	142
	7745	56	30	26	1	1	0	114
	7746	58	42	19	12	18	31	180
	7747	33	39	32	27	16	1	148
	7748	30	18	15	0	0	0	63
	7749	57	27	26	21	10	15	156
	7750	47	25	8	0	5	33	118
	7751	44	23	10	0	0	2	79
Females,200 mg/kg/day	91	44	42	16	25	3	17	147
	92	52	40	40	18	29	0	179
	93	33	43	21	0	5	0	102
	94	42	35	19	30	0	0	126
	95	33	27	32	20	22	16	150
	96	43	42	23	14	2	4	128
	97	49	59	37	30	30	9	214
	98	38	49	24	7	17	8	143
	99	65	35	20	7	9	0	136

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 14. Untransformed Individual Motor Activity Counts – Females (continued)

Week 4 Sex, Dose	Animal ID	Epochs 1	2	3	4	5	6	Total
Females,0 mg/kg/day	7722	44	40	21	20	25	17	167
	7723	20	32	35	16	0	5	108
	7724	59	47	32	17	1	0	156
	7725	40	39	34	9	0	3	125
	7726	39	44	28	30	19	10	170
	7727	43	34	36	32	10	25	180
	7728	48	20	24	56	54	23	225
	7729	39	24	29	29	28	33	182
	7730	50	26	28	46	0	0	150
	7731	47	39	32	24	37	12	191
Females,10 mg/kg/day	7732	39	40	6	0	25	4	114
	7733	30	27	20	6	6	18	107
	7734	48	4	23	11	15	0	101
	7735	62	33	32	11	11	0	149
	7736	53	22	44	9	17	23	168
	7737	49	63	37	22	11	8	190
	7738	53	38	26	25	30	13	185
	7739	49	32	45	18	26	18	188
	7740	59	57	24	34	12	18	204
	7741	69	30	37	37	44	48	265
Females,100 mg/kg/day	7742	31	20	16	5	9	11	92
	7743	49	25	36	36	24	13	183
	7744	69	66	48	24	38	16	261
	7745	58	40	53	30	20	7	208
	7746	61	69	20	16	20	17	203
	7747	36	32	28	22	38	14	170
	7748	34	24	14	12	20	22	126
	7749	55	24	31	14	28	22	174
	7750	54	20	19	44	6	10	153
	7751	41	32	47	28	27	11	186
Females,200 mg/kg/day	91	21	26	18	14	44	9	132
	92	28	16	27	29	22	25	147
	93	39	33	22	4	27	9	134
	94	46	34	18	7	4	12	121
	95	29	10	3	0	0	4	46
	96	37	37	26	14	16	19	149
	97	26	30	4	2	7	10	79
	98	36	61	55	21	23	13	209
	99	32	23	21	18	17	16	127

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 15. Ophthalmic Observations – Males

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7682	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7683	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7684	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7685	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7686	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Left
		30	30	Disposition, Scheduled Necropsy
	7687	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7688	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7689	-7	-7	No Remarkable Observations
		29	29	Eye, Periocular Soiling, Clear, Right
		30	30	Disposition, Scheduled Necropsy
	7690	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7691	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Right
		30	30	Disposition, Scheduled Necropsy
10 mkd				
	7692	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 15. Ophthalmic Observations – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
10 mkd				
	7693	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7694	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7695	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7696	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7697	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7698	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Bilateral
		30	30	Disposition, Scheduled Necropsy
	7699	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Right
		30	30	Disposition, Scheduled Necropsy
	7700	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7701	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
100 mkd				
	7702	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7703	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 15. Ophthalmic Observations – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
100 mkd				
	7704	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7705	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Right
		29	29	Eye, Periocular Soiling, Red, Right
		30	30	Disposition, Scheduled Necropsy
	7706	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7707	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Bilateral
		30	30	Disposition, Scheduled Necropsy
	7708	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Right
		29	29	Eye, Pale Fundus, Right
		30	30	Disposition, Scheduled Necropsy
	7709	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7710	-7	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	7711	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Right
		30	30	Disposition, Scheduled Necropsy
200 mkd				
	81	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	82	-14	-14	Eye, Dilation Incomplete, Left
		29	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 15. Ophthalmic Observations – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
200 mkd				
	83	-14	29	Eye, Cloudy Cornea, Left
		29	29	Eye, Pale Fundus, Left
		30	30	Disposition, Scheduled Necropsy
	84	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	85	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	86	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	87	-14	-14	Eye, Dilation Incomplete, Right
		29	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	88	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	89	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	90	-14	-14	No Remarkable Observations
		29	29	Eye, Periocular Soiling, Red, Left
		30	30	Disposition, Scheduled Necropsy
1000 mkd				
	7712	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7713	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 15. Ophthalmic Observations – Males (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
1000 mkd				
	7714	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7715	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7716	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7717	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7718	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7719	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7720	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7721	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 16. Ophthalmic Observations – Females

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
0.0 mkd				
	7722	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7723	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7724	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7725	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7726	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7727	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7728	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7729	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Left
		31	31	Disposition, Scheduled Necropsy
	7730	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7731	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
10 mkd				
	7732	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7733	-7	29	No Remarkable Observations

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 16. Ophthalmic Observations – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
10 mkd				
	7733	31	31	Disposition, Scheduled Necropsy
	7734	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7735	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Right
		31	31	Disposition, Scheduled Necropsy
	7736	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7737	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7738	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7739	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7740	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7741	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
100 mkd				
	7742	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Left
		31	31	Disposition, Scheduled Necropsy
	7743	-7	-7	No Remarkable Observations
		29	29	Eye, Cloudy Cornea, Left
		29	29	Eye, Pale Fundus, Left
		31	31	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 16. Ophthalmic Observations – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
100 mkd				
	7744	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7745	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7746	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7747	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7748	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7749	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7750	-7	29	No Remarkable Observations
		31	31	Disposition, Scheduled Necropsy
	7751	-7	-7	No Remarkable Observations
		29	29	Eye, Pale Fundus, Right
		31	31	Disposition, Scheduled Necropsy
200 mkd				
	91	-14	-14	Eye, Microphthalmia, Right
		29	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	92	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	93	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	94	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 16. Ophthalmic Observations – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
200 mkd				
	95	-14	29	Eye, Microphthalmia, Bilateral
		30	30	Disposition, Scheduled Necropsy
	96	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	97	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	98	-14	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
	99	-14	-14	Eye, Periocular Soiling, Red, Right
		29	29	No Remarkable Observations
		30	30	Disposition, Scheduled Necropsy
1000 mkd				
	7752	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7753	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7754	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7755	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 16. Ophthalmic Observations – Females (continued)

Dose	Animal Number	Day Observed First	Day Observed Last	Observation/Comment
1000 mkd				
	7756	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7757	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7758	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7759	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7760	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed
	7761	-7	-7	No Remarkable Observations
		5	5	Disposition, Removed

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
0	7682	118.3	131.7	13.4	152.6	34.3	165.1	46.8	184.9	66.6	197.9	79.6	212.3	94.0
	7683	121.0	137.1	16.1	158.6	37.6	177.2	56.2	199.9	78.9	213.2	92.2	227.4	106.4
	7684	119.5	134.4	14.9	152.6	33.1	166.6	47.1	186.8	67.3	198.6	79.1	214.9	95.4
	7685	123.9	139.0	15.1	158.0	34.1	171.0	47.1	192.2	68.3	204.0	80.1	223.2	99.3
	7686	126.4	143.5	17.1	164.6	38.2	182.3	55.9	202.9	76.5	217.8	91.4	231.4	105.0
	7687	128.5	145.5	17.0	170.5	42.0	186.3	57.8	209.2	80.7	223.6	95.1	236.6	108.1
	7688	129.6	145.3	15.7	164.6	35.0	182.5	52.9	202.9	73.3	214.4	84.8	233.4	103.8
	7689	135.0	154.3	19.3	179.9	44.9	194.5	59.5	214.2	79.2	228.8	93.8	243.9	108.9
	7690	132.8	147.8	15.0	168.0	35.2	184.1	51.3	206.0	73.2	214.7	81.9	229.7	96.9
	7691	131.4	145.7	14.3	167.8	36.4	180.2	48.8	202.2	70.8	213.7	82.3	228.1	96.7
	MEAN	126.6	142.4	15.8	163.7	37.1	179.0	52.3	200.1	73.5	212.7	86.0	228.1	101.5
	S.D.	5.8	6.8	1.7	8.5	3.8	9.2	4.8	9.5	5.2	10.0	6.4	9.5	5.6
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	7692	124.9	143.0	18.1	170.3	45.4	187.2	62.3	209.2	84.3	220.5	95.6	238.5	113.6
	7693	118.3	131.1	12.8	149.4	31.1	164.6	46.3	184.9	66.6	198.3	80.0	214.5	96.2
	7694	121.6	138.0	16.4	161.6	40.0	177.7	56.1	202.2	80.6	214.9	93.3	230.7	109.1
	7695	126.7	143.7	17.0	162.6	35.9	175.2	48.5	195.9	69.2	206.8	80.1	222.9	96.2
	7696	124.6	139.4	14.8	159.8	35.2	173.4	48.8	195.6	71.0	207.1	82.5	224.2	99.6
	7697	129.2	147.3	18.1	171.6	42.4	190.0	60.8	214.6	85.4	225.2	96.0	240.8	111.6
	7698	131.2	151.3	20.1	177.8	46.6	193.9	62.7	218.4	87.2	229.1	97.9	243.4	112.2
	7699	129.8	144.5	14.7	162.2	32.4	172.7	42.9	195.1	65.3	208.1	78.3	226.2	96.4
	7700	128.7	144.4	15.7	165.9	37.2	180.6	51.9	202.3	73.6	213.5	84.8	228.0	99.3
	7701	137.0	157.8	20.8	182.3	45.3	201.4	64.4	224.0	87.0	234.8	97.8	250.3	113.3
	MEAN	127.2	144.1	16.9	166.4	39.2	181.7	54.5	204.2	77.0	215.8	88.6	232.0	104.8
	S.D.	5.2	7.3	2.5	9.5	5.6	11.2	7.8	12.2	8.8	11.4	8.2	11.0	7.8
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
100	7702	117.8	132.8	15.0	145.2	27.4	155.6	37.8	176.4	58.6	190.3	72.5	202.8	85.0
	7703	126.4	139.6	13.2	152.6	26.2	164.4	38.0	182.3	55.9	191.2	64.8	206.4	80.0
	7704	125.0	138.5	13.5	147.1	22.1	158.9	33.9	180.1	55.1	193.5	68.5	206.9	81.9
	7705	128.1	145.0	16.9	156.7	28.6	169.9	41.8	190.4	62.3	203.5	75.4	216.0	87.9
	7706	125.0	139.5	14.5	153.4	28.4	163.5	38.5	182.7	57.7	192.8	67.8	209.9	84.9
	7707	126.4	142.1	15.7	150.6	24.2	161.5	35.1	181.3	54.9	194.3	67.9	213.2	86.8
	7708	127.1	137.6	10.5	153.8	26.7	162.9	35.8	185.6	58.5	195.3	68.2	210.4	83.3
	7709	131.2	143.9	12.7	161.0	29.8	168.8	37.6	192.8	61.6	201.4	70.2	218.5	87.3
	7710	132.7	149.5	16.8	161.0	28.3	172.8	40.1	191.9	59.2	203.9	71.2	215.7	83.0
	7711	132.3	144.8	12.5	158.6	26.3	171.6	39.3	188.6	56.3	201.5	69.2	218.7	86.4
	MEAN	127.2	141.3	14.1	154.0	26.8	165.0	37.8	185.2	58.0	196.8	69.6	211.9	84.7
	S.D.	4.4	4.7	2.0	5.4	2.3	5.7	2.4	5.5	2.6	5.2	2.9	5.4	2.6
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	81	187.2	191.8	4.6	187.2	0.0	184.5	-2.7	188.6	1.4	---	---	196.2	9.0
	82	166.5	158.7	-7.8	126.6	-39.9	124.1	-42.4#	136.1	-30.4	---	---	156.7	-9.8
	83	161.6	158.1	-3.5	133.6	-28.0	138.1	-23.5	143.2	-18.4	---	---	148.0	-13.6
	84	154.5	159.8	5.3	152.7	-1.8	150.1	-4.4	154.7	0.2	---	---	158.5	4.0
	85	169.4	171.3	1.9	162.7	-6.7	163.9	-5.5	166.3	-3.1	---	---	170.1	0.7
	86	171.7	177.5	5.8	151.3	-20.4	156.7	-15.0	162.1	-9.6	---	---	162.7	-9.0
	87	181.6	178.9	-2.7	167.2	-14.4	167.0	-14.6	169.5	-12.1	---	---	173.9	-7.7
	88	175.9	179.3	3.4	175.9	0.0	174.5	-1.4	177.0	1.1	---	---	175.6	-0.3
	89	174.3	176.3	2.0	166.4	-7.9	165.5	-8.8	172.9	-1.4	---	---	176.5	2.2
	90	153.5	154.7	1.2	148.4	-5.1	151.2	-2.3	156.1	2.6	---	---	157.1	3.6
	MEAN	169.6	170.6	1.0	157.2	-12.4	157.6	-12.1	162.7	-7.0	===	===	167.5	-2.1
	S.D.	11.0	12.2	4.4	18.5	13.3	17.6	12.8	15.8	10.7	===	===	13.9	7.4
	N=	10	10	10	10	10	10	10	10	10	0	0	10	10

STATISTICAL OUTLIERS INCLUDED
--- NO DATA
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
1000	7712	115.7	92.0	-23.7	***	***	***	***	***	***	***	***	***	***
	7713	125.4	100.5	-24.9	***	***	***	***	***	***	***	***	***	***
	7714	118.8	96.2	-22.6	***	***	***	***	***	***	***	***	***	***
	7715	121.3	99.5	-21.8	***	***	***	***	***	***	***	***	***	***
	7716	127.0	102.4	-24.6	***	***	***	***	***	***	***	***	***	***
	7717	130.1	104.8	-25.3	***	***	***	***	***	***	***	***	***	***
	7718	130.2	101.1	-29.1	***	***	***	***	***	***	***	***	***	***
	7719	128.4	97.4	-31.0	***	***	***	***	***	***	***	***	***	***
	7720	135.9	102.1	-33.8	***	***	***	***	***	***	***	***	***	***
	7721	141.7	108.4	-33.3	***	***	***	***	***	***	***	***	***	***
	MEAN	127.5	100.4	-27.0	===	===	===	===	===	===	===	===	===	===
	S.D.	7.8	4.6	4.4	===	===	===	===	===	===	===	===	===	===
	N=	10	10	10	0	0	0	0	0	0	0	0	0	0

*** DEAD ANIMAL
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
0	7682	118.3	226.0	107.7
	7683	121.0	247.4	126.4
	7684	119.5	234.6	115.1
	7685	123.9	242.2	118.3
	7686	126.4	251.8	125.4
	7687	128.5	259.1	130.6
	7688	129.6	252.3	122.7
	7689	135.0	264.1	129.1
	7690	132.8	244.3	111.5
	7691	131.4	254.3	122.9
	MEAN	126.6	247.6	121.0
	S.D.	5.8	11.4	7.6
	N=	10	10	10
10	7692	124.9	259.4	134.5
	7693	118.3	236.8	118.5
	7694	121.6	248.6	127.0
	7695	126.7	249.1	122.4
	7696	124.6	242.4	117.8
	7697	129.2	265.6	136.4
	7698	131.2	266.6	135.4
	7699	129.8	248.7	118.9
	7700	128.7	250.5	121.8
	7701	137.0	275.2	138.2
	MEAN	127.2	254.3	127.1
	S.D.	5.2	12.0	8.2
	N=	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males (continued)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
100	7702	117.8	226.0	108.2
	7703	126.4	226.7	100.3
	7704	125.0	231.1	106.1
	7705	128.1	237.9	109.8
	7706	125.0	231.6	106.6
	7707	126.4	230.4	104.0
	7708	127.1	236.2	109.1
	7709	131.2	241.4	110.2
	7710	132.7	236.1	103.4
	7711	132.3	240.4	108.1
	MEAN	127.2	233.8	106.6
	S.D.	4.4	5.4	3.2
	N=	10	10	10
200	81	187.2	207.3	20.1
	82	166.5	176.0	9.5
	83	161.6	158.7	-2.9
	84	154.5	166.8	12.3
	85	169.4	178.2	8.8
	86	171.7	176.4	4.7
	87	181.6	192.5	10.9
	88	175.9	187.4	11.5
	89	174.3	186.4	12.1
	90	153.5	173.6	20.1
	MEAN	169.6	180.3	10.7
	S.D.	11.0	13.7	6.7
	N=	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 17. Body Weight/Body Weight Gains (G) – Males (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
1000	7712	115.7	***	***
	7713	125.4	***	***
	7714	118.8	***	***
	7715	121.3	***	***
	7716	127.0	***	***
	7717	130.1	***	***
	7718	130.2	***	***
	7719	128.4	***	***
	7720	135.9	***	***
	7721	141.7	***	***
	MEAN	127.5	===	===
	S.D.	7.8	===	===
	N=	10	0	0

*** DEAD ANIMAL
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
0	7722	101.8	110.3	8.5	122.3	20.5	128.1	26.3	137.1	35.3	139.6	37.8	144.5	42.7
	7723	100.1	108.6	8.5	120.6	20.5	126.0	25.9	136.2	36.1	140.1	40.0	150.6	50.5
	7724	101.3	109.8	8.5	118.6	17.3	122.7	21.4	130.3	29.0	132.7	31.4	137.3	36.0
	7725	100.0	106.7	6.7	115.9	15.9	122.0	22.0	127.8	27.8	131.3	31.3	135.9	35.9
	7726	102.2	114.8	12.6	125.0	22.8	130.8	28.6	139.4	37.2	145.6	43.4	151.6	49.4
	7727	106.1	114.6	8.5	123.5	17.4	129.7	23.6	138.0	31.9	142.2	36.1	147.6	41.5
	7728	106.4	116.1	9.7	124.6	18.2	131.9	25.5	137.9	31.5	142.0	35.6	148.1	41.7
	7729	107.8	115.2	7.4	126.0	18.2	129.6	21.8	136.8	29.0	139.1	31.3	144.3	36.5
	7730	110.1	119.3	9.2	131.4	21.3	141.3	31.2	152.2	42.1	153.3	43.2	161.3	51.2
	7731	111.9	119.0	7.1	130.5	18.6	137.9	26.0	147.0	35.1	150.7	38.8	156.5	44.6
	MEAN	104.8	113.4	8.7	123.8	19.1	130.0	25.2	138.3	33.5	141.7	36.9	147.8	43.0
	S.D.	4.3	4.4	1.7	4.8	2.1	6.1	3.1	7.1	4.5	6.9	4.6	7.9	5.9
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	7732	99.2	108.2	9.0	118.2	19.0	124.0	24.8	132.9	33.7	135.1	35.9	138.9	39.7
	7733	99.5	108.2	8.7	115.1	15.6	122.1	22.6	129.2	29.7	130.6	31.1	134.7	35.2
	7734	103.4	111.3	7.9	120.8	17.4	126.9	23.5	133.1	29.7	133.9	30.5	138.1	34.7
	7735	104.4	113.7	9.3	122.6	18.2	128.9	24.5	135.3	30.9	136.5	32.1	141.1	36.7
	7736	101.4	110.9	9.5	119.9	18.5	126.3	24.9	132.7	31.3	137.0	35.6	140.9	39.5
	7737	106.8	115.6	8.8	122.6	15.8	128.6	21.8	137.4	30.6	135.3	28.5	142.7	35.9
	7738	107.2	114.3	7.1	125.3	18.1	131.7	24.5	138.9	31.7	145.0	37.8	148.2	41.0
	7739	110.2	117.7	7.5	131.3	21.1	138.5	28.3	146.0	35.8	147.5	37.3	156.2	46.0
	7740	111.8	118.0	6.2	130.7	18.9	138.0	26.2	142.4	30.6	146.4	34.6	155.0	43.2
	7741	104.8	112.6	7.8	123.9	19.1	130.4	25.6	138.0	33.2	141.2	36.4	145.4	40.6
	MEAN	104.9	113.1	8.2	123.0	18.2	129.5	24.7	136.6	31.7	138.9	34.0	144.1	39.3
	S.D.	4.2	3.5	1.1	5.1	1.6	5.4	1.8	5.0	2.0	5.8	3.2	7.1	3.7
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females (continued)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
100	7742	100.2	105.7	5.5	112.2	12.0	115.5	15.3	121.9	21.7	124.3	24.1	129.5#	29.3
	7743	100.0	107.9	7.9	116.4	16.4	119.9	19.9	132.2	32.2	133.0	33.0	142.0	42.0
	7744	104.9	111.6	6.7	118.0	13.1	124.9	20.0	133.2	28.3	133.7	28.8	139.0	34.1
	7745	106.9	113.7	6.8	122.3	15.4	124.7	17.8	132.7	25.8	131.9	25.0	142.1	35.2
	7746	104.5	109.4	4.9	115.7	11.2	121.1	16.6	126.8	22.3	128.9	24.4	141.3	36.8
	7747	101.0	109.0	8.0	114.4	13.4	120.9	19.9	129.2	28.2	127.8	26.8	140.9	39.9
	7748	108.7	116.8	8.1	121.0	12.3	126.4	17.7	133.7	25.0	134.9	26.2	143.5	34.8
	7749	107.5	115.4	7.9	121.1	13.6	126.0	18.5	133.7	26.2	137.8	30.3	143.7	36.2
	7750	108.8	114.7	5.9	120.5	11.7	123.6	14.8	128.9	20.1	130.8	22.0	141.5	32.7
	7751	108.7	115.4	6.7	121.0	12.3	123.5	14.8	134.2	25.5	135.3	26.6	143.5	34.8
	MEAN	105.1	112.0	6.8	118.3	13.1	122.7	17.5	130.7	25.5	131.8	26.7	140.7	35.6
	S.D.	3.6	3.8	1.1	3.4	1.7	3.3	2.1	4.0	3.6	4.0	3.2	4.2	3.5
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	91	115.0	115.5	0.5	116.8	1.8	113.4	-1.6	115.6	0.6	---	---	117.3	2.3
	92	113.6	114.3	0.7	112.3	-1.3	114.5	0.9	119.0	5.4	---	---	126.9	13.3
	93	113.6	117.6	4.0	119.7	6.1	117.1	3.5	121.6	8.0	---	---	129.6	16.0
	94	127.6	127.8	0.2	129.3	1.7	132.0	4.4	133.7	6.1	---	---	135.9	8.3
	95	110.7	112.0	1.3	109.7	-1.0	102.8	-7.9	109.0	-1.7	---	---	107.9	-2.8
	96	126.7	128.8	2.1	125.8	-0.9	125.5	-1.2	130.3	3.6	---	---	136.6	9.9
	97	109.6	112.7	3.1	114.6	5.0	114.9	5.3	116.5	6.9	---	---	121.9	12.3
	98	133.8	135.7	1.9	132.9	-0.9	135.3	1.5	139.7	5.9	---	---	146.8	13.0
	99	125.7	127.8	2.1	124.6	-1.1	125.4	-0.3	128.5	2.8	---	---	138.4	12.7
	MEAN	119.6	121.4	1.8	120.6	1.0	120.1	0.5	123.8	4.2	===	===	129.0	9.4
	S.D.	8.8	8.7	1.2	8.0	2.8	10.3	4.0	9.9	3.2	===	===	12.0	6.0
	N=	9	9	9	9	9	9	9	9	9	0	0	9	9

STATISTICAL OUTLIERS INCLUDED.
--- NO DATA
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females (continued)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1	4	GAIN	8	GAIN	11	GAIN	15	GAIN	18	GAIN	22	GAIN
1000	7752	102.1	88.4	-13.7	***	***	***	***	***	***	***	***	***	***
	7753	102.1	86.0	-16.1	***	***	***	***	***	***	***	***	***	***
	7754	102.6	86.7	-15.9	***	***	***	***	***	***	***	***	***	***
	7755	105.3	89.2	-16.1	***	***	***	***	***	***	***	***	***	***
	7756	104.2	87.7	-16.5	***	***	***	***	***	***	***	***	***	***
	7757	104.5	86.6	-17.9	***	***	***	***	***	***	***	***	***	***
	7758	106.4	89.1	-17.3	***	***	***	***	***	***	***	***	***	***
	7759	101.6	86.0	-15.6	***	***	***	***	***	***	***	***	***	***
	7760	107.1	91.1	-16.0	***	***	***	***	***	***	***	***	***	***
	7761	109.4	92.5	-16.9	***	***	***	***	***	***	***	***	***	***
	MEAN	104.5	88.3	-16.2	===	===	===	===	===	===	===	===	===	===
	S.D.	2.6	2.2	1.1	===	===	===	===	===	===	===	===	===	===
	N=	10	10	10	0	0	0	0	0	0	0	0	0	0

*** DEAD ANIMAL
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
0	7722	101.8	156.2	54.4
	7723	100.1	156.6	56.5
	7724	101.3	148.7	47.4
	7725	100.0	146.7	46.7
	7726	102.2	169.2	67.0
	7727	106.1	161.5	55.4
	7728	106.4	153.8	47.4
	7729	107.8	160.1	52.3
	7730	110.1	173.8	63.7
	7731	111.9	172.8	60.9
	MEAN	104.8	159.9	55.2
	S.D.	4.3	9.5	7.1
	N=	10	10	10
10	7732	99.2	148.6	49.4
	7733	99.5	147.8	48.3
	7734	103.4	150.6	47.2
	7735	104.4	153.9	49.5
	7736	101.4	151.8	50.4
	7737	106.8	154.2	47.4
	7738	107.2	155.5	48.3
	7739	110.2	165.8	55.6#
	7740	111.8	159.4	47.6
	7741	104.8	156.5	51.7
	MEAN	104.9	154.4	49.5
	S.D.	4.2	5.4	2.6
	N=	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
100	7742	100.2	140.0#	39.8
	7743	100.0	153.7	53.7
	7744	104.9	152.9	48.0
	7745	106.9	153.1	46.2
	7746	104.5	150.8	46.3
	7747	101.0	153.1	52.1
	7748	108.7	156.3	47.6
	7749	107.5	159.9	52.4
	7750	108.8	152.7	43.9
	7751	108.7	156.7	48.0
	MEAN	105.1	152.9	47.8
	S.D.	3.6	5.2	4.2
	N=	10	10	10
200	91	115.0	131.0	16.0
	92	113.6	127.2	13.6
	93	113.6	140.3	26.7
	94	127.6	148.8	21.2
	95	110.7	111.5	0.8
	96	126.7	142.2	15.5
	97	109.6	127.6	18.0
	98	133.8	159.2	25.4
	99	125.7	155.6	29.9
	MEAN	119.6	138.2	18.6
	S.D.	8.8	15.3	8.7
	N=	9	9	9

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 18. Body Weight/Body Weight Gains (G) – Females (continued)

DOSE (MKD)	ANIMAL NUMBER	DAYS ON TEST 1	29	GAIN
1000	7752	102.1	***	***
	7753	102.1	***	***
	7754	102.6	***	***
	7755	105.3	***	***
	7756	104.2	***	***
	7757	104.5	***	***
	7758	106.4	***	***
	7759	101.6	***	***
	7760	107.1	***	***
	7761	109.4	***	***
	MEAN	104.5	===	===
	S.D.	2.6	===	===
	N=	10	0	0

*** DEAD ANIMAL
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 19. Feed Consumption (G/Day) – Males (0, 10 and 100 mg/kg/day)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
0	7682	14.0	14.8	15.0	16.0	16.8	17.0	16.5
	7683	14.4	14.8	16.9	17.6	17.8	17.9	18.5
	7684	14.3	15.3	18.5@	15.2@	16.8	17.5	19.3
	7685	14.9	15.0	15.7	17.0	17.5	18.6	17.8
	7686	15.0	15.3	17.4	17.6	19.1	18.7	17.9
	7687	14.9	16.1	17.4	18.2	18.6	17.8	19.6
	7688	15.9	15.9	17.7	17.7	18.3	19.3	18.1
	7689	16.5	16.9	17.0	18.2	18.4	19.0	20.4
	7690	15.9	15.9	17.7	18.2	17.6	18.8	18.2
	7691	14.3	15.7	15.7	16.6	17.0	17.5	17.7
	MEAN	15.0	15.6	16.7	17.5	17.8	18.2	18.4
	S.D.	0.8	0.7	1.0	0.8	0.8	0.8	1.1
	N=	10	10	9	9	10	10	10
10	7692	15.2	17.3	17.5	18.1	18.1	19.0	18.4
	7693	13.5	13.4	15.0	15.8	16.6	16.6	16.6
	7694	14.4	15.0	16.7	17.5	17.8	18.3	18.2
	7695	15.3	15.2	16.1	16.5	16.2	17.4	18.0
	7696	14.2	14.4	15.5	16.4	16.4	17.5	17.3
	7697	15.5	16.8	18.6	19.4	18.8	19.3	19.3
	7698	16.1	16.8	17.9	19.6	18.9	19.2	19.3
	7699	14.9	15.0	14.6	16.9	16.9	17.6	17.5
	7700	15.5	15.7	16.9	17.6	16.4	17.8	18.4
	7701	16.9	16.8	18.7	18.9	18.6	19.0	18.6
	MEAN	15.2	15.6	16.8	17.7	17.5	18.2	18.2
	S.D.	1.0	1.3	1.4	1.3	1.1	0.9	0.9
	N=	10	10	10	10	10	10	10

@ VALUES EXCLUDED FROM ANALYSIS.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 19. Feed Consumption (G/Day) – Males (0, 10 and 100 mg/kg/day) (continued)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
100	7702	13.5	12.0	12.9	15.2	14.9	15.8	15.9
	7703	13.7	13.3	14.2	15.5	14.8	16.9	16.8
	7704	13.8	11.8	12.9	15.5	16.0	16.1	17.3
	7705	14.8	13.9	15.5	16.5	17.3	17.9	18.1
	7706	13.9	13.3	14.0	16.0	15.4	17.2	17.7
	7707	14.7	12.3	13.6	15.2	16.1	17.7	16.9
	7708	12.6	12.7	13.1	15.3	14.6	15.8	16.2
	7709	14.0	14.1	13.8	16.3	15.7	17.2	17.3
	7710	14.6	14.0	14.3	16.8	16.3	17.1	18.0
	7711	14.5	13.4	14.3	15.7	16.5	17.4	16.7
	MEAN	14.0	13.1	13.9	15.8	15.8	16.9	17.1
	S.D.	0.7	0.8	0.8	0.6	0.9	0.8	0.7
	N=	10	10	10	10	10	10	10
1000	7712	3.1	***	***	***	***	***	***
	7713	2.9	***	***	***	***	***	***
	7714	3.5	***	***	***	***	***	***
	7715	2.9	***	***	***	***	***	***
	7716	2.7	***	***	***	***	***	***
	7717	2.5	***	***	***	***	***	***
	7718	2.3	***	***	***	***	***	***
	7719	2.0	***	***	***	***	***	***
	7720	1.7	***	***	***	***	***	***
	7721	1.9	***	***	***	***	***	***
	MEAN	2.6	===	===	===	===	===	===
	S.D.	0.6	===	===	===	===	===	===
	N=	10	0	0	0	0	0	0

*** DEAD ANIMAL
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 20. Feed Consumption (G/Day) – Males (200 mg/kg/day)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-22	22-29
200	81	15.3	10.1	11.5	12.3	10.2	11.3
	82	9.2	2.8	5.8	10.4	10.1	11.0
	83	10.4	5.1	7.6	9.4	8.3	9.2
	84	11.8	8.7	8.2	10.4	8.7	9.0
	85	12.2	8.6	8.7	11.6	10.2	10.9
	86	13.4	6.3	8.7	10.6	9.0	10.6
	87	12.7	8.3	17.0@	10.0	9.2	11.0
	88	13.1	10.8	9.0	12.0	9.7	9.7
	89	11.9	9.4	8.6	12.2	9.8	10.6
	90	9.7	7.9	8.9	10.7	8.9	10.7
	MEAN	12.0	7.8	8.6	11.0	9.4	10.4
	S.D.	1.8	2.4	1.5	1.0	0.7	0.8
	N=	10	10	9	10	10	10

@ VALUES EXCLUDED FROM ANALYSIS.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 21. Feed Consumption (G/Day) – Females (0, 10, and 100 mg/kg/day)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
0	7722	11.7	12.6	12.5	12.4	11.7	13.1	11.9
	7723	11.8	11.5	12.5	13.2	13.1	13.8	11.7
	7724	11.6	11.6	11.8	11.5	11.4	11.9	11.8
	7725	11.3	11.5	12.3	12.5	11.2	11.4	11.4
	7726	11.8	12.3	12.7	13.0	12.5	13.2	12.9
	7727	11.9	12.1	12.8	12.9	12.2	13.3	12.5
	7728	13.0	13.3	14.0	12.9	13.4	12.7	11.9
	7729	11.2	12.0	12.0	12.1	11.8	12.3	12.2
	7730	12.7	12.6	13.2	14.1	13.3	13.8	13.2
	7731	12.7	13.7	13.8	14.2	13.3	13.7	13.8
	MEAN	12.0	12.3	12.8	12.9	12.4	12.9	12.3
	S.D.	0.6	0.7	0.7	0.8	0.8	0.8	0.8
	N=	10	10	10	10	10	10	10
10	7732	11.2	11.7	11.7	12.5	12.0	12.3	12.1
	7733	11.5	11.5	12.7	11.3	10.8	12.4	11.7
	7734	11.7	11.6	12.2	11.7	10.2	11.8	10.8
	7735	11.8	11.3	12.0	11.9	11.3	11.9	11.3
	7736	12.0	12.2	11.8	11.7	12.5	12.1	11.7
	7737	12.1	11.3	11.8	12.3	11.1	12.8	11.5
	7738	11.6	12.0	11.9	12.5	12.7	12.4	11.5
	7739	11.9	13.1	12.7	12.1	12.4	12.8	12.0
	7740	12.0	12.7	13.2	12.7	12.4	13.7	11.7
	7741	11.9	12.7	13.1	12.9	13.0	13.7	12.5
	MEAN	11.8	12.0	12.3	12.2	11.8	12.6	11.7
	S.D.	0.3	0.6	0.6	0.5	0.9	0.7	0.5
	N=	10	10	10	10	10	10	10

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 21. Feed Consumption (G/Day) – Females (0, 10, and 100 mg/kg/day) (continued)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	18-22	22-29
100	7742	10.7	10.1	10.0	11.2	10.9	11.9!	10.9
	7743	11.0	10.6	11.1	12.1	10.6	13.4	12.0
	7744	10.9	10.6	12.0	12.4	11.0	12.8	12.1
	7745	10.9	11.2	9.8	11.2	10.6	13.4	11.8
	7746	11.2	10.0	11.6	11.9	10.8	13.4	12.0
	7747	10.8	10.6	10.2	11.6	10.2	13.1	11.7
	7748	11.4	10.8	11.1	12.1	10.7	13.2	12.2
	7749	11.5	10.6	11.0	11.9	11.5	12.9	12.3
	7750	11.1	10.6	10.5	11.0	10.2	12.9	12.9
	7751	11.1	10.8	11.1	12.8	10.8	13.2	12.3
	MEAN	11.1	10.6	10.8	11.8	10.7	13.1	12.0
	S.D.	0.3	0.3	0.7	0.6	0.4	0.2	0.5
	N=	10	10	10	10	10	9	10
1000	7752	3.0	***	***	***	***	***	***
	7753	2.7	***	***	***	***	***	***
	7754	2.1	***	***	***	***	***	***
	7755	2.4	***	***	***	***	***	***
	7756	2.2	***	***	***	***	***	***
	7757	2.9	***	***	***	***	***	***
	7758	2.0	***	***	***	***	***	***
	7759	2.0	***	***	***	***	***	***
	7760	2.6	***	***	***	***	***	***
	7761	2.7	***	***	***	***	***	***
	MEAN	2.5	===	===	===	===	===	===
	S.D.	0.4	===	===	===	===	===	===
	N=	10	0	0	0	0	0	0

*** DEAD ANIMAL
! STATISTICAL OUTLIERS EXCLUDED.
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 22. Feed Consumption (G/Day) – Females (200 mg/kg/day)

DOSE MKD	ANIMAL NUMBER	DAYS ON TEST 1-4	4-8	8-11	11-15	15-18	15-22	18-22	22-29
200	91	9.3	8.7	6.1	8.2	---	7.3	---	9.0
	92	8.8	8.0	7.7	8.8	---	8.6	---	8.0
	93	10.4	8.8	6.6	9.3	---	9.3	---	9.6
	94	9.2	9.3	8.1	9.8	---	8.9	---	9.5
	95	8.5	6.8	5.7	9.1	---	7.0	---	7.5
	96	9.6	8.6	7.4	9.8	---	9.1	---	9.7
	97	9.3	8.5	7.2	8.3	---	8.2	---	8.3
	98	10.4	8.4	8.8	9.9	---	9.5	---	10.0
	99	9.9	8.1	7.6	9.2	---	9.4	---	10.0
	MEAN	9.5	8.4	7.2	9.2	===	8.6	===	9.1
	S.D.	0.7	0.7	1.0	0.6	===	0.9	===	0.9
	N=	9	9	9	9	0	9	0	9

--- NO DATA
=== NO DATA AVAILABLE FOR MEAN AND S.D.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 23. Prothrombin Time – Males

DOSE MKD	ANIMAL NUMBER	PT SECONDS
0	7682	11.6
	7683	11.1
	7684	12.2
	7685	11.6
	7686	11.8
	7687	11.5
	7688	11.8
	7689	11.0
	7690	12.3
	7691	12.2
	MEAN	11.7
	S.D.	0.4
	N=	10
10	7692	11.1
	7693	11.6
	7694	12.0
	7695	11.4
	7696	10.9
	7697	11.6
	7698	13.7
	7699	12.1
	7700	12.4
	7701	11.7
	MEAN	11.9
	S.D.	0.8
	N=	10

PT=PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 23. Prothrombin Time – Males (continued)

DOSE MKD	ANIMAL NUMBER	PT SECONDS
100	7702	11.8
	7703	11.6
	7704	11.6
	7705	11.5
	7706	11.2
	7707	12.2
	7708	11.9
	7709	12.4
	7710	12.9
	7711	11.8
	MEAN	11.9
	S.D.	0.5
	N=	10
200	81	12.1
	82	12.7
	83	12.9
	84	12.6
	85	12.5
	86	12.5
	87	12.6
	88	12.5
	89	12.8
	90	13.6
	MEAN	12.7
	S.D.	0.4
	N=	10

PT=PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 24. Prothrombin Time – Females

DOSE MKD	ANIMAL NUMBER	PT SECONDS
0	7722	11.3
	7723	12.1
	7724	12.0
	7725	11.6
	7726	12.7
	7727	11.1
	7728	11.7
	7729	11.7
	7730	11.7
	7731	11.8
	MEAN	11.8
	S.D.	0.4
	N=	10
10	7732	12.2
	7733	11.3
	7734	12.2
	7735	12.2
	7736	12.0
	7737	11.5
	7738	11.6
	7739	11.8
	7740	12.2
	7741	12.7
	MEAN	12.0
	S.D.	0.4
	N=	10

PT=PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 24. Prothrombin Time – Females (continued)

DOSE MKD	ANIMAL NUMBER	PT SECONDS
100	7742	12.1
	7743	11.9
	7744	12.1
	7745	12.0
	7746	12.8
	7747	11.4
	7748	12.1
	7749	11.9
	7750	12.0
	7751	12.1
	MEAN	12.0
	S.D.	0.3
	N=	10
200	91	12.0
	92	12.7
	93	12.6
	94	13.3
	95	13.1
	96	12.5
	97	12.4
	98	12.3
	99	13.0
	MEAN	12.7
	S.D.	0.4
	N=	9

PT=PROTHROMBIN TIME

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 25. Hematology – Males

DOSE MKD	ANIMAL NUMBER	WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
0	7682	9.17	8.36	15.3	44.7	53.5	18.3	34.3	831
	7683	8.70	8.14	15.1	44.0	54.0	18.6	34.4	789
	7684	9.14	8.10	15.1	43.5	53.7	18.6	34.7	722
	7685	7.25	8.22	15.3	43.7	53.2	18.7	35.1	704
	7686	9.42	8.14	15.1	43.7	53.7	18.6	34.6	775
	7687	10.68	8.38	15.6	44.9	53.6	18.7	34.8	812
	7688	9.82	8.17	15.2	43.9	53.8	18.6	34.6	770
	7689	11.54	8.77	16.1#	46.8#	53.4	18.3	34.3	750
	7690	10.69	8.50	15.6	44.7	52.6	18.4	34.9	741
	7691	10.44	8.18	15.2	43.2	52.8	18.6	35.2	764
	MEAN	9.69	8.30	15.4	44.3	53.4	18.5	34.7	766
	S.D.	1.23	0.21	0.3	1.0	0.4	0.2	0.3	39
	N=	10	10	10	10	10	10	10	10
10	7692	9.55	8.02	15.2	43.5	54.2	19.0	35.0	738
	7693	6.57#	7.91	15.0	42.5	53.8	18.9	35.2	780
	7694	8.97	7.97	15.1	42.4	53.2	19.0	35.7	769
	7695	9.18	7.90	14.6	42.6	53.9	18.5	34.3	794
	7696	9.59	7.88	14.9	42.1	53.5	18.9	35.3	776
	7697	10.12	8.21	15.5	43.8	53.4	18.8	35.3	751
	7698	11.01	8.31	15.5	44.7	53.8	18.6	34.6	731
	7699	9.60	8.03	14.9	42.3	52.7	18.5	35.2	792
	7700	9.94	8.18	15.1	43.3	52.9	18.5	34.9	780
	7701	10.75	8.26	15.1	43.4	52.6	18.3	34.7	697
	MEAN	9.53	8.07	15.1	43.1	53.4	18.7	35.0	761
	S.D.	1.22	0.16	0.3	0.8	0.5	0.2	0.4	31
	N=	10	10	10	10	10	10	10	10

# STATISTICAL OUTLIERS INCLUDED.
WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 25. Hematology – Males (continued)

DOSE MKD	ANIMAL NUMBER	WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
100	7702	8.96	7.93	15.3	43.4	54.7	19.3	35.2	808
	7703	11.32	8.09	15.2	43.3	53.5	18.8	35.2	745
	7704	9.63	7.93	15.0	42.7	53.8	18.9	35.1	771
	7705	9.33	8.19	15.5	43.6	53.2	18.9	35.4	762
	7706	7.65	8.16	15.2	43.5	53.3	18.6	34.9	757
	7707	7.25	8.05	15.0	43.1	53.5	18.7	34.9	781
	7708	9.76	8.19	15.4	44.4	54.2	18.8	34.7	824
	7709	10.55	8.20	15.2	43.3	52.8	18.6	35.2	788
	7710	9.85	8.44	15.6	45.0	53.3	18.5	34.7	748
	7711	11.95	8.22	15.4	44.2	53.7	18.8	34.9	728
	MEAN	9.63	8.14	15.3	43.7	53.6	18.8	35.0	771
	S.D.	1.46	0.15	0.2	0.7	0.5	0.2	0.2	30
	N=	10	10	10	10	10	10	10	10
200	81	12.57	8.75	15.5	44.1	50.4	17.8	35.2	800
	82	7.97	7.70	13.9	40.0	51.9	18.1	34.9	862
	83	13.05	8.38	15.1	42.4	50.6	18.0	35.5	822
	84	8.59	8.41	15.3	42.8	50.9	18.1	35.6	782
	85	9.98	8.84	16.0	45.0	50.9	18.0	35.5	823
	86	6.80	8.40	14.9	42.8	50.9	17.7	34.8	812
	87	7.26	8.23	15.0	41.9	50.8	18.2	35.9	837
	88	10.53	8.56	15.2	42.9	50.1	17.8	35.5	674
	89	7.35	8.59	15.4	44.0	51.2	17.9	35.0	776
	90	7.99	8.33	14.8	41.9	50.3	17.8	35.4	661
	MEAN	9.21	8.42	15.1	42.8	50.8	17.9	35.3	785
	S.D.	2.23	0.32	0.5	1.4	0.5	0.2	0.3	67
	N=	10	10	10	10	10	10	10	10

WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 26. Hematology – Females

DOSE MKD	ANIMAL NUMBER	WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
0	7722	4.93	7.75	15.0	40.8	52.7	19.4	36.8	784
	7723	3.16	7.97	15.1	42.1	52.9	18.9	35.8	814
	7724	5.96	7.92	14.9	41.6	52.5	18.8	35.8	821
	7725	7.58	8.03	15.2	42.1	52.5	19.0	36.1	756
	7726	5.41	7.86	15.0	41.1	52.3	19.1	36.5	748
	7727	5.50	7.89	15.2	42.4	53.7	19.2	35.7	801
	7728	5.88	7.99	14.9	42.5	53.1	18.6	35.1	715
	7729	9.50	7.54	14.4	40.3	53.4	19.1	35.8	739
	7730	8.23	7.47	14.4	40.2	53.8	19.3	35.9	757
	7731	8.28	7.85	15.1	40.9	52.1	19.3	36.9	781
	MEAN	6.44	7.83	14.9	41.4	52.9	19.1	36.0	772
	S.D.	1.91	0.19	0.3	0.9	0.6	0.2	0.6	34
	N=	10	10	10	10	10	10	10	10
10	7732	6.27	7.91	15.3	41.5	52.4	19.3	36.8	738
	7733	6.07	7.94	15.0	41.5	52.3	18.9	36.1	738
	7734	9.10	7.49	14.3	39.3	52.5	19.1	36.4	743
	7735	6.62	7.72	14.7	39.8	51.6	19.1	36.9	780
	7736	10.10	8.02	15.1	41.9	52.3	18.8	36.0	824
	7737	6.83	7.70	14.6	39.9	51.8	19.0	36.7	910
	7738	7.10	8.05	15.1	42.8	53.2	18.7	35.2	776
	7739	5.68	7.55	14.5	40.1	53.1	19.2	36.1	797
	7740	6.48	7.83	14.9	41.4	52.8	19.0	36.0	712
	7741	10.37	8.34	15.7	43.5	52.2	18.8	36.1	703
	MEAN	7.46	7.86	14.9	41.2	52.4	19.0	36.2	772
	S.D.	1.73	0.25	0.4	1.4	0.5	0.2	0.5	61
	N=	10	10	10	10	10	10	10	10

WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 26. Hematology – Females (continued)

DOSE MKD	ANIMAL NUMBER	WBC E3/UL	RBC E6/UL	HGB G/DL	HCT PCNT	MCV FL	MCH PG	MCHC G/DL	PLT E3/UL
100	7742	6.97	7.73	14.8	40.9	52.9	19.2	36.2	807
	7743	7.76	7.67	14.6	40.5	52.8	19.0	36.0	799
	7744	8.16	7.57	14.7	40.0	52.9	19.4	36.7	836
	7745	6.87	7.70	14.7	40.7	52.9	19.1	36.2	857
	7746	6.12	7.61	14.5	39.8	52.2	19.0	36.4	719
	7747	6.60	7.58	14.8	39.7	52.4	19.5	37.2	849
	7748	7.01	7.94	15.0	42.0	52.9	18.9	35.8	851
	7749	6.04	7.52	14.4	40.3	53.6	19.1	35.7	804
	7750	9.64	7.75	14.7	41.0	52.9	19.0	36.0	751
	7751	6.42	7.64	14.4	40.3	52.8	18.8	35.6	840
	MEAN	7.16	7.67	14.7	40.5	52.8	19.1	36.2	811
	S.D.	1.10	0.12	0.2	0.7	0.4	0.2	0.5	46
	N=	10	10	10	10	10	10	10	10
200	91	10.80	7.63	14.3	38.5	50.4	18.8	37.2	725
	92	8.65	7.91	14.5	40.0	50.6	18.3	36.3	714
	93	12.07	7.93	14.8	41.2	52.0	18.7	36.0	797
	94	8.77	7.65	14.1	39.0	51.0	18.4	36.0	804
	95	8.92	8.53	15.2	42.6	49.9	17.9	35.8	611
	96	12.47	8.01	14.7	40.3	50.4	18.3	36.4	708
	97	5.23	8.13	14.9	41.8	51.4	18.3	35.5	779
	98	6.36	7.60	14.1	38.5	50.6	18.5	36.5	792
	99	9.86	7.58	13.9	39.1	51.6	18.4	35.6	766
	MEAN	9.24	7.89	14.5	40.1	50.9	18.4	36.1	744
	S.D.	2.41	0.31	0.4	1.5	0.7	0.3	0.5	62
	N=	9	9	9	9	9	9	9	9

WBC=TOTAL LEUKOCYTE COUNT, RBC=ERYTHROCYTE COUNT, HGB=HEMOGLOBIN CONCENTRATION, HCT=HEMATOCRIT, MCV=MEAN CORPUSCULAR VOLUME, MCH=MEAN CORPUSCULAR HEMOGLOBIN, MCHC=MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION, PLT=PLATELET COUNT

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 27. Differential WBC – Males

DOSE MKD	ANIMAL NUMBER	NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
0	7682	18.7	74.4	2.3	1.2	0.8	2.6
	7683	17.2	78.2	2.0	0.7	0.5	1.4
	7684	19.0	75.8	1.6	0.9	0.8	1.8
	7685	17.3	77.5	2.5	0.4	0.3	2.0
	7686	21.0	73.1	2.1	0.5	0.6	2.6
	7687	20.3	74.0	2.0	0.7	0.6	2.3
	7688	21.9	73.9	1.6	0.4	0.6	1.7
	7689	15.1	78.2	2.6	1.0	0.5	2.6
	7690	16.9	78.1	1.9	0.8	0.6	1.8
	7691	21.4	72.0	2.3	0.6	0.9	2.8
	MEAN	18.9	75.5	2.1	0.7	0.6	2.2
	S.D.	2.2	2.3	0.3	0.3	0.2	0.5
	N=	10	10	10	10	10	10
10	7692	18.1	76.7	2.2	0.6	0.6	1.9
	7693	15.0	81.1	1.7	0.5	0.5	1.3
	7694	18.1	76.4	2.4	1.0#	0.4	1.7
	7695	17.3	78.1	1.7	0.5	0.6	1.8
	7696	20.8	74.1	2.4	0.7	0.4	1.6
	7697	19.7	74.7	2.3	0.6	0.7	2.0
	7698	18.8	75.5	2.2	0.5	0.6	2.4
	7699	17.6	78.4	1.9	0.6	0.3	1.2
	7700	15.7	80.5	1.4	0.5	0.5	1.5
	7701	14.3	80.2	2.3	0.4	0.6	2.2
	MEAN	17.5	77.6	2.1	0.6	0.5	1.8
	S.D.	2.1	2.5	0.4	0.2	0.1	0.4
	N=	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED
@ WBC DIFFERENTIAL NOT STATISTICALLY COMPARED
NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE, ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS
AUTOMATIC DIFFERENTIAL COUNTING

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 27. Differential WBC – Males (continued)

DOSE MKD	ANIMAL NUMBER	NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
100	7702	15.8	80.6	1.8	0.5	0.3	1.1
	7703	19.1	76.0	1.9	0.6	0.6	1.8
	7704	16.7	79.6	1.4	0.5	0.5	1.4
	7705	24.9	69.7	2.3	1.1	0.4	1.6
	7706	17.1	77.8	2.0	0.6	0.9	1.7
	7707	15.2	80.5	1.8	0.7	0.5	1.3
	7708	20.3	75.5	1.7	0.4	0.7	1.5
	7709	17.7	77.8	1.9	0.6	0.4	1.7
	7710	14.4	82.2	1.5	0.2	0.4	1.3
	7711	15.1	81.2	1.4	0.4	0.6	1.3
	MEAN	17.6	78.1	1.8	0.6	0.5	1.5
	S.D.	3.2	3.7	0.3	0.2	0.2	0.2
	N=	10	10	10	10	10	10
200	81	20.0	75.0	1.9	0.9	0.4	1.9
	82	20.3	76.2	1.8	0.4	0.3	1.0
	83	32.9	60.4	2.5	1.1	0.9#	2.1
	84	27.6	68.0	1.8	1.0	0.4	1.2
	85	25.7	69.6	2.0	1.0	0.4	1.3
	86	25.7	71.1	1.4	0.6	0.2	0.9
	87	20.5	75.4	1.9	0.8	0.2	1.2
	88	34.0	61.7	1.9	0.8	0.4	1.1
	89	29.7	66.6	1.7	1.0	0.3	0.6
	90	34.3	61.4	2.3	1.0	0.1	0.9
	MEAN	27.1	68.5	1.9	0.9	0.4	1.2
	S.D.	5.6	6.0	0.3	0.2	0.2	0.5
	N=	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED
@ WBC DIFFERENTIAL NOT STATISTICALLY COMPARED
NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE, ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS
AUTOMATIC DIFFERENTIAL COUNTING

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 28. Differential WBC – Females

DOSE MKD	ANIMAL NUMBER	NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
0	7722	15.4	79.5	1.6	1.8	0.4	1.3
	7723	24.2	70.4	2.6	1.3	0.1	1.4
	7724	28.3	67.6	1.7	1.1	0.2	1.2
	7725	13.7	81.8	2.2	0.9	0.2	1.1
	7726	21.0	73.3	2.3	1.6	0.2	1.6
	7727	22.6	73.6	1.5	1.2	0.2	0.8
	7728	18.0	77.0	2.4	1.4	0.3	0.9
	7729	13.0	82.8	1.7	0.7	0.6	1.2
	7730	16.3	78.4	2.3	0.5	0.9#	1.6
	7731	14.4	80.8	2.1	1.3	0.2	1.3
	MEAN	18.7	76.5	2.0	1.2	0.3	1.2
	S.D.	5.1	5.1	0.4	0.4	0.2	0.3
	N=	10	10	10	10	10	10
10	7732	20.6	74.1	2.3	1.3	0.2	1.4
	7733	16.2	78.8	1.4	1.2	0.9	1.6
	7734	15.8	80.2	1.7	1.0	0.3	1.0
	7735	22.7	73.5	1.5	0.9	0.3	1.1
	7736	19.1	75.4	2.6	0.7	0.4	1.9
	7737	17.2	78.6	2.1	0.8	0.3	1.0
	7738	16.5	79.8	1.5	1.1	0.4	0.8
	7739	12.2	84.4	1.9	0.5	0.2	0.8
	7740	18.8	75.2	2.6	1.2	0.7	1.5
	7741	18.2	75.7	2.4	1.7	0.5	1.5
	MEAN	17.7	77.6	2.0	1.0	0.4	1.3
	S.D.	2.9	3.4	0.5	0.3	0.2	0.4
	N=	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED
@ WBC DIFFERENTIAL NOT STATISTICALLY COMPARED
NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE, ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS
AUTOMATIC DIFFERENTIAL COUNTING

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 28. Differential WBC – Females (continued)

DOSE MKD	ANIMAL NUMBER	NEUT PCNT	LYMP PCNT	MONO PCNT	EOS PCNT	BASO PCNT	LUC PCNT
100	7742	17.4	78.2	2.0	0.9	0.2	1.2
	7743	26.1#	69.7	1.3	0.6	0.5	1.9
	7744	15.8	80.3	1.3	1.1	0.3	1.1
	7745	18.9	77.0	1.3	0.8	0.5	1.6
	7746	16.2	79.1	1.8	1.0	0.3	1.5
	7747	15.8	80.0	1.5	1.2	0.3	1.2
	7748	13.8	82.8	1.4	0.9	0.3	0.7
	7749	14.4	82.0	1.3	0.9	0.3	1.0
	7750	15.3	79.8	1.5	0.9	0.8	1.7
	7751	21.0	74.4	1.5	1.0	0.5	1.5
	MEAN	17.5	78.3	1.5	0.9	0.4	1.3
	S.D.	3.7	3.9	0.2	0.2	0.2	0.4
	N=	10	10	10	10	10	10
200	91	18.6	76.5	1.9	1.5	0.2	1.3
	92	16.1	80.3	1.5	0.8	0.2	1.0
	93	25.4	69.9	1.9	1.0	0.4	1.4
	94	22.3	74.2	1.4	1.0	0.3	0.8
	95	15.1	81.1	1.5	0.8	0.3	1.2
	96	16.2	79.7	1.5	1.1	0.4	1.1
	97	17.4	79.7	1.0	0.6	0.4	1.0
	98	12.8	84.3	1.3	0.5	0.2	0.8
	99	18.2	78.6	1.1	0.7	0.4	1.0
	MEAN	18.0	78.3	1.5	0.9	0.3	1.1
	S.D.	3.8	4.2	0.3	0.3	0.1	0.2
	N=	9	9	9	9	9	9

STATISTICAL OUTLIERS INCLUDED
@ WBC DIFFERENTIAL NOT STATISTICALLY COMPARED
NEUT=NEUTROPHILS, LYMP=LYMPHOCYTES, MONO=MONOCYTES, EOS=EOSINOPHILS, BASO=BASOPHILS, LUC=LARGE UNSTAINED CELLS WHICH INCLUDE, ATYPICAL LYMPHOCYTES, LARGE LYMPHOCYTES, PLASMA CELLS AND BLASTS
AUTOMATIC DIFFERENTIAL COUNTING

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 29. Clinical Chemistry – Males

DOSE MKD	ANIMAL NUMBER	UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
0	7682	16	48	202	96	86	6.5	3.5	45	0.1	0.4
	7683	14	47	207	100	118	6.3	3.3	35	0.1	0.3
	7684	14	50	205	95	97	6.3	3.4	38	0.1	0.4
	7685	14	41	211	89	109	6.2	3.3	43	0.1	0.4
	7686	15	41	206	86	105	6.2	3.3	38	0.1	0.4
	7687	16	45	187	98	127	6.5	3.4	46	0.1	0.3
	7688	15	42	202	77	114	6.2	3.3	38	0.1	0.3
	7689	19	48	178	96	134	6.4	3.4	41	0.1	0.4
	7690	14	36	173	85	103	6.0	3.3	38	0.1	0.3
	7691	13	42	189	83	98	6.4	3.3	35	0.1	0.3
	MEAN	15	44	196	91	109	6.3	3.4	40	0.1	0.4
	S.D.	2	4	13	8	15	0.2	0.1	4	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
10	7692	14	43	188	101	98	6.3	3.3	39	0.1	0.3
	7693	16	38	203	96	99	6.2	3.3	41	0.1	0.3
	7694	14	40	179	85	102	6.3	3.3	42	0.1	0.2
	7695	15	37	205	79	113	6.2	3.3	41	0.1	0.4
	7696	15	36	182	82	96	6.0	3.2	41	0.1	0.3
	7697	14	42	209	85	117	6.3	3.3	40	0.1	0.3
	7698	15	49	185	86	122	6.4	3.4	36	0.1	0.4
	7699	14	35	180	84	121	5.8	3.1	37	0.1	0.3
	7700	16	36	186	72	117	6.1	3.3	38	0.1	0.3
	7701	12	40	187	77	128	6.3	3.3	37	0.1	0.3
	MEAN	15	40	190	85	111	6.2	3.3	39	0.1	0.3
	S.D.	1	4	11	9	12	0.2	0.1	2	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10

UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 29. Clinical Chemistry – Males (continued)

DOSE MKD	ANIMAL NUMBER	UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
100	7702	16	38	197	84	99	6.4	3.4	42	0.1	0.4#
	7703	14	47	178	89	85	6.2	3.4	41	0.1	0.3
	7704	14	43	181	93	111	6.2	3.3	45	0.1	0.3
	7705	16	37	175	78	108	6.2	3.3	43	0.1	0.3
	7706	15	41	185	84	115	6.2	3.3	41	0.1	0.3
	7707	15	44	159	88	121	5.9	3.3	42	0.1	0.3
	7708	14	39	167	75	103	6.3	3.4	44	0.1	0.3
	7709	14	36	171	75	97	6.1	3.3	46	0.1	0.3
	7710	16	34	174	70	114	6.1	3.3	38	0.1	0.3
	7711	16	36	167	70	109	6.2	3.3	49	0.1	0.3
	MEAN	15	40	175	81	106	6.2	3.3	43	0.1	0.3
	S.D.	1	4	11	8	10	0.1	0.0	3	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10
200	81	16	64	112	102	78	6.8	3.5	69	0.1	0.3
	82	13	37	127	83	74	6.0	3.2	66	0.1	0.3
	83	15	42	105	83	77	5.9	3.1	85	0.1	0.3
	84	15	36	106	75	80	6.2	3.3	77	0.1	0.3
	85	17	35	113	89	125#	6.1	3.2	78	0.1	0.3
	86	15	38	101	84	73	6.0	3.1	83	0.1	0.2#
	87	15	36	107	80	91	6.1	3.2	71	0.1	0.3
	88	16	66	113	125#	104	6.3	3.3	66	0.1	0.3
	89	14	53	106	89	85	6.4	3.4	72	0.1	0.3
	90	15	141#	123	195#	71	6.2	3.3	69	0.1	0.3
	MEAN	15	55	111	101	86	6.2	3.3	74	0.1	0.3
	S.D.	1	32	8	36	17	0.3	0.1	7	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10

# STATISTICAL OUTLIERS INCLUDED
UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 30. Clinical Chemistry – Females

DOSE (MKD)	ANIMAL NUMBER	UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
0	7722	18	37	162	119	91	6.3	3.3	85	0.2#	0.3
	7723	18	83#	161	167	86	6.4	3.3	75	0.2#	0.4
	7724	15	38	170	114	74	6.0	3.1	65	0.1	0.3
	7725	18	37	154	87	101	5.7	3.1	68	0.1	0.4
	7726	18	47	168	124	99	6.4	3.3	74	0.1	0.4
	7727	18	42	170	111	97	6.4	3.4	87	0.1	0.4
	7728	15	37	130	87	74	5.9	3.2	70	0.1	0.3
	7729	15	29	146	78	88	5.8	3.2	83	0.1	0.3
	7730	14	29	137	77	92	5.9	3.1	70	0.1	0.3
	7731	15	29	147	85	96	6.0	3.2	79	0.1	0.3
	MEAN	16	41	155	105	90	6.1	3.2	76	0.1	0.3
	S.D.	2	16	14	28	10	0.3	0.1	8	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10
10	7732	17	37	144	103	76	5.9	3.2	65	0.1	0.3
	7733	16	35	156	90	85	6.2	3.3	72	0.1	0.3
	7734	16	32	146	88	97	5.7	3.1	69	0.1	0.3
	7735	15	38	157	86	102	6.1	3.3	78	0.1	0.4
	7736	17	31	163	104	80	5.8	3.2	68	0.1	0.3
	7737	16	44	154	110	99	5.8	3.2	68	0.1	0.3
	7738	16	63#	152	148	70	6.2	3.4	70	0.2#	0.4
	7739	15	32	158	79	89	6.0	3.2	73	0.1	0.3
	7740	16	41	134	100	79	5.9	3.1	69	0.1	0.3
	7741	15	39	153	109	74	5.8	3.1	64	0.1	0.2
	MEAN	16	39	152	102	85	5.9	3.2	70	0.1	0.3
	S.D.	1	9	8	19	11	0.2	0.1	4	0.0	0.1
	N=	10	10	10	10	10	10	10	10	10	10

# STATISTICAL OUTLIERS INCLUDED
UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 30. Clinical Chemistry – Females (continued)

DOSE MKD	ANIMAL NUMBER	UN MG/DL	ALT U/L	ALP U/L	AST U/L	GLUC MG/DL	TP G/DL	ALB G/DL	CHOL MG/DL	TBIL MG/DL	CREA MG/DL
100	7742	17	38	145	117#	77	5.7	3.2	74	0.1	0.3
	7743	16	33	151	91	91	5.8	3.2	68	0.1	0.3
	7744	13	32	120	87	89	5.8	3.2	74	0.1	0.3
	7745	16	37	141	93	75	5.9	3.1	66	0.1	0.3
	7746	17	32	135	96	83	5.7	3.1	70	0.1	0.3
	7747	19	38	160	103	86	6.1	3.3	79	0.1	0.3
	7748	14	34	146	89	98	5.8	3.2	74	0.1	0.3
	7749	16	34	147	87	95	5.9	3.2	75	0.1	0.3
	7750	16	36	128	89	75	5.4	3.0	70	0.1	0.2#
	7751	16	35	146	88	89	5.6	3.1	76	0.1	0.2#
	MEAN	16	35	142	94	86	5.8	3.2	73	0.1	0.3
	S.D.	2	2	12	9	8	0.2	0.1	4	0.0	0.0
	N=	10	10	10	10	10	10	10	10	10	10
200	91	17	57	135	145	104	6.0	3.2	75	0.1	0.3
	92	17	33	119	89	94	5.7	3.1	79	0.1	0.3
	93	16	35	121	86	86	5.7	3.2	62	0.1	0.2#
	94	15	39	116	103	83	5.8	3.2	70	0.1	0.3
	95	17	34	118	81	92	5.6	3.2	67	0.1	0.3
	96	17	57	127	123	85	5.9	3.2	76	0.1	0.3
	97	15	51	121	117	92	6.2	3.3	50	0.1	0.3
	98	18	117#	133	176	102	6.5	3.4	78	0.1	0.3
	99	15	38	129	84	80	5.6	3.1	70	0.1	0.2#
	MEAN	16	51	124	112	91	5.9	3.2	70	0.1	0.3
	S.D.	1	26	7	32	8	0.3	0.1	9	0.0	0.0
	N=	9	9	9	9	9	9	9	9	9	9

# STATISTICAL OUTLIERS INCLUDED
UN=UREA NITROGEN, ALT=ALANINE AMINOTRANSFERASE, ALP=ALKALINE PHOSPHATASE, AST=ASPARTATE AMINOTRANSFERASE, GLUC=GLUCOSE, TP=TOTAL PROTEIN, ALB=ALBUMIN, CHOL=CHOLESTEROL, TBIL=TOTAL BILIRUBIN, CREA=CREATININE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 31. Electrolytes – Males

DOSE MKD	ANIMAL NUMBER	CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
0	7682	12.8	13.6	151	6.1	97
	7683	12.4	12.7	148	5.4	96
	7684	12.5	13.6	150	6.0	96
	7685	12.0	13.1	148	5.6	97
	7686	12.2	12.7	150	5.5	98
	7687	12.2	12.7	148	5.4	98
	7688	12.3	12.8	148	5.8	97
	7689	12.5	13.1	149	5.9	98
	7690	12.0	12.4	150	5.7	98
	7691	12.6	12.3	149	6.0	98
	MEAN	12.4	12.9	149	5.7	97
	S.D.	0.3	0.4	1	0.3	1
	N=	10	10	10	10	10
10	7692	12.0	12.7	148	5.6	96
	7693	12.1	12.7	149	5.5	96
	7694	12.0	12.7	147	5.5	95
	7695	12.0	12.6	150	5.7	97
	7696	11.9	12.2	147	5.5	97
	7697	11.6	12.5	148	5.5	97
	7698	12.1	12.5	149	5.8	97
	7699	12.0	12.8	148	5.5	98
	7700	12.3	12.8	149	5.8	98
	7701	12.7	13.8#	150	6.2#	97
	MEAN	12.1	12.7	149	5.7	97
	S.D.	0.3	0.4	1	0.2	1
	N=	10	10	10	10	10

# STATISTICAL OUTLIERS INCLUDED
CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 31. Electrolytes – Males (continued)

DOSE MKD	ANIMAL NUMBER	CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
100	7702	12.3	13.0	149	5.7	97
	7703	12.4	13.7	149	6.3	97
	7704	11.9	11.9	148	5.2	97
	7705	11.7	12.5	147	5.4	97
	7706	12.2	13.7	148	5.6	96
	7707	12.2	13.3	148	5.8	98
	7708	12.5	12.9	149	5.9	96
	7709	12.0	12.7	150	5.4	98
	7710	12.3	13.2	150	6.0	97
	7711	12.2	13.0	149	5.9	96
	MEAN	12.2	13.0	149	5.7	97
	S.D.	0.2	0.5	1	0.3	1
	N=	10	10	10	10	10
200	81	12.0	12.4	151	6.9	98
	82	11.8	13.0	150	6.4	98
	83	11.3	11.2	150	6.2	99
	84	11.5	11.7	149	6.1	96
	85	11.8	13.1	150	6.4	100
	86	11.5	11.4	151	6.2	100
	87	11.3	11.9	150	6.0	99
	88	12.2	14.1	152	7.1	98
	89	11.5	12.1	149	6.8	96
	90	11.4	13.3	149	7.3	98
	MEAN	11.6	12.4	150	6.5	98
	S.D.	0.3	0.9	1	0.5	1
	N=	10	10	10	10	10

CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 32. Electrolytes – Females

DOSE MKD	ANIMAL NUMBER	CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
0	7722	12.0	12.3	148	6.6	100
	7723	12.5	15.7	149	8.1	101
	7724	11.4	11.9	148	6.5	100
	7725	11.9	12.8	148	6.0	99
	7726	12.4	14.0	148	7.9	100
	7727	11.4	12.7	149	6.8	99
	7728	11.7	12.4	147	6.1	99
	7729	11.6	11.4	149	5.7	100
	7730	11.4	10.3	148	5.5	99
	7731	12.3	13.5	151	6.5	102
	MEAN	11.9	12.7	149	6.6	100
	S.D.	0.4	1.5	1	0.9	1
	N=	10	10	10	10	10
10	7732	11.4	11.3	147	6.2	99
	7733	11.4	10.2	150	6.2	102
	7734	11.1	11.2	149	5.7	101
	7735	11.8	12.0	149	6.3	101
	7736	11.4	12.7	148	6.2	99
	7737	11.8	13.0	148	6.5	99
	7738	11.9	14.1	149	7.5	100
	7739	12.1	12.5	149	6.4	100
	7740	11.8	12.3	149	6.7	101
	7741	11.8	13.1	148	6.6	101
	MEAN	11.7	12.2	149	6.4	100
	S.D.	0.3	1.1	1	0.5	1
	N=	10	10	10	10	10

CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 32. Electrolytes – Females (continued)

DOSE MKD	ANIMAL NUMBER	CA MG/DL	PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
100	7742	11.7	13.0	147	6.3	99
	7743	11.2	12.3	149	6.3	104
	7744	11.3	11.6	148	6.7	101
	7745	11.4	11.6	150	6.4	102
	7746	11.6	13.0	149	6.7	102
	7747	12.0	14.1	147	6.0	101
	7748	11.4	12.5	150	5.7	101
	7749	11.0	11.0	149	5.8	101
	7750	11.3	12.0	150	6.3	101
	7751	11.2	10.7	146	6.0	100
	MEAN	11.4	12.2	149	6.2	101
	S.D.	0.3	1.0	1	0.3	1
	N=	10	10	10	10	10
200	91	12.0	14.7	150	7.8	102
	92	11.2	12.0	149	6.3	99
	93	11.1	12.2	150	6.0	98
	94	11.4	12.3	151	6.7	101
	95	11.3	11.5	148	5.7	99
	96	11.1	12.2	150	6.6	99
	97	11.5	12.7	151	7.2	100
	98	12.1	14.5	149	8.6	101
	99	11.4	12.5	150	6.3	100
	MEAN	11.5	12.7	150	6.8	100
	S.D.	0.4	1.1	1	0.9	1
	N=	9	9	9	9	9

CA=CALCIUM, PHOS=PHOSPHORUS, NA=SODIUM, K=POTASSIUM, CL=CHLORIDE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 33. Urinalysis – Males

DOSE MKD	ANIMAL NUMBER	URINE VOL (ML)	SPECIFIC GRAVITY	COLOR	APPEAR	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
0	7682	4.0	1.068	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	NEG	<=1
	7683	4.5	1.072	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	NEG	<=1
	7684	5.2	1.072	YELLOW	SL. CL	7.0	++	NEG	TRC	NEG	NEG	<=1
	7685	5.5	1.056	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	++	<=1
	7686	5.6	1.056	YELLOW	SL. CL	7.0	+	NEG	+	NEG	NEG	<=1
	7687	4.4	1.078	YELLOW	SL. CL	6.5	++	NEG	+	NEG	NEG	<=1
	7688	3.6	1.074	YELLOW	SL. CL	7.0	++	NEG	+	NEG	NEG	<=1
	7689	14.8#	1.032#	YELLOW	SL. CL	7.0	TRC	NEG	NEG	NEG	NEG	<=1
	7690	5.0	1.068	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	NEG	<=1
	7691	3.8	1.068	YELLOW	SL. CL	7.0	++	NEG	TRC	NEG	NEG	<=1
	MEAN	5.6	1.064									
	S.D.	3.3	0.013									
	N=	10	10									
10	7692	4.1	1.074	YELLOW	SL. CL	7.0	++	NEG	+	NEG	NEG	<=1
	7693	3.7	1.080	YELLOW	SL. CL	7.0	++	NEG	TRC	NEG	NEG	<=1
	7694	5.0	1.072	YELLOW	SL. CL	7.0	++	NEG	TRC	NEG	NEG	<=1
	7695	3.9	1.072	YELLOW	SL. CL	7.0	++	NEG	+	+	NEG	<=1
	7696	4.0	1.074	YELLOW	SL. CL	6.5	++	NEG	TRC	NEG	NEG	<=1
	7697	5.8	1.062	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7698	4.8	1.074	YELLOW	SL. CL	6.5	++	NEG	TRC	NEG	NEG	<=1
	7699	3.7	1.074	YELLOW	SL. CL	7.0	++	NEG	+	NEG	NEG	<=1
	7700	3.4	1.082	YELLOW	SL. CL	6.5	++	NEG	TRC	+	++	<=1
	7701	5.6	1.054	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	NEG	<=1
	MEAN	4.4	1.072									
	S.D.	0.8	0.008									
	N=	10	10									

SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS. ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE. THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF ANIMALS IN THE DOSE GROUP N = NORMAL; + = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE EU/DL=EHRLICH UNITS/DECILITER
STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 33. Urinalysis – Males (continued)

DOSE MKD	ANIMAL NUMBER	URINE VOL (ML)	SPECIFIC GRAVITY	COLOR	APPEAR	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
100	7702	2.3	1.090	YELLOW	SL. CL	7.0	++	NEG	+	+	++	<=1
	7703	3.0	1.092	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	7704	3.4	1.082	YELLOW	SL. CL	6.5	++	NEG	+	+	+	<=1
	7705	5.0	1.070	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7706	3.2	1.086	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	7707	2.6	1.088	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	7708	2.5	1.092	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7709	3.7	1.078	YELLOW	SL. CL	6.5	++	NEG	TRC	+	NEG	<=1
	7710	3.0	1.080	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	7711	2.3	1.094	YELLOW	SL. CL	6.0	++	NEG	TRC	+	NEG	<=1
	MEAN	3.1	1.085									
	S.D.	0.8	0.008									
	N=	10	10									
200	81	1.7	1.086	YELLOW	SL. CL	7.5	++	NEG	+	+	NEG	<=1
	82	3.1	1.068	YELLOW	SL. CL	8.5	+	NEG	TRC	NEG	NEG	<=1
	83	0.9	1.120	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	84	1.1	1.098	YELLOW	SL. CL	7.0	++	NEG	+	+	NEG	<=1
	85	2.0	1.084	YELLOW	SL. CL	7.0	++	NEG	+	+	NEG	<=1
	86	2.4	1.052	YELLOW	SL. CL	7.5	+	NEG	TRC	NEG	+	<=1
	87	1.8	1.082	YELLOW	SL. CL	7.5	++	NEG	+	+	NEG	<=1
	88	2.7	1.068	YELLOW	SL. CL	7.5	+	NEG	TRC	NEG	NEG	<=1
	89	2.5	1.080	YELLOW	SL. CL	7.0	+	NEG	+	+	NEG	<=1
	90	1.4	1.114	YELLOW	SL. CL	6.5	++	NEG	+	+	NEG	<=1
	MEAN	2.0	1.085									
	S.D.	0.7	0.021									
	N=	10	10									

SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS. ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE. THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF ANIMALS IN THE DOSE GROUP N = NORMAL; + = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE EU/DL=EHRLICH UNITS/DECILITER

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 34. Urinalysis – Females

DOSE MKD	ANIMAL NUMBER	URINE VOL (ML)	SPECIFIC GRAVITY	COLOR	APPEAR	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
0	7722	2.7	1.072	YELLOW	SL. CL	7.0	+	NEG	TRC	+	+	<=1
	7723	8.5	1.027	YELLOW	SL. CL	7.5	NEG	NEG	NEG	NEG	NEG	<=1
	7724	1.9	1.080	YELLOW	SL. CL	7.5	+	NEG	TRC	+	NEG	<=1
	7725	2.8	1.078	YELLOW	SL. CL	6.0	+	NEG	TRC	+	NEG	<=1
	7726	5.8	1.042	YELLOW	SL. CL	7.0	TRC	NEG	NEG	NEG	NEG	<=1
	7727	3.3	1.058	YELLOW	SL. CL	7.0	+	NEG	TRC	NEG	+	<=1
	7728	3.0	1.072	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7729	2.4	1.076	YELLOW	SL. CL	6.5	+	NEG	TRC	+	NEG	<=1
	7730	5.0	1.062	YELLOW	SL. CL	7.0	+	NEG	NEG	NEG	NEG	<=1
	7731	5.0	1.044	YELLOW	SL. CL	7.0	NEG	NEG	NEG	NEG	NEG	<=1
	MEAN	4.0	1.061									
	S.D.	2.0	0.018									
	N=	10	10									
10	7732	4.5	1.056	YELLOW	SL. CL	7.5	TRC	NEG	NEG	NEG	NEG	<=1
	7733	3.4	1.052	YELLOW	SL. CL	8.5	+	NEG	NEG	NEG	NEG	<=1
	7734	3.9	1.056	YELLOW	SL. CL	7.5	TRC	NEG	NEG	NEG	NEG	<=1
	7735	3.7	1.052	YELLOW	SL. CL	8.5	+	NEG	TRC	NEG	++	<=1
	7736	4.3	1.060	YELLOW	SL. CL	7.5	+	NEG	TRC	NEG	+	<=1
	7737	4.7	1.048	YELLOW	SL. CL	7.0	TRC	NEG	NEG	NEG	NEG	<=1
	7738	2.6	1.078	YELLOW	SL. CL	7.0	+	NEG	TRC	+	+	<=1
	7739	3.4	1.066	YELLOW	SL. CL	6.5	+	NEG	TRC	+	NEG	<=1
	7740	3.3	1.062	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7741	2.0	1.088	YELLOW	SL. CL	6.0	++	NEG	TRC	+	NEG	<=1
	MEAN	3.6	1.062									
	S.D.	0.8	0.013									
	N=	10	10									

SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS. ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE. THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF ANIMALS IN THE DOSE GROUP N = NORMAL; + = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE EU/DL=EHRLICH UNITS/DECILITER

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 34. Urinalysis – Females (continued)

DOSE MKD	ANIMAL NUMBER	URINE VOL (ML)	SPECIFIC GRAVITY	COLOR	APPEAR	pH	PROTEIN (MG/DL)	GLUCOSE (MG/DL)	KETONES (MG/DL)	BILI-RUBIN	BLOOD	UROBIL-INOGEN
100	7742	1.3	1.094	YELLOW	SL. CL	6.5	+	NEG	TRC	+	+	<=1
	7743	2.0	1.068	YELLOW	SL. CL	7.0	+	NEG	TRC	+	NEG	<=1
	7744	2.3	1.078	YELLOW	SL. CL	7.0	+	NEG	TRC	+	NEG	<=1
	7745	2.8	1.076	YELLOW	SL. CL	7.0	+	NEG	TRC	+	+	<=1
	7746	2.8	1.068	YELLOW	SL. CL	7.0	+	NEG	TRC	+	NEG	<=1
	7747	1.5	1.094	YELLOW	SL. CL	6.5	++	NEG	TRC	+	++	<=1
	7748	2.8	1.072	YELLOW	SL. CL	6.5	+	NEG	TRC	+	+	<=1
	7749	1.3	1.088	YELLOW	SL. CL	6.5	++	NEG	TRC	+	NEG	<=1
	7750	3.4	1.066	YELLOW	SL. CL	6.5	+	NEG	TRC	NEG	NEG	<=1
	7751	1.4	1.098	YELLOW	SL. CL	6.0	++	NEG	TRC	+	NEG	<=1
	MEAN	2.2	1.080									
	S.D.	0.8	0.012									
	N=	10	10									
200	0091	1.6	1.076	YELLOW	SL. CL	8.0	+	NEG	TRC	+	NEG	<=1
	0092	0.8	1.096	YELLOW	SL. CL	7.5	++	NEG	TRC	+	NEG	<=1
	0093	1.2	1.098	YELLOW	SL. CL	7.0	++	NEG	+	+	NEG	<=1
	0094	1.4	1.090	YELLOW	SL. CL	6.0	+	NEG	TRC	+	NEG	<=1
	0095	0.2	1.120	YELLOW	SL. CL	7.0	+++	NEG	+	++	NEG	<=1
	0096	0.6	1.117	YELLOW	SL. CL	8.5	++	NEG	+	+	++	<=1
	0097	1.5	1.082	YELLOW	SL. CL	7.0	+	NEG	TRC	+	NEG	<=1
	0098	0.7	1.120	YELLOW	SL. CL	7.0	++	NEG	+	+	++	<=1
	0099	2.8	1.064	YELLOW	SL. CL	8.5	+	NEG	TRC	NEG	NEG	<=1
	MEAN	1.2	1.096									
	S.D.	0.8	0.020									
	N=	9	9									

SPECIFIC GRAVITY VALUES ARE MEAN AND S.D. FOR THE SPECIFIED NUMBER (N) OF ANIMALS. ALL OTHER DATA TABULATED AS NUMBER OF ANIMALS (N) WITH THE STATED VALUE. THE TOTAL NUMBER OF ANIMALS FOR SOME PARAMETERS MAY NOT EQUAL THE NUMBER OF ANIMALS IN THE DOSE GROUP N = NORMAL; + = SLIGHT; ++ = MODERATE; +++ = SEVERE NEG=NEGATIVE TRC=TRACE EU/DL=EHRLICH UNITS/DECILITER

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 35. Organ and Organ/Body Weights – Males

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
0	7682	207.6	0.068#	0.033#	0.741	0.357	1.799	0.867	6.542	3.151	1.887	0.909	0.498	0.240
	7683	226.4	0.039	0.017	0.852	0.376	1.905	0.841	8.151	3.600	1.825	0.806	0.536	0.237
	7684	214.5	0.038	0.018	0.779	0.363	1.739	0.811	6.879	3.207	1.865	0.869	0.510	0.238
	7685	220.4	0.039	0.018	0.838	0.380	1.869	0.848	7.228	3.279	1.881	0.853	0.517	0.235
	7686	229.3	0.035	0.015	0.875	0.382	1.924	0.839	7.562	3.298	1.820	0.794	0.512	0.223
	7687	235.8	0.039	0.017	0.946	0.401	1.986	0.842	8.534	3.619	1.820	0.772	0.543	0.230
	7688	231.4	0.038	0.016	0.894	0.386	2.008	0.868	7.884	3.407	1.864	0.806	0.528	0.228
	7689	238.3	0.042	0.018	0.892	0.374	2.034	0.854	8.237	3.457	1.871	0.785	0.489	0.205
	7690	222.3	0.035	0.016	0.870	0.391	1.919	0.863	7.062	3.177	1.899	0.854	0.529	0.238
	7691	228.6	0.036	0.016	0.817	0.357	1.901	0.832	7.231	3.163	1.848	0.808	0.565	0.247
	MEAN	225.5	0.041	0.018	0.850	0.377	1.908	0.846	7.531	3.336	1.858	0.826	0.523	0.232
	S.D.	9.5	0.010	0.005	0.060	0.015	0.091	0.018	0.651	0.176	0.029	0.044	0.022	0.012
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	7692	235.0	0.043	0.018	0.829	0.353	2.004	0.853	8.121	3.456	1.848	0.786	0.563	0.240
	7693	216.4	0.039	0.018	0.804	0.372	1.888	0.872	7.032	3.250	1.839	0.850	0.525	0.243
	7694	227.7	0.036	0.016	0.847	0.372	1.959	0.860	7.671	3.369	1.846	0.811	0.533	0.234
	7695	227.1	0.037	0.016	0.942	0.415	1.921	0.846	7.493	3.299	1.884	0.830	0.552	0.243
	7696	223.4	0.037	0.017	0.886	0.397	1.926	0.862	7.296	3.266	1.823	0.816	0.525	0.235
	7697	242.2	0.039	0.016	0.958	0.396	2.088	0.862	8.200	3.386	1.864	0.770	0.555	0.229
	7698	241.3	0.041	0.017	0.957	0.397	2.050	0.850	8.311	3.444	1.830	0.758	0.566	0.235
	7699	229.4	0.038	0.017	0.860	0.375	2.036	0.888	7.518	3.277	1.905	0.830	0.568	0.248
	7700	228.0	0.040	0.018	0.845	0.371	2.034	0.892	7.554	3.313	1.848	0.811	0.554	0.243
	7701	248.6	0.042	0.017	0.896	0.360	2.211	0.889	8.478	3.410	1.928	0.776	0.587	0.236
	MEAN	231.9	0.039	0.017	0.882	0.381	2.012	0.867	7.767	3.347	1.862	0.804	0.553	0.238
	S.D.	9.8	0.002	0.001	0.055	0.019	0.095	0.017	0.479	0.076	0.034	0.030	0.020	0.006
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 35. Organ and Organ/Body Weights – Males (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
100	7702	202.6	0.060#	0.030#	0.786	0.388	1.764	0.871	7.016	3.463	1.878	0.927	0.517	0.255
	7703	204.5	0.038	0.019	0.779	0.381	1.823	0.891	7.151	3.497	1.840	0.900	0.491	0.240
	7704	208.7	0.038	0.018	0.749	0.359	1.991	0.954	7.702	3.690	1.838	0.881	0.495	0.237
	7705	215.1	0.033	0.015	0.798	0.371	1.945	0.904	7.709	3.584	1.829	0.850	0.512	0.238
	7706	209.4	0.033	0.016	0.781	0.373	1.902	0.908	7.148	3.414	1.826	0.872	0.511	0.244
	7707	208.7	0.034	0.016	0.794	0.380	1.791	0.858	7.007	3.357	1.874	0.898	0.553	0.265
	7708	213.0	0.036	0.017	0.801	0.376	1.851	0.869	7.279	3.417	1.875	0.880	0.524	0.246
	7709	217.8	0.039	0.018	0.812	0.373	1.989	0.913	7.390	3.393	1.863	0.855	0.503	0.231
	7710	215.2	0.042	0.020	0.912#	0.424	2.025	0.941	7.377	3.428	1.851	0.860	0.525	0.244
	7711	218.7	0.036	0.016	0.773	0.353	1.990	0.910	7.619	3.484	1.858	0.850	0.496	0.227
	MEAN	211.4	0.039	0.018	0.799	0.378	1.907	0.902	7.340	3.473	1.853	0.877	0.513	0.243
	S.D.	5.5	0.008	0.004	0.044	0.019	0.094	0.031	0.267	0.099	0.019	0.025	0.019	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	81	185.5	0.056	0.030	0.661	0.356	1.818	0.980	6.661	3.591	1.817	0.980	0.433	0.233
	82	161.1	0.053	0.033	0.599	0.372	1.579	0.980	5.350	3.321	1.749	1.086	0.400	0.248
	83	144.9	0.040	0.028	0.538	0.371	1.382	0.954	4.917	3.393	1.752	1.209	0.401	0.277
	84	152.4	0.053	0.035	0.547	0.359	1.517	0.995	4.954	3.251	1.734	1.138	0.394	0.259
	85	159.5	0.047	0.029	0.557	0.349	1.498	0.939	5.253	3.293	1.784	1.118	0.416	0.261
	86	158.5	0.044	0.028	0.562	0.355	1.512	0.954	5.196	3.278	1.818	1.147	0.426	0.269
	87	171.8	0.068	0.040	0.592	0.345	1.653	0.962	5.733	3.337	1.781	1.037	0.418	0.243
	88	169.7	0.049	0.029	0.582	0.343	1.622	0.956	5.655	3.332	1.773	1.045	0.434	0.256
	89	170.0	0.050	0.029	0.598	0.352	1.706	1.004	5.696	3.351	1.814	1.067	0.423	0.249
	90	154.8	0.037	0.024	0.531	0.343	1.493	0.964	5.345	3.453	1.730	1.118	0.395	0.255
	MEAN	162.8	0.050	0.030	0.577	0.354	1.578	0.969	5.476	3.360	1.775	1.094	0.414	0.255
	S.D.	11.6	0.009	0.004	0.039	0.011	0.125	0.020	0.505	0.099	0.034	0.066	0.015	0.012
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 35. Organ and Organ/Body Weights – Males (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	TESTES (G)	TESTES (G/100)	THYMUS (G)	THYMUS (G/100)	EPIDIDYMIDES (G)	EPIDIDYMIDES (G/100)
0	7682	207.6	2.798	1.348	0.329	0.158	0.543	0.262
	7683	226.4	2.855	1.261	0.355	0.157	0.583	0.258
	7684	214.5	2.792	1.302	0.233#	0.109#	0.516	0.241
	7685	220.4	2.930	1.329	0.333	0.151	0.559	0.254
	7686	229.3	2.996	1.307	0.361	0.157	0.611	0.266
	7687	235.8	2.947	1.250	0.369	0.156	0.588	0.249
	7688	231.4	3.001	1.297	0.346	0.150	0.578	0.250
	7689	238.3	3.018	1.266	0.298	0.125#	0.677	0.284
	7690	222.3	2.956	1.330	0.354	0.159	0.580	0.261
	7691	228.6	3.014	1.318	0.354	0.155	0.608	0.266
	MEAN	225.5	2.931	1.301	0.333	0.148	0.584	0.259
	S.D.	9.5	0.086	0.033	0.041	0.017	0.043	0.012
	N=	10	10	10	10	10	10	10
10	7692	235.0	2.959	1.259	0.356	0.151	0.661	0.281
	7693	216.4	2.784	1.287	0.333	0.154	0.534	0.247
	7694	227.7	2.844	1.249	0.365	0.160	0.569	0.250
	7695	227.1	2.976	1.310	0.390	0.172	0.540	0.238
	7696	223.4	2.964	1.327	0.378	0.169	0.578	0.259
	7697	242.2	2.975	1.228	0.312	0.129	0.616	0.254
	7698	241.3	2.943	1.220	0.336	0.139	0.612	0.254
	7699	229.4	2.991	1.304	0.382	0.167	0.547	0.238
	7700	228.0	2.910	1.276	0.321	0.141	0.548	0.240
	7701	248.6	3.023	1.216	0.348	0.140	0.653	0.263
	MEAN	231.9	2.937	1.268	0.352	0.152	0.586	0.252
	S.D.	9.8	0.073	0.039	0.027	0.015	0.047	0.013
	N=	10	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 35. Organ and Organ/Body Weights – Males (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	TESTES (G)	TESTES (G/100)	THYMUS (G)	THYMUS (G/100)	EPIDIDYMIDES (G)	EPIDIDYMIDES (G/100)
100	7702	202.6	2.748	1.356	0.339	0.167	0.515	0.254
	7703	204.5	2.965	1.450	0.314	0.154	0.588	0.288
	7704	208.7	2.842	1.362	0.350	0.168	0.612	0.293
	7705	215.1	2.883	1.340	0.324	0.151	0.622	0.289
	7706	209.4	2.981	1.424	0.339	0.162	0.567	0.271
	7707	208.7	2.865	1.373	0.334	0.160	0.503	0.241
	7708	213.0	2.911	1.367	0.335	0.157	0.541	0.254
	7709	217.8	2.954	1.356	0.356	0.163	0.565	0.259
	7710	215.2	2.939	1.366	0.340	0.158	0.551	0.256
	7711	218.7	2.907	1.329	0.388	0.177	0.571	0.261
	MEAN	211.4	2.900	1.372	0.342	0.162	0.564	0.267
	S.D.	5.5	0.069	0.037	0.020	0.008	0.038	0.018
	N=	10	10	10	10	10	10	10
200	81	185.5	3.165	1.706	0.242	0.130	0.695	0.375
	82	161.1	2.783	1.727	0.206	0.128	0.572	0.355
	83	144.9	2.449	1.690	0.177	0.122	0.440	0.304
	84	152.4	2.962	1.944#	0.191	0.125	0.536	0.352
	85	159.5	2.824	1.771	0.206	0.129	0.579	0.363
	86	158.5	2.769	1.747	0.165	0.104	0.560	0.353
	87	171.8	3.045	1.772	0.186	0.108	0.625	0.364
	88	169.7	2.951	1.739	0.205	0.121	0.593	0.349
	89	170.0	3.027	1.781	0.211	0.124	0.659	0.388
	90	154.8	2.819	1.821	0.183	0.118	0.535	0.346
	MEAN	162.8	2.879	1.770	0.197	0.121	0.579	0.355
	S.D.	11.6	0.199	0.072	0.022	0.009	0.071	0.022
	N=	10	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 36. Organ and Organ/Body Weights – Females

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
0	7722	141.6	0.050	0.035	0.513	0.362	1.181	0.834	4.401	3.108	1.680	1.186	0.400	0.282
	7723	141.0	0.048	0.034	0.540	0.383	1.163	0.825	4.622	3.278	1.750	1.241	0.367	0.260
	7724	133.3	0.051	0.038	0.495	0.371	1.183	0.887	4.427	3.321	1.699	1.275	0.388	0.291
	7725	133.5	0.049	0.037	0.525	0.393	1.138	0.852	4.154	3.112	1.678	1.257	0.343	0.257
	7726	149.9	0.049	0.033	0.556	0.371	1.263	0.843	4.800	3.202	1.761	1.175	0.419	0.280
	7727	143.7	0.049	0.034	0.549	0.382	1.221	0.850	4.481	3.118	1.780	1.239	0.384	0.267
	7728	142.2	0.046	0.032	0.516	0.363	1.165	0.819	4.370	3.073	1.693	1.191	0.372	0.262
	7729	145.0	0.050	0.034	0.537	0.370	1.238	0.854	4.500	3.103	1.633	1.126	0.427	0.294
	7730	155.1	0.050	0.032	0.563	0.363	1.230	0.793	4.737	3.054	1.764	1.137	0.460	0.297
	7731	154.6	0.056	0.036	0.551	0.356	1.219	0.788	4.718	3.052	1.730	1.119	0.447	0.289
	MEAN	144.0	0.050	0.035	0.535	0.372	1.200	0.835	4.521	3.142	1.717	1.195	0.401	0.278
	S.D.	7.6	0.003	0.002	0.022	0.011	0.040	0.030	0.199	0.094	0.047	0.056	0.037	0.015
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
10	7732	134.9	0.032	0.024	0.521	0.386	1.136	0.842	4.287	3.178	1.738	1.288	0.370	0.274
	7733	131.1	0.049	0.037	0.522	0.398	1.101	0.840	4.112	3.137	1.709	1.304	0.360	0.275
	7734	136.3	0.048	0.035	0.523	0.384	1.189	0.872	4.162	3.054	1.720	1.262	0.396	0.291
	7735	138.4	0.047	0.034	0.512	0.370	1.236	0.893	4.140	2.991	1.744	1.260	0.380	0.275
	7736	137.1	0.041	0.030	0.527	0.384	1.101	0.803	3.981	2.904	1.701	1.241	0.359	0.262
	7737	139.6	0.046	0.033	0.526	0.377	1.148	0.822	4.191	3.002	1.587#	1.137	0.400	0.287
	7738	140.3	0.052	0.037	0.516	0.368	1.166	0.831	4.575	3.261	1.726	1.230	0.378	0.269
	7739	151.3	0.051	0.034	0.557#	0.368	1.315	0.869	4.599	3.040	1.799#	1.189	0.408	0.270
	7740	145.9	0.055	0.038	0.517	0.354	1.220	0.836	4.562	3.127	1.735	1.189	0.381	0.261
	7741	140.3	0.043	0.031	0.508	0.362	1.176	0.838	4.170	2.972	1.716	1.223	0.407	0.290
	MEAN	139.5	0.046	0.033	0.523	0.375	1.179	0.845	4.278	3.066	1.718	1.232	0.384	0.275
	S.D.	5.7	0.007	0.004	0.013	0.013	0.066	0.026	0.221	0.108	0.053	0.050	0.018	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 36. Organ and Organ/Body Weights – Females (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	ADRENAL GLANDS (G)	ADRENAL GLANDS (G/100)	HEART (G)	HEART (G/100)	KIDNEYS (G)	KIDNEYS (G/100)	LIVER (G)	LIVER (G/100)	BRAIN (G)	BRAIN (G/100)	SPLEEN (G)	SPLEEN (G/100)
100	7742	128.1#	0.041	0.032	0.443#	0.346	1.067	0.833	4.099	3.200	1.682	1.313	0.346	0.270
	7743	137.2	0.049	0.036	0.523	0.381	1.309	0.954	4.723	3.442	1.699	1.238	0.418	0.305
	7744	136.0	0.047	0.035	0.511	0.376	1.203	0.885	4.325	3.180	1.717	1.263	0.392	0.288
	7745	139.6	0.045	0.032	0.536	0.384	1.248	0.894	4.300	3.080	1.748	1.252	0.404	0.289
	7746	137.2	0.048	0.035	0.520	0.379	1.223	0.891	4.707	3.431	1.713	1.249	0.386	0.281
	7747	137.4	0.044	0.032	0.527	0.384	1.178	0.857	4.317	3.142	1.719	1.251	0.377	0.274
	7748	139.0	0.046	0.033	0.531	0.382	1.206	0.868	4.238	3.049	1.715	1.234	0.415	0.299
	7749	140.4	0.052	0.037	0.502	0.358	1.253	0.892	4.780	3.405	1.590	1.132	0.421	0.300
	7750	138.6	0.044	0.032	0.513	0.370	1.167	0.842	4.304	3.105	1.778	1.283	0.403	0.291
	7751	141.6	0.050	0.035	0.499	0.352	1.229	0.868	4.421	3.122	1.692	1.195	0.402	0.284
	MEAN	137.5	0.047	0.034	0.511	0.371	1.208	0.878	4.421	3.216	1.705	1.241	0.396	0.288
	S.D.	3.7	0.003	0.002	0.027	0.014	0.064	0.034	0.233	0.152	0.049	0.049	0.023	0.011
	N=	10	10	10	10	10	10	10	10	10	10	10	10	10
200	91	117.3	0.038	0.032	0.431	0.367	1.046	0.892	3.754	3.200	1.665	1.419	0.355	0.303
	92	115.1	0.033	0.029	0.418	0.363	1.079	0.937	3.566	3.098	1.708	1.484	0.326	0.283
	93	123.9	0.045	0.036	0.475	0.383	1.125	0.908	3.879	3.131	1.671	1.349	0.348	0.281
	94	136.0	0.042	0.031	0.481	0.354	1.246	0.916	3.990	2.934	1.732	1.274	0.383	0.282
	95	103.8	0.030	0.029	0.416	0.401	0.972	0.936	3.058	2.946	1.615	1.556	0.322	0.310
	96	130.3	0.034	0.026	0.489	0.375	1.255	0.963	3.987	3.060	1.721	1.321	0.367	0.282
	97	114.7	0.037	0.032	0.411	0.358	1.035	0.902	3.400	2.964	1.651	1.439	0.302	0.263
	98	143.7	0.048	0.033	0.486	0.338	1.318	0.917	4.670	3.250	1.751	1.219	0.391	0.272
	99	135.3	0.040	0.030	0.481	0.356	1.233	0.911	4.262	3.150	1.756	1.298	0.432	0.319
	MEAN	124.5	0.039	0.031	0.454	0.366	1.145	0.920	3.841	3.081	1.697	1.373	0.358	0.288
	S.D.	12.8	0.006	0.003	0.034	0.018	0.121	0.022	0.474	0.114	0.049	0.109	0.040	0.018
	N=	9	9	9	9	9	9	9	9	9	9	9	9	9

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 36. Organ and Organ/Body Weights – Females (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	THYMUS (G)	THYMUS (G/100)
0	7722	141.6	0.263	0.186
	7723	141.0	0.265	0.188
	7724	133.3	0.255	0.191
	7725	133.5	0.221	0.166
	7726	149.9	0.341	0.227
	7727	143.7	0.309	0.215
	7728	142.2	0.297	0.209
	7729	145.0	0.293	0.202
	7730	155.1	0.345	0.222
	7731	154.6	0.305	0.197
	MEAN	144.0	0.289	0.200
	S.D.	7.6	0.039	0.019
	N=	10	10	10
10	7732	134.9	0.283	0.210
	7733	131.1	0.274	0.209
	7734	136.3	0.263	0.193
	7735	138.4	0.302	0.218
	7736	137.1	0.350#	0.255
	7737	139.6	0.290	0.208
	7738	140.3	0.295	0.210
	7739	151.3	0.277	0.183
	7740	145.9	0.264	0.181
	7741	140.3	0.290	0.207
	MEAN	139.5	0.289	0.207
	S.D.	5.7	0.025	0.021
	N=	10	10	10

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 36. Organ and Organ/Body Weights – Females (continued)

DOSE MKD	ANIMAL NUMBER	FINAL BODY WT. (G)	THYMUS (G)	THYMUS (G/100)
100	7742	128.1#	0.269	0.210
	7743	137.2	0.286	0.208
	7744	136.0	0.275	0.202
	7745	139.6	0.263	0.188
	7746	137.2	0.281	0.205
	7747	137.4	0.298	0.217
	7748	139.0	0.320	0.230
	7749	140.4	0.266	0.189
	7750	138.6	0.319	0.230
	7751	141.6	0.300	0.212
	MEAN	137.5	0.288	0.209
	S.D.	3.7	0.021	0.014
	N=	10	10	10
200	91	117.3	0.216	0.184
	92	115.1	0.249	0.216
	93	123.9	0.280	0.226
	94	136.0	0.277	0.204
	95	103.8	0.218	0.210
	96	130.3	0.258	0.198
	97	114.7	0.270	0.235
	98	143.7	0.286	0.199
	99	135.3	0.281	0.208
	MEAN	124.5	0.259	0.209
	S.D.	12.8	0.027	0.015
	N=	9	9	9

STATISTICAL OUTLIERS INCLUDED.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis

LabDiet PMI NUTRITION

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0220827-1
Lot Code: AUG 02 02 2A
Entered: 8/20/2002

Assay	Analysis	Units
PROTEIN	21.4	%
FAT ACID (HYDRO.)	6.2	%
FIBER (CRUDE)	4.03	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.076	PPM
CALCIUM	0.893	%
LEAD	0.215	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.633	%
SELENIUM	0.397	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis (continued)

LabDiet PMI NUTRITION INTERNATIONAL

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0222607-3
Lot Code: SEP 08 02 3C
Entered: 9/24/2002

Assay	Analysis	Units
PROTEIN	21	%
FAT ACID (HYDRO.)	6.09	%
FIBER (CRUDE)	4.43	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	LESS THAN 0.05	PPM
CALCIUM	0.836	%
LEAD	0.164	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.589	%
SELENIUM	0.176	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis (continued)

LabDiet PMI NUTRITION INTERNATIONAL

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0223019-2
Lot Code: SEP 18 02 3B
Entered: 10/3/2002

Assay	Analysis	Units
PROTEIN	21.3	%
FAT ACID (HYDRO.)	5.66	%
FIBER (CRUDE)	4.12	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.056	PPM
CALCIUM	0.834	%
LEAD	0.137	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.637	%
SELENIUM	0.174	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis (continued)

LabDiet PMI NUTRITION INTERNATIONAL

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0225649-2
Lot Code: NOV 08 02 1B
Entered: 11/25/2002

Assay	Analysis	Units
PROTEIN	21.3	%
FAT ACID (HYDRO.)	5.62	%
FIBER (CRUDE)	4.67	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.056	PPM
CALCIUM	1.02	%
LEAD	0.176	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.695	%
SELENIUM	0.164	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis (continued)

LabDiet PMI NUTRITION INTERNATIONAL

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0226410-3
Lot Code: DEC 01 02 3A
Entered: 12/19/2002

Assay	Analysis	Units
PROTEIN	21.4	%
FAT ACID (HYDRO.)	6.02	%
FIBER (CRUDE)	3.97	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.097	PPM
CALCIUM	0.876	%
LEAD	0.173	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.659	%
SELENIUM	0.345	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 37. Feed Analysis (continued)

LabDiet PMI NUTRITION International

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0227342-3
Lot Code: DEC 12 02 2C
Entered: 1/3/2003

Assay	Analysis	Units
PROTEIN	21.4	%
FAT ACID (HYDRO.)	5.64	%
FIBER (CRUDE)	3.89	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.111	PPM
CALCIUM	0.949	%
LEAD	0.166	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.690	%
SELENIUM	0.222	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	0.03
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15

Aflatoxin	Aflatoxins	LESS THAN 5 PPB

No notes.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 38. Municipal Water Analysis

MONTHLY DISTRIBUTION WATER ANALYSIS REPORT*
MIDLAND WATER TREATMENT PLANT

MONTH: JANUARY 2003

PARAMETER	RESULTS		
	Average	Maximum	Minimum
TOTAL COLIFORMS	ND	ND	ND
HETEROTROPHIC PLATE COUNT	0	3	0
TEMPERATURE - °C	7	11	5
pH	8.3	8.5	8.1
CONDUCTIVITY, uS/CM	218	233	211
TURBIDITY, NTU	0.10	0.70	0.06
ODOR# AT 60°C	**	**	**
TOTAL HARDNESS, (mg/L) as $CaCO_3$	100	105	95
TOTAL ALKALINITY, (mg/L) as $CaCO_3$	70	74	67
CARBONATE ALKALINITY, (mg/L) as $CaCO_3$	2	4	2
BICARBONATE ALKALINITY, (mg/L) as $CaCO_3$	67	72	63
CALCIUM, as $CaCO_3$	70	73	67
CALCIUM, (mg/L)	28	29	27
MAGNESIUM, (mg/L)	7.5	8.0	6.8
FLUORIDE, (mg/L)	1.08	1.14	1.03
Free Chlorine, (mg/L)	0.82	1.25	0.50
TOTAL IRON, (mg/L)	**	**	**
LANGELIER SATURATION INDEX@	-0.2	0.0	-0.5

* STANDARD METHODS FOR EXAMINATION OF WATER AND WASTE WATER, 16TH ED. (1985), AMERICAN PUBLIC HEALTH ASSOCIATION AND AMERICAN WATER WORKS; WASHINGTON, D.C.
NTU - NEPHELOMETRIC TURBIDITY UNITS
\# INTENSITY LEVEL RECORDED AS I THROUGH IV
M - MUSTY
** NO DATA GIVEN
@ INDICATES WATER CORROSIVITY (A POSITIVE VALUE INDICATES WATER WILL DEPOSIT MINERALS, A NEGATIVE VALUE INDICATES WATER WILL TAKE UP MINERALS)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 38. Water Analysis (continued)

MONTHLY DISTRIBUTION WATER ANALYSIS REPORT*
MIDLAND WATER TREATMENT PLANT

MONTH: FEBRUARY 2003

PARAMETER	RESULTS		
	Average	Maximum	Minimum
TOTAL COLIFORMS	ND	ND	ND
HETEROTROPHIC PLATE COUNT	1	6	0
TEMPERATURE - °C	6	8	3
pH	8.4	8.7	8.1
CONDUCTIVITY, uS/CM	224	238	207
TURBIDITY, NTU	.09	0.16	0.06
ODOR# AT 60°C	**	**	**
TOTAL HARDNESS, (mg/L) as $CaCO_3$	105	113	95
TOTAL ALKALINITY, (mg/L) as $CaCO_3$	74	80	63
CARBONATE ALKALINITY, (mg/L) as $CaCO_3$	4	6	2
BICARBONATE ALKALINITY, (mg/L) as $CaCO_3$	70	75	59
CALCIUM, as $CaCO_3$	73	80	61
CALCIUM, (mg/L)	29	32	24
MAGNESIUM, (mg/L)	7.7	8.3	7.3
FLUORIDE, (mg/L)	1.06	1.22	.97
Free Chlorine, (mg/L)	0.83	1.10	0.55
TOTAL IRON, (mg/L)	**	**	**
LANGELIER SATURATION INDEX@	-0.1	0.2	-0.5

* STANDARD METHODS FOR EXAMINATION OF WATER AND WASTE WATER, 16TH ED. (1985), AMERICAN PUBLIC HEALTH ASSOCIATION AND AMERICAN WATER WORKS; WASHINGTON, D.C.
NTU - NEPHELOMETRIC TURBIDITY UNITS
\# INTENSITY LEVEL RECORDED AS I THROUGH IV
M - MUSTY
** NO DATA GIVEN
@ INDICATES WATER CORROSIVITY (A POSITIVE VALUE INDICATES WATER WILL DEPOSIT MINERALS, A NEGATIVE VALUE INDICATES WATER WILL TAKE UP MINERALS)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 38. Water Analysis (continued)

MONTHLY DISTRIBUTION WATER ANALYSIS REPORT*
MIDLAND WATER TREATMENT PLANT

MONTH: MARCH 2003

PARAMETER	RESULTS		
	Average	Maximum	Minimum
TOTAL COLIFORMS	ND	ND	ND
HETEROTROPHIC PLATE COUNT	1	6	0
TEMPERATURE - °C	5	8	3
pH	8.9	9.0	8.5
CONDUCTIVITY, uS/CM	224	235	209
TURBIDITY, NTU	.09	0.14	0.07
ODOR# AT 60°C	**	**	**
TOTAL HARDNESS, (mg/L) as $CaCO_3$	107	113	99
TOTAL ALKALINITY, (mg/L) as $CaCO_3$	77	82	71
CARBONATE ALKALINITY, (mg/L) as $CaCO_3$	10	12	6
BICARBONATE ALKALINITY, (mg/L) as $CaCO_3$	67	73	61
CALCIUM, as $CaCO_3$	74	80	68
CALCIUM, (mg/L)	30	32	27
MAGNESIUM, (mg/L)	7.9	8.5	7.5
FLUORIDE, (mg/L)	0.16	0.50	0.09
Free Chlorine, (mg/L)	0.86	1.15	0.50
TOTAL IRON, (mg/L)	**	**	**
LANGELIER SATURATION INDEX@	0.3	0.5	-0.1

* STANDARD METHODS FOR EXAMINATION OF WATER AND WASTE WATER, 16TH ED. (1985), AMERICAN PUBLIC HEALTH ASSOCIATION AND AMERICAN WATER WORKS; WASHINGTON, D.C.
NTU - NEPHELOMETRIC TURBIDITY UNITS
\# INTENSITY LEVEL RECORDED AS I THROUGH IV
M - MUSTY
** NO DATA GIVEN
@ INDICATES WATER CORROSIVITY (A POSITIVE VALUE INDICATES WATER WILL DEPOSIT MINERALS, A NEGATIVE VALUE INDICATES WATER WILL TAKE UP MINERALS)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 39. Analytical Water Analysis

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 39. Analytical Water Analysis (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 39. Analytical Water Analysis (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 39. Analytical Water Analysis (continued)

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report

Animal No.: 7682 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 208g

Organ Weights:

ADRENAL GLANDS	:	0.068g<	BRAIN	:	1.887g	KIDNEYS	:	1.799g
EPIDIDYMIDES	:	0.543g	HEART	:	0.741g<	LIVER	:	6.542g
SPLEEN	:	0.498g	TESTES	:	2.798g	THYMUS	:	0.329g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL
LYMPH NODE - MESENTERIC		MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
PROSTATE	RECTUM	SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	TESTES

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7682 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7683 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 226g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.825g	KIDNEYS	: 1.905g
EPIDIDYMIDES	:	0.583g	HEART	:	0.852g<	LIVER	: 8.151g
SPLEEN	:	0.536g	TESTES	:	2.855g	THYMUS	: 0.355g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG	LYMPH NODE - MEDIASTINAL	
LYMPH NODE - MESENTERIC		MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX	

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7683 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
PROSTATE	RECTUM	SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	TESTES
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7684 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 215g

Organ Weights:

ADRENAL GLANDS	:	0.038g<	BRAIN	:	1.865g	KIDNEYS	: 1.739g
EPIDIDYMIDES	:	0.516g	HEART	:	0.779g<	LIVER	: 6.879g
SPLEEN	:	0.510g	TESTES	:	2.792g	THYMUS	: 0.233g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
Aggregates Of Macrophages - Histiocytes; adjacent to necrotic or degenerative hepatocytes; very slight

PROSTATE;
Inflammation; subacute to chronic; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	EYE	HEART	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG	LYMPH NODE - MEDIASTINAL

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7684 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

LYMPH NODE - MESENTERIC		MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	TESTES
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7685 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 220g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.881g	KIDNEYS	: 1.869g
EPIDIDYMIDES	:	0.559g	HEART	:	0.838g<	LIVER	: 7.228g
SPLEEN	:	0.517g	TESTES	:	2.930g	THYMUS	: 0.333g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG	LYMPH NODE - MEDIASTINAL	
LYMPH NODE - MESENTERIC		MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX	

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7685 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
PROSTATE	RECTUM	SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	TESTES
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7686 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 229g

Organ Weights:

ADRENAL GLANDS	:	0.035g<	BRAIN	:	1.820g	KIDNEYS	: 1.924g
EPIDIDYMIDES	:	0.611g	HEART	:	0.875g<	LIVER	: 7.562g
SPLEEN	:	0.512g	TESTES	:	2.996g	THYMUS	: 0.361g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BRAIN;
Degeneration; axonal; optic tract; unilateral; multifocal; very slight

CRANIAL NERVE - OPTIC;
Degeneration; axonal; unilateral; multifocal; very slight

EYE;
Atrophy; retina; unilateral; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7686 Group: 1 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	HEART
ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC		MEDIASTINAL TISSUE
MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS	PARATHYROID GLAND
PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM	SALIVARY GLAND
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR		
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7687 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 236g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.820g	KIDNEYS	: 1.986g
EPIDIDYMIDES	:	0.588g	HEART	:	0.946g<	LIVER	: 8.534g
SPLEEN	:	0.543g	TESTES	:	2.947g	THYMUS	: 0.369g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7687 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7688 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 231g

Organ Weights:

ADRENAL GLANDS	:	0.038g<	BRAIN	:	1.864g	KIDNEYS	: 2.008g
EPIDIDYMIDES	:	0.578g	HEART	:	0.894g<	LIVER	: 7.884g
SPLEEN	:	0.528g	TESTES	:	3.001g	THYMUS	: 0.346g

Gross Pathology Observations:

GENERAL;
Comment: The transponder was broken at necropsy.

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7688 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS
PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7689 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 238g

Organ Weights:

ADRENAL GLANDS	:	0.042g<	BRAIN	:	1.871g	KIDNEYS	: 2.034g
EPIDIDYMIDES	:	0.677g	HEART	:	0.892g<	LIVER	: 8.237g
SPLEEN	:	0.489g	TESTES	:	3.018g	THYMUS	: 0.298g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7689 Group: 1 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND	
LARYNX	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS
PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7690 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 222g

Organ Weights:

ADRENAL GLANDS	:	0.035g<	BRAIN	:	1.899g	KIDNEYS	: 1.919g
EPIDIDYMIDES	:	0.580g	HEART	:	0.870g<	LIVER	: 7.062g
SPLEEN	:	0.529g	TESTES	:	2.956g	THYMUS	: 0.354g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	COAGULATING GLAND	COLON	CRANIAL NERVE - OPTIC		DUODENUM
EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7690 Group: 1 Sex: Male (continued)

The following tissues were within normal limits: (continued)

PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7691 Group: 1 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 229g

Organ Weights:

ADRENAL GLANDS	:	0.036g<	BRAIN	:	1.848g	KIDNEYS	: 1.901g
EPIDIDYMIDES	:	0.608g	HEART	:	0.817g<	LIVER	: 7.231g
SPLEEN	:	0.565g	TESTES	:	3.014g	THYMUS	: 0.354g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BRAIN;
Degeneration; axonal; optic tract; unilateral; multifocal; very slight

CRANIAL NERVE - OPTIC;
Degeneration; axonal; unilateral; multifocal; very slight

EYE;
Atrophy; retina; unilateral; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7691 Group: 1 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	CECUM
COAGULATING GLAND	COLON	DUODENUM	EPIDIDYMIDES	ESOPHAGUS	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	PANCREAS
PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	PROSTATE	RECTUM
SALIVARY GLAND	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	TESTES	THYMUS	THYROID GLAND	TRACHEA
URINARY BLADDER					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7722 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 142g

Organ Weights:

ADRENAL GLANDS	: 0.050g<	BRAIN	: 1.680g	KIDNEYS	: 1.181g
HEART	: 0.513g<	LIVER	: 4.401g	SPLEEN	: 0.400g
THYMUS	: 0.263g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:
LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	EYE	HEART	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG	LYMPH NODE - MEDIASTINAL	
LYMPH NODE - MESENTERIC		MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX
ORAL TISSUE	OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7722 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7723 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 141g

Organ Weights:

ADRENAL GLANDS	: 0.048g<	BRAIN	: 1.750g	KIDNEYS	: 1.163g
HEART	: 0.540g<	LIVER	: 4.622g	SPLEEN	: 0.367g
THYMUS	: 0.265g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	HEART	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND	
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7723 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7724 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 133g

Organ Weights:

ADRENAL GLANDS	0.051g<	BRAIN	1.699g	KIDNEYS	1.183g
HEART	0.495g<	LIVER	4.427g	SPLEEN	0.388g
THYMUS	0.255g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	EYE	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7724 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7725 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 134g

Organ Weights:

ADRENAL GLANDS	0.049g<	BRAIN	1.678g	KIDNEYS	1.138g
HEART	0.525g<	LIVER	4.154g	SPLEEN	0.343g
THYMUS	0.221g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7725 Group: 1 Sex: Female (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM	ESOPHAGUS
HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND	
LARYNX	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7726 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
Soiling, Periocular; Red

Palpable Mass Details:
None

Terminal Body Weight: 150g

Organ Weights:

ADRENAL GLANDS	0.049g<	BRAIN	1.761g	KIDNEYS	1.263g
HEART	0.556g<	LIVER	4.800g	SPLEEN	0.419g
THYMUS	0.341g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND
LARYNX	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7726 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7727 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 144g

Organ Weights:

ADRENAL GLANDS	: 0.049g<	BRAIN	: 1.780g	KIDNEYS	: 1.221g
HEART	: 0.549g<	LIVER	: 4.481g	SPLEEN	: 0.384g
THYMUS	: 0.309g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	EYE	HEART	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7727 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7728 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 142g

Organ Weights:

ADRENAL GLANDS	0.046g<	BRAIN	1.693g	KIDNEYS	1.165g
HEART	0.516g<	LIVER	4.370g	SPLEEN	0.372g
THYMUS	0.297g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight: Comment: Very slight hypocellularity is more prominent in the femoral marrow.

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM	ESOPHAGUS
EYE	HEART	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND	
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7728 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7729 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 145g

Organ Weights:

ADRENAL GLANDS	0.050g<	BRAIN	1.633g	KIDNEYS	1.238g
HEART	0.537g<	LIVER	4.500g	SPLEEN	0.427g
THYMUS	0.293g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BRAIN;
Degeneration; axonal; optic tract; unilateral; multifocal; very slight

CRANIAL NERVE - OPTIC;
Degeneration; axonal; unilateral; multifocal; slight

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7729 Group: 1 Sex: Female (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	CECUM
CERVIX	COLON	DUODENUM	ESOPHAGUS	HEART	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC		MAMMARY GLAND
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES
OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR	
SPLEEN	STOMACH	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER
UTERUS	VAGINA				

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7730 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 155g

Organ Weights:

ADRENAL GLANDS	: 0.050g<	BRAIN	: 1.764g	KIDNEYS	: 1.230g
HEART	: 0.563g<	LIVER	: 4.737g	SPLEEN	: 0.460g
THYMUS	: 0.345g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	EYE	HEART	ILEUM	JEJUNUM	KIDNEYS
LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL
LYMPH NODE - MESENTERIC		MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX
ORAL TISSUE	OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA	Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7731 Group: 1 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 0.0 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 155g

Organ Weights:

ADRENAL GLANDS	: 0.056g<	BRAIN	: 1.730g	KIDNEYS	: 1.219g
HEART	: 0.551g<	LIVER	: 4.718g	SPLEEN	: 0.447g
THYMUS	: 0.305g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		DUODENUM
ESOPHAGUS	HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC
MAMMARY GLAND	MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
OVARIES	OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	
PITUITARY GLAND	RECTUM	SALIVARY GLAND	SKELETAL MUSCLE	SKIN AND SUBCUTIS	
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	STOMACH	THYMUS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7731 Group: 1 Sex: Female (continued)

The following tissues were within normal limits: (continued)

THYROID GLAND	TRACHEA	URINARY BLADDER	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7692 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 235g

Organ Weights:

ADRENAL GLANDS	:	0.043g<	BRAIN	:	1.848g	KIDNEYS	:	2.004g
EPIDIDYMIDES	:	0.661g	HEART	:	0.829g<	LIVER	:	8.121g
SPLEEN	:	0.563g	TESTES	:	2.959g	THYMUS	:	0.356g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7693 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 216g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.839g	KIDNEYS	: 1.888g
EPIDIDYMIDES	:	0.534g	HEART	:	0.804g<	LIVER	: 7.032g
SPLEEN	:	0.525g	TESTES	:	2.784g	THYMUS	: 0.333g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

PROSTATE;
Inflammation; subacute to chronic; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC
MESENTERIC TISSUE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH THYMUS

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7694 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 228g

Organ Weights:

ADRENAL GLANDS	:	0.036g<	BRAIN	:	1.846g	KIDNEYS	: 1.959g
EPIDIDYMIDES	:	0.569g	HEART	:	0.847g<	LIVER	: 7.671g
SPLEEN	:	0.533g	TESTES	:	2.844g	THYMUS	: 0.365g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7695 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 227g

Organ Weights:

ADRENAL GLANDS	:	0.037g<	BRAIN	:	1.884g	KIDNEYS	:	1.921g
EPIDIDYMIDES	:	0.540g	HEART	:	0.942g<	LIVER	:	7.493g
SPLEEN	:	0.552g	TESTES	:	2.976g	THYMUS	:	0.390g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	PROSTATE	SALIVARY GLAND
SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH	THYMUS		

The following tissues have not been examined:

LYMPH NODE - MESENTERIC; MISSING
MESENTERIC TISSUE; MISSING

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7696 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 223g

Organ Weights:

ADRENAL GLANDS	:	0.037g<	BRAIN	:	1.823g	KIDNEYS	: 1.926g
EPIDIDYMIDES	:	0.578g	HEART	:	0.886g<	LIVER	: 7.296g
SPLEEN	:	0.525g	TESTES	:	2.964g	THYMUS	: 0.378g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7697 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 242g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.864g	KIDNEYS	:	2.088g
EPIDIDYMIDES	:	0.616g	HEART	:	0.958g<	LIVER	:	8.200g
SPLEEN	:	0.555g	TESTES	:	2.975g	THYMUS	:	0.312g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7698 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 241g

Organ Weights:

ADRENAL GLANDS	:	0.041g<	BRAIN	:	1.830g	KIDNEYS	:	2.050g
EPIDIDYMIDES	:	0.612g	HEART	:	0.957g<	LIVER	:	8.311g
SPLEEN	:	0.566g	TESTES	:	2.943g	THYMUS	:	0.336g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7699 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 229g

Organ Weights:

ADRENAL GLANDS	:	0.038g<	BRAIN	:	1.905g	KIDNEYS	: 2.036g
EPIDIDYMIDES	:	0.547g	HEART	:	0.860g<	LIVER	: 7.518g
SPLEEN	:	0.568g	TESTES	:	2.991g	THYMUS	: 0.382g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7700 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 228g

Organ Weights:

ADRENAL GLANDS	:	0.040g<	BRAIN	:	1.848g	KIDNEYS	: 2.034g
EPIDIDYMIDES	:	0.548g	HEART	:	0.845g<	LIVER	: 7.554g
SPLEEN	:	0.554g	TESTES	:	2.910g	THYMUS	: 0.321g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7701 Group: 2 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 249g

Organ Weights:

ADRENAL GLANDS	:	0.042g<	BRAIN	:	1.928g	KIDNEYS	: 2.211g
EPIDIDYMIDES	:	0.653g	HEART	:	0.896g<	LIVER	: 8.478g
SPLEEN	:	0.587g	TESTES	:	3.023g	THYMUS	: 0.348g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC	
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	STOMACH
THYMUS					

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7732 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
Skin, Reddened; Multifocal

Palpable Mass Details:
None

Terminal Body Weight: 135g

Organ Weights:

ADRENAL GLANDS	0.032g<	BRAIN	1.738g	KIDNEYS	1.136g
HEART	0.521g<	LIVER	4.287g	SPLEEN	0.370g
THYMUS	0.283g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7733 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 131g

Organ Weights:

ADRENAL GLANDS	: 0.049g<	BRAIN	: 1.709g	KIDNEYS	: 1.101g
HEART	: 0.522g<	LIVER	: 4.112g	SPLEEN	: 0.360g
THYMUS	: 0.274g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7734 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 136g

Organ Weights:

ADRENAL GLANDS	0.048g<	BRAIN	1.720g	KIDNEYS	1.189g
HEART	0.523g<	LIVER	4.162g	SPLEEN	0.396g
THYMUS	0.263g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7735 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
Eye, Cloudy; Right

Palpable Mass Details:
None

Terminal Body Weight: 138g

Organ Weights:

ADRENAL GLANDS	:	0.047g<	BRAIN	:	1.744g	KIDNEYS	:	1.236g
HEART	:	0.512g<	LIVER	:	4.140g	SPLEEN	:	0.380g
THYMUS	:	0.302g						

Gross Pathology Observations:

EYE;
Cloudy; cornea; right

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Atrophy; retina; unilateral; very slight
Mineralization; cornea; unilateral; multifocal; very slight

STOMACH;
Dilatation; glandular; glandular mucosa; focal; slight

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7736 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 137g

Organ Weights:

ADRENAL GLANDS	0.041g<	BRAIN	1.701g	KIDNEYS	1.101g
HEART	0.527g<	LIVER	3.981g	SPLEEN	0.359g
THYMUS	0.350g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7737 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 140g

Organ Weights:

ADRENAL GLANDS	0.046g<	BRAIN	1.587g	KIDNEYS	1.148g
HEART	0.526g<	LIVER	4.191g	SPLEEN	0.400g
THYMUS	0.290g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7738 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 140g

Organ Weights:

ADRENAL GLANDS	: 0.052g<	BRAIN	: 1.726g	KIDNEYS	: 1.166g
HEART	: 0.516g<	LIVER	: 4.575g	SPLEEN	: 0.378g
THYMUS	: 0.295g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7739 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 151g

Organ Weights:

ADRENAL GLANDS	: 0.051g<	BRAIN	: 1.799g	KIDNEYS	: 1.315g
HEART	: 0.557g<	LIVER	: 4.599g	SPLEEN	: 0.408g
THYMUS	: 0.277g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7740 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 146g

Organ Weights:

ADRENAL GLANDS	: 0.055g<	BRAIN	: 1.735g	KIDNEYS	: 1.220g
HEART	: 0.517g<	LIVER	: 4.562g	SPLEEN	: 0.381g
THYMUS	: 0.264g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7741 Group: 2 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 10 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 140g

Organ Weights:

ADRENAL GLANDS	: 0.043g<	BRAIN	: 1.716g	KIDNEYS	: 1.176g
HEART	: 0.508g<	LIVER	: 4.170g	SPLEEN	: 0.407g
THYMUS	: 0.290g				

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	STOMACH	THYMUS	UTERUS	VAGINA

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7702 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 203g

Organ Weights:

ADRENAL GLANDS	:	0.060g<	BRAIN	:	1.878g	KIDNEYS	: 1.764g
EPIDIDYMIDES	:	0.515g	HEART	:	0.786g<	LIVER	: 7.016g
SPLEEN	:	0.517g	TESTES	:	2.748g	THYMUS	: 0.339g

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; pylorus; neck mucous cell; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7702 Group: 3 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7703 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 205g

Organ Weights:

ADRENAL GLANDS	:	0.038g<	BRAIN	:	1.840g	KIDNEYS	:	1.823g
EPIDIDYMIDES	:	0.588g	HEART	:	0.779g<	LIVER	:	7.151g
SPLEEN	:	0.491g	TESTES	:	2.965g	THYMUS	:	0.314g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7703 Group: 3 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7704 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 209g

Organ Weights:

ADRENAL GLANDS	:	0.038g<	BRAIN	:	1.838g	KIDNEYS	:	1.991g
EPIDIDYMIDES	:	0.612g	HEART	:	0.749g<	LIVER	:	7.702g
SPLEEN	:	0.495g	TESTES	:	2.842g	THYMUS	:	0.350g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7704 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC	MESENTERIC TISSUE
PROSTATE	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7705 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
Soiling, Periocular; Red

Palpable Mass Details:
None

Terminal Body Weight: 215g

Organ Weights:

ADRENAL GLANDS	:	0.033g<	BRAIN	:	1.829g	KIDNEYS	:	1.945g
EPIDIDYMIDES	:	0.622g	HEART	:	0.798g<	LIVER	:	7.709g
SPLEEN	:	0.512g	TESTES	:	2.883g	THYMUS	:	0.324g

Gross Pathology Observations:

EYE;
Cloudy; cornea; right

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

EYE;
Comment: There was no histologic correlate for the gross diagnosis of 'cloudy cornea' in the sections examined.

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7705 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	EYE	LYMPH NODE - MESENTERIC
MESENTERIC TISSUE	PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7706 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 209g

Organ Weights:

ADRENAL GLANDS	:	0.033g<	BRAIN	:	1.826g	KIDNEYS	:	1.902g
EPIDIDYMIDES	:	0.567g	HEART	:	0.781g<	LIVER	:	7.148g
SPLEEN	:	0.511g	TESTES	:	2.981g	THYMUS	:	0.339g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7706 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Inflammation; chronic active; nonglandular mucosa; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC	MESENTERIC TISSUE
PROSTATE	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7707 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 209g

Organ Weights:

ADRENAL GLANDS	:	0.034g<	BRAIN	:	1.874g	KIDNEYS	: 1.791g
EPIDIDYMIDES	:	0.503g	HEART	:	0.794g<	LIVER	: 7.007g
SPLEEN	:	0.553g	TESTES	:	2.865g	THYMUS	: 0.334g

Gross Pathology Observations:

EYE;
Cloudy; cornea; bilateral

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; focal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7707 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC	MESENTERIC TISSUE
PROSTATE	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7708 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

Eye, Cloudy; Right
Eye, Enlarged or Protruding; Right

Palpable Mass Details:

None

Terminal Body Weight: 213g

Organ Weights:

ADRENAL GLANDS	:	0.036g<	BRAIN	:	1.875g	KIDNEYS	:	1.851g
EPIDIDYMIDES	:	0.541g	HEART	:	0.801g<	LIVER	:	7.279g
SPLEEN	:	0.524g	TESTES	:	2.911g	THYMUS	:	0.335g

Gross Pathology Observations:

EYE;
Cloudy; cornea; right

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight

EYE;
Inflammation; subacute; cornea; focal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7708 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; pylorus; neck mucous cell; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7709 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 218g

Organ Weights:

ADRENAL GLANDS	:	0.039g<	BRAIN	:	1.863g	KIDNEYS	:	1.989g
EPIDIDYMIDES	:	0.565g	HEART	:	0.812g<	LIVER	:	7.390g
SPLEEN	:	0.503g	TESTES	:	2.954g	THYMUS	:	0.356g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7709 Group: 3 Sex: Male (continued)

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
PROSTATE	SALIVARY GLAND	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7710 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 215g

Organ Weights:

ADRENAL GLANDS	:	0.042g<	BRAIN	:	1.851g	KIDNEYS	:	2.025g
EPIDIDYMIDES	:	0.551g	HEART	:	0.912g<	LIVER	:	7.377g
SPLEEN	:	0.525g	TESTES	:	2.939g	THYMUS	:	0.340g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; very slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7710 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Inflammation; chronic active; nonglandular mucosa; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	LYMPH NODE - MESENTERIC	MESENTERIC TISSUE
PROSTATE	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7711 Group: 3 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/25/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/25/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 219g

Organ Weights:

ADRENAL GLANDS	:	0.036g<	BRAIN	:	1.858g	KIDNEYS	: 1.990g
EPIDIDYMIDES	:	0.571g	HEART	:	0.773g<	LIVER	: 7.619g
SPLEEN	:	0.496g	TESTES	:	2.907g	THYMUS	: 0.388g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

PROSTATE;
Inflammation; subacute to chronic; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7711 Group: 3 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	BONE MARROW	COAGULATING GLAND	DUODENUM	LYMPH NODE - MESENTERIC
MESENTERIC TISSUE	SEMINAL VESICLES	SKIN AND SUBCUTIS	THYMUS	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7742 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 128g

Organ Weights:

ADRENAL GLANDS	0.041g<	BRAIN	1.682g	KIDNEYS	1.067g
HEART	0.443g<	LIVER	4.099g	SPLEEN	0.346g
THYMUS	0.269g				

Gross Pathology Observations:

LIVER;
Focus; pale; papillary process

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

LIVER;
Comment: There was no histologic correlate for the gross diagnosis of
'pale focus, papillary process' in the section examined.

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7742 Group: 3 Sex: Female (continued)

Histo Pathology Observations: (continued)

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

The following tissues were within normal limits:

BONE MARROW	CERVIX	LIVER	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7743 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 137g

Organ Weights:

ADRENAL GLANDS	:	0.049g<	BRAIN	:	1.699g	KIDNEYS	: 1.309g
HEART	:	0.523g<	LIVER	:	4.723g	SPLEEN	: 0.418g
THYMUS	:	0.286g					

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; very slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7743 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE	SALIVARY GLAND
SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7744 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 136g

Organ Weights:

ADRENAL GLANDS	:	0.047g<	BRAIN	:	1.717g	KIDNEYS	:	1.203g
HEART	:	0.511g<	LIVER	:	4.325g	SPLEEN	:	0.392g
THYMUS	:	0.275g						

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7744 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE	SALIVARY GLAND
SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7745 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
GI, Maloccluded Incisors; Not Clipped

Palpable Mass Details:
None

Terminal Body Weight: 140g

Organ Weights:

ADRENAL GLANDS	0.045g<	BRAIN	1.748g	KIDNEYS	1.248g
HEART	0.536g<	LIVER	4.300g	SPLEEN	0.404g
THYMUS	0.263g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7745 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE	SALIVARY GLAND
SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7746 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 137g

Organ Weights:

ADRENAL GLANDS	0.048g<	BRAIN	1.713g	KIDNEYS	1.223g
HEART	0.520g<	LIVER	4.707g	SPLEEN	0.386g
THYMUS	0.281g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7746 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7747 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 137g

Organ Weights:

ADRENAL GLANDS	0.044g<	BRAIN	1.719g	KIDNEYS	1.178g
HEART	0.527g<	LIVER	4.317g	SPLEEN	0.377g
THYMUS	0.298g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7747 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE	SALIVARY GLAND
SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7748 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 139g

Organ Weights:

ADRENAL GLANDS	:	0.046g<	BRAIN	:	1.715g	KIDNEYS	:	1.206g
HEART	:	0.531g<	LIVER	:	4.238g	SPLEEN	:	0.415g
THYMUS	:	0.320g						

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7748 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE	SALIVARY GLAND
SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7749 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 140g

Organ Weights:

ADRENAL GLANDS	:	0.052g<	BRAIN	:	1.590g	KIDNEYS	:	1.253g
HEART	:	0.502g<	LIVER	:	4.780g	SPLEEN	:	0.421g
THYMUS	:	0.266g						

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7749 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7750 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 139g

Organ Weights:

ADRENAL GLANDS	:	0.044g<	BRAIN	:	1.778g	KIDNEYS	:	1.167g
HEART	:	0.513g<	LIVER	:	4.304g	SPLEEN	:	0.403g
THYMUS	:	0.319g						

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; focal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; epithelium; nonglandular mucosa; multifocal; slight
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7750 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7751 Group: 3 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 100 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 02/26/2003 Study Day No. (Week): 31 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 02/26/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 142g

Organ Weights:

ADRENAL GLANDS	0.050g<	BRAIN	1.692g	KIDNEYS	1.229g
HEART	0.499g<	LIVER	4.421g	SPLEEN	0.402g
THYMUS	0.300g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; multifocal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; epithelium; nonglandular mucosa; multifocal; moderate
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 7751 Group: 3 Sex: Female (continued)

The following tissues were within normal limits:

BONE MARROW	CERVIX	DUODENUM	LYMPH NODE - MESENTERIC		MESENTERIC TISSUE
SALIVARY GLAND	SKIN AND SUBCUTIS	THYMUS	UTERUS	VAGINA	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 9994 Group: 4 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 1000 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : . Study Day No. (Week): Unknown Mode of Death: Unknown
Date of Necropsy: Unknown Necropsy Pathologist: Unknown

Pathologist: Unknown

Last Clinical Observations:
Removed

Palpable Mass Details:
None

Terminal Body Weight: None

Gross Pathology Observations: None

Histo Pathology Observations: None

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 9998 Group: 4 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 1000 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : . Study Day No. (Week): Unknown Mode of Death: Unknown
Date of Necropsy: Unknown Necropsy Pathologist: Unknown

Pathologist: Unknown

Last Clinical Observations:
Removed

Palpable Mass Details:
None

Terminal Body Weight: None

Gross Pathology Observations: None

Histo Pathology Observations: None

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 81 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 186g<

Organ Weights:

ADRENAL GLANDS	:	0.056g<	BRAIN	:	1.817g	KIDNEYS	:	1.818g
EPIDIDYMIDES	:	0.695g	HEART	:	0.661g<	LIVER	:	6.661g
SPLEEN	:	0.433g	TESTES	:	3.165g	THYMUS	:	0.242g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight: Comment: In all affected animals, the hypertrophic cells of the zona fasciculata contained finely vacuolated cytoplasm consistent with increased steroid hormone synthesis.

BONE MARROW;
Hypocellularity; all cell lines; diffuse; slight

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 81 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight: Comment: In all affected animals, the overall thickness of the mucosa is slightly increased. Crypts are more elongated and lined by hyperplastic epithelium with increased numbers of mitoses. There is variable increase in the numbers and/or size of the goblet cells lining the crypts and villi. The mucosa is also hyperemic.
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; adjacent to necrotic or degenerative hepatocytes; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight: Comments: In all affected animals, compared to that of controls, there is variable increase in the numbers of histiocytes in the sinusoids of some of the lymph nodes in the mesenteric lymph node chain. . Along with the histiocytes there are also variable numbers of mast cells, plasma cells and red blood cells in the sinusoids, consistent with draining of ulcerated and inflammed stomach.

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 81 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate: Comment: In all affected animals, the thickness of the adipose tissue in the deep dermis is decreased.
Atrophy; hair follicle; sebaceous gland; diffuse; moderate: Comment: In all affected animals, the hair follicles and sebaceous glands are atrophied with very few or no deep seated plump anagen follicles.

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate: Comment: In all affected animals, the nonglandular gastric mucosa is variably ulcerated, hyperplastic and hyperkeratotic. There is chronic active inflammation of the mucosa and variably the submucosa characterized by fibrosis, infiltration with eosinophils, neutrophils and lesser numbers of lymphocytes and macrophages. In some animals, there are occasional free hair shafts, or vegetable matter in the lamina propria surrounded by macrophages or multinucleated giant cells.
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

THYMUS;
Atrophy; very slight

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG
LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 81 Group: 5 Sex: Male (continued)

The following tissues were within normal limits: (continued)

PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR		SPLEEN	TESTES
THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 82 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 161g<

Organ Weights:

ADRENAL GLANDS	:	0.053g<	BRAIN	:	1.749g	KIDNEYS	: 1.579g
EPIDIDYMIDES	:	0.572g	HEART	:	0.599g<	LIVER	: 5.350g
SPLEEN	:	0.400g	TESTES	:	2.783g	THYMUS	: 0.206g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 82 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

NASAL TISSUE - PHARYNX;
Inflammation; chronic active; respiratory epithelium; multifocal; very slight

PROSTATE;
Decreased Secretory Material; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 82 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	ORAL TISSUE	PANCREAS
PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM	SKELETAL MUSCLE
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	TESTES	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER			

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 83 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 145g<

Organ Weights:

ADRENAL GLANDS	:	0.040g<	BRAIN	:	1.752g	KIDNEYS	:	1.382g
EPIDIDYMIDES	:	0.440g	HEART	:	0.538g<	LIVER	:	4.917g
SPLEEN	:	0.401g	TESTES	:	2.449g	THYMUS	:	0.177g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

BRAIN;
Degeneration; axonal; optic tract; unilateral; multifocal; very slight

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 83 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

CRANIAL NERVE - OPTIC;
Degeneration; axonal; unilateral; multifocal; slight

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Atrophy; retina; unilateral; moderate
Mineralization; cornea; bilateral; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; focal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 83 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	CECUM	COLON	EPIDIDYMIDES
ESOPHAGUS	ILEUM	JEJUNUM	LACRIMAL/HARDERIAN GLAND		LARYNX
LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 84 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 152g<

Organ Weights:

ADRENAL GLANDS	:	0.053g<	BRAIN	:	1.734g	KIDNEYS	:	1.517g
EPIDIDYMIDES	:	0.536g	HEART	:	0.547g<	LIVER	:	4.954g
SPLEEN	:	0.394g	TESTES	:	2.962g	THYMUS	:	0.191g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 84 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

THYMUS;
Atrophy; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 84 Group: 5 Sex: Male (continued)

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
TESTES	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 85 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 160g<

Organ Weights:

ADRENAL GLANDS	:	0.047g<	BRAIN	:	1.784g	KIDNEYS	:	1.498g
EPIDIDYMIDES	:	0.579g	HEART	:	0.557g<	LIVER	:	5.253g
SPLEEN	:	0.416g	TESTES	:	2.824g	THYMUS	:	0.206g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 85 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight
Inflammation; subacute to chronic; multifocal; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 85 Group: 5 Sex: Male (continued)

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	EYE	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
TESTES	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 86 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 159g<

Organ Weights:

ADRENAL GLANDS	:	0.044g<	BRAIN	:	1.818g	KIDNEYS	:	1.512g
EPIDIDYMIDES	:	0.560g	HEART	:	0.562g<	LIVER	:	5.196g
SPLEEN	:	0.426g	TESTES	:	2.769g	THYMUS	:	0.165g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 86 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; focal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; adjacent to necrotic or degenerative hepatocytes; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; moderate

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 86 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

THYMUS;
Atrophy; very slight

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	EYE	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG
LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
PANCREAS	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM	SKELETAL MUSCLE
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	TESTES	THYROID GLAND
TRACHEA	URINARY BLADDER				

The following tissues have not been examined:

PARATHYROID GLAND; MISSING

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 87 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 172g<

Organ Weights:

ADRENAL GLANDS	:	0.068g<	BRAIN	:	1.781g	KIDNEYS	:	1.653g
EPIDIDYMIDES	:	0.625g	HEART	:	0.592g<	LIVER	:	5.733g
SPLEEN	:	0.418g	TESTES	:	3.045g	THYMUS	:	0.186g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 87 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

KIDNEYS;
Degeneration; with regeneration; tubule; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; moderate

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight
Inflammation; subacute to chronic; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 87 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

THYMUS;
Atrophy; very slight

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	HEART	ILEUM
JEJUNUM	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER	LUNG
LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	TESTES
THYROID GLAND	TRACHEA	URINARY BLADDER			

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 88 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 170g<

Organ Weights:

ADRENAL GLANDS	:	0.049g<	BRAIN	:	1.773g	KIDNEYS	:	1.622g
EPIDIDYMIDES	:	0.593g	HEART	:	0.582g<	LIVER	:	5.655g
SPLEEN	:	0.434g	TESTES	:	2.951g	THYMUS	:	0.205g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 88 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; adjacent to necrotic or degenerative hepatocytes; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight
Inflammation; subacute to chronic; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 88 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; slight
Ulcer; nonglandular mucosa

THYMUS;
Atrophy; very slight

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	EYE	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LUNG
LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE
PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	TESTES
THYROID GLAND	TRACHEA	URINARY BLADDER			

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 89 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 170g<

Organ Weights:

ADRENAL GLANDS	:	0.050g<	BRAIN	:	1.814g	KIDNEYS	: 1.706g
EPIDIDYMIDES	:	0.659g	HEART	:	0.598g<	LIVER	: 5.696g
SPLEEN	:	0.423g	TESTES	:	3.027g	THYMUS	: 0.211g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; very slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 89 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

LIVER;
Aggregates Of Macrophages - Histiocytes; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; very slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; slight
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; slight

THYMUS;
Atrophy; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 89 Group: 5 Sex: Male (continued)

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	EYE	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX	
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
TESTES	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 90 Group: 5 Sex: Male Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
Soiling, Periocular; Red

Palpable Mass Details:
None

Terminal Body Weight: 155g<

Organ Weights:

ADRENAL GLANDS	:	0.037g<	BRAIN	:	1.730g	KIDNEYS	: 1.493g
EPIDIDYMIDES	:	0.535g	HEART	:	0.531g<	LIVER	: 5.345g
SPLEEN	:	0.395g	TESTES	:	2.819g	THYMUS	: 0.183g

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

ADRENAL GLANDS;
Hypertrophy; zona fasciculata; bilateral; very slight

BONE MARROW;
Hypocellularity; all cell lines; diffuse; moderate

COAGULATING GLAND;
Decreased Secretory Material; bilateral; slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 90 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

DUODENUM; (continued)
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; moderate

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

PROSTATE;
Decreased Secretory Material; slight
Inflammation; subacute to chronic; multifocal; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight: Comment: In all the affected animals, there is slight diffuse hypertrophy of the acini of the submandibular salivary gland.

SEMINAL VESICLES;
Decreased Secretory Material; bilateral; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; moderate
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 90 Group: 5 Sex: Male (continued)

Histo Pathology Observations: (continued)

THYMUS;
Atrophy; very slight

The following tissues were within normal limits:

AORTA	BONE	BONE - JOINT	BRAIN	CECUM	COLON
CRANIAL NERVE - OPTIC		EPIDIDYMIDES	ESOPHAGUS	EYE	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LIVER	LUNG	LYMPH NODE - MEDIASTINAL		MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX
ORAL TISSUE	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
TESTES	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 91 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 117g<

Organ Weights:

ADRENAL GLANDS	: 0.038g<	BRAIN	: 1.665g	KIDNEYS	: 1.046g
HEART	: 0.431g<	LIVER	: 3.754g	SPLEEN	: 0.355g
THYMUS	: 0.216g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

CERVIX;
Atrophy; very slight

DUODENUM;
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; multifocal; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 91 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; slight
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	ILEUM	JEJUNUM
KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER	LUNG
LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC		MAMMARY GLAND	MEDIASTINAL TISSUE
MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES	OVIDUCT
PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER			

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 92 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 115g<

Organ Weights:

ADRENAL GLANDS	0.033g<	BRAIN	1.708g	KIDNEYS	1.079g
HEART	0.418g<	LIVER	3.566g	SPLEEN	0.326g
THYMUS	0.249g				

Gross Pathology Observations:

LIVER;
Hernia; right medial lobe

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 92 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

LIVER;
Architecture Altered Secondary To Diaphragmatic Hernia; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; moderate

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
CERVIX	COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	EYE
HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND	
LARYNX	LUNG	LYMPH NODE - MEDIASTINAL		MAMMARY GLAND	MEDIASTINAL TISSUE
NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES	OVIDUCT	PANCREAS

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 92 Group: 5 Sex: Female (continued)

The following tissues were within normal limits: (continued)

PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL	PITUITARY GLAND	RECTUM	SKELETAL MUSCLE
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR		SPLEEN	THYMUS	THYROID GLAND
TRACHEA	URINARY BLADDER			

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 93 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 124g<

Organ Weights:

ADRENAL GLANDS	0.045g<	BRAIN	1.671g	KIDNEYS	1.125g
HEART	0.475g<	LIVER	3.879g	SPLEEN	0.348g
THYMUS	0.280g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

CERVIX;
Atrophy; very slight

DUODENUM;
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 93 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	EYE	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LIVER	LUNG	LYMPH NODE - MEDIASTINAL		MAMMARY GLAND	MEDIASTINAL TISSUE
NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES	OVIDUCT	PANCREAS
PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM	SKELETAL MUSCLE
SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	THYMUS	THYROID GLAND
TRACHEA	URINARY BLADDER				

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 94 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 136g

Organ Weights:

ADRENAL GLANDS	:	0.042g<	BRAIN	:	1.732g	KIDNEYS	: 1.246g
HEART	:	0.481g<	LIVER	:	3.990g	SPLEEN	: 0.383g
THYMUS	:	0.277g					

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

DUODENUM;
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 94 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; very slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
CERVIX	COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	EYE
HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND	
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		MAMMARY GLAND
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES
OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR		
SPLEEN	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 95 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

Eye, Cloudy; Left
Misc, Thin

Palpable Mass Details:

None

Terminal Body Weight: 104g<

Organ Weights:

ADRENAL GLANDS	0.030g<	BRAIN	1.615g	KIDNEYS	0.972g<
HEART	0.416g<	LIVER	3.058g	SPLEEN	0.322g
THYMUS	0.218g				

Gross Pathology Observations:

CRANIAL NERVE - OPTIC;
Neither optic nerve could be located at necropsy.
Absent; bilateral

LIVER;
Hernia; left medial lobe

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 95 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

CERVIX;
Atrophy; very slight

CRANIAL NERVE - OPTIC;
Aplasia; bilateral

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Atrophy; retina; bilateral; moderate: Comment: There is moderate thinning of the inner nuclear layer and slight atrophy of the ganglion cell layer. Also there are focal rosettes in both retinas. Stringy thick network of vitreous material contains occasional small capillaries (organization) and adherent to the inner limiting membrane of the retina.
Mineralization; cornea; unilateral; multifocal; very slight

HEART;
Degeneration; with or without inflammation; myocardium; multifocal; slight

LIVER;
Architecture Altered Secondary To Diaphragmatic Hernia; very slight

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 95 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

STOMACH; (continued)
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; very slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
COLON	ESOPHAGUS	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND
LARYNX	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MAMMARY GLAND	MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES
OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SKIN AND SUBCUTIS	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR		
SPLEEN	THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER	

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 96 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 130g

Organ Weights:

ADRENAL GLANDS	:	0.034g<	BRAIN	:	1.721g	KIDNEYS	: 1.255g
HEART	:	0.489g<	LIVER	:	3.987g	SPLEEN	: 0.367g
THYMUS	:	0.258g					

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

CERVIX;
Atrophy; very slight

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 96 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; adipose tissue; dermis; diffuse; slight
Atrophy; hair follicle; sebaceous gland; diffuse; moderate

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	HEART	ILEUM
JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX	LIVER
LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC		MAMMARY GLAND
MEDIASTINAL TISSUE	MESENTERIC TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES
OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 97 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:

No Abnormalities Detected

Palpable Mass Details:

None

Terminal Body Weight: 115g<

Organ Weights:

ADRENAL GLANDS	:	0.037g<	BRAIN	:	1.651g	KIDNEYS	:	1.035g
HEART	:	0.411g<	LIVER	:	3.400g	SPLEEN	:	0.302g
THYMUS	:	0.270g						

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

CERVIX;
Atrophy; slight

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 97 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; very slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight

UTERUS;
Atrophy; endometrium; myometrium; slight

VAGINA;
Atrophy; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	EYE	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MAMMARY GLAND	MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES
OVIDUCT	PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND
RECTUM	SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN
THYMUS	THYROID GLAND	TRACHEA	URINARY BLADDER		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 98 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 144g

Organ Weights:

ADRENAL GLANDS	0.048g<	BRAIN	1.751g	KIDNEYS	1.318g
HEART	0.486g<	LIVER	4.670g	SPLEEN	0.391g
THYMUS	0.286g				

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

BONE MARROW;
Hypocellularity; all cell lines; diffuse; very slight

DUODENUM;
Dilatation; crypt; multifocal; very slight
Hyperplasia; epithelium; mucosa; diffuse; very slight

EYE;
Mineralization; cornea; bilateral; multifocal; very slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 98 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

ORAL TISSUE;
Inflammation; chronic active; periodontal tissue; focal; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; moderate
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BRAIN	CECUM
CERVIX	COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS	HEART
ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND		LARYNX
LIVER	LUNG	LYMPH NODE - MEDIASTINAL		LYMPH NODE - MESENTERIC	
MAMMARY GLAND	MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		OVARIES	OVIDUCT
PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	VAGINA		

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 99 Group: 5 Sex: Female Species:Rat Strain: Fischer 344

Test Material: HQDGE Dose: 200 mkd Route: Dietary Study Type: Subchronic Toxicity
Date of Death : 03/04/2003 Study Day No. (Week): 30 (5) Mode of Death: SCHEDULED NECROPSY
Date of Necropsy: 03/04/2003 Necropsy Pathologist: Johnson Thomas ** NECROPSY COMPLETE **

Pathologist: Johnson Thomas ** EXAMINATION COMPLETE **

Last Clinical Observations:
No Abnormalities Detected

Palpable Mass Details:
None

Terminal Body Weight: 135g

Organ Weights:

ADRENAL GLANDS	:	0.040g<	BRAIN	:	1.756g	KIDNEYS	: 1.233g
HEART	:	0.481g<	LIVER	:	4.262g	SPLEEN	: 0.432g
THYMUS	:	0.281g					

Gross Pathology Observations:

STOMACH;
Thickened; nonglandular mucosa; diffuse

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

DUODENUM;
Dilatation; crypt; multifocal; very slight
Necrosis; individual cell; crypt; epithelium; multifocal; very slight

EYE;
Mineralization; cornea; unilateral; multifocal; very slight

LYMPH NODE - MESENTERIC;
Sinus Histiocytosis; increased; slight

Codes Used:.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX TABLE 40. Individual Animal Pathology Report (continued)

Animal No.: 99 Group: 5 Sex: Female (continued)

Histo Pathology Observations: (continued)

MESENTERIC TISSUE;
Atrophy; adipose tissue; slight

SALIVARY GLAND;
Hypertrophy; acinus; diffuse; slight

SKIN AND SUBCUTIS;
Atrophy; hair follicle; sebaceous gland; diffuse; slight

STOMACH;
Dilatation; glandular lumen; pylorus; multifocal; very slight
Hyperkeratosis; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; epithelium; nonglandular mucosa; diffuse; moderate
Hyperplasia; pylorus; neck mucous cell; slight
Inflammation; chronic active; nonglandular mucosa; slight
Necrosis; individual cell; glandular; pylorus; multifocal; very slight
Ulcer; nonglandular mucosa

UTERUS;
Atrophy; endometrium; myometrium; slight

The following tissues were within normal limits:

ADRENAL GLANDS	AORTA	BONE	BONE - JOINT	BONE MARROW	BRAIN
CECUM	CERVIX	COLON	CRANIAL NERVE - OPTIC		ESOPHAGUS
HEART	ILEUM	JEJUNUM	KIDNEYS	LACRIMAL/HARDERIAN GLAND	
LARYNX	LIVER	LUNG	LYMPH NODE - MEDIASTINAL		MAMMARY GLAND
MEDIASTINAL TISSUE	NASAL TISSUE - PHARYNX		ORAL TISSUE	OVARIES	OVIDUCT
PANCREAS	PARATHYROID GLAND	PERIPHERAL NERVE - TIBIAL		PITUITARY GLAND	RECTUM
SKELETAL MUSCLE	SPINAL CORD - CERVICAL, THORACIC AND LUMBAR			SPLEEN	THYMUS
THYROID GLAND	TRACHEA	URINARY BLADDER	VAGINA		

Codes Used:.

APPENDIX A. Explicitly Defined Scales for DCOs and Sensory Evaluation

DCO Examination Conduct

The clinical examination is conducted in a careful and systematic format. The examination begins at the head of the animal and gradually works towards the tail as outlined below.

A. Cage-side observations are made first.

1. Categorical observations include: Unusual body movements (*e.g.*, tremors, convulsions), abnormal behaviors (*e.g.*, circling, stereotypy) and changes in posture (*e.g.*, arched back, splayed stance).

2. Resistance to Removal: The degree to which the animal attempts to escape capture is scored. The observer will slowly present a gloved hand into the cage and will grasp the animal over the shoulder area or by the tail.

   1 = Decrease – clearly less resistance to capture than typical
   2 = Typical – minimally to actively avoids capture and may be mildly aggressive
   3 = Increase – clearly more resistance to capture than typical and is very aggressive (attempts to bite)

B. Eye observations: Eyes are bilaterally examined for these effects; however, if a unilateral observation is made, a concurrent observation is not made for the other eye if it is within typical limits.

1. Palpebral closure:

   1 = Closed (50% to completely closed)
   2 = Open
   3 = Protruding eyes

2. Pupil size (aided by penlight): Under typical examination conditions (white light), the typical appearance of the pupils in albino animals is complete constriction. Therefore a decrease in pupil size cannot be observed.

   0 = Unable to evaluate
   1 = Decrease – clearly decreased pupil size compared to typical
   2 = Typical – completely constricted pupils
   3 = Increase – clearly increased pupil size compared to typical

3. Lacrimation (clear wetness): Under typical examination conditions, corneal dryness is not observed in rodents, nor are the eyelids excessively wet.

   1 = Decrease – extremely dry appearance of cornea
   2 = Typical – glistening cornea (moderate dryness or wetness)
   3 = Increase – extensive wetness around the eyes

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX A. Explicitly Defined Scales For DCOs and Sensory Evaluation (continued)

C. Degree of salivation: Under typical examination conditions, dryness of the oral cavity is not observed in rodents.

1 = Decrease – oral dryness
2 = Typical – limited to moderate perioral wetness, but lips and chin are dry
3 = Increase – extensive wetness around the mouth and lips

D. Muscle tone: An assessment of muscle tone at the time of the hand-held observations.

1 = Decrease – clearly less muscle tone than typical
2 = Typical – animal is neither very relaxed nor very tense
3 = Increase – clearly more muscle tone than typical

E. Extensor-thrust response: Extent of reflex response to brisk pushes (by finger) on the plantar surface of the hindfeet.

1 = Decrease – clearly less response than typical
2 = Typical – clearly detectable extensor-thrust response
3 = Increase – clearly more response than typical

F. Reactivity to handling: The degree to which an animal struggles to get free from hand-held restraint is ranked.

1 = Decrease – very slight or no struggling
2 = Typical – mild to moderate struggling, animal may vocalize
3 = Increase – aggressive escape behavior, may try to bite observer and usually vocalizes

G. Observations made in the open-field.

1. Responsiveness to touch: The ventral aspect of the tail is lightly stroked using a finger. Typically, the animal will lift its tail and wrap it around the finger when lightly touched.

1 = Decrease – does not lift tail, but may briefly hold tail in the air when manually lifted; no response to touch
2 = Typical – lifts tail when touched
3 = Increase – lifts tail and acts startled, may turn towards finger in an attack response

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX A. Explicitly Defined Scales For DCOs and Sensory Evaluation (continued)

2. Gait evaluation: Open-field observations are used for gait evaluation. If the animal remains motionless in the open-field, it may be forced to walk on its forelegs while the hindlegs are held off the floor of the observation box ("the wheel-barrow test").

   1 = Unable to walk
   2 = Clear knuckling, stumbling and poor coordination, may include falling and/or dragging of one or more limbs
   3 = Typical – smooth and coordinated gait

H. Categorical Observations: These observations can be made at anytime during the DCOs. For the categories listed below, the observer directly records the positive observation.

1.	Abnormal behavior	Description
2.	Abnormalities of the eye	Description
3.	Abnormal urine or feces	Description
4.	Abnormalities of the gastrointestinal tract	Description
5.	Injury	Description
6.	Missing extremity	Description
7.	Abnormal muscle movements	Description
8.	Palpable mass/swellings	Description
9.	Abnormal posture	Description
10.	Abnormalities of the reproductive system	Description
11.	Abnormal respiration	Description
12.	Abnormal skin or hair coat/mucous membranes	Description
13.	Excessive soiling	Description
14.	General abnormalities	Description

Sensory Evaluation

1. Responsiveness to tail pinch (nociception): The animal should be stationary when this response is elicited, however, with very active animals it may be necessary to perform the procedure while the animal is moving. To elicit the nociceptive reflex, firmly pinch the tail approximately 2 cm from the tip of the tail.

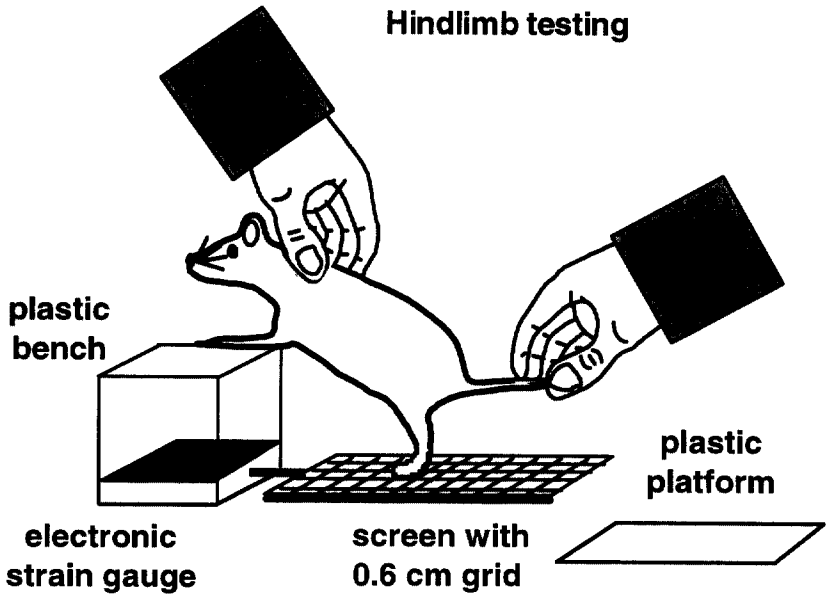
   1 = None; no response to pinch
   2 = Minimal flinch, does not vocalize or bend toward tail
   3 = Moderate flinch, and/or vocalizes
   4 = Pronounced flinch, animal bends towards the tail and vocalizes
   5 = Exaggerated response to pinch; same as a 4 but includes an attempt to attack the source of the stimulation

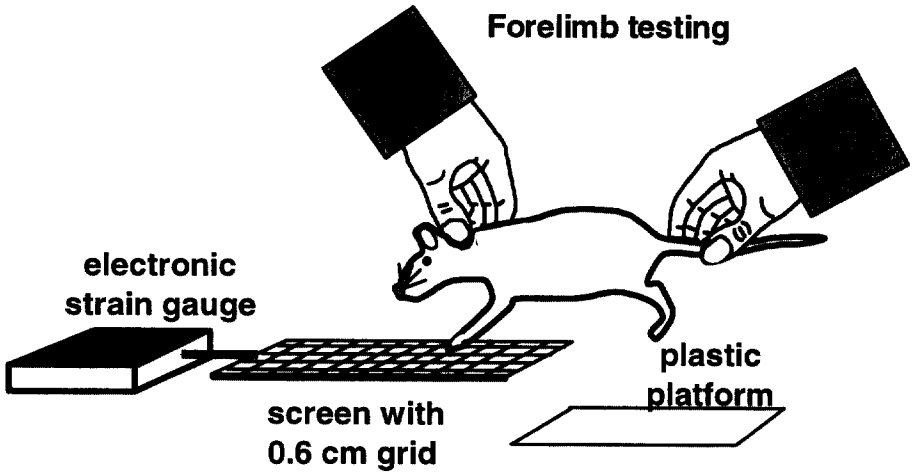
2. Responsive to sharp noise: An approximately 100 dB click stimulus is elicited by button activation of a Coulbourn click module. The goal is to present the stimulus when the animal is stationary, however, if the animal is too active, present stimulus when the animal is least active.

   1 = None; no response to click
   2 = Minimal; only the ears move
   3 = Moderate; clear movement of the head, neck and ears
   4 = Pronounced; clear movement of head, neck and ears, plus clear movement of body.
   5 = Exaggerated; whole body response to stimulus, more intense than 4

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX B. Grip Performance Apparatus





HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX C. Motor Activity

Motor activity is conducted in special devices (usually referred to as motor activity cages or chambers) which are visually isolated from each other and are located in a quiet, light-attenuated room. The devices are monitored using a commercially available system (Med Associates, St. Albans, Vermont) and rats are tested one per cage. Each of the motor activity chambers consists of two concentric cylinders that form an alley between them (similar to that of Richelle *et al.,* 1967 and Fontaine *et al.,* 1966). The cylinders are made of clear acrylic. The whole device has a circular lid that has small ventilation holes drilled in it. The outer diameter of the outer cylinder is ~35.6 cm, the outer diameter of the inner cylinder is ~14 cm, the width of the alley is ~10.2 cm. The height of the cylinders is ~13.3 cm. A photocell consisting of an emitter and a receiver is mounted at a height of ~3.5 cm from the base just outside of the outer cylinder. The emitter and the receiver are mounted opposite to each other. Figures C-1 and C-2 illustrate this device. The photocell emitter produces an infrared (IR) photobeam that falls on the receiver, bisecting the chamber so that the beam crosses the alley in two locations. Whenever an animal crosses in front of a beam, an interruption in the beam is detected. If the beam is broken for more than 100 msec following an inter-beam break duration that is greater than 100 msec, then that beam break is recorded as an activity count (these minimum durations were set to try and minimize recording of tail-flicking, head-bobbing, etc.). Motor activity data are reported as the square root of activity counts and as untransformed counts.

HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX C. Motor Activity (continued)

Figure C-1. Side View of Motor Activity Device

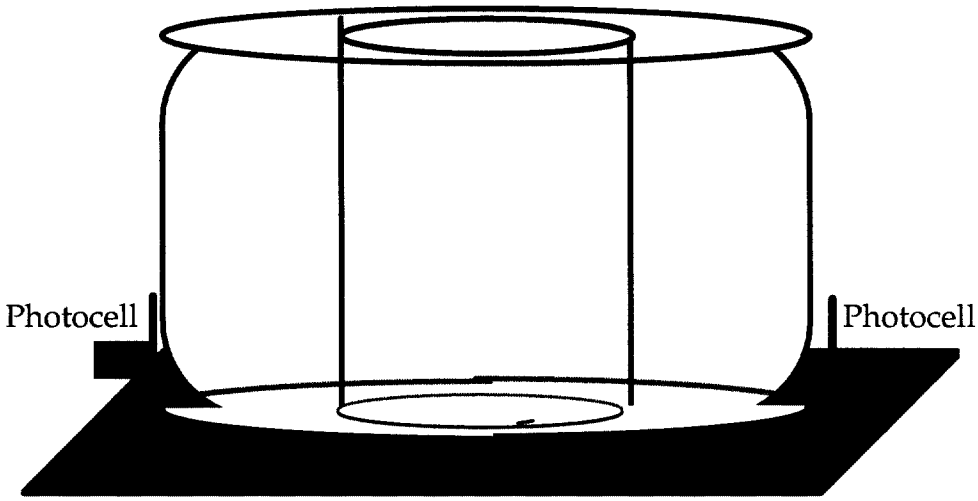
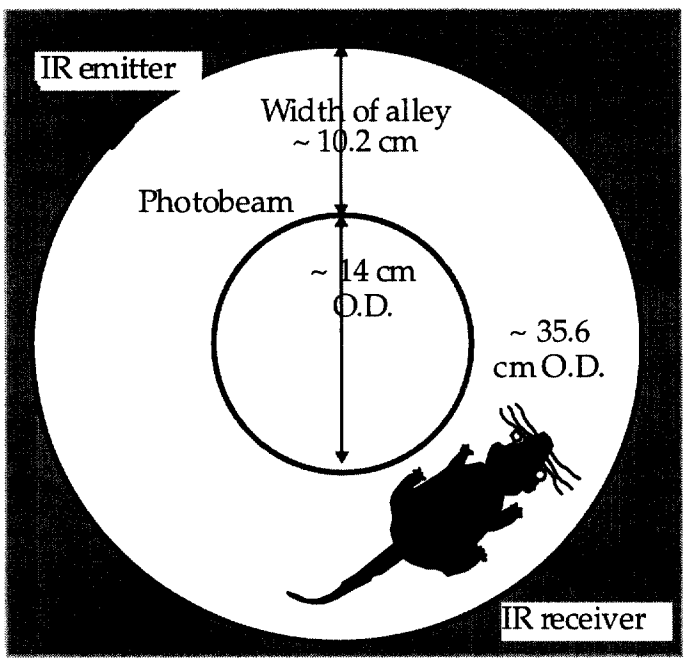


Figure C-2. Top-Down View of Motor Activity Device.



HQDGE: 28-DAY DIETARY TOXICITY STUDY IN FISCHER 344 RATS

APPENDIX C. Motor Activity (continued)