TRADE SECRET

Study Title

H-24678: Two-Week Inhalation Toxicity Study in Male Rats

Laboratory Project ID: DuPont-8685

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STUDY COMPLETED ON: April 2, 2003

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
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WORK REQUEST NUMBER: [redacted]

SERVICE CODE NUMBER: [redacted]

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA TSCA (40 CFR part 792) Good Laboratory Practice Standards except for the item documented below. The item listed does not impact the validity of the study.

The test substance is commercially available and was characterized by the supplier prior to the initiation of this study. An analysis was provided. Although the characterization was not performed under Good Laboratory Practice Standards, based on our knowledge of the performing laboratory and its experience with analyzing this chemical, we have no reason to doubt the validity of the analysis.

Applicant / Sponsor: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Director: _____ 2-APR-2003
David P. Kelly, B.S. Date
Research Toxicologist

Applicant / Sponsor: _____ _____
DuPont Representative Date

QUALITY ASSURANCE STATEMENT

Haskell Sample Number(s):

24678

Dates of Inspections:

Protocol: August 2, 2002

Conduct: August 5,8,13, 2002

Records, Reports: March 3-7,11, 2003

Dates Findings Reported to:

Study Director: March 20, 2003

Management: March 26, 2003

Reported by: Matthew T. Frentzel, BS. 2-Apr-2003
Quality Assurance Auditor Date

CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Clinical Pathology Evaluation Reported by: _____ 28-MAR-2003
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Diplomate A.C.V.P.
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Anatomic Pathology Evaluation Reported by: _____ 2-April-2003
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STUDY INFORMATION

Substance Tested: [redacted]

Synonyms/Codes:
- [redacted]
- H-24678
- [redacted]

Haskell Number: 24678

Composition: [redacted]

Known Impurities: [redacted]

Physical Characteristics: [redacted]

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Study Initiated/Completed: August 2, 2002 / (see report cover page)

In-Life Initiated/Completed: August 5, 2002 / August 29, 2002

STUDY PERSONNEL

Study Director:	David P. Kelly, B.S.
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Laboratory Veterinarian:	William Singleton, D.V.M., A.C.L.A.M.

SUMMARY

Four groups of 15 male rats each were exposed to concentrations of H-24678 aerosol targeted to 0.2, 2, or 20 mg/m³ (actual mean concentrations were 0.22, 1.9, and 20 mg/m³). The mass median aerodynamic equivalent diameter of the aerosols ranged from 0.90 to 2.1 μm. All rats were exposed nose-only for 6 hours per day for a total of 9 exposures over a two-week period. A similarly comprised control group of 15 male rats was simultaneously exposed to air only.

The first 10 rats per group were designated for standard toxicity testing. The remaining 5 rats were designated for blood fluoride analysis sampling. On the day of the last exposure, collection of an overnight urine specimen was initiated for each standard toxicity rat. On the day following the last exposure, blood samples were collected for clinical analyses from each standard toxicity rat, and 5 rats per group were sacrificed for anatomic pathology examination. All remaining rats were allowed to recover for a 15-day period. At the end of the recovery period, blood and urine samples were collected for clinical analyses from each standard toxicity rat, and all surviving rats were sacrificed. Only the standard toxicity rats were given an anatomic pathology examination.

No deleterious effects were observed in clinical observations during the exposure or recovery periods, and body weights were similar in test and control rats. Clinical pathology evaluations, including fluoride measurements, showed no effects in urine, hematology, or blood chemistry parameters as a result of exposure to H-24678.

Small amounts of fluorine (approximately 2 ppm), slightly above background, were detected in the blood of rats in the 20 mg/m³ group on test days 0, 3, and 9 (compared to test day 9 control data) indicating the presence of the test compound or its metabolites. No above-background fluorine was detected in rats exposed at this concentration after the 2-week recovery period (test day 24) compared to the test day 24 control group. No fluorine was detected above background levels in the 0.2 and the 2 mg/m³ groups on test day 9 (the last day of the exposure period).

Weight analysis of the major organs showed no effects attributable to the test substance. Histological findings were confined to the respiratory tract. There were no adverse effects in any other evaluated organs. Compound-related microscopic observations were present in the lungs and larynx of test day 10 sacrifice rats at concentrations of 2 and 20 mg/m³. Inflammation in the lungs, characterized by mixed inflammatory cells within scattered alveolar lumina was observed at 2 mg/m³ in 1 of 5 rats and at 20 mg/m³ in 3 of 5 rats. In addition, minimal to mild squamous metaplasia of the mucosa lining the ventral floor of the larynx was observed at 2 mg/m³ in 4 of 5 rats and at 20 mg/m³ in 5 of 5 rats.

There were no compound-related microscopic lesions observed in test day 24 sacrifice rats, indicating the reversibility of compound-related lesions in the lung and larynx.

The no-observed-effect level (NOEL) for this study is defined as the highest concentration at which no toxicologically important effects attributable to the test substance were detected. Thus for this study, the NOEL is equivalent to the NOEL as defined by the United States

Environmental Protection Agency (1985) and to the no-observed-adverse-effect level (NOAEL) as defined by the European Union (1994).

Based on the above findings in the respiratory tract of rats exposed to H-24678 for 2 weeks, the NOEL for repeated inhalation exposure was 0.2 mg/m^3.

INTRODUCTION

The purpose of this 2-week inhalation study was to investigate the effects of repeated inhalation exposure in rats to airborne concentrations of H-24678 aerosol. Inhalation is an expected route of human exposure. The data will be used to provide information for safe handling of the test substance. In a previous study at this laboratory with the same compound, the 4-hour approximate lethal concentration (ALC) in nose-only exposed rats was 57 mg/m³; no rats died after exposure to 23 mg/m³.[1] Immediately prior to the present study, a rangefinding experiment was conducted in groups of rats exposed nose-only for approximately 5 ½-to-6 hours/day for 6 days, within an 8-day period, to a mean concentration of approximately 18 mg/m³ of the test compound. No significant clinical signs of toxicity were observed. Following a 3-day period without exposure, the same rats were exposed for 5 hours to a mean concentration of approximately 44 mg/m³ followed by a final 4 hour and 20 minute exposure to a mean concentration of 69 mg/m³ of H-24678. Five of 6 rats died within 2 days of the last exposure. Clinical signs of toxicity observed immediately following the last exposure included: red nasal discharge, irregular respiration, and lethargy. The day following the last exposure lung noise and severe weight loss were also observed.

Based on the above information, exposure concentrations of 0.2, 2, and 20 mg/m³ were chosen for the 2-week inhalation study described in this report.

STUDY DESIGN

Four groups of 15 male rats each were exposed to concentrations of H-24678 targeted to 0, 0.2, 2, or 20 mg/m³. All rats were exposed nose-only for 6 hours per day for a total of 9 exposures.

The first 10 rats per group were designated for standard toxicity testing. Immediately following the last exposure, collection of an overnight urine specimen was initiated for each rat. On the day following the last exposure, blood samples were collected for clinical analyses from each standard toxicity rat, and 5 rats per group were sacrificed for anatomic pathology examination. All remaining rats were allowed to recover for a 15-day period. At the end of the recovery period, standard toxicity rats were fasted overnight, blood and urine samples were collected for clinical analyses from each rat, and all surviving standard toxicity rats were sacrificed for anatomic pathology examination.

The remaining 5 rats per group were designated for total fluorine analysis sampling. Blood for total fluorine analysis was collected from each rat during the exposure phase on test days 0, 3, and 9, and during the recovery period on test days 14 and 24. Selected blood samples were subsequently analyzed for fluorine, and the remaining samples were saved for possible future analysis. At the end of the recovery period, all rats were sacrificed without further examination.

All rats were weighed and individually observed for clinical signs of toxicity throughout the exposure period. Group clinical signs were observed during each exposure. In addition, the

alerting response to an auditory stimulus was checked before and during each exposure. After each exposure, rats were checked for the alerting response to an auditory stimulus prior to removal from restrainers and were observed for clinical signs immediately after they were returned to their cages. Surviving rats were weighed and individually observed for clinical signs of toxicity throughout the recovery period.

MATERIALS AND METHODS

A. Test Substance

The test substance, H-24678, was supplied by the sponsor as [redacted] Purity was [redacted] The test substance was expected to be stable throughout the exposure phase of the study; no evidence of instability was observed.

B. Animals

A total of 63 male Crl:CD®(SD)IGS BR rats was received from Charles River Laboratories, Inc., Raleigh, North Carolina. The rats were approximately 6 weeks old on the day of arrival.

Rats have historically been used in safety evaluation studies for inhalation toxicity testing. The Crl:CD®(SD)IGS BR rat was selected based on consistently acceptable health status and on extensive experience with the strain at Haskell Laboratory.

C. Animal Husbandry

1. Temporary Animal Identification and Quarantine

Upon arrival, each rat was assigned a temporary, 1- to 2-digit identification number. Rats were quarantined for 7 days prior to test initiation. During the quarantine period rats were weighed and observed 3 times for clinical signs of disease.

2. Housing

Rats were housed singly in stainless steel, wire-mesh cages suspended above cage boards.

3. Animal Room Environment

Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted to be within a temperature range of 23 ± 1°C and a relative humidity range of 50 ± 10%. Excursions outside of these ranges were of insufficient magnitude and/or duration to have adversely affected the validity of the study.

4. Animal Selection and Permanent Identification

Prior to the end of the quarantine period, rats were assigned to 4 groups of 15 male rats each. Rats were divided into groups with the aid of a computerized, stratified, randomization program, so that mean body weights for each group were similar. Rats were approximately 8 weeks old and weighed between 231 and 276 grams at the start of the exposures.

Upon grouping, each rat was assigned a unique 6-digit animal number. Following grouping, a 3-digit identification number was tattooed onto the tail of each rat.

Rats that were not assigned to a test group were sacrificed by carbon dioxide asphyxiation and discarded without anatomic pathology evaluation.

5. Feed and Water

Except during exposure, tap water was available *ad libitum*. PMI® Nutrition International, LLC Certified Rodent LabDiet® 5002 was available *ad libitum* except during exposure and fasting periods prior to necropsy.

6. Health Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Feed samples are analyzed for total bacterial, spore, and fungal counts.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Evaluation of these data did not indicate any conditions that affected the validity of the study.

D. Inhalation Exposure System
(Figure 1)

1. Atmosphere Generation

Chamber atmospheres were generated by nebulization of the test substance in air with a Spraying Systems Nebulizer. The test substance was metered into the nebulizer with a Harvard Apparatus model 22 Syringe Infusion Pump. Filtered, high-pressure air, metered into the nebulizer by a Brooks model 5878 Mass Flow Controllers, atomized the test substance and carried the resulting atmosphere through a cyclone, through a glass flow-splitter, and into the exposure chamber. The flow splitter diverted aerosol to the hood exhaust to reduce the amount of test material reaching the exposure chamber. Dilution air, metered into the chamber by a Brooks model 5878 Mass Flow Controller, helped to evenly distribute the test substance throughout the exposure chamber. The infusion pump and mass flow controllers were controlled and monitored by the Camile Inhalation Toxicology Automated Data System (CITADS). Fine control of the chamber concentration was accomplished by varying the test substance feed rate to the nebulizer.

Test atmospheres were exhausted through an MSA filter cartridge prior to discharge into the fume hood.

2. Chamber Construction and Design

All exposure chambers were constructed of stainless steel and glass (NYU style) with a nominal internal volume of 150 L. A polycarbonate baffle at the chamber inlet promoted uniform chamber distribution of the test atmosphere.

3. Exposure Mode

During exposure, animals were individually restrained in perforated stainless steel cylinders with conical nose pieces. The restrainers were inserted into a polymethylmethacrylate faceplate which was attached to the exposure chamber so that the nose of each animal protruded into the exposure chamber. Before the start of the exposure phase, animals were placed in restrainers on 2 separate days for approximately 15 minutes each day to acclimate the animals to the restrainers.

E. Characterization of Chamber Atmosphere

1. Test Substance Sampling and Analysis

The atmospheric concentration of H-24678 was determined by gravimetric analysis at approximately 60-minute intervals during each exposure. The control chamber was sampled once during the study. Known volumes of chamber atmosphere were drawn from the breathing zone of the animals through a 25 mm filter cassette that contained a pre-weighed Gelman glass fiber (Type A/E) filter. The filters were weighed on a Cahn model C-30 or C-31 Microbalance®. The filter weights were automatically transferred to CITADS, which calculated the chamber concentrations based on the difference in pre- and post-sampling filter weights divided by the

volume of chamber atmosphere sampled. Gravimetric sample start- and stop-times for each sample were controlled and recorded by CITADS.

2. Particle Size Determination

Samples to determine the aerosol particle size distribution (mass median aerodynamic diameter and geometric standard deviation) were taken once per week in the 2 and 20 mg/m³ chambers with a Sierra® Series 210 Cyclone Preseparator/Cascade Impactor and Sierra® Series 110 Constant Flow Air Sampler.(2) On the last exposure day of the study, the aerosol particle size in all 3 chambers was measured in duplicate with a QCM Impactor.(3) The QCM uses piezo-crystal sensors and allows measurement of a small mass of aerosol. The QCM sensitivity was needed to measure the particle size in the 0.2 mg/m³ test chamber.

3. Environmental Monitoring

Chamber airflows were set at the beginning of each exposure to achieve at least 12 air changes per hour and were monitored continually with a calibrated Brooks model 5878 Mass Flow Controller. Chamber temperature was targeted at 23 ± 2°C and was measured with an Omega type J Thermocouple Thermometer. Chamber relative humidity was targeted at 50 ± 10% and was measured with Jumo model PT100 wet-bulb/dry-bulb resistance temperature detectors. Airflow, temperature, and relative humidity were monitored continually with the CITADS and recorded at 15-minute intervals during each exposure. On 3 occasions, the relative humidity was not measured in one or more chambers over periods of 15 minutes to approximately 2 hours due to sensor problems. Based on the overall stability of the relative humidity measurements over the duration of the study, the inability to measure humidity over these 3 periods was considered not to have an effect on the study outcome. Chamber oxygen concentration was targeted to be at least 19%. Chamber oxygen concentration was measured with a Biosystems model 3100R Oxygen Analyzer and was recorded 3 times during each exposure.

F. Body Weights and Clinical Observations

During the exposure phase of the study, all rats were weighed on exposure days and individually observed for clinical signs of toxicity before and after each exposure. Group clinical observations were made during exposures. In addition, rats were checked for an alerting response to an auditory stimulus prior to each exposure, approximately every 2 hours during each exposure, and after each exposure. During the recovery period, all remaining rats were weighed and individually observed twice per week.

G. Blood Fluorine Analysis

Blood for total fluorine analyses was collected (0.5 to 1 mL) from 5 rats per group on the afternoons of test days 0, 3 and 9. Blood was also taken during the recovery period on test days 14 and 24. The blood samples were frozen for total fluorine analysis as needed. Whole blood was analyzed for fluorine in rats exposed to 20 mg/m³ of H-24678 and sampled immediately after exposure on test days 0, 3, and 9, and after a 15-day recovery period (test

day 24). Whole blood from the remaining groups was analyzed on test day 9, the last day of exposure. Unanalyzed samples were stored for possible future fluorine analysis.

The total fluorine content of the blood samples was determined using a Wickbold torch combustion method followed by analysis with a fluoride ion selective electrode.[4] The liquid whole blood was decomposed or volatilized in the presence of wet oxygen and swept through an oxy-hydrogen flame in a closed quartz apparatus. The combustion products were collected in an aqueous absorbing solution and analyzed using a fluoride ion selective electrode.

H. Clinical Pathology Evaluation

A clinical pathology evaluation was conducted on all rats designated for standard toxicity testing approximately 10 days after initiation of the study. The day before collection of samples for the clinical pathology evaluation, the animals were placed in metabolism cages. These animals were fasted overnight (approximately 16 hours) and urine was collected from each animal. Blood samples for hematology and clinical chemistry measurements were collected from the orbital sinus of each animal while the animal was under light carbon dioxide anesthesia. Blood samples for fluoride analysis were collected at sacrifice from the abdominal *vena cava* of each animal while the animal was under carbon dioxide anesthesia. Additional blood collected from the *vena cava* was placed in a serum tube, processed to serum, and frozen at -80°C. Serum was discarded without analysis because further tests were not required to support experimental findings. Bone marrow smears were prepared at sacrifice from all surviving animals. Bone marrow smears were stained with Wright's stain and coverslipped, but analysis was not necessary to support experimental findings.

1. Hematology

Blood samples were evaluated for quality by visual examination prior to analysis. Complete blood counts, including reticulocytes, were determined on a Bayer® Advia 120 hematology analyzer or determined from microscopic evaluation of the blood smear. Wright-stained blood smears from all animals were examined microscopically for confirmation of automated results and evaluation of cellular morphology. Blood smears, stained with new methylene blue, were prepared from each animal undergoing a hematology evaluation but were not needed for examination.

The following hematology parameters were determined:

red blood cell count
hemoglobin
hematocrit
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin concentration
red cell distribution width
absolute reticulocyte count
platelet count
white blood cell count
differential white blood cell count
microscopic blood smear examination

2. Clinical Chemistry

Serum clinical chemistry parameters were determined on a Roche Diagnostics (BMC)/Hitachi® 717 clinical chemistry analyzer. Plasma fluorides were determined using a phi12 pH meter and a fluoride-selective electrode.

The following clinical chemistry parameters were determined:

aspartate aminotransferase	glucose
alanine aminotransferase	total protein
sorbitol dehydrogenase	albumin
alkaline phosphatase	globulin
total bilirubin	calcium
urea nitrogen	inorganic phosphorus
creatinine	sodium
cholesterol	potassium
triglycerides	chloride
	fluoride[a]

3. Urinalysis

Urine volume was measured. Urine fluorides were determined using a phi12 pH meter and a fluoride-selective electrode.

The following urinalysis parameters were determined:

volume	fluoride[b]

4. Recovery

Clinical pathology evaluation including hematology, clinical chemistry, and plasma and urine fluoride were performed at the end of the recovery period (test day 24) according to the methods detailed above.

I. Anatomic Pathology Evaluation

Male rats were exposed to the test substance for 2 weeks (total of 9 exposures for 6 hours/exposures). Ten animals per group were exposed to the following: air only (Control Group I) and to H-24678 at 0.2 mg/m³ (Low Exposure Group III), 2 mg/m³ (Intermediate Exposure Group V), and 20 mg/m³ (High Exposure Group VII). Five animals per group were sacrificed and necropsied following the last exposure (test day 10 sacrifice). Another 5 animals

[a] Fluoride determination was analyzed on EDTA plasma.
[b] Fluoride determination was analyzed from urine with EDTA added.

per group were allowed to recover and were sacrificed and necropsied on the 15th day of recovery (test day 24 sacrifice).

Rats were euthanatized by carbon dioxide anesthesia and exsanguination. Gross examinations were performed on all rats.

The following tissues were collected from the standard toxicity study rats.

Digestive System	Respiratory System	Nervous System
liver	lungs	brain (3 cross sections)
esophagus	trachea	spinal cord (3 cross sections)
stomach	nose (4 cross sections)	peripheral nerve (sciatic)
duodenum	pharynx/larynx	
jejunum		Musculoskeletal System
ileum	Cardiovascular System	sternum
cecum	heart	
colon		Reproductive System
rectum	Hematopoietic System	testes
pancreas	spleen	epididymides
	thymus	prostate
Urinary System	mesenteric lymph node	seminal vesicles
kidneys	bone marrow[a]	
urinary bladder		Miscellaneous
	Endocrine System	eyes (including optic nerve)
	thyroid gland	gross observations
	parathyroid glands	
	adrenal glands	

a Bone marrow was collected with the sternum.

The liver, kidneys, lungs, brain, and testes were weighed at necropsy, and organ weight/final body weight and organ weight/brain weight ratios were calculated. Final body weights determined just prior to necropsy were used in the assessment of organ weight changes.

Gross lesions which were diagnosed at necropsy and for which microscopic examination was not appropriate (e.g., fluid accumulation, ruffled fur, missing anatomic parts) were generally not collected. Gross lesions for which a microscopic diagnosis would not be additive (e.g., osteoarthritis, pododermatitis, chronic dermatitis of the tail, urinary calculi, and deformity of the teeth, toe, tail, or pinna) were saved but were generally not processed for microscopic evaluation.

Testes, epididymides, and eyes were fixed in Bouin's solution. All other tissues were fixed in 10% neutral buffered formalin. Processed tissues were embedded in paraffin, cut at a nominal thickness of 5 micrometers, stained with hematoxylin and eosin (H&E), and examined microscopically.

All collected tissues from the test day 10 sacrifice rats in the control and high exposure groups were processed and received a full histopathological examination. Liver, kidneys, lungs, pharynx/larynx, testes and nose from the test day 10 sacrifice rats in the low and intermediate exposure groups (III and V) and from the test day 24 sacrifice standard toxicity rats in the control and high exposure groups (I and VII) were processed and examined microscopically.

The key to the pathology lesion grading system used in this study can be found within the pathology tables and appendices.

J. Statistical Analyses

Significance was judged at $p < 0.05$.

<table>
<tr><td rowspan="2"></td><td rowspan="2"></td><td colspan="2">Method of Statistical Analysis</td></tr>
<tr><td>Parameter</td><td>Preliminary Test</td><td>If preliminary test is not significant</td><td>If preliminary test is significant</td></tr>
<tr><td>Exposure Concentration
Data
Environmental Data</td><td>None</td><td colspan="2">Descriptive statistics (e.g., mean, standard deviation)</td></tr>
<tr><td>Blood Fluorine Analysis</td><td>None</td><td colspan="2">Student's T-test[5]</td></tr>
<tr><td rowspan="3">Body Weight
Body Weight Gain
Organ Weight</td><td>Test for lack of trend[6]</td><td>Sequential application[7] of the Jonckheere-Terpstra trend test[8]</td><td>Preliminary tests for pairwise comparison</td></tr>
<tr><td colspan="2">OR[a]</td></tr>
<tr><td>Levene's test for homogeneity[9] and Shapiro-Wilk test[10] for normality[b]</td><td>One-way analysis of variance[5] followed with Dunnett's test[11]</td><td>Kruskal-Wallis test[12] followed with Dunn's test[13]</td></tr>
<tr><td>Incidence of Clinical Observations</td><td>None</td><td colspan="2">Cochran-Armitage test for trend[5]c</td></tr>
<tr><td>Clinical Pathology[d]</td><td>Levene's test for homogeneity[9] and Shapiro-Wilk test[10] for normality[b]</td><td>One-way analysis of variance[5] followed with Dunnett's test[11]</td><td>Kruskal-Wallis test[12] followed with Dunn's test[13]</td></tr>
</table>

a Pairwise comparisons and associated preliminary tests were only conducted if the test for lack of trend was significant.

b If the Shapiro-Wilk test was not significant but Levene's test was significant, a robust version of Dunnett's test was used. If the Shapiro-Wilk test was significant, Kruskal-Wallis test was followed by Dunn's test.

c If the incidence was not significant, but a significant lack of fit occurred, then Fisher's Exact test[12] with a Bonferroni correction was used.

d When an individual observation was recorded as being less than a certain value, calculations were performed on half the recorded value. For example, if bilirubin was reported as <0.1, 0.05 was used for any calculations performed with that bilirubin data.

RESULTS AND DISCUSSION

In-Life Animal Measurements

A. Chamber Atmosphere Concentrations of H-24678 and Chamber Environmental Conditions

(Tables 1-3, Appendices A-B)

The mean chamber concentrations of H-24678 and chamber environmental conditions during the exposures are located in Tables 1 and 2, respectively. The mean, analytically determined, aerosol concentrations for the 9 exposures were 0.22, 1.9 and 20 mg/m^3 for target concentrations of 0.2, 2, and 20 mg/m^3, respectively. Targeted concentrations are used throughout this report. No aerosol was detected in the control chamber. The mass median aerodynamic equivalent diameter of the H-24678 aerosol measured in the test atmospheres ranged from 0.90 to 2.1 μm.

The chamber oxygen concentrations were 21% in all chambers. The daily mean relative humidities for the chambers ranged from 36 to 67%, and the daily mean temperatures ranged from 19 to 25°C. Although in some cases the relative humidity and temperature measurements were slightly out of range, these deviations were minor and were not expected to affect the study outcome.

B. Body Weights and Clinical Observations

(Tables 4-6, Figure 2, Appendices C-D)

The mean body weights of male and female rats exposed to H-24678 were not statistically different from those of the control rats during the overall course of the study. There was a slightly depressed weight gain on test day 7 in the 20 mg/m^3 group but the group body weights were not statistically different from those of the controls.

Nasal and ocular discharges were observed in many rats, including controls, immediately after exposure. This is a frequent observation in inhalation studies where rats are exposed in restrainers, and is not considered to be deleterious.

During the study there were no notable clinical observations that may have been related to the test treatment.

Blood Fluorine Analysis

A. Blood Fluorine Analysis
(Table 7, Appendix E)

Small amounts of fluorine (approximately 2 ppm), slightly above background (approximately 1.3 ppm in controls at test day 9), were detected in the blood of rats in the 20 mg/m³ group on test days 0, 3, and 9 (compared to test day 9 control data) indicating the presence of the test compound or its metabolites. No above-background fluorine was detected in rats exposed at this concentration after the 2-week recovery period (test day 24) compared to the test day 24 control group. No fluorine was detected above background levels in the 0.2 and the 2 mg/m³ groups on test day 9 (the last day of the exposure period).

Clinical Pathology Evaluation

A. Hematology
(Table 8, Appendix F)

There were no treatment-related or statistically significant changes in hematologic parameters in rats exposed to H-24678.

B. Clinical Chemistry
(Table 9, Appendix F)

There were no adverse changes in clinical chemistry parameters in male rats exposed to H-24678. The following statistically significant and/or treatment-related change in mean clinical chemistry parameters were considered to be non-adverse or not related to exposure to the test compound:

- Urea nitrogen was minimally decreased in males exposed to 20 mg/m³ after 10 days of treatment, and at the end of the recovery period (test days 10 and 24). At both time-points, urea nitrogen concentrations in males exposed to 20 mg/m³ were generally within the range of those in other groups, and similar to historical control values. There were no alterations in other related clinical pathology parameters (urine volume, creatinine, phosphorus), and no alterations in renal histopathology. Therefore, this change was unlikely to be related to treatment. Regardless, minimally decreased urea nitrogen has no toxicologic significance, and thus was considered non-adverse.

- Albumin was minimally increased in males exposed to 0.2 mg/m³ on test day 10. There was no dose-relationship to the response, so this change was considered to be unrelated to treatment.

C. Urine Volume
(Table 10, Appendix F)

There were no treatment-related changes in urine volume.

D. Plasma and Urine Fluoride

Exposure to H-24678 did not result in changes in plasma or urine fluoride.

E. Conclusions

In conclusion, exposure of male rats to 20 mg/m^3 H-24678 did not result in adverse changes in clinical pathology parameters. Therefore, under the conditions of this study and for the clinical pathology parameters measured, the no-adverse-effect level for male rats was 20 mg/m^3 H-24678, the highest exposure in this study.

Anatomic Pathology Evaluation

A. Mortality
(Tables 15-16)

There were no compound-related deaths in this study.

B. Organ Weights
(Tables 11-12, Appendix G)

There were no compound-related organ weight effects at either sacrifice in animals exposed to H-24678. There were no statistically significant organ weight changes at the test day 10 sacrifice. Higher mean absolute liver weight than control in high exposure group rats from the test day 24 sacrifice was attributed to higher final body weight in that group.

C. Gross Observations
(Tables 13-14, Appendix H)

There were no compound-related gross observations in this study. Discoloration of the lung was observed in 1 high exposure rat from the test day 24 sacrifice. This observation was not considered to be compound-related because there was no corresponding microscopic lesion in this rat. Other gross observations occurred in low incidences and were randomly distributed across control and treatment groups.

CONCLUSIONS

Four groups of 15 male rats each were exposed to concentrations of H-24678 aerosol targeted to 0.2, 2, or 20 mg/m³ (actual mean concentrations were 0.22, 1.9, and 20 mg/m³). The mass median aerodynamic equivalent diameter of the aerosols ranged from 0.90 to 2.1 μm. All rats were exposed nose-only for 6 hours per day for a total of 9 exposures over a 2-week period. A similarly comprised control group of 15 male rats was simultaneously exposed to air only.

No deleterious effects were observed in clinical observations during the exposure or recovery periods, and body weights were similar in test and control rats. Clinical pathology evaluations, including fluoride measurements, showed no effects in urine, hematology, or blood chemistry parameters as a result of exposure to H-24678.

Small amounts of fluorine (approximately 2 ppm), slightly above background, were detected in the blood of rats in the 20 mg/m³ group on test days 0, 3, and 9 (compared to test day 9 control data) indicating the presence of the test compound or its metabolites. No above-background fluorine was detected in rats exposed at this concentration after the 2-week recovery period (test day 24) compared to the test day 24 control group. No fluorine was detected above background levels in the 0.2 and the 2 mg/m³ groups on test day 9 (the last day of the exposure period).

Weight analysis of the major organs showed no effects attributable to the test substance. Histological findings were confined to the respiratory tract. There were no adverse effects in any other evaluated organs. Compound-related microscopic observations were present in the lungs and larynx of test day 10 sacrifice rats at concentrations of 2 and 20 mg/m³. Inflammation in the lungs, characterized by mixed inflammatory cells within scattered alveolar lumina was observed at 2 mg/m³ in 1 of 5 rats and at 20 mg/m³ in 3 of 5 rats. In addition, minimal to mild squamous metaplasia of the mucosa lining the ventral floor of the larynx was observed at 2 mg/m³ in 4 of 5 rats and at 20 mg/m³ in 5 of 5 rats.

There were no compound-related microscopic lesions observed in test day 24 sacrifice rats, indicating the reversibility of compound-related lesions in the lung and larynx.

The no-observed-effect level (NOEL) for this study is defined as the highest concentration at which no toxicologically important effects attributable to the test substance were detected. Thus for this study, the NOEL is equivalent to the NOEL as defined by the United States Environmental Protection Agency (1985) and to the no-observed-adverse-effect level (NOAEL) as defined by the European Union (1994).

Based on the above findings in the respiratory tract of rats exposed to H-24678 for 2 weeks, the NOEL for repeated inhalation exposure was 0.2 mg/m³.

RECORDS AND SAMPLE STORAGE

A sample of the test substance was collected for archive purposes and retained at Haskell Laboratory, Newark, Delaware. Specimens (if applicable), raw data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware (formerly known as the E.I. du Pont de Nemours and Company Records Management Center).

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TABLES

TABLES

EXPLANATORY NOTES

ABBREVIATIONS:

Chamber Concentrations of H-24678
Chamber Environmental Conditions

S.E.M. - standard error of the mean
mg/m^3 - milligrams per cubic meter
n - number of samples

Summary of Hematology Values

RBC - red blood cell count
HGB - hemoglobin
HCT - hematocrit
MCV - mean corpuscular volume
MCH - mean corpuscular hemoglobin
MCHC - mean corpuscular hemoglobin concentration
RDW - red cell distribution width
ARET - absolute reticulocyte count
PLT - platelet count
WBC - white blood cell count
ANEU - absolute neutrophil (all forms)
ALYM - absolute lymphocyte
AMON - absolute monocyte
AEOS - absolute eosinophil
ABAS - absolute basophil
ALUC - absolute large unstained cell

TABLES

EXPLANATORY NOTES (Continued)

ABBREVIATIONS (Continued):

Summary of Serum and Plasma Chemistry Values

AST - aspartate aminotransferase
ALT - alanine aminotransferase
SDH - sorbitol dehydrogenase
ALKP - alkaline phosphatase
BILI - total bilirubin
BUN - urea nitrogen
CREA - creatinine
CHOL - cholesterol
TRIG - triglycerides
GLUC - glucose
TP - total protein
ALB - albumin
GLOB - globulin
CALC - calcium
IPHS - inorganic phosphorous
NA - sodium
K - potassium
CL - chloride
PFLU - plasma fluoride

Summary of Urinalysis Values

VOL - volume
UFLU - urine fluoride

TABLES

EXPLANATORY NOTES (Continued)

NOTES:

Chamber Concentrations of H-24678
Particle Size Distribution of H-24678
Chamber Environmental Conditions
Values are reported to 2 significant figures.
Means and standard errors of the mean were calculated prior to rounding values.

Summary of Hematology Values
Summary of Serum and Plasma Chemistry Values
Summary of Urinalysis Values
When an individual observation was recorded as being less than a certain value, calculations were performed on half the recorded value. For example, if bilirubin was reported as <0.1, 0.05 was used for any calculations performed with that bilirubin data.

TABLE 1

CHAMBER CONCENTRATIONS OF H-24678

DESIGN CONCENTRATION (mg/m^3)	MEASURED CONCENTRATION[a] (mg/m^3)			
	MEAN	S.E.M.	RANGE	n
0	0	[b]	0	1
0.2	0.22	0.011	0.15 - 0.26	9
2	1.9	0.13	1.2 - 2.6	9
20	20	0.38	18 - 22	9

a Values represent the mean, standard error of the mean (S.E.M.), and range of the daily mean values obtained from n exposures.
b Value not calculable from sample size.

TABLE 2

PARTICLE SIZE DISTRIBUTION OF H-24678

DESIGN CONCENTRATION (mg/m^3)	EXPOSURE NUMBER	MASS MEDIAN AERODYNAMIC DIAMETER (μm)	GEOMETRIC STANDARD DEVIATION	% PARTICLES BY MASS		
				<1 μm	<3 μm	<10 μm
0.2	9[a]	2.1	2.1	16	68	ND[c]
2	4[b]	1.4	2.1	34	85	100
	8[b]	0.90	1.7	58	98	100
	9[a]	1.0	1.7	50	98	ND
20	3[b]	0.90	1.9	52	93	100
	7[b]	1.3	1.6	32	96	100
	9[a]	1.1	2.2	48	92	ND

a Mean of 2 samples determined with QCM Impactor.
b Single sample determined with Sierra Impactor.
c ND = not determined.

TABLE 3

CHAMBER ENVIRONMENTAL CONDITIONS

DESIGN CONCENTRATION (mg/m^3)[a]	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)	AIRFLOW (L/min)	n
0	21 - 24	36 - 67	35	9
0.2	20 - 24	51 - 59	65	9
2	20 - 25	50 - 56	65	9
20	19 - 24	37 - 50	50	9

a Values represent the range of the daily mean values obtained from n exposures.

TABLE 4

MEAN BODY WEIGHTS OF MALE RATS

DAYS ON TEST	MEAN BODY WEIGHTS (g) Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
EXPOSURE				
0	255.1 10.3(15)	255.1 11.6(15)	254.6 9.9(15)	256.4 11.9(15)
1	253.2 11.8(15)	252.0 10.6(15)	254.1 10.1(15)	255.0 12.0(15)
2	257.0 11.6(15)	257.6 12.4(15)	259.0 10.5(15)	256.7 12.5(15)
3	260.4 12.5(15)	259.8 14.1(15)	262.0 10.7(15)	259.3 13.1(15)
4	261.3 12.9(15)	264.0 14.7(15)	264.3 10.9(15)	261.6 12.8(15)
6	267.4 22.1(15)	272.9 16.3(15)	274.5 12.3(15)	271.3 14.8(15)
7	270.5 17.0(15)	275.5 17.0(15)	277.5 13.4(15)	273.4 15.6(15)
8	275.4 17.1(15)	279.9 18.2(15)	281.5 13.0(15)	274.3 15.6(15)
9	276.6 21.3(15)	280.2 20.3(15)	282.6 13.8(15)	276.1 17.2(15)
10[a]	258.5 24.7(15)	258.4 23.6(15)	265.0 20.7(15)	257.5 16.7(15)

TABLE 4 (Continued)

MEAN BODY WEIGHTS OF MALE RATS

	MEAN BODY WEIGHTS (g)			
DAYS ON TEST	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
RECOVERY				
14	297.1 22.5(10)	298.2 23.6(10)	305.3 18.4(10)	296.8 19.5(10)
17	315.0 25.5(10)	311.0 30.9(10)	323.3 17.8(10)	318.1 19.7(10)
21	338.4 25.5(10)	334.6 31.4(10)	343.2 20.1(10)	339.4 22.2(10)
24	344.1 41.7(10)	338.8 41.1(10)	347.6 33.1(10)	343.1 22.2(10)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

There were no statistically significant differences from control at $p < 0.05$.

a Weight losses due to fasting of rats prior to clinical pathology evaluation.

TABLE 5

MEAN BODY WEIGHT GAINS OF MALE RATS

DAYS ON TEST	MEAN BODY WEIGHT GAINS (g) Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
EXPOSURE				
0 - 1	-1.8 4.4(15)	-3.1 3.5(15)	-0.5 4.4(15)	-1.4 3.2(15)
1 - 2	3.7 3.1(15)	5.6 3.6(15)	4.9 3.6(15)	1.7 2.2(15)
2 - 3	3.4 2.1(15)	2.2 4.4(15)	3.0 3.0(15)	2.6 3.2(15)
3 - 4	1.0 4.8(15)	4.2 4.4(15)	2.3 2.5(15)	2.3 4.3(15)
4 - 6	6.0 12.5(15)	8.9 3.5(15)	10.2 4.9(15)	9.7 3.9(15)
6 - 7	3.2 8.2(15)	2.7 2.3(15)	3.1 3.4(15)	2.1 3.3(15)
7 - 8	4.9 3.6(15)	4.4 2.5(15)	4.0 2.5(15)	0.9# 2.1(15)
8 - 9	1.2 5.6(15)	0.2 4.6(15)	1.0 2.3(15)	1.8 3.5(15)
9 - 10[a]	-18.0 13.7(15)	-21.8 11.7(15)	-17.6 13.1(15)	-18.6 13.2(15)

TABLE 5 (Continued)

MEAN BODY WEIGHT GAINS OF MALE RATS

	MEAN BODY WEIGHT GAINS (g)			
DAYS ON TEST	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
RECOVERY				
10 - 14	35.1 7.3(10)	35.8 11.2(10)	35.2 8.4(10)	33.7 15.1(10)
14 - 17	17.9 4.3(10)	12.8 11.5(10)	18.0 3.5(10)	21.3 6.2(10)
17 - 21	23.4 2.6(10)	23.6 6.0(10)	19.9 4.3(10)	21.3 6.2(10)
21 - 24	5.7 18.7(10)	4.2 15.6(10)	4.4 15.5(10)	3.7 16.8(10)
OVERALL				
0 - 10	3.4 17.0(15)	3.3 16.2(15)	10.4 14.5(15)	1.1 9.5(15)
10 - 24	82.0 16.0(10)	76.3 18.7(10)	77.4 14.1(10)	80.0 12.3(10)
0 - 24	87.4 34.8(10)	82.1 34.5(10)	91.2 28.2(10)	84.6 18.2(10)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

\# Statistically significant difference from control at $p < 0.05$ by Jonckheere-Terpstra trend test.

a Weight losses due to fasting of rats prior to clinical pathology evaluation.

TABLE 6

SUMMARY OF CLINICAL OBSERVATIONS IN MALE RATS

	Group I	Group III	Group V	Group VII
	0 mg/m³	0.2 mg/m³	2 mg/m³	20 mg/m³
ANIMAL COUNT:	15	15	15	15
Discharge				
Incidence	0 (0%)	1 (7%)	0 (0%)	0 (0%)
Mean onset (Days)	-	17	-	-
Hair Loss				
Incidence	1 (7%)	0 (0%)	1 (7%)	2 (13%)
Mean onset (Days)	6	-	10	16

Incidence - The number of animals (percent of group) for which an observation was recorded.
Mean onset (Days) - The mean of the test days each observation was first recorded for that group.
A dash indicates a clinical observation was not observed, therefore, there is no mean onset day.

There were no statistically significant differences from control at $p < 0.05$.

TABLE 7

SUMMARY OF BLOOD FLUORINE ANALYSIS

	BLOOD FLUORINE (ppm)			
DAYS ON TEST	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
0	a	a	a	1.6* 0.05(5)
3	a	a	a	2.1* 0.32(5)
9	1.3 0.04(5)	1.4 0.22(5)	1.4 0.15(5)	2.0* 0.11(5)
24	1.6 0.23(5)	a	a	1.5 0.13(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from test day 9 control at p = 0.05 by Student's T-test.

a Samples not evaluated for this timepoint.

TABLE 8

SUMMARY OF HEMATOLOGY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
RBC (x10^6/μL)				
DAY 10	6.98	7.16	7.30	7.18
	0.27(10)	0.24(10)	0.31(10)	0.50(10)
DAY 24	7.38	7.32	7.47	7.42
	0.19(5)	0.17(5)	0.28(4)	0.33(5)
HGB (g/dL)				
DAY 10	14.8	15.1	15.1	15.0
	0.4(10)	0.4(10)	0.5(10)	0.7(10)
DAY 24	15.3	15.3	15.0	14.8
	0.3(5)	0.3(5)	0.5(4)	0.2(5)
HCT (%)				
DAY 10	44.3	45.3	45.6	45.0
	1.3(10)	1.2(10)	1.9(10)	2.4(10)
DAY 24	45.1	44.7	44.4	43.9
	0.6(5)	0.6(5)	1.8(4)	1.2(5)
MCV (fl)				
DAY 10	63.6	63.3	62.5	62.8
	2.0(10)	2.1(10)	1.2(10)	2.2(10)
DAY 24	61.0	61.1	59.4	59.3
	1.0(5)	1.2(5)	1.4(4)	2.9(5)
MCH (pg)				
DAY 10	21.3	21.2	20.8	21.0
	0.5(10)	0.7(10)	0.5(10)	0.8(10)
DAY 24	20.7	20.9	20.1	20.0
	0.6(5)	0.5(5)	0.4(4)	1.1(5)
MCHC (g/dL)				
DAY 10	33.5	33.4	33.2	33.4
	0.4(10)	0.3(10)	0.3(10)	0.6(10)
DAY 24	33.9	34.2	34.0	33.7
	0.7(5)	0.7(5)	0.4(4)	0.9(5)
RDW (%)				
DAY 10	12.2	12.4	12.4	12.5
	0.4(10)	0.5(10)	0.6(10)	0.4(10)
DAY 24	12.0	11.9	11.8	12.2
	0.2(5)	0.3(5)	0.6(4)	0.4(5)

TABLE 8 (Continued)

SUMMARY OF HEMATOLOGY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
ARET (x10³/μL)				
DAY 10	180.5	210.0	207.8	198.0
	36.9(10)	48.3(10)	19.9(10)	46.5(10)
DAY 24	234.3	228.3	213.4	234.8
	28.9(5)	33.8(5)	19.4(4)	26.7(5)
PLT (x10³/μL)				
DAY 10	1162	1183	1335	1217
	173(10)	207(10)	93(10)	224(9)
DAY 24	1122	1189	1368	1319
	188(3)	206(2)	58(4)	96(4)
WBC (x10³/μL)				
DAY 10	14.89	13.87	13.47	13.51
	2.35(10)	4.14(10)	2.34(10)	3.07(10)
DAY 24	10.72	10.48	10.03	10.18
	1.44(5)	3.32(5)	1.58(4)	3.48(5)
ANEU (x10³/μL)				
DAY 10	2.02	1.50	1.64	1.79
	0.83(10)	0.45(10)	0.40(10)	0.38(10)
DAY 24	1.92	1.67	1.57	1.88
	0.46(5)	0.55(5)	0.51(4)	0.42(5)
ALYM (x10³/μL)				
DAY 10	12.28	11.75	11.23	11.02
	1.62(10)	4.05(10)	2.24(10)	2.82(10)
DAY 24	8.34	8.40	8.09	7.83
	1.25(5)	2.64(5)	1.17(4)	2.96(5)
AMON (x10³/μL)				
DAY 10	0.27	0.32	0.30	0.30
	0.15(10)	0.16(10)	0.13(10)	0.12(10)
DAY 24	0.25	0.21	0.14	0.22
	0.11(5)	0.14(5)	0.03(4)	0.08(5)
AEOS (x10³/μL)				
DAY 10	0.11	0.09	0.13	0.21
	0.05(10)	0.05(10)	0.05(10)	0.19(10)
DAY 24	0.10	0.10	0.09	0.10
	0.11(5)	0.05(5)	0.03(4)	0.05(5)

TABLE 8 (Continued)

SUMMARY OF HEMATOLOGY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
ABAS (x10³/μL)				
DAY 10	0.12	0.11	0.10	0.10
	0.07(10)	0.04(10)	0.05(10)	0.05(10)
DAY 24	0.05	0.05	0.09	0.07
	0.04(5)	0.03(5)	0.04(4)	0.03(5)
ALUC (x10³/μL)				
DAY 10	0.09	0.10	0.06	0.08
	0.05(10)	0.05(10)	0.02(10)	0.03(10)
DAY 24	0.06	0.05	0.06	0.07
	0.05(5)	0.02(5)	0.03(4)	0.05(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

There were no statistically significant differences from control at $p < 0.05$.

TABLE 9

SUMMARY OF SERUM AND PLASMA CHEMISTRY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
AST (U/L)				
DAY 10	94	94	94	103
	10(10)	12(10)	15(10)	12(10)
DAY 24	100	95	87	90
	12(5)	17(5)	11(5)	7(5)
ALT (U/L)				
DAY 10	38	39	39	41
	8(10)	7(10)	6(10)	5(10)
DAY 24	38	40	48	39
	3(5)	5(5)	23(5)	6(5)
SDH (U/L)				
DAY 10	12.1	11.4	12.4	12.5
	3.4(10)	2.0(10)	3.8(10)	2.7(10)
DAY 24	12.2	13.1	12.5	15.0
	4.7(5)	3.8(5)	2.2(5)	3.8(5)
ALKP (U/L)				
DAY 10	227	258	249	261
	18(10)	47(10)	57(10)	64(10)
DAY 24	219	213	185	219
	30(5)	50(5)	31(5)	47(5)
BILI (mg/dL)				
DAY 10	0.11	0.10	0.10	0.10
	0.03(10)	0.03(10)	0.03(10)	0.04(10)
DAY 24	0.13	0.09	0.11	0.12
	0.03(5)	0.03(5)	0.04(5)	0.05(5)
BUN (mg/dL)				
DAY 10	16	16	15	13*
	2(10)	2(10)	2(10)	2(10)
DAY 24	16	14	15	13*
	2(5)	1(5)	1(5)	1(5)
CREA (mg/dL)				
DAY 10	0.24	0.28	0.25	0.27
	0.03(10)	0.05(10)	0.03(10)	0.05(10)
DAY 24	0.31	0.29	0.36	0.29
	0.04(5)	0.05(5)	0.13(5)	0.03(5)

TABLE 9 (Continued)

SUMMARY OF SERUM AND PLASMA CHEMISTRY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
CHOL (mg/dL)				
DAY 10	66	62	61	57
	12(10)	12(10)	11(10)	12(10)
DAY 24	58	61	60	62
	10(5)	6(5)	5(5)	14(5)
TRIG (mg/dL)				
DAY 10	41	41	44	46
	15(10)	13(10)	8(10)	13(10)
DAY 24	44	53	55	52
	17(5)	21(5)	18(5)	26(5)
GLUC (mg/dL)				
DAY 10	86	86	82	85
	5(10)	6(10)	7(10)	4(10)
DAY 24	91	88	92	94
	16(5)	12(5)	7(5)	6(5)
TP (g/dL)				
DAY 10	6.1	6.2	6.1	6.1
	0.2(10)	0.2(10)	0.3(10)	0.2(10)
DAY 24	6.5	6.4	6.3	6.3
	0.2(5)	0.3(5)	0.4(5)	0.5(5)
ALB (g/dL)				
DAY 10	4.1	4.3*	4.2	4.1
	0.2(10)	0.1(10)	0.1(10)	0.2(10)
DAY 24	4.4	4.4	4.3	4.3
	0.2(5)	0.2(5)	0.2(5)	0.2(5)
GLOB (g/dL)				
DAY 10	2.1	2.0	2.0	2.0
	0.1(10)	0.1(10)	0.2(10)	0.1(10)
DAY 24	2.1	2.0	2.0	2.0
	0.1(5)	0.1(5)	0.2(5)	0.3(5)
CALC (mg/dL)				
DAY 10	11.6	11.6	11.7	11.6
	0.2(10)	0.3(10)	0.4(10)	0.3(10)
DAY 24	11.0	11.0	10.9	11.0
	0.2(5)	0.6(5)	0.4(5)	0.4(5)

TABLE 9 (Continued)

SUMMARY OF SERUM AND PLASMA CHEMISTRY VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
IPHS (mg/dL)				
DAY 10	10.5	10.7	10.9	10.5
	0.5(10)	0.5(10)	0.6(10)	0.7(10)
DAY 24	10.2	9.2	9.6	9.7
	0.6(5)	0.2(5)	0.9(5)	0.8(5)
NA (mmol/L)				
DAY 10	148.5	149.2	149.4	150.0
	2.2(10)	2.1(10)	1.9(10)	2.1(10)
DAY 24	147.3	147.1	147.2	148.4
	1.3(5)	1.5(5)	1.2(5)	1.1(5)
K (mmol/L)				
DAY 10	6.07	6.20	6.14	6.16
	0.24(10)	0.39(10)	0.22(10)	0.42(10)
DAY 24	5.92	6.13	6.09	6.02
	0.48(5)	0.46(5)	0.49(5)	0.25(5)
CL (mmol/L)				
DAY 10	102.5	102.9	104.1	105.0
	2.4(10)	3.8(10)	1.7(10)	2.8(10)
DAY 24	102.4	105.1	104.2	104.8
	3.4(5)	2.5(5)	3.0(5)	1.5(5)
PFLU (μg/mL)				
DAY 10	0.0	0.0	0.0	0.0
	0.0(5)	0.0(5)	0.0(5)	0.0(5)
DAY 24	0.1	0.1	0.1	0.1
	0.0(4)	0.0(4)	0.0(5)	0.0(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

* Statistically significant difference from control at $p < 0.05$ by Dunnett/Tamhane-Dunnett test.

TABLE 10

SUMMARY OF URINALYSIS VALUES FOR MALE RATS

TEST/ PERIOD	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
VOL (mL)				
DAY 10	7.2	7.9	9.3	9.3
	3.6(10)	6.2(10)	3.3(10)	10.6(10)
DAY 24	5.2	8.1	9.3	10.8
	3.7(5)	4.4(5)	3.1(5)	6.5(5)
UFLU (μg)				
DAY 10	8.3	7.9	8.1	10.5
	2.2(10)	2.4(10)	1.2(10)	4.8(10)
DAY 24	10.1	12.5	12.7	14.0
	2.6(5)	4.4(5)	2.6(5)	2.8(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

There were no statistically significant differences from control at $p < 0.05$.

TABLE 11

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 10 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams)				
LIVER	8.241 1.209(5)	7.898 1.292(5)	8.145 0.515(5)	7.384 1.002(5)
KIDNEYS	2.296 0.179(5)	2.315 0.445(5)	2.240 0.245(5)	2.335 0.376(5)
LUNGS	1.504 0.224(5)	1.606 0.262(5)	1.554 0.138(5)	1.572 0.239(5)
BRAIN	1.890 0.106(5)	1.934 0.096(5)	1.870 0.100(5)	1.912 0.036(5)
TESTES	2.950 0.200(5)	2.992 0.213(5)	2.862 0.358(5)	2.742 0.403(5)
FINAL BODY WEIGHT (grams)				
	251.440 18.258(5)	250.200 18.931(5)	254.680 14.201(5)	246.280 15.327(5)

TABLE 11 (Continued)

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 10 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN RELATIVE ORGAN WEIGHTS (% of body weight)				
LIVER/ FINAL BODY*100	3.269 0.339(5)	3.146 0.342(5)	3.197 0.046(5)	2.996 0.330(5)
KIDNEYS/ FINAL BODY*100	0.913 0.027(5)	0.921 0.124(5)	0.878 0.055(5)	0.947 0.134(5)
LUNGS/ FINAL BODY*100	0.600 0.092(5)	0.642 0.097(5)	0.611 0.057(5)	0.637 0.073(5)
BRAIN/ FINAL BODY*100	0.754 0.060(5)	0.776 0.062(5)	0.735 0.025(5)	0.778 0.038(5)
TESTES/ FINAL BODY*100	1.176 0.075(5)	1.198 0.071(5)	1.121 0.087(5)	1.112 0.128(5)

TABLE 11 (Continued)

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 10 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN RELATIVE ORGAN WEIGHTS (organ to brain weight ratio)				
LIVER/BRAIN	435.438 54.098(5)	407.488 56.895(5)	435.622 12.933(5)	386.133 51.265(5)
KIDNEYS/BRAIN	121.614 9.622(5)	119.407 20.504(5)	119.535 7.755(5)	121.908 17.942(5)
LUNGS/BRAIN	79.378 8.140(5)	82.699 9.683(5)	83.078 5.215(5)	82.141 11.772(5)
TESTES/BRAIN	156.562 14.659(5)	154.661 7.589(5)	152.815 14.167(5)	143.359 20.667(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

There were no statistically significant differences from control at $p < 0.05$.

TABLE 12

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 24 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN FINAL BODY AND ABSOLUTE ORGAN WEIGHTS (grams)				
LIVER	9.082 0.961(4)	9.366 1.297(4)	10.376 0.404(5)	10.477# 0.975(5)
KIDNEYS	2.644 0.246(4)	2.636 0.204(4)	2.761 0.219(5)	2.855 0.243(5)
LUNGS	1.623 0.201(4)	1.633 0.204(4)	1.840 0.264(5)	1.695 0.131(5)
BRAIN	1.991 0.027(4)	1.949 0.052(4)	1.976 0.072(5)	2.023 0.114(5)
TESTES	3.244 0.177(4)	2.813* 0.150(4)	3.209 0.261(5)	3.177 0.258(5)
FINAL BODY WEIGHT (grams)				
	310.600 13.849(4)	316.900 33.900(4)	321.560 11.341(5)	339.160# 22.606(5)

TABLE 12 (Continued)

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 24 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN RELATIVE ORGAN WEIGHTS (% of body weight)				
LIVER/ FINAL BODY*100	2.923 0.263(4)	2.952 0.201(4)	3.231 0.186(5)	3.085 0.111(5)
KIDNEYS/ FINAL BODY*100	0.851 0.065(4)	0.835 0.067(4)	0.858 0.056(5)	0.844 0.081(5)
LUNGS/ FINAL BODY*100	0.523 0.065(4)	0.517 0.055(4)	0.573 0.087(5)	0.502 0.064(5)
BRAIN/ FINAL BODY*100	0.642 0.036(4)	0.620 0.066(4)	0.616 0.044(5)	0.599 0.056(5)
TESTES/ FINAL BODY*100	1.047 0.103(4)	0.893 0.070(4)	0.997 0.064(5)	0.942 0.123(5)

TABLE 12 (Continued)

MEAN FINAL BODY AND ORGAN WEIGHTS FROM MALE RATS
DAY 24 SACRIFICE

	Group I 0 mg/m³	Group III 0.2 mg/m³	Group V 2 mg/m³	Group VII 20 mg/m³
MEAN RELATIVE ORGAN WEIGHTS (organ to brain weight ratio)				
LIVER/BRAIN	456.224 47.919(4)	481.160 71.330(4)	525.254 19.394(5)	519.153 53.128(5)
KIDNEYS/BRAIN	132.855 12.579(4)	135.373 12.688(4)	139.973 14.129(5)	141.244 10.200(5)
LUNGS/BRAIN	81.485 9.862(4)	83.779 10.007(4)	92.973 11.872(5)	83.911 6.893(5)
TESTES/BRAIN	162.866 6.801(4)	144.282 5.310(4)	162.765 17.763(5)	157.389 14.494(5)

Data arranged as: Mean
Standard deviation (Number of values included in calculation)

\# Statistically significant difference from control at $p < 0.05$ by trend test (Jonckheere-Terpstra).
* Statistically significant difference from control at $p < 0.05$ by parametric test (Dunnett/Tamhane-Dunnett).

TABLE 13

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (Numeric) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
LIVER					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 4
DISCOLORATION, TAN, MOTTLED.					1
KIDNEYS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
LUNGS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
HEART					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
SPLEEN					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
BRAIN					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
SPINAL CORD					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 13 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (Numeric) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
STOMACH					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
DUODENUM					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
JEJUNUM					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
ILEUM					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
PANCREAS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
CECUM					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
COLON					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 13 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	LESION INCIDENCE (Numeric)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
RECTUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
MESENTERIC LYMPH NODE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
THYMUS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
ADRENAL GLANDS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
SCIATIC NERVE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
THYROID GLAND				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
PARATHYROID GLANDS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 13 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	LESION INCIDENCE (Numeric)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
TRACHEA				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
ESOPHAGUS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
PHARYNX/LARYNX				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
EYE(S) WITH OPTIC NERVE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
PROSTATE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
SEMINAL VESICLES				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
URINARY BLADDER				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 13 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (Numeric) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
TESTES					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
EPIDIDYMIDES					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
STERNUM					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
NOSE					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 14

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (Numeric)			
		0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
LIVER					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
KIDNEYS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
LUNGS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 4
DISCOLORATION, RED, SCATTERED.					1
HEART					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
SPLEEN					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
BRAIN					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
SPINAL CORD					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 14 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	LESION INCIDENCE (Numeric)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
STOMACH				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
DUODENUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
JEJUNUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
ILEUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
PANCREAS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
CECUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
COLON				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 14 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	LESION INCIDENCE (Numeric)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
RECTUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
MESENTERIC LYMPH NODE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
THYMUS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 4	(5) 5
DISCOLORATION, DARK, MOTTLED.			1	
ADRENAL GLANDS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
SCIATIC NERVE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
THYROID GLAND				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
PARATHYROID GLANDS				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 14 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (Numeric) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
TRACHEA					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
ESOPHAGUS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
PHARYNX/LARYNX					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
EYE(S) WITH OPTIC NERVE					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
PROSTATE					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
SEMINAL VESICLES					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5
URINARY BLADDER					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 14 (Continued)

INCIDENCES OF GROSS OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	LESION INCIDENCE (Numeric)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
TESTES				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
EPIDIDYMIDES				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 4	(5) 5
DISCOLORATION, TAN, LEFT, TAIL, 3MM DIA..			1	
STERNUM				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5
NOSE				
NO ABNORMALITY DETECTED	(5) 5	(5) 5	(5) 5	(5) 5

Figure in parentheses is the number of animals grossly examined for this tissue
The absence of a number indicates the finding specified was not identified

TABLE 15

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
DIGESTIVE SYSTEM					
LIVER					
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL.		(5)	(4)	(5)	(4)
minimal		4	4	5	4
mild		1			
total observations per lesion		5	4	5	4
HYPERPLASIA, BILE DUCT.					
minimal					1
total observations per lesion					1
FATTY CHANGE, MEDIAN CLEFT.					
minimal		1			
total observations per lesion		1			
PANCREAS					
NO ABNORMALITY DETECTED		(5)			(5)
		5			5
ESOPHAGUS					
NO ABNORMALITY DETECTED		(5)			(5)
		5			5
STOMACH					
NO ABNORMALITY DETECTED		(5)			(5)
		5			5

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	LESION INCIDENCE (NUMERIC)			
TREATMENT	0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
DIGESTIVE SYSTEM				
DUODENUM				
NO ABNORMALITY DETECTED	(5) 5			(5) 5
JEJUNUM				
NO ABNORMALITY DETECTED	(5) 5			(5) 5
ILEUM				
NO ABNORMALITY DETECTED	(5) 5			(5) 5
CECUM				
NO ABNORMALITY DETECTED	(5) 5			(5) 5
COLON				
NO ABNORMALITY DETECTED	(5) 5			(5) 5
RECTUM				
NO ABNORMALITY DETECTED	(5) 5			(5) 5

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC)			
		0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
URINARY SYSTEM					
KIDNEYS					
NO ABNORMALITY DETECTED		(5) 4	(5) 4	(5) 4	(5) 2
NEPHROPATHY, CHRONIC PROGRESSIVE.					
minimal		1	1	1	2
total observations per lesion		1	1	1	2
HYDRONEPHROSIS, UNILATERAL.					
mild					1
total observations per lesion					1
URINARY BLADDER					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
RESPIRATORY SYSTEM					
LUNGS					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 4	(5) 2
INFLAMMATION, SUBACUTE/CHRONIC.					
minimal				1	3
total observations per lesion				1	3

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
RESPIRATORY SYSTEM					
TRACHEA					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
PHARYNX/LARYNX					
NO ABNORMALITY DETECTED		(5) 5	(5) 5	(5) 1	(5)
SQUAMOUS METAPLASIA.					
minimal				4	1
mild					4
total observations per lesion				4	5
NOSE					
NO ABNORMALITY DETECTED		(5) 5	(5) 4	(5) 4	(5) 5
INFLAMMATION, SUBACUTE/CHRONIC.					
minimal			1	1	
total observations per lesion			1	1	

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
CARDIOVASCULAR SYSTEM					
HEART		(5)			(5)
NO ABNORMALITY DETECTED		3			3
CARDIOMYOPATHY.					
minimal		2			2
total observations per lesion		2			2
LYMPHATIC AND HEMATOPOIETIC SYSTEM					
SPLEEN		(5)			(5)
NO ABNORMALITY DETECTED		5			5
THYMUS		(5)			(5)
NO ABNORMALITY DETECTED		5			5
MESENTERIC LYMPH NODE		(5)			(5)
NO ABNORMALITY DETECTED		5			5

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
ENDOCRINE SYSTEM					
THYROID GLAND					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
PARATHYROID GLANDS					
NO ABNORMALITY DETECTED		(4) 4			(5) 5
ADRENAL GLANDS					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
NERVOUS SYSTEM					
BRAIN					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
SPINAL CORD					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
SCIATIC NERVE					
NO ABNORMALITY DETECTED		(5) 5			(5) 5

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
MUSCULAR AND SKELETAL SYSTEM					
STERNUM		(5)			(5)
NO ABNORMALITY DETECTED		5			5
REPRODUCTIVE SYSTEM					
TESTES		(5)	(5)	(5)	(5)
NO ABNORMALITY DETECTED		5	5	5	5
EPIDIDYMIDES		(5)			(5)
NO ABNORMALITY DETECTED		5			4
OLIGOSPERMIA/GERM CELL DEBRIS.					
mild					1
total observations per lesion					1
PROSTATE		(5)			(5)
NO ABNORMALITY DETECTED		4			5
INFLAMMATION, SUBACUTE/CHRONIC.					
minimal		1			
total observations per lesion		1			

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 15 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 10 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
REPRODUCTIVE SYSTEM					
SEMINAL VESICLES		(5)			(5)
NO ABNORMALITY DETECTED		5			5
SPECIAL SENSES SYSTEM					
EYE(S) WITH OPTIC NERVE		(5)			(5)
NO ABNORMALITY DETECTED		5			5
OPTIC NERVE NOT PRESENT.					3

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 16

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
DIGESTIVE SYSTEM					
LIVER					
NO ABNORMALITY DETECTED		(5)			(5)
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL.					1
minimal		5			4
total observations per lesion		5			4
URINARY SYSTEM					
KIDNEYS					
NO ABNORMALITY DETECTED		(5)			(5)
NEPHROPATHY, CHRONIC PROGRESSIVE.		3			3
minimal		1			1
mild		1			
total observations per lesion		2			1
CYST.					
minimal		1			1
total observations per lesion		1			1

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

TABLE 16 (Continued)

INCIDENCES AND LESION GRADES OF MICROSCOPIC OBSERVATIONS IN MALE RATS
DAY 24 SACRIFICE

LESIONS	TREATMENT	LESION INCIDENCE (NUMERIC) 0 mg/m³ I	0.2 mg/m³ III	2 mg/m³ V	20 mg/m³ VII
RESPIRATORY SYSTEM					
LUNGS					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
PHARYNX/LARYNX					
NO ABNORMALITY DETECTED		(5) 5			(5) 5
NOSE					
NO ABNORMALITY DETECTED		(5) 4			(5) 4
DEGENERATION, TRIGEMINAL NERVE.					
mild		1			1
total observations per lesion		1			1
REPRODUCTIVE SYSTEM					
TESTES					
NO ABNORMALITY DETECTED		(5) 5			(5) 5

Figure in parentheses is number of animals microscopically examined for this tissue
The absence of a number indicates the lesion specified was not identified

FIGURES

FIGURE 1

SCHEMATIC OF EXPOSURE SYSTEM

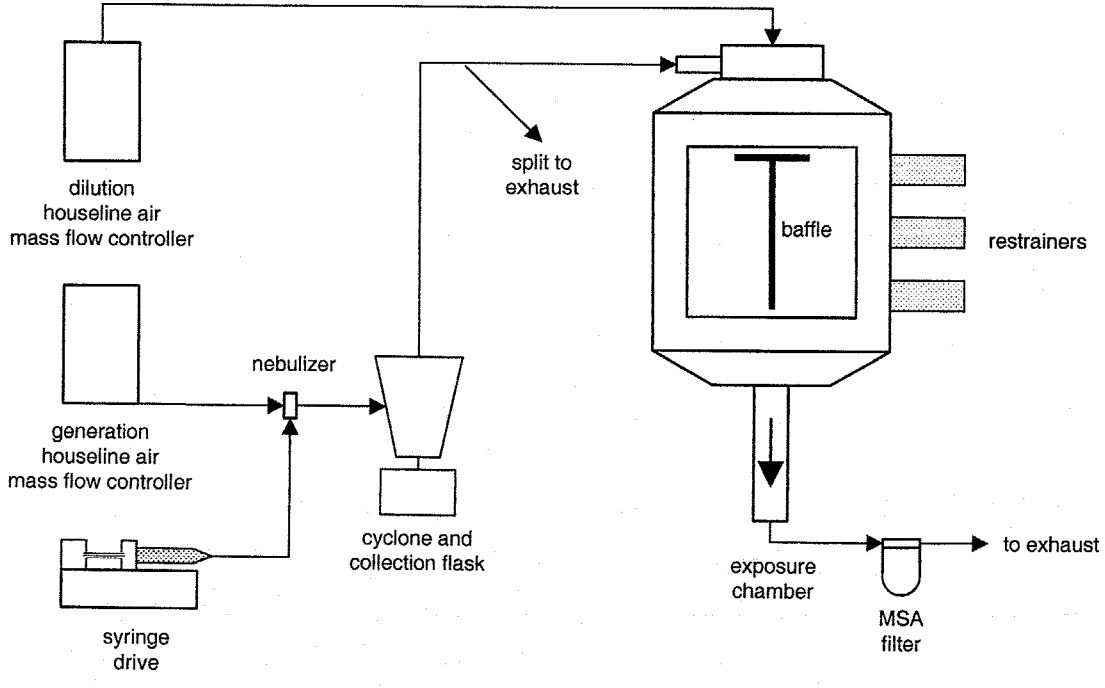
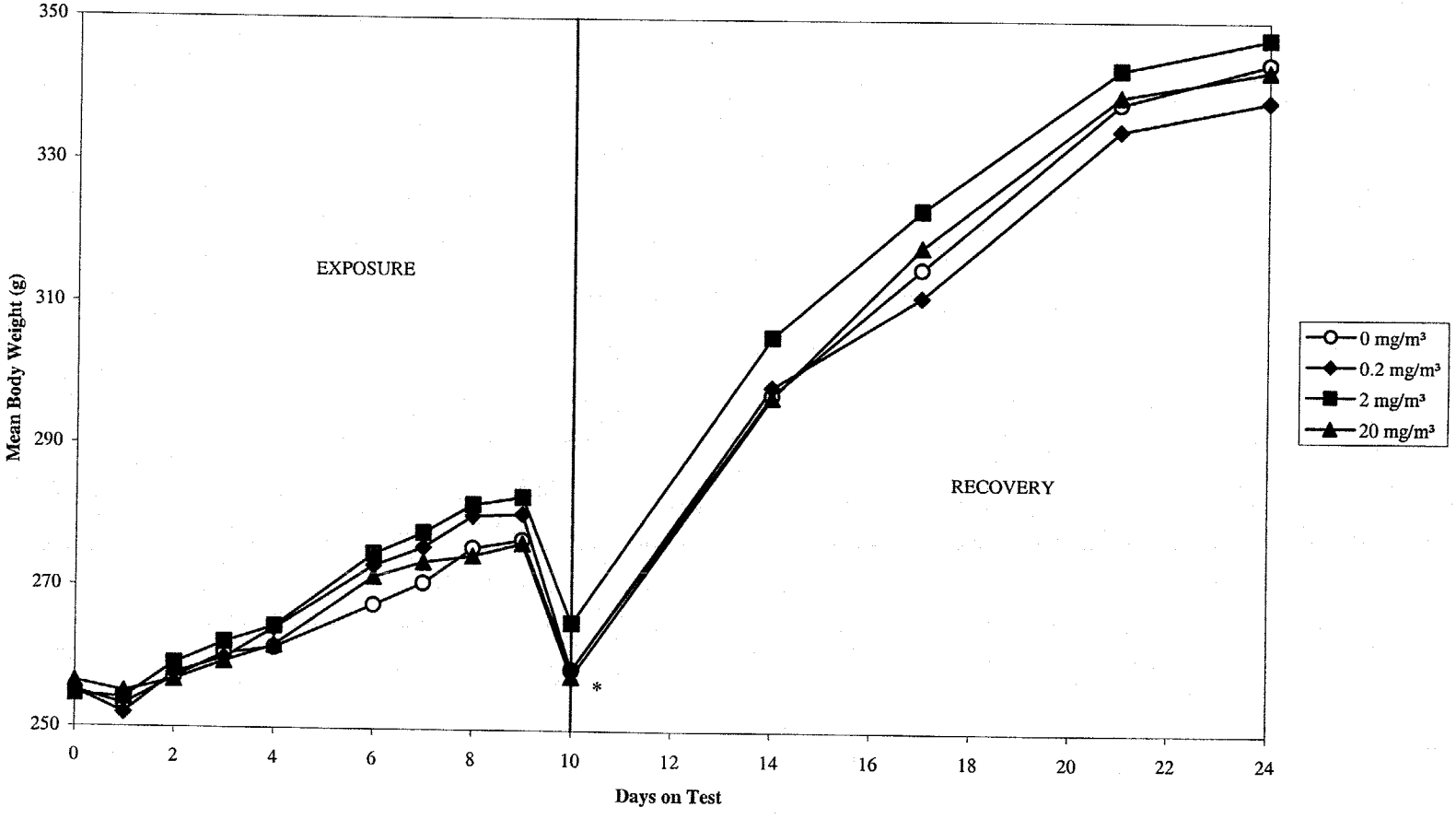


FIGURE 2

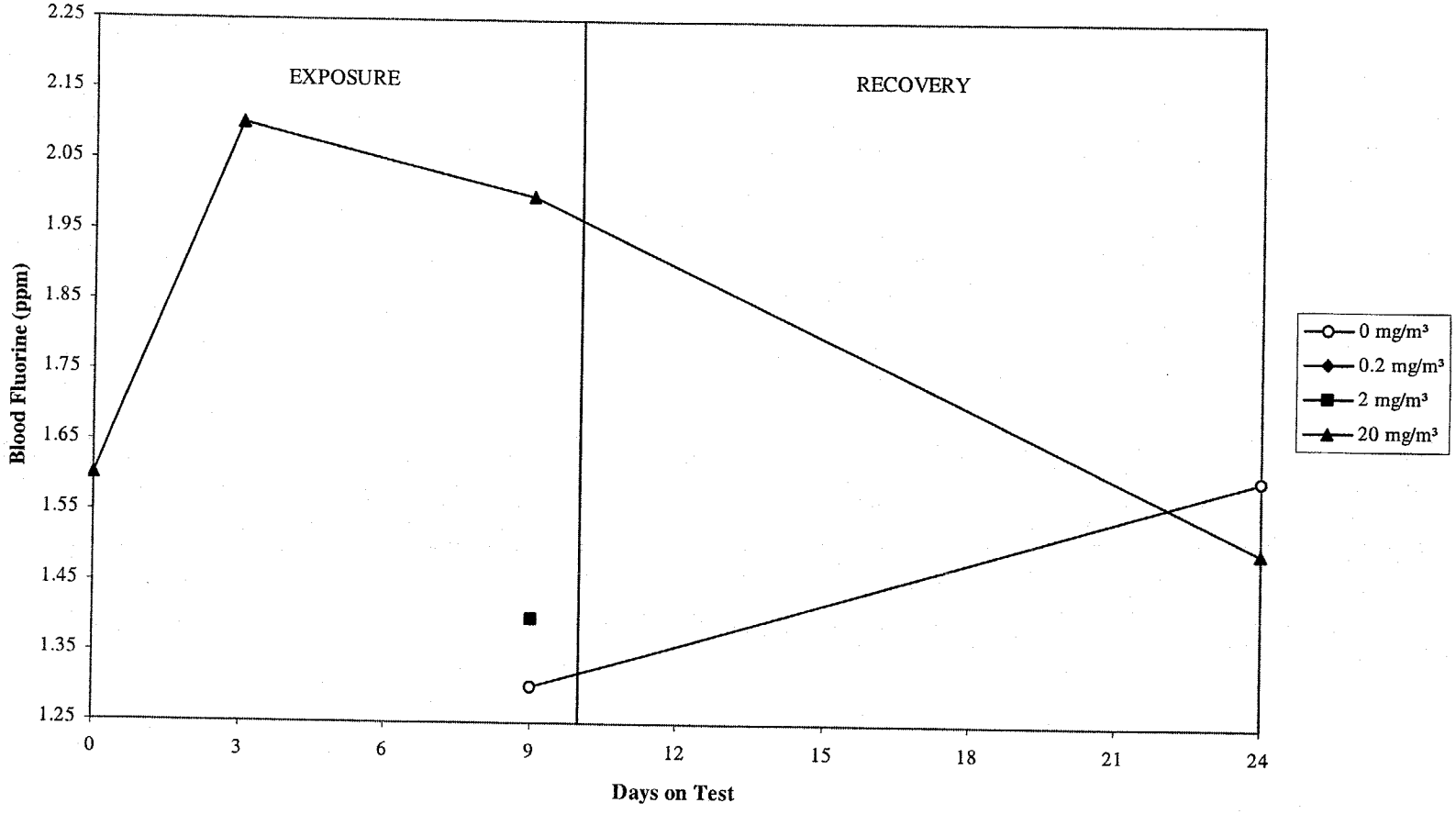
MEAN BODY WEIGHTS OF MALE RATS



* Weight losses due to fasting of rats prior to clinical pathology evaluation.

FIGURE 3

MEAN BLOOD FLUORINE OF MALE RATS



APPENDICES

APPENDIX A

Daily Chamber Concentrations

DAILY CHAMBER CONCENTRATIONS

EXPLANATORY NOTES

ABBREVIATIONS:

S.D. - standard deviation
mg/m^3 - milligrams per cubic meter
n - number of samples

FOOTNOTES:

a Chamber not sampled on this day.
b Value not calculable from sample size.

NOTES:

Values are reported to 2 significant figures.
Means and standard deviations were calculated prior to rounding values.

Daily Chamber Concentrations (mg/m³)

Exposure	0 mg/m³				0.2 mg/m³				2 mg/m³				20 mg/m³			
	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n
1	[a]				0.15	0.076	0.05 - 0.26	5	1.5	0.35	1.1 - 2.1	6	22	2.9	19 - 26	6
2	[a]				0.26	0.10	0.11 - 0.35	5	1.2	0.15	1.1 - 1.4	6	20	2.3	16 - 23	6
3	[a]				0.22	0.067	0.11 - 0.27	5	1.9	0.24	1.6 - 2.3	6	20	4.2	14 - 26	6
4	[a]				0.22	0.053	0.14 - 0.28	5	1.8	0.047	1.7 - 1.8	6	18	1.0	17 - 19	6
5	[a]				0.24	0.067	0.17 - 0.31	4	2.6	0.40	2.2 - 3.3	6	19	3.3	17 - 26	6
6	[a]				0.21	0.068	0.13 - 0.27	5	2.2	0.36	1.8 - 2.9	6	20	0.99	18 - 21	6
7	[a]				0.26	0.14	0.15 - 0.51	5	2.1	0.35	1.7 - 2.5	6	21	1.6	19 - 23	6
8	0	[b]	0	1	0.20	0.16	0.04 - 0.42	4	2.0	0.36	1.6 - 2.5	6	20	2.0	18 - 23	6
9	[a]				0.19	0.12	0.10 - 0.40	5	1.9	0.20	1.6 - 2.1	6	20	3.5	15 - 26	6

APPENDIX B

Daily Chamber Environmental Conditions

DAILY CHAMBER ENVIRONMENTAL CONDITIONS

EXPLANATORY NOTES

ABBREVIATIONS:

n - number of observations

FOOTNOTES:

a Due to technical error, samples were not taken for approximately the first 2 hours of the exposure.
b Due to technical error, false readings were omitted.

NOTES:

Values are reported to 2 significant figures.
Means and standard deviations were calculated prior to rounding values.

Daily Chamber Environmental Conditions - Temperature (ºC)

Exposure	0 mg/m³				0.2 mg/m³				2 mg/m³				20 mg/m³			
	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n
1	23	0.25	23 - 24	24	24	0.63	23 - 25	24	24	0.60	23 - 25	24	24	0.26	23 - 24	24
2	22	0.35	22 - 23	24	24	0.66	22 - 24	24	24	0.85	22 - 25	24	23	0.74	21 - 24	24
3	22	0.34	21 - 22	24	24	0.61	22 - 25	24	23	0.74	22 - 25	24	23	0.24	23	24
4	22	0.35	21 - 22	24	23	0.55	22 - 25	24	23	0.62	21 - 24	24	22	0.74	21 - 23	24
5	21	0.62	20 - 22	24	23	1.7	19 - 25	24	23	1.4	20 - 25	24	21	1.4	19 - 23	24
6	21	1.1	19 - 24	24	20	1.1	18 - 21	24	20	1.1	17 - 22	24	19	1.2	16 - 21	24
7	22	1.1	21 - 24	24	20	0.70	19 - 22	24	23	1.4	20 - 25	24	21	1.3	19 - 23	24
8	24	0.37	23 - 24	24	24	0.52	23 - 25	24	24	0.47	23 - 25	24	24	0.34	22 - 24	24
9	23	0.30	23 - 24	24	23	0.86	22 - 24	24	25	0.35	24 - 25	24	23	0.45	22 - 24	24

Daily Chamber Environmental Conditions - Relative Humidity (%)

Exposure	0 mg/m³				0.2 mg/m³				2 mg/m³				20 mg/m³			
	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n
1	53	0.72	52 - 55	16[a]	56	1.0	54 - 58	16[a]	52	3.9	48 - 68	24	38	1.3	36 - 40	16[a]
2	36	3.7	34 - 53	24	51	2.0	47 - 57	24	50	4.0	47 - 66	24	37	2.5	35 - 47	23[b]
3	55	8.9	34 - 61	24	51	2.0	48 - 57	24	51	2.6	49 - 62	24	41	1.9	37 - 44	20[b]
4	60	4.1	57 - 79	24	53	2.8	49 - 63	24	50	4.5	47 - 69	24	44	11	37 - 91	24
5	67	9.0	58 - 82	24	52	3.2	48 - 58	24	51	2.8	48 - 58	24	50	7.5	44 - 77	24
6	58	1.9	53 - 63	24	59	2.8	56 - 66	24	56	2.1	54 - 63	24	48	6.8	44 - 70	24
7	54	2.6	50 - 58	24	59	1.9	56 - 62	24	55	1.8	51 - 59	24	48	3.3	42 - 58	24
8	54	1.3	52 - 58	24	54	1.2	52 - 57	24	54	0.94	52 - 56	24	44	1.4	42 - 46	24
9	53	1.5	50 - 56	24	54	1.6	52 - 57	24	53	1.3	50 - 55	24	43	1.5	41 - 46	24

Daily Chamber Environmental Conditions - Airflow (L/min)

Exposure	0 mg/m³				0.2 mg/m³				2 mg/m³				20 mg/m³			
	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n	Mean	S.D.	Range	n
1	35	0.017	35	24	65	0.071	65	24	65	0.052	65	24	50	0.029	50	24
2	35	0.031	35	24	65	0.036	65	24	62	3.1	59 - 65	24	50	0.046	50	24
3	35	0.081	35	24	65	0.033	65	24	65	0.038	65	24	50	0.046	50	24
4	35	0.018	35 - 36	24	65	0.065	65	24	65	0.045	65	24	50	0.20	50 - 51	24
5	35	0.12	35	24	65	0.040	65	24	65	0.040	65	24	50	0.032	50	24
6	35	0.040	35	24	65	0.042	65	24	65	0.040	65	24	50	0.034	50	24
7	35	0.024	35 - 36	24	65	0.039	65	24	65	0.040	65	24	50	0.033	50	24
8	35	0.026	35	24	65	0.029	65	24	65	0.026	65	24	50	0.030	50	24
9	35	0.033	35	24	65	0.024	65	24	65	0.024	65	24	50	0.026	50	24

APPENDIX C

Individual Body Weights

INDIVIDUAL BODY WEIGHTS

EXPLANATORY NOTES

FOOTNOTES:

a Weight losses due to fasting of rats prior to clinical pathology evaluation

Individual Body Weights

	Body Weight g Day 0	Body Weight g Day 1	Body Weight g Day 2	Body Weight g Day 3	Body Weight g Day 4	Body Weight g Day 6	Body Weight g Day 7	Body Weight g Day 8	Body Weight g Day 9
Male, I 0 mg/m³									
662482	256.8	261.5	260.5	264.3	263.1	272.9	277.9	280.6	286.5
662483	274.2	271.7	273.9	276.6	278.9	292.8	291.1	295.4	297.1
662484	245.1	244.0	247.8	252.5	251.7	264.0	269.8	271.9	276.8
662485	246.6	251.9	257.6	261.0	261.4	270.3	272.7	276.8	273.5
662486	236.9	232.3	237.0	239.2	243.9	250.6	249.1	251.7	252.0
662487	252.1	242.1	242.9	246.4	249.0	254.9	256.0	262.4	262.5
662488	252.0	252.9	259.0	258.3	265.0	271.1	270.8	279.3	282.3
662489	252.1	249.5	251.2	254.3	258.8	261.6	264.2	262.4	263.9
662490	258.4	261.2	260.2	263.3	263.8	273.3	264.4	270.0	268.6
662491	242.4	236.1	240.3	239.3	242.9	248.2	253.7	255.9	254.5
662492	266.0	267.0	269.3	274.4	273.4	284.0	283.9	287.7	290.7
662493	264.2	257.3	261.8	266.4	267.7	281.0	284.3	286.5	293.8
662494	264.6	262.7	273.3	277.1	281.1	291.0	293.7	301.5	307.0
662495	249.6	243.9	251.9	257.6	243.4	205.8	235.6	248.1	232.4
662496	265.3	264.5	267.9	274.7	275.8	289.0	290.9	300.8	306.7

	Body Weight g Day 10	Body Weight g Day 14	Body Weight g Day 17	Body Weight g Day 21	Body Weight g Day 24
Male, I 0 mg/m³					
662482	261.3				
662483	276.4				
662484	248.1				
662485	243.0				
662486	228.4				
662487	233.4	276.6	289.3	309.5	299.4[a]
662488	253.6	297.0	314.6	338.3	321.7[a]
662489	238.7	278.3	292.7	318.7	310.2[a]
662490	243.4	286.5	306.4	330.9	319.3[a]
662491	229.4	263.2	280.6	303.3	291.2[a]
662492	286.8	311.0	335.0	354.2	377.2
662493	290.7	321.3	340.7	368.0	394.2
662494	297.1	321.3	339.8	361.7	380.6
662495	250.9	286.7	297.6	323.2	342.6
662496	296.5	329.3	353.0	376.4	404.4

Individual Body Weights

	Body Weight g Day 0	Body Weight g Day 1	Body Weight g Day 2	Body Weight g Day 3	Body Weight g Day 4	Body Weight g Day 6	Body Weight g Day 7	Body Weight g Day 8	Body Weight g Day 9
Male, III 0.2 mg/m³									
662497	259.3	251.1	255.0	255.0	259.1	267.8	268.9	274.4	274.2
662498	276.3	275.2	282.7	286.9	293.4	302.1	304.9	311.1	313.6
662499	232.7	233.3	238.4	240.1	242.4	246.8	252.3	254.7	257.8
662500	252.0	250.4	250.6	257.6	263.7	275.8	276.0	278.9	284.0
662501	239.2	236.8	243.8	243.4	249.8	261.4	262.2	270.0	266.8
662502	247.8	248.0	248.1	249.0	248.3	254.7	256.1	258.2	256.6
662503	255.7	252.7	264.3	267.7	276.5	289.2	295.3	301.6	304.2
662504	247.6	247.8	251.2	246.2	252.9	252.9	251.7	252.2	250.4
662505	254.1	253.9	258.1	251.6	263.1	270.0	274.4	277.6	279.3
662506	252.4	247.1	248.8	250.1	255.7	265.1	265.8	272.9	260.5
662507	264.3	260.9	266.0	266.9	266.1	277.7	282.9	283.1	286.1
662508	261.9	258.9	268.3	271.2	279.2	287.1	292.3	299.5	298.4
662509	264.7	252.2	259.7	269.6	265.3	277.9	279.7	282.2	287.0
662510	247.2	245.1	251.1	258.3	256.2	265.7	269.9	275.6	271.6
662511	270.8	266.6	278.3	283.5	287.9	298.7	300.4	306.6	311.8

	Body Weight g Day 10	Body Weight g Day 14	Body Weight g Day 17	Body Weight g Day 21	Body Weight g Day 24
Male, III 0.2 mg/m³					
662497	248.1				
662498	279.8				
662499	228.1				
662500	252.5				
662501	242.5				
662502	227.0	271.5	252.6	287.5	278.3[a]
662503	266.8	322.4	342.6	371.9	361.4[a]
662504	231.7	259.8	270.9	287.4	278.9[a]
662505	247.1	292.8	311.4	329.8	312.6[a]
662506	236.5	278.6	297.0	319.2	314.7[a]
662507	277.8	307.0	321.5	343.4	357.4
662508	297.8	320.7	337.1	359.0	371.3
662509	279.8	304.3	315.8	341.2	363.2
662510	267.2	292.3	310.2	326.9	347.1
662511	292.6	332.7	350.7	379.6	402.7

Individual Body Weights

	Body Weight g Day 0	Body Weight g Day 1	Body Weight g Day 2	Body Weight g Day 3	Body Weight g Day 4	Body Weight g Day 6	Body Weight g Day 7	Body Weight g Day 8	Body Weight g Day 9
Male, V 2 mg/m³									
662512	263.7	261.2	273.6	274.2	275.6	285.7	289.4	291.9	290.3
662513	262.0	267.0	270.7	274.1	275.2	289.0	294.4	298.3	301.1
662514	246.4	247.6	254.8	256.6	259.2	270.6	271.3	276.5	279.9
662515	252.0	241.7	248.3	251.4	252.7	264.9	267.4	275.2	277.6
662516	231.3	235.1	238.5	240.5	240.1	251.0	249.4	253.3	254.6
662517	253.9	255.2	254.1	263.9	266.1	268.6	277.9	281.3	283.0
662518	247.6	249.6	256.6	254.8	255.3	257.6	262.6	264.7	265.7
662519	254.5	253.7	256.3	261.0	265.6	278.2	274.6	282.8	284.1
662520	255.6	260.1	259.0	265.0	266.3	274.2	278.9	278.8	279.7
662521	252.8	253.6	254.3	256.2	261.5	268.8	272.6	274.2	274.1
662522	270.2	266.6	272.2	277.2	275.3	293.1	294.5	300.1	303.5
662523	265.1	267.2	273.5	278.2	280.4	294.0	299.8	300.5	304.7
662524	264.9	258.8	264.7	264.3	271.0	279.1	286.0	288.3	289.9
662525	244.7	238.8	246.5	251.4	252.0	270.4	272.6	278.4	275.0
662526	254.3	255.2	261.6	260.9	267.5	271.7	271.6	278.5	275.2

	Body Weight g Day 10	Body Weight g Day 14	Body Weight g Day 17	Body Weight g Day 21	Body Weight g Day 24
Male, V 2 mg/m³					
662512	267.4				
662513	268.1				
662514	252.5				
662515	252.0				
662516	233.4				
662517	250.3	289.5	313.8	334.5	325.9[a]
662518	240.0	276.8	295.6	309.9	301.8[a]
662519	258.3	301.6	316.0	334.1	323.1[a]
662520	257.1	301.2	320.6	340.7	330.3[a]
662521	250.7	293.2	312.2	337.9	326.7[a]
662522	296.4	330.1	342.9	362.6	385.6
662523	300.6	333.3	354.5	374.5	400.2
662524	296.6	321.1	337.3	364.0	380.7
662525	275.4	312.1	331.2	351.9	368.5
662526	276.2	294.4	309.1	321.9	332.8

Individual Body Weights

	Body Weight g Day 0	Body Weight g Day 1	Body Weight g Day 2	Body Weight g Day 3	Body Weight g Day 4	Body Weight g Day 6	Body Weight g Day 7	Body Weight g Day 8	Body Weight g Day 9
Male, VII 20 mg/m³									
662527	267.8	266.2	268.5	268.9	272.6	277.9	276.6	279.9	281.6
662528	275.5	275.1	275.3	278.2	278.0	289.1	289.4	288.4	292.4
662529	233.6	233.9	235.5	235.7	239.6	246.2	248.4	250.8	251.0
662530	247.2	244.2	242.4	250.2	256.0	262.4	269.4	273.1	271.6
662531	237.5	239.2	241.3	240.0	246.3	252.8	248.4	246.8	247.0
662532	259.0	265.2	268.9	274.8	275.4	290.1	294.7	297.7	295.5
662533	258.1	259.7	263.7	270.0	277.1	295.0	299.3	299.7	303.6
662534	255.0	252.6	254.9	260.5	265.8	273.5	281.7	281.5	291.1
662535	258.0	254.1	259.5	257.9	261.0	271.8	272.8	274.0	275.9
662536	251.1	250.0	248.3	252.3	255.4	267.2	272.2	272.9	272.5
662537	265.8	264.2	264.4	270.0	260.7	270.9	272.9	274.7	276.9
662538	262.1	261.8	266.7	265.4	270.8	274.1	275.3	271.2	273.5
662539	269.1	263.5	263.5	262.9	266.3	277.9	278.1	278.5	286.4
662540	244.0	237.7	238.4	240.1	237.7	246.0	248.0	250.0	246.8
662541	262.1	257.9	258.9	262.8	261.7	275.2	274.3	275.6	276.1

	Body Weight g Day 10	Body Weight g Day 14	Body Weight g Day 17	Body Weight g Day 21	Body Weight g Day 24
Male, VII 20 mg/m³					
662527	258.8				
662528	263.9				
662529	227.3				
662530	245.7				
662531	235.7				
662532	267.3	318.4	340.1	353.4	346.2[a]
662533	272.1	325.9	349.5	379.4	371.1[a]
662534	254.8	306.7	330.9	351.3	343.2[a]
662535	250.8	291.5	314.3	337.1	321.7[a]
662536	238.6	272.0	307.9	332.5	313.6[a]
662537	271.9	298.0	317.6	334.2	358.0
662538	267.9	277.9	296.1	307.4	324.2
662539	287.3	312.5	327.1	351.7	367.2
662540	246.3	269.1	284.0	304.1	318.8
662541	274.0	295.8	313.2	342.5	366.5

APPENDIX D

Individual Clinical Observations and Mortality Records

Individual Clinical Observations and Mortality Records

Sex	Group	Animal	Observation	Days
M	I	662482	General observation, No Abnormality Detected	0-4
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Hair Loss, Forelimb, Bilateral	6-10
			Hair Loss, Forepaw, Bilateral	6-10
			Sacrificed by design	10
M	I	662483	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	I	662484	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	I	662485	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	I	662486	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	I	662487	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Accidentally killed	24
M	I	662488	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	I	662489	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	I	662490	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Bilateral	24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	24
M	I	662491	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	I	662492	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	I	662493	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	I	662494	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	I	662495	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	I	662496	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24

Individual Clinical Observations and Mortality Records

Sex	Group	Animal	Observation	Days
M	III	662497	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	III	662498	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	III	662499	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	III	662500	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	III	662501	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	III	662502	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Accidentally killed	24
M	III	662503	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	III	662504	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	III	662505	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	III	662506	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	III	662507	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	III	662508	General observation, No Abnormality Detected	0-14,21-24
			Discharge, Nose, Black	17
			Sacrificed by design	24
M	III	662509	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	III	662510	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	III	662511	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24

Individual Clinical Observations and Mortality Records

Sex	Group	Animal	Observation	Days
M	V	662512	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	V	662513	General observation, No Abnormality Detected	0-9
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Hair Loss, Forepaw, Bilateral	10
			Sacrificed by design	10
M	V	662514	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	V	662515	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	V	662516	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	V	662517	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10,24
			Sacrificed by design	24
M	V	662518	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	V	662519	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	V	662520	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	V	662521	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	V	662522	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	V	662523	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	V	662524	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	V	662525	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	V	662526	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24

Individual Clinical Observations and Mortality Records

Sex	Group	Animal	Observation	Days
M	VII	662527	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	VII	662528	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	VII	662529	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	VII	662530	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	VII	662531	General observation, No Abnormality Detected	0-10
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Sacrificed by design	10
M	VII	662532	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	VII	662533	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	VII	662534	General observation, No Abnormality Detected	0-21
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Hair Loss, Forepaw, Bilateral	24
			Sacrificed by design	24
M	VII	662535	General observation, No Abnormality Detected	0-24
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Sacrificed by design	24
M	VII	662536	General observation, No Abnormality Detected	0-7
			Eye Observations, Bled via Orbital for Clin Path, Left	10
			Eye Observations, Bled via Orbital for Clin Path, Right	24
			Hair Loss, Forelimb, Bilateral	8-24
			Hair Loss, Forepaw, Bilateral	17-24
			Sacrificed by design	24
M	VII	662537	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	VII	662538	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	VII	662539	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	VII	662540	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24
M	VII	662541	General observation, No Abnormality Detected	0-24
			Sacrificed by design	24

APPENDIX E

Individual Animal Blood Fluorine

INDIVIDUAL ANIMAL BLOOD FLUORINE

EXPLANATORY NOTES

FOOTNOTES:

a Insufficient sample size for accurate analysis.

Individual Animal Blood Fluorine

	Blood Fluorine ppm Day 0	Blood Fluorine ppm Day 3	Blood Fluorine ppm Day 9	Blood Fluorine ppm Day 24
Male, Group I - 0 mg/m³				
662492			1.3	1.6
662493			1.3	1.4
662494			1.3	1.8
662495			1.3	1.9
662496			1.4	1.4
Male, Group III - 0.2 mg/m³				
662507			1.3[a]	
662508			1.3	
662509			1.8[a]	
662510			1.5	
662511			1.3	
Male, Group V - 2 mg/m³				
662522			1.4	
662523			1.2	
662524			1.5	
662525			1.5	
662526			1.6[a]	
Male, Group VII - 20 mg/m³				
662537	1.6	1.9	2.0	1.4
662538	1.5	2.0	2.0	1.4
662539	1.5	2.2	1.9	1.6
662540	1.6	2.6	2.1	1.6
662541	1.6	1.8	1.8	1.7

APPENDIX F

Individual Animal Clinical Pathology Data

INDIVIDUAL ANIMAL CLINICAL PATHOLOGY DATA

EXPLANATORY NOTES

ABBREVIATIONS:

General:

ADEQ	-	adequate
CLOT	-	sample clotted
DECR	-	decreased
NSR	-	no sample received for testing
NT	-	not taken or not performed
OK	-	sample condition OK for testing
RNV	-	result not valid
UTD	-	unable to determine
<	-	less than

Individual Hematology Values:

COND	-	sample condition
RBC	-	red blood cell count
HGB	-	hemoglobin
HCT	-	hematocrit
MCV	-	mean corpuscular volume
MCH	-	mean corpuscular hemoglobin
MCHC	-	mean corpuscular hemoglobin concentration
RDW	-	red cell distribution width
ARET	-	absolute reticulocyte count
PLT	-	platelet count
WBC	-	white blood cell count
ANEU	-	absolute neutrophil (all forms)
ALYM	-	absolute lymphocyte
AMON	-	absolute monocyte
AEOS	-	absolute eosinophil
ABAS	-	absolute basophil
ALUC	-	absolute large unstained cell

Individual Red Blood Cell Morphology Values:

NORM	-	Normal
ANIS	-	anisocytosis
MIC	-	microcytes
MAC	-	macrocytes
POLY	-	polychromasia
HYPO	-	hypochromasia
ECHI	-	echinocytes
ACAN	-	acanthocytes
TARG	-	Target cells
RX	-	rouleaux
HJB	-	Howell-Jolly body
-	-	not observed or not examined; see whole blood sample condition

Individual White Blood Cell / Platelet Morphology Values:

NORM	-	Normal
SM	-	Smudge white blood cells
TOX	-	toxic neutrophils
DB	-	Döhle bodies
VC	-	vacuolated cytoplasm
BC	-	basophilic cytoplasm
PCE	-	platelet clumps / estimate
GP	-	giant platelets
BP	-	bizarre platelets
-	-	not observed or not examined; see whole blood sample condition

INDIVIDUAL ANIMAL CLINICAL PATHOLOGY DATA

EXPLANATORY NOTES (Continued)

ABBREVIATIONS: (Continued)

Individual Serum and Plasma Chemistry Values:

SHEM	-	serum hemolysis
SLIP	-	serum lipemia
SICT	-	serum icterus
AST	-	aspartate aminotransferase
ALT	-	alanine aminotransferase
SDH	-	sorbitol dehydrogenase
ALKP	-	alkaline phosphatase
BILI	-	total bilirubin
BUN	-	urea nitrogen
CREA	-	creatinine
CHOL	-	cholesterol
TRIG	-	triglycerides
GLUC	-	glucose
TP	-	total protein
ALB	-	albumin
GLOB	-	globulin
CALC	-	calcium
IPHS	-	inorganic phosphorous
NA	-	sodium
K	-	potassium
CL	-	chloride
PHEM	-	plasma hemolysis from blood sample for fluoride determination
PLIP	-	plasma lipemia from blood sample for fluoride determination
PICT	-	plasma icterus from blood sample for fluoride determination
PFLU	-	plasma fluoride

Individual Urinalysis Values:

VOL	-	volume
UFLU	-	urine fluoride

NOTES:

When individual animal data are not reported, it may be due to one of the following reasons or other reasons, all of which are explained in the study records:

the sample was clotted (CLOT)
there was insufficient sample for testing (QNS)
a valid result could not be obtained (RNV)
the sample was not suitable for testing
the animal died prior to sample collection
no sample was available for testing (NSR)

When an individual observation was recorded as being less than a certain value, calculations were performed on half the recorded value. For example, if bilirubin was reported as <0.1, 0.05 was used for any calculations performed with that bilirubin data.

Individual Hematology Values

Animal Number	COND	RBC $x10^6/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	ARET $x10^3/\mu L$	PLT $x10^3/\mu L$	WBC $x10^3/\mu L$
Male, Group I - 0 mg/m³ - Day 10											
662482	OK	7.36	14.8	43.9	59.6	20.1	33.8	12.5	218.9	1178	17.93
662483	OK	6.82	14.7	43.5	63.7	21.5	33.7	12.7	219.1	1538	17.84
662484	OK	6.59	14.4	43.1	65.4	21.9	33.5	12.0	178.3	1135	17.46
662485	OK	7.10	15.4	46.0	64.8	21.7	33.5	12.2	211.3	1117	13.71
662486	OK	7.30	15.4	45.5	62.4	21.1	33.8	11.5	185.2	989	15.25
662487	OK	7.04	14.7	43.1	61.3	20.9	34.1	12.1	149.4	1337	13.83
662488	OK	6.70	14.1	42.8	63.9	21.1	33.0	12.3	183.2	1198	14.36
662489	OK	6.72	14.7	44.4	66.0	21.9	33.1	13.0	155.7	1143	15.20
662490	OK	6.94	14.8	44.4	64.0	21.3	33.2	11.8	101.7	1046	10.83
662491	OK	7.22	15.4	46.6	64.5	21.4	33.1	12.2	202.6	938	12.49
Male, Group III - 0.2 mg/m³ - Day 10											
662497	OK	7.61	15.3	45.6	59.9	20.1	33.5	12.4	204.8	1283	11.58
662498	OK	7.01	14.7	44.2	63.0	21.0	33.3	13.3	209.0	1436	11.68
662499	OK	7.25	15.0	45.2	62.3	20.6	33.1	11.4	183.1	1274	16.15
662500	OK	7.17	15.2	44.9	62.7	21.2	33.9	12.6	256.5	1197	11.01
662501	OK	7.25	14.7	44.1	60.8	20.2	33.3	12.3	239.7	1311	13.98
662502	OK	7.32	16.1	47.5	65.0	22.0	33.9	12.6	154.9	1033	24.81
662503	OK	6.80	14.8	44.0	64.7	21.8	33.7	12.7	305.3	1366	12.72
662504	OK	7.24	15.0	45.6	63.0	20.8	33.0	12.6	139.9	1126	13.34
662505	OK	7.08	15.5	46.9	66.3	21.9	33.0	11.9	195.7	717	11.64
662506	OK	6.86	15.1	44.9	65.5	22.0	33.6	12.4	211.0	1089	11.75

Individual Hematology Values

Animal Number	COND	RBC $x10^6/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	ARET $x10^3/\mu L$	PLT $x10^3/\mu L$	WBC $x10^3/\mu L$
Male, Group V - 2 mg/m³ - Day 10											
662512	OK	7.14	14.7	44.2	61.9	20.6	33.3	12.6	213.3	1340	12.23
662513	OK	7.31	15.0	45.2	61.9						

Individual Hematology Values

Animal Number	ANEU $x10^3/\mu L$	ALYM $x10^3/\mu L$	AMON $x10^3/\mu L$	AEOS $x10^3/\mu L$	ABAS $x10^3/\mu L$	ALUC $x10^3/\mu L$
Male, Group I - 0 mg/m³ - Day 10						
662482	3.58	13.49	0.46	0.21	0.09	0.09
662483	2.14	14.78	0.50	0.17	0.14	0.10
662484	3.01	13.45	0.44	0.07	0.30	0.19
662485	1.75	11.57	0.13	0.11	0.09	0.07
662486	2.56	12.18	0.22	0.11	0.11	0.07
662487	1.61	11.86	0.14	0.07	0.08	0.07
662488	1.74	12.27	0.15	0.07	0.07	0.05
662489	1.05	13.52	0.29	0.06	0.12	0.15
662490	0.95	9.54	0.11	0.10	0.06	0.07
662491	1.84	10.09	0.29	0.08	0.13	0.05
Male, Group III - 0.2 mg/m³ - Day 10						
662497	1.97	9.04	0.25	0.05	0.18	0.09
662498	1.96	9.25	0.19	0.10	0.10	0.08
662499	1.74	13.34	0.62	0.20	0.15	0.11
662500	1.03	9.41	0.24	0.07	0.16	0.09
662501	0.97	12.27	0.46	0.06	0.10	0.12
662502	1.60	22.53	0.23	0.11	0.13	0.21
662503	2.19	9.72	0.50	0.14	0.08	0.09
662504	1.18	11.70	0.27	0.05	0.08	0.05
662505	1.09	9.99	0.31	0.08	0.10	0.07
662506	1.23	10.22	0.13	0.07	0.06	0.05

Individual Hematology Values

Animal Number	ANEU $x10^3/\mu L$	ALYM $x10^3/\mu L$	AMON $x10^3/\mu L$	AEOS $x10^3/\mu L$	ABAS $x10^3/\mu L$	ALUC $x10^3/\mu L$
Male, Group V - 2 mg/m³ - Day 10						
662512	2.21	9.21	0.46	0.10	0.16	0.10
662513	1.88	10.43	0.41	0.22	0.04	0.05
662514	1.19	10.53	0.17	0.15	0.07	0.08
662515	1.50	16.24	0.29	0.16	0.17	0.08
662516	1.91	10.05	0.32	0.17	0.11	0.06
662517	1.67	12.94	0.13	0.07	0.12	0.05
662518	2.21	12.07	0.52	0.14	0.15	0.07
662519	1.16	8.11	0.16	0.08	0.05	0.03
662520	1.28	11.54	0.31	0.15	0.07	0.06
662521	1.41	11.18	0.23	0.06	0.07	0.06
Male, Group VII - 20 mg/m³ - Day 10						
662527	1.55	12.46	0.55	0.29	0.19	0.09
662528	2.26	11.23	0.46	0.19	0.09	0.10
662529	1.27	8.84	0.15	0.13	0.09	0.06
662530	1.90	12.86	0.29	0.71	0.17	0.10
662531	1.80	15.48	0.29	0.20	0.13	0.10
662532	2.03	9.99	0.23	0.10	0.07	0.07
662533	1.91	12.73	0.16	0.26	0.10	0.11
662534	2.18	11.44	0.33	0.08	0.07	0.07
662535	1.10	10.21	0.28	0.10	0.06	0.04
662536	1.88	4.99	0.30	0.06	0.04	0.03

Individual Hematology Values

Animal Number	COND	RBC $x10^6/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	ARET $x10^3/\mu L$	PLT $x10^3/\mu L$	WBC $x10^3/\mu L$
Male, Group I - 0 mg/m³ - Day 24											
662487	OK	7.58	14.9	45.5	60.0	19.7	32.8	12.1	228.2	RNV	13.17
662488	OK	7.48	15.5	45.9	61.4	20.8	33.9	12.2	264.8	RNV	10.45
662489	OK	7.13	15.1	44.2	61.9	21.2	34.3	12.0	226.6	1321	9.67
662490	OK	7.24	15.4	44.9	61.9	21.3	34.4	11.8	193.0	1098	10.60
662491	OK	7.49	15.4	44.9	59.9	20.6	34.3	12.1	259.1	947	9.69
Male, Group III - 0.2 mg/m³ - Day 24											
662502	OK	7.31	15.2	45.6	62.4	20.8	33.3	12.4	236.4	RNV	16.04
662503	OK	7.07	15.0	43.8	62.0	21.3	34.3	12.0	259.8	1335	10.21
662504	OK	7.54	15.4	44.7	59.3	20.4	34.4	11.7	197.3	RNV	9.69
662505	OK	7.37	15.8	44.8	60.7	21.5	35.3	11.5	188.5	RNV	7.17
662506	OK	7.30	15.1	44.5	61.0	20.7	33.9	11.9	259.5	1043	9.28
Male, Group V - 2 mg/m³ - Day 24											
662517	OK	7.83	15.7	47.0	60.0	20.0	33.4	11.3	228.6	1375	11.95
662518	OK	7.57	14.9	43.4	57.3	19.7	34.4	12.7	186.3	1421	10.42
662519	OK	7.22	14.5	43.1	59.6	20.1	33.8	11.5	226.1	1286	8.17
662520	CLOT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
662521	OK	7.27	15.0	44.0	60.5	20.7	34.2	11.7	212.4	1388	9.59
Male, Group VII - 20 mg/m³ - Day 24											
662532	OK	7.49	14.8	45.2	60.4	19.8	32.8	12.0	267.8	1395	12.18
662533	OK	7.41	14.9	45.1	60.9	20.1	32.9	11.7	213.7	1406	11.54
662534	OK	6.91	15.0	42.9	62.1	21.7	35.0	12.3	203.6	1220	10.73
662535	OK	7.84	14.5	42.9	54.7	18.5	33.9	12.1	236.0	1253	12.39
662536	OK	7.45	14.7	43.3	58.2	19.7	33.8	12.8	253.1	RNV	4.06

Individual Hematology Values

Animal Number	ANEU $x10^3/\mu L$	ALYM $x10^3/\mu L$	AMON $x10^3/\mu L$	AEOS $x10^3/\mu L$	ABAS $x10^3/\mu L$	ALUC $x10^3/\mu L$
Male, Group I - 0 mg/m³ - Day 24						
662487	2.28	10.05	0.33	0.28	0.09	0.14
662488	1.15	9.20	0.10	0.00	0.00	0.00
662489	1.91	7.20	0.36	0.08	0.07	0.06
662490	2.29	8.02	0.17	0.04	0.03	0.04
662491	1.95	7.25	0.29	0.09	0.04	0.06
Male, Group III - 0.2 mg/m³ - Day 24						
662502	2.50	12.82	0.45	0.14	0.06	0.08
662503	1.93	7.80	0.20	0.12	0.09	0.06
662504	1.30	8.12	0.15	0.04	0.04	0.04
662505	1.13	5.74	0.11	0.14	0.02	0.03
662506	1.50	7.50	0.16	0.05	0.04	0.04
Male, Group V - 2 mg/m³ - Day 24						
662517	2.30	9.25	0.10	0.10	0.12	0.08
662518	1.52	8.46	0.13	0.10	0.13	0.09
662519	1.34	6.48	0.16	0.11	0.05	0.03
662520	NT	NT	NT	NT	NT	NT
662521	1.12	8.15	0.15	0.05	0.07	0.05
Male, Group VII - 20 mg/m³ - Day 24						
662532	2.23	9.28	0.31	0.11	0.11	0.14
662533	1.98	9.06	0.21	0.15	0.07	0.07
662534	2.16	8.02	0.30	0.08	0.10	0.07
662535	1.85	10.08	0.19	0.13	0.06	0.08
662536	1.18	2.70	0.11	0.03	0.03	0.01

Individual Red Blood Cell Morphology Values

Animal Number	NORM	ANIS	MIC	MAC	POLY	HYPO	ECHI	ACAN	TARG	RX	HJB
Male, Group I - 0 mg/m³ - Day 10											
662482	NO	-	-	-	TRACE	-	-	-	-	-	-
662483	NO	TRACE	TRACE	-	TRACE	-	-	-	-	-	-
662484	NO	-	-	-	TRACE	-	FEW	TRACE	-	-	-
662485	NO	-	-	-	TRACE	-	-	-	-	-	-
662486	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662487	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662488	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662489	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662490	NO	-	-	-	TRACE	-	-	-	-	-	-
662491	NO	-	-	-	TRACE	-	-	-	-	-	-
Male, Group III - 0.2 mg/m³ - Day 10											
662497	NO	-	-	-	TRACE	-	-	-	-	-	-
662498	NO	-	-	-	TRACE	-	-	-	-	-	-
662499	NO	-	-	-	TRACE	-	FEW	-	-	-	-
662500	NO	-	-	-	TRACE	-	-	-	-	-	-
662501	NO	-	-	-	TRACE	-	FEW	TRACE	-	-	-
662502	NO	-	-	-	TRACE	-	FEW	TRACE	-	-	-
662503	NO	-	-	-	FEW	-	TRACE	TRACE	-	-	-
662504	NO	-	-	-	TRACE	-	-	-	-	-	-
662505	NO	-	-	-	TRACE	-	-	-	-	-	-
662506	NO	-	-	-	TRACE	-	-	-	-	-	-

Individual Red Blood Cell Morphology Values

Animal Number	NORM	ANIS	MIC	MAC	POLY	HYPO	ECHI	ACAN	TARG	RX	HJB
Male, Group V - 2 mg/m³ - Day 10											
662512	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662513	NO	-	-	-	TRACE	-	FEW	TRACE	-	-	-
662514	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
662515	NO	-	-	-	TRACE	-	-	-	-	-	-
662516	NO	-	-	-	TRACE	-	-	-	-	-	-
662517	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
662518	NO	-	-	-	TRACE	-	-	-	-	-	-
662519	NO	-	-	-	TRACE	-	-	-	-	-	-
662520	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662521	NO	-	-	-	TRACE	-	-	-	-	-	-
Male, Group VII - 20 mg/m³ - Day 10											
662527	NO	-	-	-	TRACE	-	-	-	-	-	-
662528	NO	-	-	-	TRACE	-	-	-	-	-	-
662529	NO	TRACE	TRACE	-	TRACE	-	TRACE	TRACE	-	-	-
662530	NO	-	-	-	TRACE	-	-	-	-	-	-
662531	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
662532	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662533	NO	-	-	-	TRACE	-	-	-	-	-	-
662534	NO	-	-	-	TRACE	-	-	-	-	-	-
662535	NO	-	-	-	TRACE	-	-	-	-	-	-
662536	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-

Individual Red Blood Cell Morphology Values

Animal Number	NORM	ANIS	MIC	MAC	POLY	HYPO	ECHI	ACAN	TARG	RX	HJB
Male, Group I - 0 mg/m³ - Day 24											
662487	NO	-	-	-	TRACE	-	MODERATE	TRACE	-	-	-
662488	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662489	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662490	NO	-	-	-	TRACE	-	-	-	-	-	-
662491	NO	-	-	-	TRACE	-	FEW	MODERATE	-	-	-
Male, Group III - 0.2 mg/m³ - Day 24											
662502	NO	-	-	-	TRACE	-	FEW	FEW	-	-	-
662503	NO	-	-	-	TRACE	-	-	-	-	-	-
662504	NO	-	-	-	TRACE	-	-	-	-	-	-
662505	NO	-	-	-	TRACE	-	-	-	-	-	-
662506	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
Male, Group V - 2 mg/m³ - Day 24											
662517	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
662518	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662519	NO	-	-	-	TRACE	-	-	-	-	-	-
662520	CLOT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
662521	NO	-	-	-	TRACE	-	TRACE	-	-	-	-
Male, Group VII - 20 mg/m³ - Day 24											
662532	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662533	NO	-	-	-	TRACE	-	-	TRACE	-	-	-
662534	NO	-	-	-	TRACE	-	-	-	-	-	-
662535	NO	-	-	-	TRACE	-	TRACE	TRACE	-	-	-
662536	NO	-	-	-	TRACE	-	FEW	FEW	-	-	-

Individual White Blood Cell / Platelet Morphology Values

Animal Number	NORM	SM	TOX	DB	VC	BC	PCE	GP	BP
Male, Group I - 0 mg/m³ - Day 10									
662482	YES	-	-	-	-	-	-	-	-
662483	YES	-	-	-	-	-	-	-	-
662484	YES	-	-	-	-	-	-	-	-
662485	YES	-	-	-	-	-	-	-	-
662486	YES	-	-	-	-	-	-	-	-
662487	YES	-	-	-	-	-	-	-	-
662488	YES	-	-	-	-	-	-	-	-
662489	YES	-	-	-	-	-	-	-	-
662490	YES	-	-	-	-	-	-	-	-
662491	YES	-	-	-	-	-	-	-	-
Male, Group III - 0.2 mg/m³ - Day 10									
662497	YES	-	-	-	-	-	-	-	-
662498	YES	-	-	-	-	-	-	-	-
662499	YES	-	-	-	-	-	-	-	-
662500	YES	-	-	-	-	-	-	-	-
662501	YES	-	-	-	-	-	-	-	-
662502	YES	-	-	-	-	-	-	-	-
662503	YES	-	-	-	-	-	-	-	-
662504	YES	-	-	-	-	-	-	-	-
662505	YES	-	-	-	-	-	-	-	-
662506	YES	-	-	-	-	-	-	-	-

Individual White Blood Cell / Platelet Morphology Values

Animal Number	NORM	SM	TOX	DB	VC	BC	PCE	GP	BP
Male, Group V - 2 mg/m³ - Day 10									
662512	YES	-	-	-	-	-	-	-	-
662513	YES	-	-	-	-	-	-	-	-
662514	YES	-	-	-	-	-	-	-	-
662515	YES	-	-	-	-	-	-	-	-
662516	YES	-	-	-	-	-	-	-	-
662517	YES	-	-	-	-	-	-	-	-
662518	YES	-	-	-	-	-	-	-	-
662519	YES	-	-	-	-	-	-	-	-
662520	YES	-	-	-	-	-	-	-	-
662521	YES	-	-	-	-	-	-	-	-
Male, Group VII - 20 mg/m³ - Day 10									
662527	YES	-	-	-	-	-	-	-	-
662528	YES	-	-	-	-	-	-	-	-
662529	YES	-	-	-	-	-	-	-	-
662530	YES	-	-	-	-	-	-	-	-
662531	YES	-	-	-	-	-	-	-	-
662532	NO	-	-	-	-	-	YES/UTD	-	-
662533	YES	-	-	-	-	-	-	-	-
662534	YES	-	-	-	-	-	-	-	-
662535	YES	-	-	-	-	-	-	-	-
662536	YES	-	-	-	-	-	-	-	-

Individual White Blood Cell / Platelet Morphology Values

Animal Number	NORM	SM	TOX	DB	VC	BC	PCE	GP	BP
Male, Group I - 0 mg/m³ - Day 24									
662487	NO	-	-	-	-	-	YES/UTD	-	-
662488	NO	-	-	-	-	-	YES/UTD	-	-
662489	YES	-	-	-	-	-	-	-	-
662490	YES	-	-	-	-	-	-	-	-
662491	YES	-	-	-	-	-	-	-	-
Male, Group III - 0.2 mg/m³ - Day 24									
662502	NO	-	-	-	-	-	YES/DECR	-	-
662503	YES	-	-	-	-	-	-	-	-
662504	NO	-	-	-	-	-	YES/ADEQ	-	-
662505	NO	-	-	-	-	-	YES/UTD	-	-
662506	YES	-	-	-	-	-	-	-	-
Male, Group V - 2 mg/m³ - Day 24									
662517	YES	-	-	-	-	-	-	-	-
662518	YES	-	-	-	-	-	-	-	-
662519	YES	-	-	-	-	-	-	-	-
662520	CLOT	NT	NT	NT	NT	NT	NT	NT	NT
662521	YES	-	-	-	-	-	-	-	-
Male, Group VII - 20 mg/m³ - Day 24									
662532	YES	-	-	-	-	-	-	-	-
662533	YES	-	-	-	-	-	-	-	-
662534	YES	-	-	-	-	-	-	-	-
662535	YES	-	-	-	-	-	-	-	-
662536	NO	-	-	-	-	-	YES/DECR	-	-

Individual Serum and Plasma Chemistry Values

Animal Number	SHEM	SLIP	SICT	AST U/L	ALT U/L	SDH U/L	ALKP U/L	BILI mg/dL	BUN mg/dL	CREA mg/dL	CHOL mg/dL
Male, Group I - 0 mg/m³ - Day 10											
662482	TRACE	NONE	NONE	107	45	11.9	233	0.12	16	0.20	67
662483	NONE	NONE	NONE	107	41	19.9	189	0.10	15	0.23	68
662484	TRACE	NONE	NONE	106	54	16.3	214	0.16	14	0.24	96
662485	NONE	NONE	NONE	90	37	11.0	223	<0.10	14	0.24	67
662486	NONE	NONE	NONE	80	37	10.7	231	<0.10	18	0.26	58
662487	NONE	NONE	NONE	81	27	11.1	241	0.10	16	0.21	59
662488	TRACE	NONE	NONE	94	38	10.7	218	0.12	17	0.23	53
662489	NONE	NONE	NONE	89	36	10.2	256	0.11	17	0.27	61
662490	TRACE	NONE	NONE	87	29	7.9	227	0.11	14	0.21	70
662491	TRACE	NONE	NONE	99	36	11.6	237	0.13	18	0.27	65
Male, Group III - 0.2 mg/m³ - Day 10											
662497	NONE	NONE	NONE	99	51	12.9	330	0.14	15	0.25	68
662498	TRACE	NONE	NONE	114	42	9.3	192	0.12	17	0.30	55
662499	TRACE	NONE	NONE	78	29	7.3	246	<0.10	16	0.20	58
662500	TRACE	NONE	NONE	108	42	12.7	323	0.11	19	0.36	41
662501	NONE	NONE	NONE	89	30	13.0	219	0.12	13	0.35	79
662502	NONE	NONE	NONE	74	34	9.6	250	<0.10	16	0.27	63
662503	NONE	NONE	NONE	103	48	12.2	252	0.10	13	0.23	67
662504	NONE	NONE	NONE	91	41	12.4	224	0.11	15	0.25	58
662505	TRACE	NONE	NONE	95	42	12.7	231	0.12	18	0.31	79
662506	TRACE	NONE	NONE	93	33	11.4	310	0.11	15	0.28	56

Individual Serum and Plasma Chemistry Values

Animal Number	SHEM	SLIP	SICT	AST U/L	ALT U/L	SDH U/L	ALKP U/L	BILI mg/dL	BUN mg/dL	CREA mg/dL	CHOL mg/dL
Male, Group V - 2 mg/m³ - Day 10											
662512	TRACE	NONE	NONE	107	41	20.5	227	0.12	13	0.25	45
662513	TRACE	NONE	NONE	128	46	9.4	390	<0.10	12	0.25	55
662514	NONE	NONE	NONE	87	40	11.2	236	<0.10	13	0.21	64
662515	TRACE	NONE	NONE	96	46	13.4	252	0.10	15	0.25	62
662516	TRACE	NONE	NONE	91	42	16.8	266	0.12	18	0.28	84
662517	NONE	NONE	NONE	77	29	8.1	196	0.11	14	0.28	49
662518	TRACE	NONE	NONE	98	43	12.8	248	0.13	20	0.26	60
662519	TRACE	NONE	NONE	79	30	8.5	229	<0.10	15	0.20	58
662520	NONE	NONE	NONE	87	40	11.7	268	0.11	14	0.21	60
662521	NONE	NONE	NONE	91	33	11.2	182	0.11	16	0.28	68
Male, Group VII - 20 mg/m³ - Day 10											
662527	TRACE	NONE	NONE	102	36	12.0	325	0.11	15	0.38	58
662528	TRACE	NONE	NONE	103	42	14.7	212	0.11	15	0.27	43
662529	NONE	NONE	NONE	109	44	14.0	197	<0.10	14	0.29	51
662530	NONE	NONE	NONE	126	43	18.2	230	0.15	9	0.16	43
662531	TRACE	NONE	NONE	106	48	12.3	327	0.12	15	0.27	54
662532	NONE	NONE	NONE	88	39	11.2	193	<0.10	14	0.29	71
662533	NONE	NONE	NONE	93	36	13.0	261	0.11	12	0.28	69
662534	TRACE	NONE	NONE	88	39	8.5	224	<0.10	12	0.24	49
662535	NONE	NONE	NONE	94	34	10.9	253	0.12	14	0.25	76
662536	TRACE	NONE	NONE	117	47	10.5	383	0.14	13	0.27	53

Individual Serum and Plasma Chemistry Values

Animal Number	TRIG mg/dL	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	CALC mg/dL	IPHS mg/dL	NA mmol/L	K mmol/L	CL mmol/L	PHEM
Male, Group I - 0 mg/m³ - Day 10											
662482	36	85	6.1	4.0	2.1	11.5	11.2	144.9	6.48	98.6	NONE
662483	47	79	6.2	4.1	2.1	11.9	10.2	146.9	6.39	100.3	NONE
662484	77	87	6.2	4.2	2.0	11.6	10.0	146.5	5.67	99.7	NONE
662485	48	76	6.0	3.9	2.1	11.4	10.6	147.9	6.06	102.4	NONE
662486	40	89	6.0	3.9	2.1	11.2	10.7	148.0	5.84	103.3	NONE
662487	34	90	5.8	3.8	2.0	11.4	10.3	147.6	6.13	102.8	NT
662488	21	91	6.0	4.1	1.9	11.8	10.9	150.7	6.08	103.3	NT
662489	35	85	6.2	4.2	2.0	11.4	10.4	151.2	6.01	105.9	NT
662490	44	88	6.3	4.0	2.3	11.6	9.8	150.7	5.93	106.1	NT
662491	30	85	6.4	4.4	2.0	11.9	11.3	150.8	6.07	102.9	NT
Male, Group III - 0.2 mg/m³ - Day 10											
662497	52	81	6.5	4.4	2.1	11.9	11.0	145.6	6.28	93.3	NONE
662498	42	84	6.4	4.4	2.0	11.6	10.4	146.4	5.95	101.6	NONE
662499	27	82	6.1	4.2	1.9	11.8	11.0	147.7	6.07	102.7	NONE
662500	32	89	6.1	4.3	1.8	11.8	11.8	148.4	6.23	102.3	NONE
662501	35	81	6.1	4.2	1.9	11.2	10.1	151.1	6.23	106.6	NONE
662502	35	84	6.5	4.5	2.0	12.0	11.0	149.7	5.97	105.4	NT
662503	69	86	6.3	4.2	2.1	12.0	10.1	149.1	6.71	103.3	NT
662504	33	98	6.0	4.2	1.8	11.5	10.7	151.6	6.10	104.9	NT
662505	37	96	6.3	4.3	2.0	11.1	10.7	151.6	5.56	102.7	NT
662506	50	79	5.9	4.0	1.9	11.3	10.6	150.3	6.94	105.8	NT

Individual Serum and Plasma Chemistry Values

Animal Number	TRIG mg/dL	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	CALC mg/dL	IPHS mg/dL	NA mmol/L	K mmol/L	CL mmol/L	PHEM
Male, Group V - 2 mg/m³ - Day 10											
662512	44	78	5.9	4.1	1.8	11.4	10.5	146.5	6.13	104.0	NONE
662513	45	68	5.8	4.2	1.6	11.0	10.7	146.3	5.73	100.9	NONE
662514	34	72	6.4	4.3	2.1	11.5	10.6	148.6	5.93	103.7	NONE
662515	55	83	6.0	4.1	1.9	11.5	10.5	149.4	6.22	105.6	NONE
662516	46	91	6.4	4.3	2.1	11.6	10.6	148.5	5.96	102.7	NONE
662517	35	84	6.5	4.3	2.2	12.1	10.5	151.0	6.27	104.8	NT
662518	49	87	6.6	4.4	2.2	12.1	10.2	151.7	6.32	106.9	NT
662519	40	86	5.9	3.9	2.0	11.4	11.6	149.9	6.28	104.5	NT
662520	56	84	5.9	4.2	1.7	11.8	11.1	150.7	6.49	105.3	NT
662521	38	88	6.0	4.1	1.9	12.2	12.2	151.0	6.09	102.7	NT
Male, Group VII - 20 mg/m³ - Day 10											
662527	40	82	6.3	4.3	2.0	11.9	10.0	147.9	6.11	101.4	NONE
662528	30	84	6.2	4.1	2.1	11.5	10.1	148.0	5.78	102.6	NONE
662529	40	81	6.1	4.2	1.9	11.6	10.0	147.6	6.28	103.0	NONE
662530	39	88	5.7	3.8	1.9	11.2	10.5	148.5	5.31	104.5	NONE
662531	56	88	6.5	4.3	2.2	11.4	9.9	149.2	6.20	105.0	NONE
662532	75	76	6.0	4.0	2.0	11.6	11.6	151.0	6.55	104.6	NT
662533	57	84	6.2	4.2	2.0	12.1	10.9	152.7	6.38	106.0	NT
662534	34	88	5.8	4.0	1.8	11.3	9.5	150.0	5.93	105.8	NT
662535	45	90	6.2	4.1	2.1	11.5	10.6	152.0	6.29	105.5	NT
662536	39	85	5.9	4.1	1.8	11.6	11.4	153.3	6.80	111.8	NT

Individual Serum and Plasma Chemistry Values

Animal Number	PLIP	PICT	PFLU µg/mL
Male, Group I - 0 mg/m³ - Day 10			
662482	NONE	NONE	0.1
662483	NONE	NONE	0.0
662484	NONE	NONE	0.0
662485	NONE	NONE	0.0
662486	NONE	NONE	0.0
662487	NT	NT	NT
662488	NT	NT	NT
662489	NT	NT	NT
662490	NT	NT	NT
662491	NT	NT	NT
Male, Group III - 0.2 mg/m³ - Day 10			
662497	NONE	NONE	0.1
662498	NONE	NONE	0.0
662499	NONE	NONE	0.0
662500	NONE	NONE	0.0
662501	NONE	NONE	0.0
662502	NT	NT	NT
662503	NT	NT	NT
662504	NT	NT	NT
662505	NT	NT	NT
662506	NT	NT	NT

Individual Serum and Plasma Chemistry Values

Animal Number	PLIP	PICT	PFLU µg/mL
Male, Group V - 2 mg/m³ - Day 10			
662512	NONE	NONE	0.1
662513	NONE	NONE	0.0
662514	NONE	NONE	0.0
662515	NONE	NONE	0.0
662516	NONE	NONE	0.0
662517	NT	NT	NT
662518	NT	NT	NT
662519	NT	NT	NT
662520	NT	NT	NT
662521	NT	NT	NT
Male, Group VII - 20 mg/m³ - Day 10			
662527	NONE	NONE	0.1
662528	NONE	NONE	0.0
662529	NONE	NONE	0.0
662530	NONE	NONE	0.0
662531	NONE	NONE	0.0
662532	NT	NT	NT
662533	NT	NT	NT
662534	NT	NT	NT
662535	NT	NT	NT
662536	NT	NT	NT

Individual Serum and Plasma Chemistry Values

Animal Number	SHEM	SLIP	SICT	AST U/L	ALT U/L	SDH U/L	ALKP U/L	BILI mg/dL	BUN mg/dL	CREA mg/dL	CHOL mg/dL
Male, Group I - 0 mg/m³ - Day 24											
662487	TRACE	NONE	NONE	82	39	14.2	238	0.17	15	0.28	58
662488	SMALL	NONE	NONE	106	41	17.1	191	0.10	16	0.38	43
662489	TRACE	NONE	NONE	96	34	10.7	240	0.13	19	0.28	69
662490	TRACE	NONE	NONE	99	38	14.1	245	0.13	13	0.32	63
662491	TRACE	NONE	NONE	115	38	4.8	182	0.12	18	0.30	56
Male, Group III - 0.2 mg/m³ - Day 24											
662502	TRACE	NONE	NONE	106	46	17.9	229	0.11	13	0.36	63
662503	TRACE	NONE	NONE	69	44	11.9	205	0.11	14	0.29	60
662504	NONE	NONE	NONE	88	39	14.3	168	0.10	14	0.22	54
662505	NONE	NONE	NONE	101	35	7.4	171	0.10	15	0.29	70
662506	NONE	NONE	NONE	112	36	13.8	290	<0.10	13	0.28	56
Male, Group V - 2 mg/m³ - Day 24											
662517	TRACE	NONE	NONE	77	34	14.0	166	0.12	13	0.29	57
662518	TRACE	NONE	NONE	79	41	13.9	211	0.15	17	0.36	61
662519	TRACE	NONE	NONE	87	34	8.8	170	0.11	14	0.27	57
662520	TRACE	NONE	NONE	104	89	11.9	225	<0.10	15	0.58	56
662521	NONE	NONE	NONE	87	40	13.7	153	0.11	15	0.28	67
Male, Group VII - 20 mg/m³ - Day 24											
662532	TRACE	NONE	NONE	83	38	18.5	174	0.11	13	0.33	70
662533	TRACE	NONE	NONE	88	40	14.4	240	0.15	13	0.30	74
662534	TRACE	NONE	NONE	99	49	19.1	194	0.11	13	0.27	46
662535	NONE	NONE	NONE	84	32	12.7	196	<0.10	14	0.27	74
662536	NONE	NONE	NONE	96	35	10.1	290	0.17	14	0.26	48

Individual Serum and Plasma Chemistry Values

Animal Number	TRIG mg/dL	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	CALC mg/dL	IPHS mg/dL	NA mmol/L	K mmol/L	CL mmol/L	PHEM
Male, Group I - 0 mg/m³ - Day 24											
662487	49	85	6.4	4.2	2.2	11.1	9.4	146.5	6.31	98.5	NSR
662488	17	90	6.4	4.3	2.1	10.8	10.1	148.4	5.88	99.8	NONE
662489	65	81	6.6	4.5	2.1	11.0	10.0	145.4	5.87	102.1	NONE
662490	43	118	6.9	4.6	2.3	11.4	10.9	147.8	5.16	105.3	NONE
662491	45	80	6.3	4.4	1.9	10.8	10.4	148.2	6.37	106.3	NONE
Male, Group III - 0.2 mg/m³ - Day 24											
662502	80	72	6.9	4.7	2.2	11.9	9.6	147.9	6.64	102.5	NSR
662503	64	101	6.4	4.3	2.1	11.1	9.2	145.2	6.44	102.3	NONE
662504	29	88	6.2	4.3	1.9	10.7	9.2	147.2	6.28	105.8	NONE
662505	34	97	6.4	4.4	2.0	10.4	9.2	146.1	5.55	107.2	NONE
662506	60	83	6.3	4.3	2.0	11.0	9.0	149.1	5.75	107.5	NONE
Male, Group V - 2 mg/m³ - Day 24											
662517	47	93	6.5	4.4	2.1	11.0	8.8	146.1	5.98	101.0	NONE
662518	58	101	6.8	4.5	2.3	11.5	8.8	148.2	5.49	103.8	NONE
662519	36	95	6.3	4.2	2.1	10.7	10.4	145.8	6.13	104.0	NONE
662520	52	82	5.6	3.9	1.7	10.3	10.7	147.7	6.84	109.1	NONE
662521	84	89	6.2	4.3	1.9	11.1	9.2	148.4	6.02	103.2	NONE
Male, Group VII - 20 mg/m³ - Day 24											
662532	52	90	6.6	4.4	2.2	10.6	9.5	147.8	6.29	102.9	NONE
662533	68	98	6.8	4.6	2.2	11.7	9.9	149.2	5.88	105.2	NONE
662534	22	102	6.0	4.2	1.8	10.9	10.4	146.7	5.86	104.7	NONE
662535	87	88	6.5	4.4	2.1	10.8	8.5	149.0	5.78	104.1	NONE
662536	32	90	5.7	4.1	1.6	10.8	10.3	149.2	6.28	106.9	NONE

Individual Serum and Plasma Chemistry Values

Animal Number	PLIP	PICT	PFLU µg/mL
Male, Group I - 0 mg/m³ - Day 24			
662487	NT	NT	NT
662488	NONE	NONE	0.1
662489	NONE	NONE	0.1
662490	NONE	NONE	0.1
662491	NONE	NONE	0.1
Male, Group III - 0.2 mg/m³ - Day 24			
662502	NT	NT	NT
662503	NONE	NONE	0.1
662504	NONE	NONE	0.1
662505	NONE	NONE	0.1
662506	NONE	NONE	0.1
Male, Group V - 2 mg/m³ - Day 24			
662517	NONE	NONE	0.2
662518	NONE	NONE	0.1
662519	NONE	NONE	0.1
662520	NONE	NONE	0.1
662521	NONE	NONE	0.1
Male, Group VII - 20 mg/m³ - Day 24			
662532	NONE	NONE	0.1
662533	NONE	NONE	0.1
662534	NONE	NONE	0.1
662535	NONE	NONE	0.1
662536	NONE	NONE	0.1

Individual Urinalysis Values

Animal Number	VOL mL	UFLU µg
Male, Group I - 0 mg/m³ - Day 10		
662482	4.6	12.0
662483	10.0	9.6
662484	12.6	10.3
662485	9.0	8.4
662486	9.8	10.4
662487	9.4	6.0
662488	7.4	6.7
662489	5.8	7.0
662490	2.0	5.6
662491	1.6	6.9
Male, Group III - 0.2 mg/m³ - Day 10		
662497	3.4	5.9
662498	13.0	10.7
662499	6.8	8.6
662500	6.0	5.4
662501	3.0	5.6
662502	6.2	5.9
662503	23.4	12.9
662504	9.0	8.8
662505	3.0	7.5
662506	5.4	7.7

Individual Urinalysis Values

Animal Number	VOL mL	UFLU µg
Male, Group V - 2 mg/m³ - Day 10		
662512	6.4	7.3
662513	13.6	9.8
662514	14.0	9.5
662515	8.2	6.6
662516	10.8	8.4
662517	6.6	7.4
662518	4.8	7.1
662519	13.0	9.4
662520	8.8	8.4
662521	6.8	6.9
Male, Group VII - 20 mg/m³ - Day 10		
662527	1.6	7.0
662528	4.2	8.4
662529	6.0	9.2
662530	38.2	23.2
662531	3.0	5.9
662532	5.0	9.8
662533	7.6	10.1
662534	13.0	13.1
662535	6.6	9.8
662536	7.8	8.8

Individual Urinalysis Values

Animal Number	VOL mL	UFLU µg
Male, Group I - 0 mg/m³ - Day 24		
662487	3.4	11.5
662488	4.8	9.4
662489	2.2	7.7
662490	11.6	14.0
662491	4.2	8.1
Male, Group III - 0.2 mg/m³ - Day 24		
662502	5.4	10.9
662503	16.0	19.8
662504	6.6	8.0
662505	6.8	11.7
662506	5.8	12.1
Male, Group V - 2 mg/m³ - Day 24		
662517	9.0	13.7
662518	4.6	8.7
662519	13.4	15.9
662520	10.0	12.2
662521	9.6	12.9
Male, Group VII - 20 mg/m³ - Day 24		
662532	6.8	12.1
662533	8.0	15.5
662534	22.4	18.1
662535	8.0	11.0
662536	9.0	13.1

APPENDIX G

Individual Animal Final Body and Organ Weights

Individual Animal Final Body and Organ Weights - Day 10 Sacrifice

Group: I Concentration: 0 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662482	261.30	1.883	0.7206	2.477	0.9480	131.55	8.352	3.1963	443.55	1.450	0.5549	77.005	2.770	1.0601	147.11
662483	276.40	1.853	0.6704	2.453	0.8875	132.38	9.450	3.4190	509.98	1.497	0.5416	80.788	3.294	1.1918	177.77
662484	248.10	2.048	0.8255	2.316	0.9335	113.09	9.376	3.7791	457.81	1.886	0.7602	92.090	2.898	1.1681	141.50
662485	243.00	1.910	0.7860	2.166	0.8914	113.40	7.203	2.9642	377.12	1.334	0.5490	69.843	2.895	1.1914	151.57
662486	228.40	1.756	0.7688	2.066	0.9046	117.65	6.826	2.9886	388.72	1.355	0.5933	77.164	2.895	1.2675	164.86
Mean	251.44	1.890	0.7543	2.296	0.9130	121.61	8.241	3.2694	435.44	1.504	0.5998	79.378	2.950	1.1758	156.56
S.D.	18.26	0.106	0.0601	0.179	0.0266	9.6225	1.209	0.3389	54.098	0.224	0.0919	8.1399	0.200	0.0748	14.659

Group: III Concentration: 0.2 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662497	248.10	2.100	0.8464	2.572	1.0367	122.48	8.815	3.5530	419.76	1.984	0.7997	94.476	3.237	1.3047	154.14
662498	279.80	1.935	0.6916	2.980	1.0650	154.01	9.691	3.4635	500.83	1.774	0.6340	91.680	3.109	1.1112	160.67
662499	228.10	1.882	0.8251	2.027	0.8886	107.70	6.878	3.0153	365.46	1.479	0.6484	78.587	2.668	1.1697	141.76
662500	252.50	1.891	0.7489	1.998	0.7913	105.66	7.335	2.9050	387.89	1.400	0.5545	74.035	3.001	1.1885	158.70
662501	242.50	1.863	0.7682	1.997	0.8235	107.19	6.772	2.7926	363.50	1.392	0.5740	74.718	2.944	1.2140	158.02
Mean	250.20	1.934	0.7760	2.315	0.9210	119.41	7.898	3.1459	407.49	1.606	0.6421	82.699	2.992	1.1976	154.66
S.D.	18.93	0.096	0.0618	0.445	0.1240	20.504	1.292	0.3415	56.895	0.262	0.0965	9.6828	0.213	0.0709	7.5886

FBW - Final Body Weight

Individual Animal Final Body and Organ Weights - Day 10 Sacrifice

Group: V Concentration: 2 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662512	267.40	1.961	0.7334	2.419	0.9046	123.36	8.707	3.2562	444.01	1.580	0.5909	80.571	3.289	1.2300	167.72
662513	268.10	1.899	0.7083	2.441	0.9105	128.54	8.558	3.1921	450.66	1.463	0.5457	77.041	3.199	1.1932	168.46
662514	252.50	1.816	0.7192	2.144	0.8491	118.06	7.910	3.1327	435.57	1.556	0.6162	85.683	2.576	1.0202	141.85
662515	252.00	1.949	0.7734	2.341	0.9290	120.11	8.125	3.2242	416.88	1.766	0.7008	90.611	2.720	1.0794	139.56
662516	233.40	1.723	0.7382	1.854	0.7943	107.60	7.426	3.1817	430.99	1.404	0.6015	81.486	2.524	1.0814	146.49
Mean	254.68	1.870	0.7345	2.240	0.8775	119.53	8.145	3.1974	435.62	1.554	0.6110	83.078	2.862	1.1208	152.82
S.D.	14.20	0.100	0.0247	0.245	0.0552	7.7554	0.515	0.0465	12.933	0.138	0.0567	5.2152	0.358	0.0874	14.167

Group: VII Concentration: 20 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662527	258.80	1.949	0.7531	2.296	0.8872	117.80	8.490	3.2805	435.61	1.684	0.6507	86.403	3.102	1.1986	159.16
662528	263.90	1.916	0.7260	2.473	0.9371	129.07	8.199	3.1069	427.92	1.827	0.6923	95.355	3.164	1.1989	165.14
662529	227.30	1.863	0.8196	1.975	0.8689	106.01	7.137	3.1399	383.09	1.501	0.6604	80.569	2.573	1.1320	138.11
662530	245.70	1.943	0.7908	2.902	1.1811	149.36	5.970	2.4298	307.26	1.651	0.6720	84.972	2.185	0.8893	112.45
662531	235.70	1.891	0.8023	2.029	0.8608	107.30	7.125	3.0229	376.78	1.199	0.5087	63.406	2.684	1.1387	141.94
Mean	246.28	1.912	0.7784	2.335	0.9470	121.91	7.384	2.9960	386.13	1.572	0.6368	82.141	2.742	1.1115	143.36
S.D.	15.33	0.036	0.0381	0.376	0.1342	17.942	1.002	0.3299	51.265	0.239	0.0733	11.772	0.403	0.1282	20.667

FBW - Final Body Weight

Individual Animal Final Body and Organ Weights - Day 24 Sacrifice

Group: I Concentration: 0 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662488	321.70	1.988	0.6180	2.556	0.7945	128.57	8.899	2.7662	447.64	1.463	0.4548	73.592	3.193	0.9925	160.61
662489	310.20	1.959	0.6315	2.540	0.8188	129.66	8.357	2.6941	426.60	1.504	0.4848	76.774	3.089	0.9958	157.68
662490	319.30	1.992	0.6239	3.009	0.9424	151.05	10.485	3.2837	526.36	1.908	0.5976	95.783	3.193	1.0000	160.29
662491	291.20	2.024	0.6951	2.472	0.8489	122.13	8.588	2.9492	424.31	1.615	0.5546	79.792	3.499	1.2016	172.88
Mean	310.60	1.991	0.6421	2.644	0.8512	132.85	9.082	2.9233	456.22	1.623	0.5229	81.485	3.244	1.0475	162.87
S.D.	13.85	0.027	0.0357	0.246	0.0647	12.579	0.961	0.2632	47.919	0.201	0.0650	9.8624	0.177	0.1028	6.8010

Group: III Concentration: 0.2 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662503	361.40	1.968	0.5445	2.693	0.7452	136.84	10.908	3.0183	554.27	1.918	0.5307	97.459	2.982	0.8251	151.52
662504	278.90	1.957	0.7017	2.348	0.8419	119.98	8.104	2.9057	414.10	1.641	0.5884	83.853	2.729	0.9785	139.45
662505	312.60	1.876	0.6001	2.831	0.9056	150.91	9.945	3.1814	530.12	1.500	0.4798	79.957	2.652	0.8484	141.36
662506	314.70	1.996	0.6343	2.670	0.8484	133.77	8.506	2.7029	426.15	1.474	0.4684	73.848	2.890	0.9183	144.79
Mean	316.90	1.949	0.6202	2.636	0.8353	135.37	9.366	2.9521	481.16	1.633	0.5168	83.779	2.813	0.8926	144.28
S.D.	33.90	0.052	0.0657	0.204	0.0666	12.688	1.297	0.2010	71.330	0.204	0.0549	10.007	0.150	0.0696	5.3100

FBW - Final Body Weight

Individual Animal Final Body and Organ Weights - Day 24 Sacrifice

Group: V Concentration: 2 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662517	325.90	2.011	0.6171	2.787	0.8552	138.59	10.776	3.3065	535.85	2.193	0.6729	109.05	3.131	0.9607	155.69
662518	301.80	2.086	0.6912	2.613	0.8658	125.26	10.535	3.4907	505.03	1.944	0.6441	93.193	3.001	0.9944	143.86
662519	323.10	1.936	0.5992	2.484	0.7688	128.31	9.768	3.0232	504.55	1.471	0.4553	75.981	3.037	0.9400	156.87
662520	330.30	1.908	0.5777	3.039	0.9201	159.28	10.180	3.0820	533.54	1.835	0.5556	96.174	3.648	1.1045	191.19
662521	326.70	1.941	0.5941	2.881	0.8818	148.43	10.623	3.2516	547.30	1.756	0.5375	90.469	3.226	0.9875	166.20
Mean	321.56	1.976	0.6158	2.761	0.8583	139.97	10.376	3.2308	525.25	1.840	0.5731	92.973	3.209	0.9974	162.77
S.D.	11.34	0.072	0.0444	0.219	0.0558	14.129	0.404	0.1864	19.394	0.264	0.0873	11.872	0.261	0.0637	17.763

Group: VII Concentration: 20 mg/m³ Sex: MALES

ANIMAL	FBW	BRAIN		KIDNEYS			LIVER			LUNGS			TESTES		
	(Gms)	(Gms)	%FBW	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN	(Gms)	%FBW	%BRAIN
662532	346.20	2.020	0.5835	2.564	0.7406	126.93	10.670	3.0820	528.22	1.561	0.4509	77.277	2.818	0.8140	139.50
662533	371.10	2.043	0.5505	3.166	0.8531	154.97	11.637	3.1358	569.60	1.735	0.4675	84.924	3.244	0.8742	158.79
662534	343.20	2.009	0.5854	2.816	0.8205	140.17	11.124	3.2413	553.71	1.562	0.4551	77.750	3.024	0.8811	150.52
662535	321.70	1.860	0.5782	2.702	0.8399	145.27	9.507	2.9552	511.13	1.751	0.5443	94.140	3.330	1.0351	179.03
662536	313.60	2.181	0.6955	3.029	0.9659	138.88	9.446	3.0121	433.10	1.864	0.5944	85.465	3.470	1.1065	159.10
Mean	339.16	2.023	0.5986	2.855	0.8440	141.24	10.477	3.0853	519.15	1.695	0.5024	83.911	3.177	0.9422	157.39
S.D.	22.61	0.114	0.0559	0.243	0.0809	10.200	0.975	0.1109	53.128	0.131	0.0639	6.8926	0.258	0.1229	14.494

FBW - Final Body Weight

APPENDIX H

Individual Animal Pathology Data

INDIVIDUAL ANIMAL PATHOLOGY DATA

KEY TO APPENDIX

LESION GRADING:

Histopathology changes are described according to their morphologic character, distribution and severity. The distribution (extent of tissue involvement) is indicated, where appropriate, by modifiers such as focal, multifocal, diffuse, unilateral, bilateral, etc. A severity score, if appropriate, is also assigned as follows:

MINIMAL:	The amount of change present barely exceeds that which is considered to be within normal limits.
MILD:	In general, the lesion is easily identified but of limited severity. The lesion probably does not produce any functional impairment.
MODERATE:	The lesion is prominent but there is significant potential for increased severity. Limited tissue or organ dysfunction is possible.
SEVERE:	The degree of change is either as complete as considered possible or great enough in intensity or extent to expect significant tissue or organ dysfunction.

COMMENT:

Grades minimal through severe represent progressive involvement/severity along a continuum with minimal lesions being the least severe and severe lesions being the most severe. While the grades refer to the morphologic characteristics of lesions, they also indicate their relative biologic significance.

Gross observations listing multiple masses for a tissue are distinguished with letters (i.e., A, b, c, d, etc.).

Individual Animal Pathology Data

Group: I Concentration: 0 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662482	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

662483 Terminal Sacrifice
Killed on Day : 10
Exposure Group : Main
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, mild.
HEART :
CARDIOMYOPATHY, minimal.
PARATHYROID GLANDS :
MISSING.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

ORGANS NOT EXAMINED:
PARATHYROID GLANDS

Individual Animal Pathology Data

Group: I Concentration: 0 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662484	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
FATTY CHANGE, MEDIAN CLEFT, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.

No Microscopic Abnormality Observed :
LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662485	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: I Concentration: 0 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662486	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
HEART :
CARDIOMYOPATHY, minimal.
PROSTATE :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662487	Accidentally Killed Duration of dosing-days: 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, mild.
NOSE :
DEGENERATION, TRIGEMINAL NERVE, mild.

No Microscopic Abnormality Observed :
LUNGS, PHARYNX/LARYNX, TESTES

Individual Animal Pathology Data

Group: I Concentration: 0 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662488	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662489 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

Individual Animal Pathology Data

Group: I Concentration: 0 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662490	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.
CYST, minimal.

No Microscopic Abnormality Observed :
LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662491 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

Individual Animal Pathology Data

Group: III Concentration: 0.2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662497	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.

No Microscopic Abnormality Observed :
LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662498 Terminal Sacrifice
Killed on Day : 10
Exposure Group : Main
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

Individual Animal Pathology Data

Group: III Concentration: 0.2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662499	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662500 Terminal Sacrifice
Killed on Day : 10
Exposure Group : Main
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
MISSING.
NOSE :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES

ORGANS NOT EXAMINED:
LIVER

Individual Animal Pathology Data

Group: III Concentration: 0.2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662501	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662502 Accidentally Killed
Duration of dosing-days: 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

662503 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: III Concentration: 0.2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662504	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662505	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662506	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: V Concentration: 2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662512	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
NOSE :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES

Animal Ref	Microscopic & Macroscopic Findings
662513	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, TESTES, NOSE

Individual Animal Pathology Data

Group: V Concentration: 2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662514	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, TESTES, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662515	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, minimal.

No Microscopic Abnormality Observed :
LUNGS, TESTES, NOSE

Individual Animal Pathology Data

Group: V Concentration: 2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662516	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
LUNGS :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, TESTES, NOSE

662517 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

THYMUS :
DISCOLORATION, DARK, MOTTLED.

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

662518 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: V Concentration: 2 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662519	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

EPIDIDYMIDES :
DISCOLORATION, TAN, LEFT, TAIL, 3MM DIA..

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662520	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662521	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662527	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
MISSING.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.
LUNGS :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, mild.

No Microscopic Abnormality Observed :
HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

ORGANS NOT EXAMINED:
LIVER

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662528	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
HYDRONEPHROSIS, UNILATERAL, mild.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, mild.
EYE(S) WITH OPTIC NERVE :
OPTIC NERVE NOT PRESENT.

No Microscopic Abnormality Observed :
LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662529	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
LUNGS :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662530	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

LIVER :
DISCOLORATION, TAN, MOTTLED.

No Macroscopic Abnormality Observed :
KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
HYPERPLASIA, BILE DUCT, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.
LUNGS :
INFLAMMATION, SUBACUTE/CHRONIC, minimal.
HEART :
CARDIOMYOPATHY, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, mild.
EYE(S) WITH OPTIC NERVE :
OPTIC NERVE NOT PRESENT.
EPIDIDYMIDES :
OLIGOSPERMIA/GERM CELL DEBRIS, mild.

No Microscopic Abnormality Observed :
SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, STERNUM, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662531	Terminal Sacrifice Killed on Day : 10 Exposure Group : Main Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
HEART :
CARDIOMYOPATHY, minimal.
PHARYNX/LARYNX :
SQUAMOUS METAPLASIA, mild.
EYE(S) WITH OPTIC NERVE :
OPTIC NERVE NOT PRESENT.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Animal Ref	Microscopic & Macroscopic Findings
662532	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662533	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

LUNGS :
DISCOLORATION, RED, SCATTERED.

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.

No Microscopic Abnormality Observed :
KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

662534 Terminal Sacrifice
Killed on Day : 24
Exposure Group : Recovery
Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

No Microscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, PHARYNX/LARYNX, TESTES, NOSE

Individual Animal Pathology Data

Group: VII Concentration: 20 mg/m³ Sex: Males

Animal Ref	Microscopic & Macroscopic Findings
662535	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
CYST, minimal.
NOSE :
DEGENERATION, TRIGEMINAL NERVE, mild.

No Microscopic Abnormality Observed :
LUNGS, PHARYNX/LARYNX, TESTES

Animal Ref	Microscopic & Macroscopic Findings
662536	Terminal Sacrifice Killed on Day : 24 Exposure Group : Recovery Animal is signed off from necropsy

Gross Pathology :

No Macroscopic Abnormality Observed :
LIVER, KIDNEYS, LUNGS, HEART, SPLEEN, BRAIN, SPINAL CORD, STOMACH, DUODENUM, JEJUNUM, ILEUM, PANCREAS, CECUM, COLON, RECTUM, MESENTERIC LYMPH NODE, THYMUS, ADRENAL GLANDS, SCIATIC NERVE, THYROID GLAND, PARATHYROID GLANDS, TRACHEA, ESOPHAGUS, PHARYNX/LARYNX, EYE(S) WITH OPTIC NERVE, PROSTATE, SEMINAL VESICLES, URINARY BLADDER, TESTES, EPIDIDYMIDES, STERNUM, NOSE

Histopathology :

LIVER :
INFLAMMATION, SUBACUTE/CHRONIC, FOCAL, minimal.
KIDNEYS :
NEPHROPATHY, CHRONIC PROGRESSIVE, minimal.

No Microscopic Abnormality Observed :
LUNGS, PHARYNX/LARYNX, TESTES, NOSE