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Perfluoro-N-Butyl Iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

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NOTICE

TECHNICAL REVIEW AND APPROVAL

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THIS TECHNICAL REPORT HAS BEEN REVIEWED AND IS APPROVED FOR PUBLICATION

FOR THE DIRECTOR

//SIGNED//

MARK M. HOFFMAN
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14. ABSTRACT

Perfluoro-n-butyl iodide (PFBI) is an environmentally acceptable (i.e., zero ozone depletion potential) replacement solvent for cleaning oxygen systems. A 13-week study was conducted in order to develop a health risk assessment. Fischer 344 rats (15 males & 10 females per group) were exposed for 6 hr/day to 0 (Air Control), 500, 1500 or 5000 ppm of PFBI for 5 days/week for 13 consecutive weeks (at least 65 exposures) followed by a 4-week recovery period. Clinical observations, body weights, clinical pathology, thyroid function, organ weights and histopathology were conducted at the end of the treatment period for up to 10 animals/sex/group. Remaining animals (5 males/group) were held for a 4-week recovery period. The target tissue following 13 weeks of daily inhalation exposure of rats to PFBI was the thyroid. The findings consisted of a minimal thyroid follicular cell hypertrophy occasionally accompanied by hyperplasia but without an increase in thyroid weight in the 500, 1500 and 5000 ppm males; only one 5000 ppm female had similar histopathological thyroid changes.

15. SUBJECT TERMS

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PREFACE

This study was sponsored by Alion Sciences and Technology of Dayton, OH, under the management of Darol E. Dodd, PhD. Alion was contracted to AFRL/HEPB at Wright-Patterson Air Force Base (WPAFB), OH, under contract number F33615-00-C-6060. Contract oversight was provided by David R. Mattie, PhD, of AFRL/HEPB. A co-sponsor of the study was Peter J. John, PhD, of the University of Dayton Research Institute (UDRI), Dayton, OH. Contract oversight was provided by Ed C. Snyder and Lois J. Gschwender of AFRL/MLBT at WPAFB, OH.

Funding was provided by ASC/ENVV (WPAFB) under the program entitled, “Qualify Optimum Oxygen System Cleaning Solvent.” Vincent R. Johnson and Charles R. Valley served as program managers.

This study, Huntingdon Life Sciences study no. 04-6154, was performed under Test Guideline 870.3465 and conducted in compliance with the United States Environmental Protection Agency’s (EPA) Good Laboratory Practice (GLP) Standards 40 CFR Part 792 (TSCA) and with the Organization for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practices ENV/MC/CHEM/(98)17 with one exception. AFRL/HEPB conducted the serum hormone analysis; although performed in the spirit of GLP, their analysis and report do not meet compliance under GLP guidelines.

Huntingdon Life Sciences, East Millstone, NJ, and AFRL/HEPB are fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). All studies involving animals were conducted under a program of animal care accredited by the AAALAC and in accordance with the "Guide for the Care and Use of Laboratory Animals", National Research Council (1996).

The authors would like to acknowledge the following for technical assistance: Latha Narayanan of the Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) at WPAFB, OH, and Sylvie J. Gosselin, D.V.M., Ph.D., Nicholas Macri, D.V.M., Ph.D, Lionel F. Rubin, V.M.D. and Graham F. Healey of Huntingdon Life Sciences. The authors wish to thank Teresa R. Sterner (HJF) for assistance with the preparation of this technical report.

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LIST OF ABBREVIATIONS

μL	microliter(s)
μm	micrometer(s)
ANOVA	Analysis of Variance
EPA	U.S. Environmental Protection Agency
F	female(s)
FOB	Functional Observational Battery evaluations
g	gram(s)
GLP	Good Laboratory Practice
hr(s)	hours(s)
IR	infrared
L	liter(s)
Lpm	liters per minute
M	male(s)
m^3	cubic meter(s)
mg	milligram(s)
min(s)	minutes(s)
mL	milliliter(s)
PFBI	perfluoro-n-butyl iodide
ppm	parts per million
RIA	radioimmunoassay
SBIR	Small Business Innovative Research
SOP	Standard Operating Procedure
T_3	triiodothyronine
T_4	tetraiodothyronine, thyroxine
TSH	Thyroid Stimulating Hormone
UDRI	University of Dayton Research Institute
WPAFB	Wright-Patterson Air Force Base

EXECUTIVE SUMMARY

Fischer 344 rats (15 males & 10 females per group) were exposed for 6 hours/day to 0 (Air Control), 500, 1500 or 5000 ppm of PFBI for generally 5 days/week for 13 consecutive weeks (at least 65 exposures) followed by a 4-week recovery period. Exposure levels were determined using an infrared spectrophotometer 4 times per chamber per day. Particle size distribution measurements were made once weekly using a TSI Aerodynamic Particle Sizer. At the end of the treatment period, up to 10 animals/sex/group were euthanized and necropsied. Remaining animals (5 males/group) were held for a 4-week recovery period, after which they were euthanized and necropsied. Parameters evaluated during the study were: viability, clinical observations, ophthalmology, body weights, feed consumption, clinical pathology, thyroid function, organ weights, macroscopic observations and microscopic pathology.

The mean (± standard deviation) analytical exposure concentrations of PFBI were determined to be 0.0 ± 0.0, 500 + 22, 1489 ± 83 and 4931 ± 359 ppm for the Air Control and the exposure groups, respectively. Particle sizing results indicated that the atmospheres were essentially vapor only, as expected, since there was no substantial difference between the test substance chambers and the Air Control chamber.

There was one accidental death on Day 29 (one control male) and all remaining animals survived until their scheduled sacrifices. The target tissue following 13 weeks of daily inhalation exposure of rats to PFBI was the thyroid. The findings consisted of a minimal thyroid follicular cell hypertrophy occasionally accompanied by hyperplasia but without an increase in thyroid weight in the 500, 1500 and 5000 ppm males; only one 5000 ppm female had similar histopathological thyroid changes. At ≥ 500 ppm, there was also increased TSH in females and increased T_3 and T_4 in animals of both sexes. These effects resolved following a 4-week recovery period.

Other changes were several minor clinical pathology variations at all exposure levels but with no biological significance and a 9.4% reduction in absolute body weight in the 5000 ppm males. None of the organ weight changes were associated with histopathological correlates; these included increased kidney weights in the ≥ 1500 females and decreased spleen weight in the 5000 ppm males. Increased adrenal weights at ≥ 1500 ppm (both sexes) with decreased thymic weight in the 5000 ppm males were indicative of stress while the effect on the accessory sex glands at 5000 ppm were considered secondary to decreased body weight in males.

INTRODUCTION

Perfluoro-n-butyl iodide (PFBI) was identified as an environmentally acceptable (i.e., zero ozone depletion potential) replacement solvent for cleaning oxygen systems. Cleaning evaluations have shown it to be a superior wipe solvent cleaner. Initial toxicity testing was conducted under a Phase II Small Business Innovative Research (SBIR) initiative used to develop PFBI as a cleaning solvent. Acute toxicity, subchronic toxicity (4-week) and genotoxicity evaluations were reported by Dodd *et al.* (2004). Because PFBI has iodide in the compound and caused increases in thyroid hormones in the subchronic toxicity study previously conducted, a recovery group was added in order to test for a return to normal levels of thyroid hormones and TSH 4-weeks after the end of daily exposures. This study was conducted to assess the potential inhalation toxicity of PFBI when administered via nose-only inhalation exposure to rats for at least 13 weeks followed by at least a 4-week recovery period. The assessment included routine toxicology parameters as well as detailed evaluations of neurotoxicity and thyroid function parameters. This study was designed to provide the information required for a health assessment including a proposed permissible exposure limit.

MATERIALS AND METHODS

The experimental outline for this study conducted at Huntingdon Life Sciences (Testing Facility) is detailed in Table I. This study was initiated 21 November 2005. Animals were received on 8 December 2005 and exposures began 21 December. Exposures were terminated on 26 March 2006 and the animals were euthanized on 24 and 27 March. Recovery group animals were euthanized on 21 April. The final report was signed and finalized on 6 October 2006.

Justifications

Route, Duration and Frequency of Administration

The inhalation route is one of the potential routes of human exposure to this test substance. The duration and frequency of the exposures are as recommended in the relevant OECD and EPA guidelines.

Test Animal Selection

The rat is used as a surrogate for humans in the detection of chemical exposure toxicity and is a species in which known toxicants have been detected. This rodent species is commonly used in the conduct of toxicity studies and is that recommended by the relevant OECD and EPA guidelines. Historical control data are also available with this strain of rat for comparative evaluation, if necessary.

Table I. Experimental outline for 13-week inhalation study of PFBI

Group	Exposure Level (ppm)[a]	Number of Animals									
		Initial		Clinical Laboratory Studies[b]		Necropsyc				Microscopic Pathologyd	
						Terminal		Recovery			
		M	F	M	F	M	F	M	F	M	F
1 (control)	0 (air only)	15	10	9	10	9	10	5	0	15	10
2 (low)	500	15	10	10	10	10	10	5	0	15	10
3 (mid)	1500	15	10	10	10	10	10	5	0	15	10
4 (high)	5000	15	10	10	10	10	10	5	0	15	10

[a]Exposures were 6 hours/day, generally 5 days/week for at least 13 weeks for at least 65 exposures followed by at least a 4-week recovery period for 5 males/group. Exposure levels are expressed as ppm of test substance. The exposures were conducted via nose-only inhalation exposure.

[b]Hematology, coagulation and clinical chemistry were performed on all 13-week study (Main Study) animals at the end of the exposures period. Samples were also collected from all animals for RIA measurements of serum TSH, T_3 and T_4 at the end of the exposures period and at the end of the recovery period. Samples were collected and shipped to the Sponsor designated laboratory for analysis.

[c]Complete postmortem evaluation was performed on the animal (male animal no. 1010) which was found dead (accidental) during the course of the study (Day 29).

[d]Microscopic examination of a complete tissue set was performed for all Main Study animals in the control and high-exposure groups following the exposures period. In addition, the thyroid/parathyroid gland was examined for all animals following the exposures and recovery periods and the lungs were examined for all animals sacrificed at the end of the exposures period.

M = Male; F = Female; The first day of exposure was Day 1 for the study.

Number of Animals

The number of animals in the protocol was considered to be the minimum necessary for statistical, regulatory and scientific validation. The purpose of this study was to monitor for toxicity of the test substance. Historical control data indicate that clinical laboratory data, organ weight data and microscopic examination of tissues vary among individual animals. The number of animals/sex/group (10) was selected based on this variability. In addition, 5 males per group (since any effects were not expected to be sex specific) were added to allow an evaluation of recovery of effects after a 4 week period. Three test substance-treated groups receiving low, medium and high exposure levels and a negative control group were considered the minimum number of groups necessary to provide a range of effects.

Exposure Level Selection

The exposure levels for this study were selected based on results of 4-week inhalation testing (HLS study 97-6111) which showed adverse effects at 10,000 ppm (decreased body weight gain and respiratory mucosal hypertrophy/hyperplasia) but no adverse effects at 1,000 and 100 ppm (Dodd *et al.*, 2004).

Test Substance

The solvent perfluoro-n-butyl iodide (PFBI) (formula: C_4F_9I; CAS # 423-39-2) has a molecular weight of 345.9 g/mole. Pure (98.8%) PFBI (Lot # Q12C-14) was manufactured at Lubrication Technology, Inc. (Franklin Furnace, OH) and supplied by SynQuest Laboratories, Inc. (Alachua, FL). The test substance was received on 5 December 2005 and stored as specified (~4°C in the dark).

The identity, strength, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance were documented by the University of Dayton Research Institute (UDRI), Dayton, OH, before its use in the study. This documentation was maintained by the UDRI. An archival sample was taken (15 mL) and stored in the Archives of the Testing Facility. The unused portion of the test substance, as well as any empty test substance containers, was returned to AFRL/MLBT at Wright-Patterson Air Force Base (WPAFB), OH, on 18 April 2006.

Test Animals

Albino inbred VAF/Plus® Fischer 344 [CDF®(F344/ DuCrl)] rats were purchased from Charles River Laboratories, Kingston, NY. A total of 106 rats (63 males, 43 females) were received and 100 total (60 males, 40 females) were used in this study. Rats were approximately 6 weeks of age at receipt and approximately 8 weeks of age at exposure initiation.

Males weighed an average of 175.6 g (range: 155 - 200 g) at the initiation of exposure, while females weighed 123.1 g (range: 103 - 136 g). Individual weights of animals were within $\pm$ 20% of the mean weight for each sex. Females were nulliparous and non-pregnant.

Animals were acclimated for approximately two weeks. All animals were checked for viability twice daily. All animals were examined during the acclimation period to confirm suitability for study.

More animals than required for the study were purchased and acclimated. Animals considered unsuitable for the study on the basis of pretest physical examinations, outlying body weight data, or ophthalmoscopic examinations were eliminated prior to random selection for group assignment. Animals considered suitable for study were distributed into 4 groups of 15/males and 10/females by a computerized random sort program so that body weight means for each group were comparable.

Each rat was assigned a temporary number upon receipt. Each rat was identified with tail tattoo bearing its assigned animal number. The assigned animal number plus the study number comprised the unique animal number for each animal. In addition, each cage was provided with a cage card which was color-coded for exposure level identification and contained study number and animal number information.

Animals were monitored by the technical staff for any conditions requiring possible veterinary care and treated as necessary. Animals were individually housed in suspended, stainless steel wire mesh cages during the study. A twelve hour light/dark cycle controlled via an automatic timer was provided.

Temperature was monitored in accordance with Testing Facility Standard Operating Procedure (SOP) and maintained within the specified range to the maximum extent possible. The desired temperature range was 18 to 26°C; the actual range was 17 to 24°C. Excursions outside the specified range were not considered to have affected the integrity of the study.

Relative humidity was monitored in accordance with Testing Facility SOP and maintained within the specified range to the maximum extent possible. The desired humidity range was 30 to 70%; the actual range was 14 to 75%. Excursions outside the specified range were not considered to have affected the integrity of the study.

Certified Rodent Diet, No. 5002; (pellets) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly. Analysis of each feed lot used during this study was performed by the manufacturer. Results are maintained on file by the manufacturer. There were no known contaminants in the feed that were expected to interfere with the objectives of this study.

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction via an automated watering system. Monthly water analyses are conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). In addition, water samples are collected biannually from representative rooms in the Testing Facility; chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory. Results of all water analyses are maintained on file at the Testing Facility. There were no known contaminants in the water that were expected to interfere with the results of this study.

Exposure Conditions and Administration

Animals were individually housed in polycarbonate cones attached to nose-only inhalation exposure chambers. No feed or water was provided during exposure. Chamber static pressure was recorded every half-hour during exposure. Chamber temperature, airflow rate and relative humidity were monitored continuously and recorded every half-hour during exposure and maintained, to the maximum extent possible, within the desired ranges. The desired temperature range was 20 to 24°C; the actual range was 19 to 24°C. The desired relative humidity range was 40 to 60%; the actual range was 22 to 49%. Excursions outside the specified range were not considered to have affected the integrity of the study.

The route of administration was inhalation via nose-only exposures. The test substance was administered for 6 hours/day, generally 5 days per week for at least 13 weeks and at least 65 exposures. Test substance administration continued through the day prior to necropsy for all animals except the recovery animals.

The test substance was administered as a vapor in the breathing air of the animals. The test atmosphere was generated by an appropriate procedure determined during pre-study trials. The trials were performed to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure levels.

Exposure Procedure

Group 1 animals were exposed to house-line air only. For Groups 2 and 3 animals, the test substance was placed in a glass syringe (covered with a damp paper towel and an ice pack) on a syringe pump with an initial setting of 3.3 mL/hr (Group 2) and 10.5 mL/hr (Group 3). The test substance was directed, via 1/8" Teflon® tubing and a syringe adapter, from the syringe onto the glass helix of a counter current volatilization chamber. The ice pack was eliminated on Day 3, as the wet paper towel was considered adequate to keep test substance cool.

For Group 4, the test substance was contained in a flask (covered with a damp paper towel in ice bath), via 1/8" tubing, by a fluid metering pump set at an initial setting of 40% with a 1/4" piston and was directed into the glass helix of a counter current volatilization chamber. Again, use of the ice bath was eliminated on Day 3 as the wet paper towel was considered adequate to keep test substance cool.

For Groups 2-4, houseline air was delivered from an in-house system consisting of a generation flowmeter and an exhaust flowmeter. For the generation system, house-line air was delivered through a flowmeter with a built in metering valve and back pressure gauge, to the ball and socket joint at the bottom of the volatilization chamber and passed over the coil to volatilize the test substance.

The test substance laden air flowed through tubing at the top of the volatilization chamber into the calibrated MIRAN (IR) air analyzer. The air equilibrated within the cell allowing for continuous monitoring during the test substance generation. The air then exited the Miran and flowed, via tubing, to the inlet turret of the flow-past nose-only inhalation exposure chamber.

The chamber atmosphere was exhausted via tubing through a flowmeter with a built in metering valve. The chamber atmosphere was exhausted via plastic tubing and filtered through a series of two filter pots prior to entering the in-house exhaust system. The filter pot closest to the

chamber exhaust consisted of wound polypropylene and the second consisted of polyester fiber, activated charcoal and a glass fiber filter. Chamber airflow was maintained at 13.0 (Lpm) for both the 360 minute exposure and for 5 minutes post-exposure to allow the chamber to clear.

Chamber Operation

The flow-past nose-only inhalation chambers (approximately 0.7 Liters in internal volume) were each operated at a minimum flow rate of 13 Liters per minute (0.52 Lpm per test animal). The final airflow was set to provide at least one air change (calculated by dividing the chamber volume by the airflow rate) in 5.0 minutes (12 air changes/hour) and a T99 equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes. This chamber size and airflow rate was considered adequate to maintain the oxygen level at least 19% and the animal loading factor below 5%. At the end of each exposure, all animals remained in the chamber for a minimum of 30 minutes. During this time, each chamber was operated at approximately the same flow rate using clean air only. Figure 1 in the Appendix provides a diagram of the generation system and flow past the nose-only inhalation exposure chamber.

Determination of the 4 exposure levels were made using a MIRAN® Ambient Air analyzer equipped with a strip chart recorder. The test atmosphere was drawn continuously through the MIRAN® and measurements were recorded 4 times during each of the exposures. The exposure levels were determined by comparison of the measured absorbance to a calibrated response curve constructed using the same instrument settings.

Particle size samples were drawn once a week during exposure from the chambers and room air using a TSI Aerodynamic Particle Sizer. The samples were drawn for 20 seconds at a rate of 5.0 Lpm. The mass median aerodynamic diameter, geometric standard deviation and total mass concentration were calculated. A computer was used to program the system to the appropriate settings prior to sampling. The particle size distributions were calculated by the computer and printed out.

A nominal exposure concentration was calculated. The flow of air through the chamber was monitored using appropriate calibrated equipment. The test substance consumed during the exposure was divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration (ppm), which was calculated as follows:

$$Conc\,(ppm) = \frac{amount\,consumed\,(g) \times 1000\left(\frac{mg}{g}\right) \times 1000\left(\frac{\mu g}{mg}\right) \times 22.4\left(\frac{\mu L}{\mu mole}\right) \times 295°K}{\exp osure\,duration(\min) \times airflow\left(\frac{L}{\min}\right) \times MW\left(\frac{\mu g}{\mu mole}\right) \times 273°K}$$

Where: MW = 345.9 g/mole

Animal Observation

Animals were observed in their cages twice daily for mortality and signs of severe toxic or pharmacologic effects. Animals in extremely poor health or in a possible moribund condition were identified for further monitoring and possible euthanasia.

All animals were observed as a group in-chamber at least once during each exposure. Out-of-chamber, each animal was removed from its cage and examined twice pretest and once weekly during the study period. Observations during the dosing phase were performed post-exposure. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia as well as evaluations of respiration, palpation for tissue masses, circulatory effects, autonomic effects, central nervous system effects, changes in motor activity, and reactivity to handling or sensory stimuli.

All animals were examined via ophthalmoscope pretest and at study termination. Eyelids, lacrimal apparatus and conjunctiva were examined grossly; cornea, anterior chamber, lens, vitreous humor, retina and optic disc were examined by indirect opthalmoscopy. The eyes were examined after instillation of a mydriatic (Tropicamide Ophthalmic Solution 1%).

Body weights were recorded twice pretest and weekly thereafter throughout the study. Terminal, fasted weights were obtained just prior to necropsy.

Feed was available without restriction 7 days/week. Animals were presented with full feeders of known weight. After 6 or 7 days during the treatment period, feeders were reweighed and the resulting weight was subtracted from the full feeder weight to obtain the grams consumed per animal over the 7-day period. Feed consumption was measured (weighed) once pretest and once weekly during treatment and calculated.

$$Feed\ Consumption\left(\frac{g}{day}\right) = \frac{grams\ of\ \ feed\ consumed}{6\ or\ 7\ days}$$

Neurobehavioral Studies

Testing was staggered over 4 sessions during the 13th week of exposures and was conducted on non-exposure days at least 16 hours post-exposure. Each session consisted of 2-3/sex/group. Testing was performed on 20 animals per session for 13-week study (Main Study) animals. Noise level was maintained within a level of 55 to 65 decibels by a white noise generator. Temperature, humidity and illumination were measured and recorded to ensure that variations in environmental conditions were minimal during all evaluations. The functional observational battery was performed for all animals before evaluation of motor activity. No feed and water were available during the measurements.

Functional Observational Battery

A functional observational battery (FOB) (Moser, 1989) was performed on 10 Main Study animals/sex/group. Time of testing was counter-balanced across treatment groups.

The following evaluations were performed as part of the FOB:

- Home Cage Evaluations: posture, vocalization and palpebral closure.
- Handling Evaluations: reactivity to general stimuli (handling); assessment of signs of autonomic function: lacrimation, salivation, altered fur appearance, or red/crusty deposits around eyes.
- Open Field Evaluations: arousal level and gait; count of urination and defecation; convulsions, tremors, abnormal movements or behaviors, excessive or repetitive actions; piloerection and exophthalmos.
- Reflex Assessments: response to visual (approach response) and auditory (finger snap) stimuli; response to a tail pinch; pupillary function.
- Grip Strength (Meyer *et al.*, 1979): Grip strength was measured using a Grip Strength Meter (Columbus Instruments International Corporation, Columbus, Ohio).
- Landing Foot Splay: A container of dampened sand was placed on a laboratory cart or table against a wall, and the surface was smoothed with a flat-edged instrument. Each animal was released onto the sand from a height of one foot. The distance between the marks left by the hindpaws was measured in centimeters. Two trials were performed for landing foot splay, the average of which was used for comparison.
- Proprioception: Animals were gently restrained on a horizontal surface by grasping the thorax. The observer gently pulled back on the hindlimb of the rat so that the dorsal surface of the paw was on the testing surface, and released. Extent of hindlimb retraction was scored.
- Air Righting Ability: Animals were held upside down and dropped from a height of one foot into a container of bedding. The landing position of each animal was recorded.
- Body Temperature: Rectal temperature was obtained using a digital electronic thermometer (Welch Allyn SureTemp Plus).
- Body Weight: Animals were removed from their cages and weighed.

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired temperature was 18 to 26°C; the actual range was 21 to 24°C. Relative humidity was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired relative humidity was 30 to 70%; the actual was 30 to 49%.

Noise level was monitored using a Digital Sound Level Meter (Sper Scientific, Ltd., Scottsdale, AZ) and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired noise level was 55 to 65 dB; the actual level was 57 to 62 dB.

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, NY) and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired lighting was <80 footcandles; the actual level was 44 to 50 footcandles.

Motor Activity

Using a modified version of Schulze's procedures (Schulze, 1990), the locomotor activity of all animals was monitored during 13th week of exposure using an automated Photobeam Activity System (San Diego Instruments, Inc., San Diego, California). Sessions were 60 minutes in length; each session was divided into 12 intervals of 5 minutes. The time of testing was balanced across treatment groups.

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired temperature range was 18 to 26°C; the actual range was 21 to 23°C. Relative humidity also was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired humidity range was 30 to 70%; the actual range was 23 to 58%.

Noise level was monitored using a Digital Sound Level Meter (Sper Scientific, Ltd., Scottsdale, AZ) and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired noise level was 55 to 65 dB; the actual range was 60 to 63 dB.

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, NY) and recorded twice daily, just prior to the first evaluation and just after the last evaluation. The desired light level was <80 footcandles; the actual range was 43 to 47 footcandles.

Clinical Laboratory Studies

Clinical pathology procedures and parameters are based on those recommended in published guidelines (Weingand *et al.*, 1996). Blood was obtained from lightly anesthetized (Isoflurane) animals via puncture of the abdominal aorta. Rats were fasted in the morning for at least 6 hours prior to blood collection (terminal procedure by carbon dioxide inhalation – no recovery). The Main Study animals (up to 10/sex/group) were bled at the terminal interval.

Blood for hematology studies was collected (approximately 0.25 mL) into tubes containing EDTA anticoagulant. Blood samples were analyzed using the ADVIA 120 HematologyAnalyzer, (Bayer Corporation). The following tests were performed:

- Hemoglobin concentration
- Hematocrit
- Erythrocyte count
- Platelet count
- Mean platelet volume
- Mean corpuscular volume
- Mean corpuscular hemoglobin
- Mean corpuscular hemoglobin concentration
- Red cell distribution width
- Total leukocyte count
- Reticulocyte count
- Differential leukocyte count

Blood for coagulation studies was collected (approximately 1.0 mL) into tubes containing sodium citrate anticoagulant. Serum samples were analyzed using a mechanical clot detection system, STA Compact® by Diagnostica Stago Products. The following tests were performed:

- Prothrombin time
- Activated partial thromboplastin time

Blood for clinical chemistry was collected (approximately 1.0 mL) into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum. Serum samples were analyzed using a Hitachi 917, Roche Corporation Automatic Analyzer. The following tests were performed:

- Aspartate aminotransferase (Kinetic - Modified IFCC Technique)

- Alanine aminotransferase (Kinetic - Modified IFCC Technique)
- Alkaline phosphatase (Kinetic – Modified AMP Buffer)
- Lactate dehydrogenase (Kinetic - Lactate-pyruvate Technique)
- Blood urea nitrogen (Kinetic - Modified Urease)
- Creatinine (Kinetic –Modified Jaffe Method)
- Glucose (Hexokinase Method)
- Creatine kinase (Kinetic – Modified NAC Method)
- Cholesterol (Enzymatic – Modified Trinder Method)
- Total protein (Biuret Technique)
- Albumin (Bromocresol Green Method)
- Total bilirubin (Modified Wahlefield *et al.*)
- Direct bilirubin (Modified Jendrassik and Grof Method)
- Sodium (Ion Selective Electrode)
- Potassium (Ion Selective Electrode)
- Chloride (Ion Selective Electrode)
- Calcium (Cresolphthalein Complexone Method)
- Inorganic phosphorus (Phosphomolybdate - UV Method)
- Gamma-glutamyl transferase (Kinetic – Modified Persijn and Vander Silk Method)
- Triglycerides (GPO Triglyceride-lipase Method)

Additional serum chemisty tests were also performed:

- Globulin (calculated value; total protein - albumin)
- Albumin/globulin ratio (calculated value; albumin ÷ globulin)
- Indirect bilirubin (calculated value; total bilirubin – direct bilirubin)

Any remaining (frozen) serum were stored for up to six months after completion of assays and then were discarded. Peripheral blood smears were retained and archived with the study.

Thyroid Evaluation

Blood (~2.0 mL for all animals) was collected into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum for 3 sample tubes per animal. Blood was obtained from lightly anesthetized (Isoflurane) animals via puncture of the abdominal aorta as a terminal procedure (no recovery) from all animals for radioimmunoassay (RIA) measurements of serum TSH, T_3 and T_4 at the end of the exposures period and at the end of the recovery period. Rats were fasted in the morning for at least 6 hours prior to blood collection. The total amount of serum available for the sample 3 tubes was 1 mL (400 μL and 400 μL and 200 μL). The resulting samples for RIA were immediately frozen on dry ice and maintained frozen (< -70°C) at the Testing Facility until shipped for analysis (all at one interval on 3 May 06) to AFRL/HEPB. The complete results of these evaluations are reported in Narayanan and Mattie (2007).

Postmortem Evaluation

Euthanasia was performed via exsanguination following carbon dioxide inhalation. A necropsy was performed on all surviving animals after animals were treated for at least 65 exposures (Terminal sacrifice) and/or held for 4 weeks of recovery (Recovery sacrifice). Necropsy schedules were established in order to assure that approximately equal numbers of males and

females from each group was examined on each day of necropsy and that examinations of animals of both sexes from each group was performed at similar times of the day throughout the necropsy period, as appropriate.

A complete macroscopic examination was performed on all animals, including all scheduled and unscheduled deaths; all abnormal observations were recorded. The necropsy included examination of the external surface and all orifices; the external surfaces of the brain and spinal cord; the organs and tissues of the cranial, thoracic, abdominal and pelvic cavities and neck; and the remainder of the carcass.

Organs indicated in Table II were weighed for all animals at the scheduled sacrifice interval(s). Prior to weighing, the organs were carefully dissected and properly trimmed to remove adipose and other contiguous tissues in a uniform manner. Organs were weighed as soon as possible after dissection to avoid drying except the thyroid/parathyroids which were weighed after at least 2 days of fixation. Paired organs were weighed together.

All tissues indicated in Table II were preserved in 10% neutral buffered formalin. Eyes and testes were initially placed in Modified Davidson's solution and then retained in 10% formalin. Lungs were infused with formalin (gravity method) prior to their immersion into a larger volume of the same fixative.

Smear preparations of the marrow from the rib were air dried and fixed in absolute methanol. After fixation, the tissues and organs from all animals were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy. The bones were decalcified in Decalcifier II™.

After decalcification the skull was serially sectioned transversely at approximately one centimeter intervals. All sections were examined, post-fixation, for the presence of macroscopically visible morphologic abnormalities. Four sections per animal, described as follows, were processed, embedded in paraffin, cut at 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy. The first section included the area between the upper incisor tooth and incisive papilla. The second section included the area between the incisive papilla and the first palatal ridge. The third section included the area between the second palatal ridge and first upper molar tooth. The fourth section included the area between the first upper molar tooth and nasopharynx. (The fifth section posterior to the fourth section includes the nasopharynx when five sections were taken.)

Larynx sections were prepared from two sites; one was the area of the ventral diverticulum and the other was the area of the ventral seromucous glands at the base of the epiglottis. In a few instances, sections of larynx were not from the aforementioned planes of section. These were classified simply as Larynx for the purposes of data entry.

In addition, slides of the indicated tissues were prepared and examined microscopically for all Main Study animals and the thyroid gland (sectioned at ~5 μm) was examined for all animals following the exposures and recovery periods. Any abnormalities not noted during macroscopic examinations which were seen during histology processing were recorded.

Table II. Tissues evaluated during postmortem examination

Tissue	Preserved	Weighed	Microscopic Examination (Groups)	
			1, 4	2, 3
adrenal gland	X	X	X	
aorta (thoracic)	X		X	
bone (sternum, femur)	X		X	
bone marrow smear (rib)	X			
brain (medulla/pons, cerebrum and cerebellum)	X	X	X	
epididymides	X	X	X	
esophagus	X		X	
eye	X			
heart	X	X	X	
kidneys	X	X	X	
large intestine (cecum, colon, and rectum)	X		X	
lacrimal gland	X			
larynx[a]	X		X	
liver	X	X	X	
lungs (with mainstem bronchi)	X	X	X	X
lymph node (mediastinal and mesenteric)	X		X	
mammary gland	X			
muscle (biceps femoris)	X			
nasopharyngeal tissue[b]	X		X	
nerve (sciatic)	X		X	
optic nerve	X			
ovaries	X	X	X	
pancreas	X		X	
pituitary	X	X		
prostate	X	X	X	
salivary gland with submandibular lymph node	X		X	
seminal vesicles	X	X	X	
skin	X			
small intestine (duodenum, jejunum, ileum)	X		X	
spinal cord (cervical, thoracic, lumbar)	X		X	
spleen	X	X	X	
stomach	X		X	
testes	X	X	X	
thymic region	X	X	X	
thyroid (with parathyroids)	X	X	X	X
trachea	X		X	
urinary bladder	X		X	
uterus (body/horns with cervix)	X	X	X	
Zymbal's gland	X			
gross lesions	X			

[a]The laryngeal mucosa were examined. Sections of the larynx examined included the epithelium covering the base of the epiglottis, the ventral pouch and the medial surfaces of the vocal processes of the arytenoid cartilages.

[b]Four sections of the nasopharyngeal tissue were examined. This included sections through the nasal cavity and examinations of the squamous, transitional, respiratory and olfactory epithelia.

Statistical Analysis

The following parameters were analyzed statistically:

- weekly body weights and body weight changes
- feed consumption
- hematology
- coagulation
- clinical chemistry
- organ weights
- forelimb and hindlimb grip strength measurements
- landing foot splay measurements
- body temperature and body weights for FOB evaluations

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) was performed to determine if groups had equal variances. For all parameters except organ and body weights, if the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. Organ and weekly body weight data was analyzed only by parametric methods. The parametric method was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971). If significant differences among the means were indicated, additional tests were used to determine which means were significantly different from the control: Dunnett's (Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Shirley's test (Shirley, 1977) or Steel's test (Steel, 1959) were used to determine which means differed from control. Bartlett's test for equality of variance was conducted at the 1% significance level; all other statistical tests were conducted at the 5% and 1% significance levels.

Motor activity count data were analyzed using split-plot repeated measures ANOVA with model terms for group, animal within group, interval and group by interval interaction. If the group x interval interaction was statistically significant (p=0.05), indicating non-parallelism in the behavioral profile between groups, a separate one-way ANOVA for group effects was performed at each interval. If the response data passed on the parallel hypothesis, an ANOVA (using summed responses over intervals) was used to test for the overall treatment effect which constitutes the level hypothesis. If any significant overall treatment group effect was found by any of the above ANOVAs, Dunnett's t-test was used to find groups that differed from control. Analyses were performed for sexes separately and combined. Treatment group effects were deemed significant at the p=0.05 level. Plots, tables, listings, and analyses were generated using SAS® version 8.2 for WINDOWS (SAS Institute, Cary, NC).

Data Storage

All raw data, preserved specimens, and retained samples, as well as the original study protocol and the original final report are maintained in the Archives of the Testing Facility. AFRL/HEPB was responsible for the archiving and retention of any data, reports and/or specimen/samples generated at sites other than the Testing Facility.

Regulatory References

This study was designed to meet or exceed the pertinent requirements of the OECD Guidelines for Testing of Chemicals 413, adopted 12 May 1981 - Subchronic Inhalation Toxicity: 90 Day Study. The study also meets or exceeds the US EPA OPPTS Health Effects Test Guidelines 870.3465, 90-Day Inhalation Toxicity, dated August 1998.

This study was conducted in compliance with Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17 and EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA).

This study complied with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163, effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505, effective March 18, 1991.

Protocol Deviations

The following protocol deviations occurred during the study but were not considered to have compromised the validity or integrity of the study:

- Due to the nature of on-test animal identification (tail-tattoo) specified by the protocol, it was not possible for the technician performing the observations for the FOB to remain completely unaware of the animals' treatment. The technician who performed the observations for the FOB was instructed to avoid looking at the tail for the identification number in order to remain unaware of the treatment group to the best of their ability.
- Adrenal glands for Recovery Animal No. 2014 were inadvertently misplaced after weighing. The organ weight was recorded prior to the loss of this tissue.
- Due to change in computer systems at the start of study, the body weight and body weight change were evaluated by parametric methods only.
- In the Sponsor's Serum Hormone Report, the number of samples per group varied due to the inability at the Testing Facility to collect sufficient serum from a rat in each of several groups for all three hormone analyses.
- The styrofoam container used to ship the serum samples to AFRL/HEPB was broken during shipment. The entire bottom was cracked. Samples were still frozen except for one box labeled Box 3/SER3. This box contained twenty samples from the recovery group for conducting one of the thyroid hormone analyses. The samples were refrozen and stored with the rest of the samples until they were analyzed.

RESULTS AND DISCUSSION

Chamber Monitoring

Pre-study chamber distribution analyses showed that the test substance was evenly distributed within each chamber. The target and mean (± standard deviation) analytical (IR) and nominal concentrations are summarized in Table III. The analytically measured (IR) exposure levels of the airborne test substance were reasonably close to the targeted exposure levels and to the

nominal concentrations. Chamber environmental conditions averaged 22°C temperature and 43% relative humidity.

Table III. Chamber exposure concentrations

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0.00 ± 0.00	0 ± 0
2	PFBI	500	500 + 22	569 ±25
3	PFBI	1500	1489 ± 83	1522 ± 112
4	PFBI	5000	4931 ± 359	4996 ± 405

Mean particle size distribution measurements for the exposures are summarized in Table IV. These results indicated that the atmospheres were essentially vapor only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

Table IV. Chamber particle size distributions

Group	Test Substance	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m^3)
1	Air Control	2.813	1.892	2.24E-03
2	PFBI	2.368	2.000	1.87E-03
3	PFBI	1.973	1.831	2.46E-03
4	PFBI	2.135	1.828	5.56E-04

Clinical Observations

All animals survived until the termination of the study except for one control Main Study male (#1010), which was accidentally killed on Day 29 during loading into the nose-only inhalation exposure tube.

During the exposure periods, all animals observed and changes were unremarkable (Appendix Table 1). During the non-exposure periods, all animals were generally unremarkable except for an increase in ano-genital staining in the 5000 ppm exposed animals (especially the males) during the latter few weeks of the exposures period (Appendix Table 2). A recovery in the males was noted during the 4 weeks after exposures were completed.

Ophthalmoscopic examination was performed on Day 91. There were no indications of treatment-related ocular abnormalities or ocular disease in the test substance exposed animals (Appendix Table 3).

There were test substance related differences in absolute body weights and in cumulative body weight changes only in the 5000 ppm males (Appendix Figure 2, Appendix Tables 4 and 5). At the end of the treatment period, the absolute body weight in the 5000 ppm males was 9.4% lower than controls. Statistically significant decreases in body weight changes or absolute body weights were noted in the 3rd and 4th week, respectively, and continued through the end of the exposures but a recovery was rapidly seen during the 4 weeks after exposures were completed. Female body weights and cumulative bodyweight changes are shown in Appendix Figure 3 and Appendix Tables 4 and 5. Mean cumulative bodyweight changes from baseline are given in Appendix Table 5.

There were no test substance related differences in feed consumption in the test substance exposed animals, compared to the Air Control animals (Appendix Figures 4 and 5, Appendix Table 6). A few minor and transient statistically significant differences (decreased or increased feed consumption) were noted in both males and females during the 13 weeks of exposures and 4 weeks of recovery.

Neurobehavioral Studies

For motor activity, the group-by-interval interaction was not significant for either male ($p=0.9476$) or female ($p=0.1258$) rats. The test of the group effect for male rats was significant ($p=0.0374$) but none of the subsequent comparisons between treated groups and control were significant at the 5% level. The test of the group effect for female rats was not significant ($p=0.1146$) so no comparisons between treated groups and control were made. When the group-by-interval interaction was compared for the combined sexes it was not significant but the test of the group effect was significant at $p=0.0034$. The subsequent comparisons between treated groups and the control showed that the 500 ppm and the 1500 ppm groups were significantly higher than control at $p<0.01$ and $p<0.05$, respectively.

There were no test substance related effects on motor activity because the increase in motor activity in the 500 and 1500 ppm exposed groups compared to the Air Control animals was absent in the 5000 ppm group (Appendix Table 7). There were no test substance related effects on FOB parameters compared to the Air Control animals (Appendix Tables 8 and 9).

Clinical Pathology

After 13 weeks of exposures, there were no exposure-related differences in hematology values in test substance exposed animals, compared to the Air Control animals (Appendix Table 10). A few statistically significant differences in HGB, HCT, RBC, reticulocyte and WBC values were noted in all or some test substance exposed groups but the changes were slight and not dose related.

After 13 weeks of exposures, statistically significant and dose-related shorter (1.3 to 0.7 seconds) prothrombin time was noted in all test substance-exposed groups of males (Appendix Table 11). A prolongation of less than 3 seconds is not considered biologically significant.

The most consistent changes after 13 weeks of exposures were decreases in AST/ALT and/or ALKP in all test substance-exposed groups and increases in serum phosphorus in the ≥500 ppm males and ≥1500 ppm females (Appendix Table 12). Other statistically significant values

such as decreases in glucose, BUN, creatinine and cholesterol were only seen in one sex and the severity of the changes were considered slight.

Thyroid Evaluation

Inhalation exposure for 13 weeks to PFBI resulted in increased TSH at ≥500 ppm in females and increased T_3 and T_4 in animals of both sexes (Table V). Increased T_4 was the major effect and it was more pronounced in males than females. At the end of the recovery, all hormone levels observed in males returned to control values indicating the hormonal changes were only transient and not necessarily adverse.

Table V. Effects[1] on serum level of TSH, T_4 andT_3 following a 13 week inhalation exposure to PFBI

ppm	500		1500		5000	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
TSH	+6%	+32%*	+11%	+42%*	+10%	+53%*
T_4	+270%*	+65%*	+300%*	+97%*	+310%*	+210%*
T_3	-	+27%*	+20%*	+31%*	+33%*	+31%*

[1]percent increase relative to control values
*statistically significant relative to controls

Pathology

Statistically significant increases in absolute/relative adrenal weights at 1500 and 5000 ppm (both sexes) were associated with decreased absolute/relative thymic weight only in the 5000 ppm males and would suggest a stress effect (Appendix Table 13). Statistically significant lower absolute values (relative to controls) for the epididymides, prostate and seminal vesicles without an adverse effect on testicular weight were considered secondary to decreased body weight in the 5000 ppm males. All organ weight changes including increased absolute kidney weights in the ≥ 1500 ppm females and minor decreases in absolute spleen weight in the 5000 ppm males had no histopathological correlates. Most or all of the above differences were not apparent at the end of the recovery period.

Gross pathological findings are shown in Appendix Table 14; there were no gross findings considered to be related to administration of PFBI. Microscopic pathological findings following exposure are shown in Appendix Table 15. Administration of PFBI was associated with minimal thyroid follicular cell hypertrophy in males. Hypertrophy occurred in most animals, in all PFBI-exposed groups, and was occasionally associated with minimal epithelial hyperplasia. Minimal epithelial hypertrophy was also present in a single female exposed to PFBI at 5000 ppm (Table VI). Microscopic changes were associated with increased hormone levels but no thyroid weight change.

Table VI. Incidence of test substance-related findings

PFBI (ppm)	Males				Females			
	0	500	1500	5000	0	500	1500	5000
No. Animals examined	10	10	10	10	10	10	10	10
Thyroid follicular cell hypertrophy	0	6	7	7	0	0	0	1

Only the thyroids were examined from all males to assess recovery. Following a 4-week recovery period, thyroid follicular cell hypertrophy was not present in males exposed to PFBI at any exposure level, indicating recovery. One 5000 ppm male had a single focus of cystic follicular hyperplasia but since this finding was not present at the end of exposures, it is considered incidental to previous administration of PFBI.

All other microscopic findings recorded occurred sporadically or at a similar incidence in controls and test article-exposed groups and were typical of the background findings commonly seen in this species.

CONCLUSION

The target tissue following 13 weeks of daily inhalation exposure of rats to PFBI was the thyroid. The findings consisted of a minimal thyroid follicular cell hypertrophy occasionally accompanied by hyperplasia but without an increase in thyroid weight in the 500, 1500 and 5000 ppm males; only one 5000 ppm female had similar histopathological thyroid changes. At $\geq$ 500 ppm, there was also increased TSH in females and increased T_3 and T_4 in animals of both sexes. These effects resolved following a 4-week recovery.

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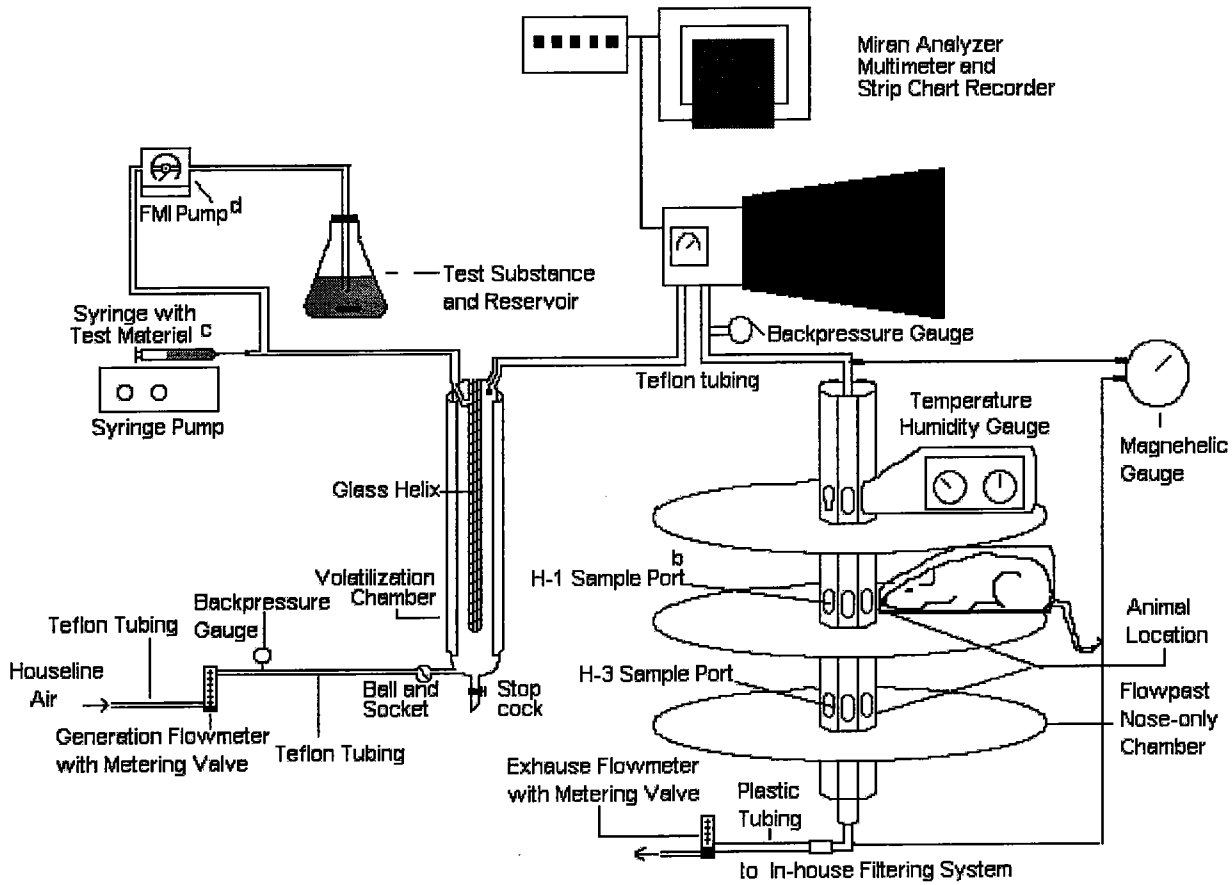
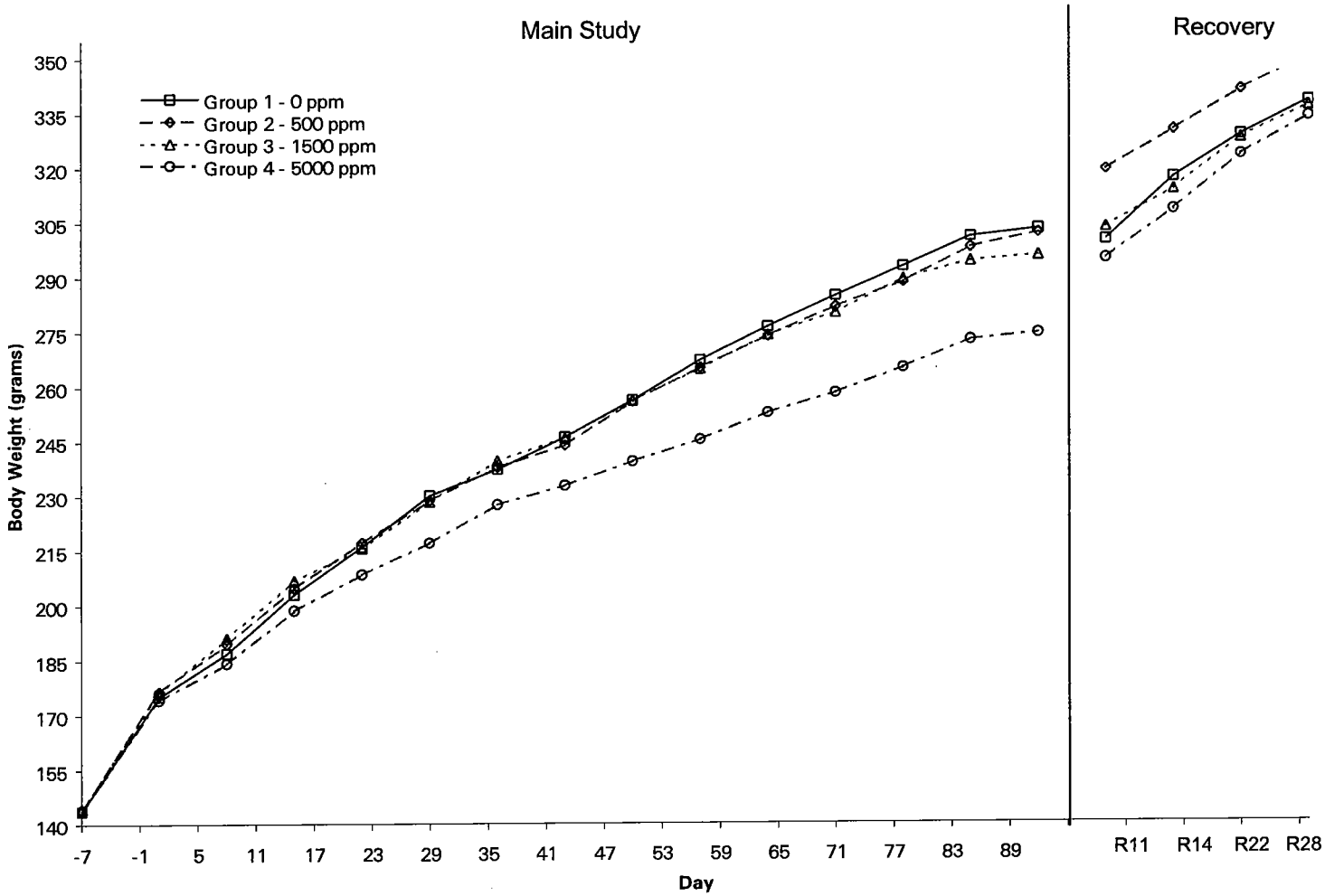
APPENDIX: FIGURES AND TABLES

	Diagram of Flow past Nose-Only Exposure Chamber and Generation System[a]	Figure 1

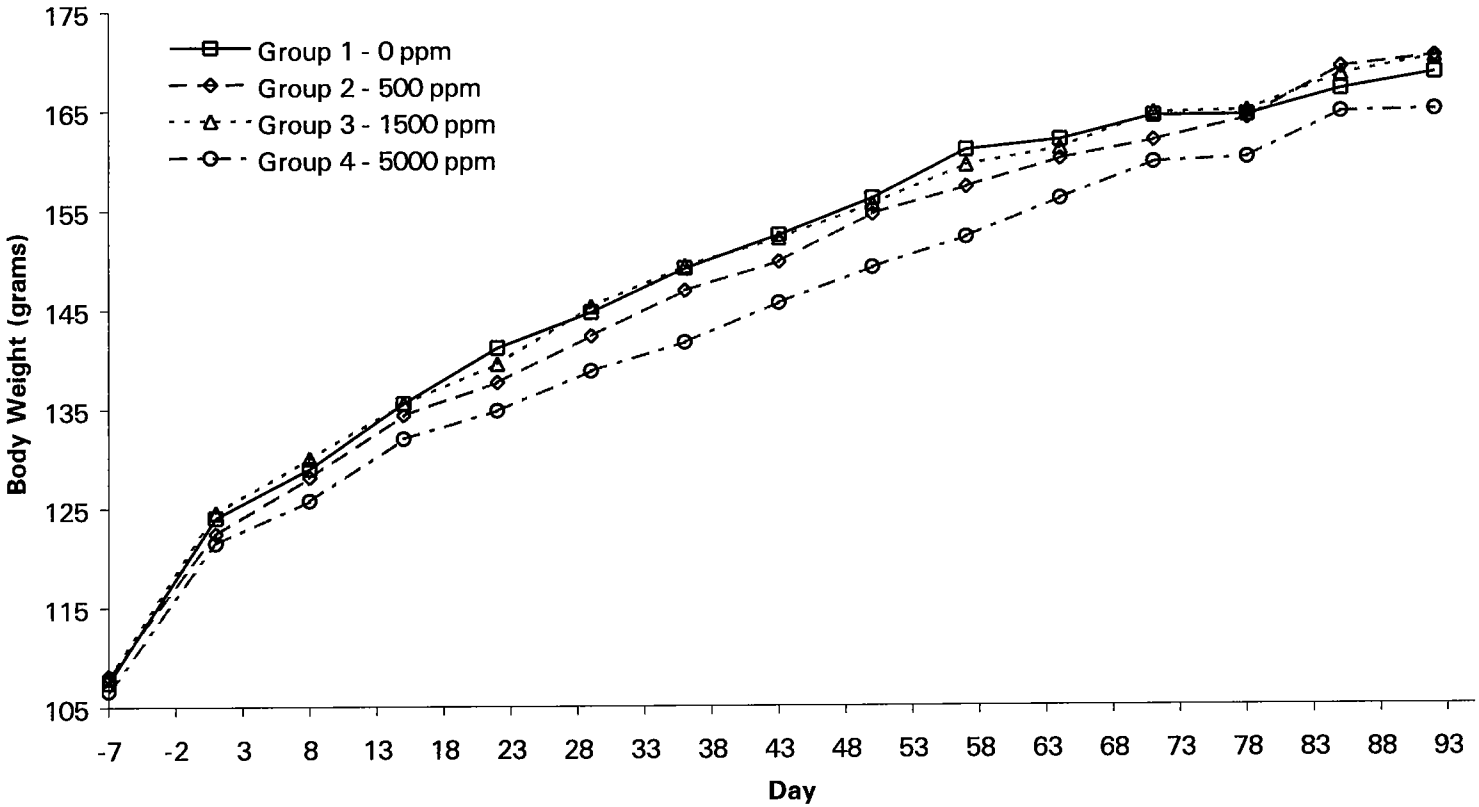


[a] The nose-only exposure chamber and generation system were contained within a exposure cabinet.
[b] The distribution sample ports (H-2 & H-4) were located on the respective side opposite the H-1 & H-3 sample ports.
[c] A damp towel and/or ice pack (Groups 2 and 3) and ice bath/paper towel for flask (Group 4) was applied to keep test material cool.
[d] Syringe was used for Groups 2 and 3 and the FMI was used for Group 4.

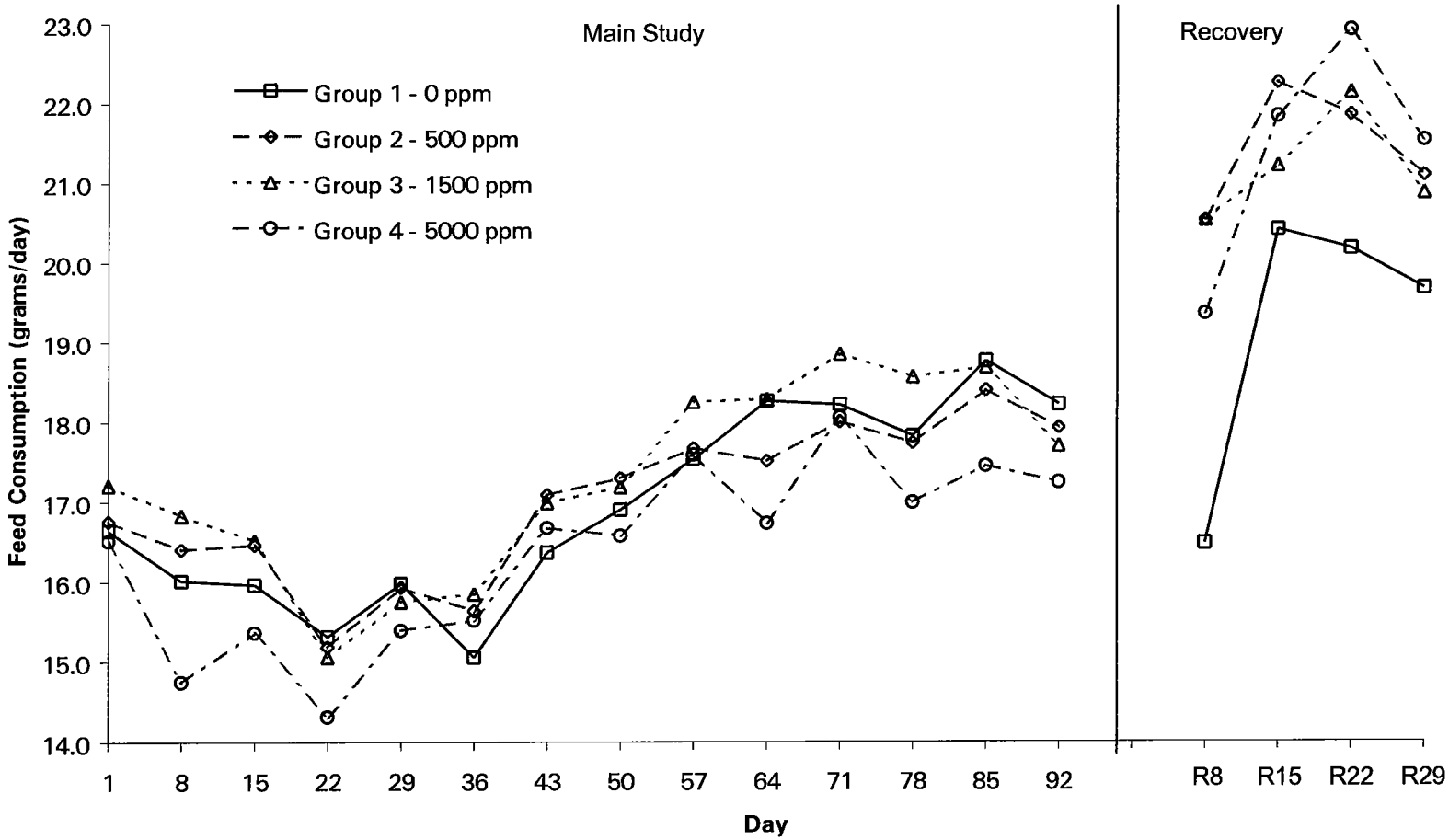
Males	Mean Body Weights (grams)	Figure 2



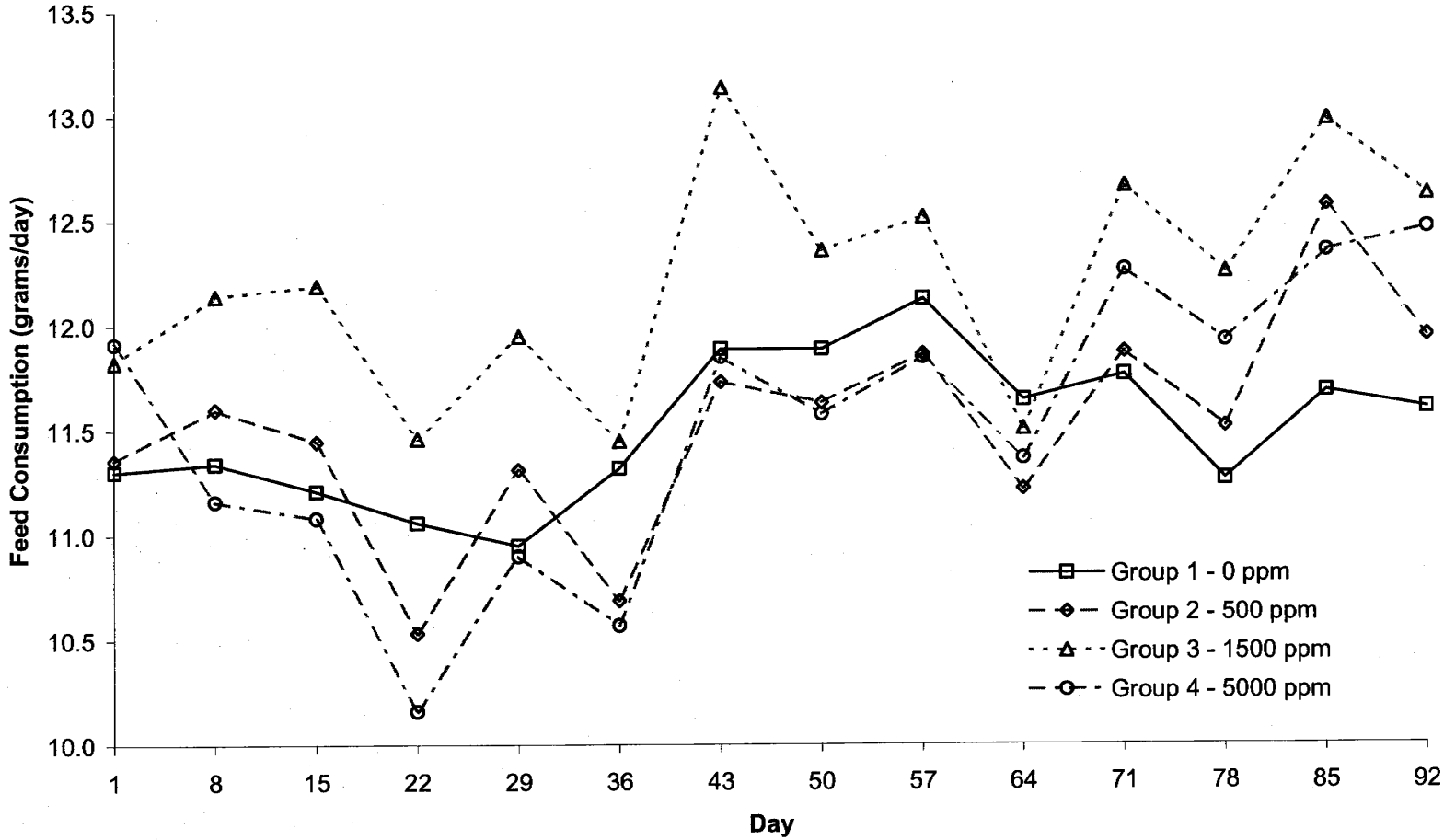
Females	Mean Body Weights (grams)	Figure 3



Males	Mean Feed Consumption (grams/animal/day)	Figure 4



Females	Mean Feed Consumption (grams/animal/day)	Figure 5



	Summary of In-Chamber Observations											Table 1			
Exposure Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Group 1 – 0 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 1500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 5000 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.

	Summary of In-Chamber Observations											Table 1				
Exposure Day	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	
Group 1 – 0 ppm																
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All	
Group 2 – 500 ppm																
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All	
Group 3 – 1500 ppm																
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All	
Group 4 – 5000 ppm																
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All	

All = 100% of the animals exhibiting a given observation.

	Summary of In-Chamber Observations											Table 1			
Exposure Day	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**
Group 1 – 0 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 1500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 5000 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.

	Summary of In-Chamber Observations											Table 1				
Exposure Day	**46**	**47**	**48**	**49**	**50**	**51**	**52**	**53**	**54**	**55**	**56**	**57**	**58**	**59**	**60**
Group 1 – 0 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 1500 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 5000 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.

	Summary of In-Chamber Observations	Table 1

Exposure Day	**61**	**62**	**63**	**64**	**65**	**66**	**67**	**68**
Group 1 – 0 ppm								
Within Normal Limits	All	All	All	All	All	All	All	All
Group 2 – 500 ppm								
Within Normal Limits	All	All	All	All	All	All	All	All
Group 3 – 1500 ppm								
Within Normal Limits	All	All	All	All	All	All	All	All
Group 4 – 5000 ppm								
Within Normal Limits	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.

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Table 2

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Clinical Signs Incidence Summary

Males

Group	Dose PPM	Clinical Sign	Day	Pretest -7	Ran. -1	Dosing phase 3	9	16	23	30
1	0									
		Total Number in Group		15	15	15	15	15	15	14
		Within Normal Limits		15	15	15	13	10	13	13
		Chromodacryorrhea		0	0	0	2	5	2	1
2	500									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		15	15	14	11	8	13	12
		Wet Fur		0	0	1	2	0	0	0
		Chromodacryorrhea		0	0	0	2	7	2	3
3	1500									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		15	15	14	13	14	13	13
		Wet Fur		0	0	1	0	0	0	0
		Chromodacryorrhea		0	0	0	2	1	2	2
4	5000									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		15	15	14	14	15	15	11
		Chromodacryorrhea		0	0	1	1	0	0	3
		Nasal Discharge		0	0	0	0	0	0	1

Table 2

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Clinical Signs Incidence Summary

				Males						
				Dosing phase						
Group	Dose PPM	Clinical Sign	Day	37	44	51	58	65	72	79
1	0									
		Total Number in Group		14	14	14	14	14	14	14
		Within Normal Limits		13	13	13	10	13	11	11
		Ano-Genital Staining		0	0	1	0	0	0	0
		Chromodacryorrhea		1	1	1	4	1	3	3
2	500									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		10	8	7	6	8	7	9
		Alopecia		0	0	0	0	1	1	1
		Ano-Genital Staining		0	0	3	4	3	3	3
		Chromodacryorrhea		5	7	7	7	4	5	3
3	1500									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		10	11	13	11	8	8	9
		Ano-Genital Staining		0	0	1	2	2	2	2
		Chromodacryorrhea		5	4	1	3	5	5	5
		Nasal Discharge		0	0	0	0	1	1	0
4	5000									
		Total Number in Group		15	15	15	15	15	15	15
		Within Normal Limits		11	13	12	10	7	6	6
		Ano-Genital Staining		0	0	2	4	4	8	8
		Chromodacryorrhea		3	2	2	1	3	2	1
		Nasal Discharge		1	0	0	0	1	0	0
		Dry Rales		0	0	0	0	0	1	0

Table 2

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Clinical Signs Incidence Summary

Males

Group	Dose PPM	Clinical Sign	Day	Dosing phase 86	Dosing phase 92	Recovery phase 9	Recovery phase 16	Recovery phase 23	Recovery phase 30
1	0								
		Total Number in Group		14	14	5	5	5	5
		Within Normal Limits		11	13	4	5	5	5
		Ano-Genital Staining		0	0	1	0	0	0
		Chromodacryorrhea		3	1	0	0	0	0
2	500								
		Total Number in Group		15	15	5	5	5	5
		Within Normal Limits		9	10	5	5	5	5
		Alopecia		1	1	0	0	0	0
		Ano-Genital Staining		3	0	0	0	0	0
		Chromodacryorrhea		3	4	0	0	0	0
3	1500								
		Total Number in Group		15	15	5	5	5	5
		Within Normal Limits		10	13	5	5	5	5
		Ano-Genital Staining		2	2	0	0	0	0
		Chromodacryorrhea		4	0	0	0	0	0
4	5000								
		Total Number in Group		15	15	5	5	5	5
		Within Normal Limits		7	10	4	4	4	5
		Alopecia		0	0	0	1	1	0
		Ano-Genital Staining		8	5	1	0	0	0
		Scab(s)		0	0	1	1	1	0

Table 2

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Clinical Signs Incidence Summary

Females

Group	Dose PPM	Clinical Sign	Day	Pretest -7	Ran. -1	Dosing phase 3	9	16	23	30	37
1	0										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		10	10	10	9	9	8	6	6
		Chromodacryorrhea		0	0	0	1	1	2	4	4
2	500										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		10	10	9	10	7	8	5	5
		Chromodacryorrhea		0	0	1	0	3	2	5	5
3	1500										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		10	10	10	9	9	9	5	3
		Chromodacryorrhea		0	0	0	1	1	1	5	7
4	5000										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		10	10	10	9	7	9	2	2
		Alopecia		0	0	0	0	0	1	4	4
		Chromodacryorrhea		0	0	0	1	3	0	7	7

Table 2

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Clinical Signs Incidence Summary

Females

Group	Dose PPM	Clinical Sign	Day	Dosing phase 44	51	58	65	72	79	86	92
1	0										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		6	6	1	3	2	1	2	7
		Alopecia		0	0	0	1	1	1	1	1
		Ano-Genital Staining		0	2	4	4	5	5	5	3
		Chromodacryorrhea		4	3	6	3	6	7	6	1
2	500										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		7	5	5	1	1	0	1	5
		Alopecia		1	0	0	0	0	0	0	0
		Ano-Genital Staining		0	3	3	4	4	4	4	4
		Chromodacryorrhea		3	2	3	7	7	7	8	2
3	1500										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		5	4	6	6	4	3	3	4
		Alopecia		0	0	0	1	1	2	2	2
		Ano-Genital Staining		0	2	1	2	2	2	2	2
		Scab(s)		0	0	0	0	0	0	0	1
		Chromodacryorrhea		5	4	4	3	6	6	6	4
4	5000										
		Total Number in Group		10	10	10	10	10	10	10	10
		Within Normal Limits		3	6	4	3	2	4	4	4
		Alopecia		4	1	1	2	2	2	2	2
		Ano-Genital Staining		0	1	4	5	6	6	6	6
		Chromodacryorrhea		5	3	1	3	4	2	2	2

Table 3. Ophthalmoscopic examination summary

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Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation
Toxicity Study in Rats with a 4-Week Recovery Period

				Males	
				Pretest phase	Dosing phase
Group	Dose PPM	Clinical Sign	Day	-6	91
1	0				
		Total Number in Group		15	14
		Within Normal Limits		15	14
2	500				
		Total Number in Group		15	15
		Within Normal Limits		15	15
3	1500				
		Total Number in Group		15	15
		Within Normal Limits		15	13
		Focal Retinopathy		0	2
4	5000				
		Total Number in Group		15	15
		Within Normal Limits		15	15

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

				Females	
				Pretest phase	Dosing phase
Group	Dose PPM	Clinical Sign	Day	-6	91
1	0				
		Total Number in Group		10	10
		Within Normal Limits		10	10
2	500				
		Total Number in Group		10	10
		Within Normal Limits		10	10
3	1500				
		Total Number in Group		10	10
		Within Normal Limits		10	9
		Conjunctivitis		0	1
4	5000				
		Total Number in Group		10	10
		Within Normal Limits		10	9
		Conjunctivitis		0	1

Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

M a l e s

Group	Dose PPM	Day	Pretest phase -7	Dosing phase 1	8	15	22
1	0	Mean	143.60	175.13	186.90	203.02	216.04
		SD	8.81	9.80	10.69	11.23	10.13
		N	15	15	15	15	15
2	500	Mean	144.13	176.58	189.49	204.80	217.21
		SD	8.53	9.94	8.62	7.53	5.79
		N	15	15	15	15	15
3	1500	Mean	144.24	176.15	191.13	206.79	215.66
		SD	9.13	8.56	7.44	8.77	9.54
		N	15	15	15	15	15
4	5000	Mean	143.93	174.23	184.21	198.65	208.48
		SD	8.87	10.34	9.73	9.40	9.70
		N	15	15	15	15	15

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Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

M a l e s

Group	Dose PPM	Day	Dosing phase 29	36	43	50	57
1	0	Mean	230.13	237.33	246.17	256.25	267.26
		SD	11.07	10.81	12.88	14.72	14.95
		N	15	14	14	14	14
2	500	Mean	228.78	237.93	243.99	255.99	265.18
		SD	5.71	7.93	8.98	11.49	14.15
		N	15	15	15	15	15
3	1500	Mean	228.47	239.70	245.91	256.24	264.87
		SD	9.85	11.07	13.00	13.74	13.01
		N	15	15	15	15	15
4	5000	Mean	217.12+	227.63*	232.87+	239.51+	245.51+
		SD	10.50	10.89	11.35	12.16	14.50
		N	15	15	15	15	15

* Significant difference from Control Group ($P < 0.05$)
\+ Significant difference from Control Group ($P < 0.01$)

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Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

M a l e s

Group	Dose PPM	Day	Dosing phase 64	71	78	85	92
1	0	Mean	276.36	284.81	292.83	300.99	303.06
		SD	15.57	15.75	16.71	17.13	17.78
		N	14	14	14	14	14
2	500	Mean	273.85	281.80	288.64	298.12	302.01
		SD	14.26	14.71	15.99	18.20	17.75
		N	15	15	15	15	15
3	1500	Mean	274.15	280.17	289.42	294.37	295.85
		SD	12.94	13.13	13.52	15.47	16.60
		N	15	15	15	15	15
4	5000	Mean	252.73+	258.21+	265.10+	272.77+	274.62+
		SD	14.72	14.94	14.38	14.89	15.18
		N	15	15	15	15	15

\+ Significant difference from Control Group ($P < 0.01$)

Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

M a l e s

Group	Dose PPM	Day	Recovery phase 8	15	22	29
1	0	Mean	300.02	317.12	328.78	338.02
		SD	39.16	19.99	17.62	17.18
		N	5	5	5	5
2	500	Mean	319.32	330.20	341.12	350.12
		SD	21.01	20.27	22.84	24.08
		N	5	5	5	5
3	1500	Mean	303.52	313.82	327.96	336.70
		SD	18.89	18.37	17.54	18.89
		N	5	5	5	5
4	5000	Mean	294.96	308.28	323.28	333.70
		SD	12.79	14.86	15.28	15.31
		N	5	5	5	5

Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

F e m a l e s

Group	Dose PPM	Day	Pretest phase	Dosing phase			
			-7	1	8	15	22
1	0	Mean	107.41	124.04	128.98	135.58	141.18
		SD	6.26	4.27	3.37	4.92	5.23
		N	10	10	10	10	10
2	500	Mean	108.09	122.44	128.11	134.40	137.69
		SD	5.29	6.01	6.64	7.28	8.07
		N	10	10	10	10	10
3	1500	Mean	108.03	124.54	130.06	135.59	139.58
		SD	5.30	5.68	6.77	7.47	8.20
		N	10	10	10	10	10
4	5000	Mean	106.57	121.47	125.75	132.02	134.85
		SD	6.96	7.37	7.65	8.76	10.06
		N	10	10	10	10	10

Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

F e m a l e s

Group	Dose PPM	Day	Dosing phase 29	36	43	50	57
1	0	Mean	144.73	149.15	152.49	156.20	161.01
		SD	6.07	5.48	5.36	5.32	5.27
		N	10	10	10	10	10
2	500	Mean	142.36	146.90	149.82	154.61	157.31
		SD	7.87	8.92	9.23	8.37	9.03
		N	10	10	10	10	10
3	1500	Mean	145.31	149.38	152.16	155.61	159.51
		SD	7.00	7.32	9.93	9.54	10.62
		N	10	10	10	10	10
4	5000	Mean	138.83	141.70	145.64	149.25	152.27
		SD	10.44	12.02	12.69	12.05	11.75
		N	10	10	10	10	10

Table 4

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Body Weights (g)

F e m a l e s

Group	Dose PPM	Day	Dosing phase 64	71	78	85	92
1	0	Mean	162.01	164.39	164.44	167.02	168.66
		SD	5.65	5.93	6.87	7.12	5.93
		N	10	10	10	10	10
2	500	Mean	160.10	161.96	164.14	169.24	170.34
		SD	7.98	8.53	9.05	8.35	8.60
		N	10	10	10	10	10
3	1500	Mean	161.16	164.68	164.88	168.50	170.26
		SD	9.09	10.14	9.91	10.83	11.47
		N	10	10	10	10	10
4	5000	Mean	156.13	159.76	160.21	164.73	164.96
		SD	13.20	13.61	11.84	11.88	10.92
		N	10	10	10	10	10

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

M a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 8	15	22	29
1	0	Mean	11.77	27.89	40.91	55.01
		SD	4.74	5.64	7.72	8.82
		N	15	15	15	15
2	500	Mean	12.91	28.22	40.63	52.20
		SD	3.63	4.85	7.52	9.52
		N	15	15	15	15
3	1500	Mean	14.99	30.64	39.51	52.32
		SD	3.78	4.53	7.31	7.33
		N	15	15	15	15
4	5000	Mean	9.97	24.42	34.25*	42.89+
		SD	2.74	4.66	6.37	7.35
		N	15	15	15	15

* Significant difference from Control Group ($P < 0.05$)

\+ Significant difference from Control Group ($P < 0.01$)

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

M a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 36	43	50	57
1	0	Mean	61.16	70.00	80.08	91.09
		SD	9.74	10.33	12.23	12.67
		N	14	14	14	14
2	500	Mean	61.35	67.41	79.41	88.60
		SD	12.51	12.37	14.08	16.90
		N	15	15	15	15
3	1500	Mean	63.55	69.77	80.09	88.72
		SD	8.24	10.35	11.83	12.23
		N	15	15	15	15
4	5000	Mean	53.39	58.63*	65.27+	71.27+
		SD	8.63	9.83	10.93	13.11
		N	15	15	15	15

* Significant difference from Control Group ($P < 0.05$)

\+ Significant difference from Control Group ($P < 0.01$)

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

M a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 64	71	78
1	0	Mean	100.19	108.64	116.66
		SD	13.67	14.22	14.97
		N	14	14	14
2	500	Mean	97.27	105.22	112.06
		SD	17.70	18.51	19.55
		N	15	15	15
3	1500	Mean	98.00	104.03	113.27
		SD	11.80	12.58	11.85
		N	15	15	15
4	5000	Mean	78.50+	83.97+	90.87+
		SD	13.02	13.36	13.45
		N	15	15	15

\+ Significant difference from Control Group ($P < 0.01$)

Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

M a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 85	Dosing phase 92	Recovery phase 8
1	0	Mean	124.81	126.89	123.26
		SD	14.58	14.77	37.41
		N	14	14	5
2	500	Mean	121.54	125.43	144.52
		SD	22.20	22.23	25.12
		N	15	15	5
3	1500	Mean	118.23	119.70	129.04
		SD	14.45	15.03	19.03
		N	15	15	5
4	5000	Mean	98.54+	100.39+	119.74
		SD	13.89	14.77	14.75
		N	15	15	5

\+ Significant difference from Control Group ($P < 0.01$)

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

M a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Recovery phase 15	22	29
1	0	Mean	140.36	152.02	161.26
		SD	19.29	18.56	18.51
		N	5	5	5
2	500	Mean	155.40	166.32	175.32
		SD	24.67	26.97	28.19
		N	5	5	5
3	1500	Mean	139.34	153.48	162.22
		SD	19.33	18.29	20.67
		N	5	5	5
4	5000	Mean	133.06	148.06	158.48
		SD	17.01	17.53	17.63
		N	5	5	5

Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

F e m a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 8	15	22	29
1	0	Mean	4.94	11.54	17.14	20.69
		SD	2.17	1.95	2.69	4.09
		N	10	10	10	10
2	500	Mean	5.67	11.96	15.25	19.92
		SD	2.62	4.14	5.42	5.82
		N	10	10	10	10
3	1500	Mean	5.52	11.05	15.04	20.77
		SD	1.99	3.32	4.47	3.14
		N	10	10	10	10
4	5000	Mean	4.28	10.55	13.38	17.36
		SD	2.74	3.36	4.57	5.76
		N	10	10	10	10

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

F e m a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 36	43	50
1	0	Mean	25.11	28.45	32.16
		SD	3.02	4.66	4.44
		N	10	10	10
2	500	Mean	24.46	27.38	32.17
		SD	6.71	6.99	5.99
		N	10	10	10
3	1500	Mean	24.84	27.62	31.07
		SD	3.55	5.63	5.39
		N	10	10	10
4	5000	Mean	20.23	24.17	27.78
		SD	6.94	7.36	7.11
		N	10	10	10

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

F e m a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 57	64	71
1	0	Mean	36.97	37.97	40.35
		SD	5.12	5.79	6.02
		N	10	10	10
2	500	Mean	34.87	37.66	39.52
		SD	6.81	6.31	6.57
		N	10	10	10
3	1500	Mean	34.97	36.62	40.14
		SD	6.36	5.02	6.02
		N	10	10	10
4	5000	Mean	30.80	34.66	38.29
		SD	6.98	7.80	7.81
		N	10	10	10

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Table 5

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Mean Cumulative Body Weight Change from Baseline (g)

F e m a l e s

Baseline day: 1 of Dosing phase

Group	Dose PPM	Day	Dosing phase 78	85	92
1	0	Mean	40.40	42.98	44.62
		SD	6.74	7.08	5.17
		N	10	10	10
2	500	Mean	41.70	46.80	47.90
		SD	7.12	6.97	6.80
		N	10	10	10
3	1500	Mean	40.34	43.96	45.72
		SD	5.39	6.68	7.38
		N	10	10	10
4	5000	Mean	38.74	43.26	43.49
		SD	6.32	6.61	5.83
		N	10	10	10

Males	Mean Feed Consumption Values (grams/animal/day)	Table 6

	Dosing Phase Day								
	1	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**57**
Group 1 – 0 ppm									
Mean	16.6	16.0	16.0	15.3	16.0	15.1	16.4	16.9	17.5
SD	1.7	1.6	1.4	1.4	1.2	1.4	1.8	1.9	1.9
N	15	15	15	15	15	14	14	14	14
Group 2 – 500 ppm									
Mean	16.8	16.4	16.5	15.2	15.9	15.6	17.1	17.3	17.7
SD	1.2	1.1	2.2	1.1	1.6	1.5	1.2	2.0	1.3
N	15	15	15	15	15	15	14	15	15
Group 3 – 1500 ppm									
Mean	17.2	16.8	16.5	15.1	15.8	15.9	17.0	17.2	18.3
SD	1.0	0.9	1.0	0.9	1.1	1.5	1.8	1.6	1.6
N	15	15	15	15	15	15	15	15	15
Group 4 – 5000 ppm									
		**							
Mean	16.5	14.7	15.4	14.3	15.4	15.5	16.7	16.6	17.6
SD	1.9	1.1	1.1	3.6	1.0	0.8	1.0	1.0	2.0
N	15	15	14	14	14	14	14	14	14

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Males	Mean Feed Consumption Values (grams/animal/day)	Table 6

	Dosing Phase Day				
	64	**71**	**78**	**85**	**92**
Group 1 – 0 ppm					
Mean	18.3	18.2	17.8	18.8	18.2
SD	2.1	1.8	1.8	1.8	1.4
N	14	14	14	14	14
Group 2 – 500 ppm					
Mean	17.5	18.0	17.7	18.4	17.9
SD	1.4	1.3	1.4	1.7	1.3
N	15	15	15	15	15
Group 3 – 1500 ppm					
Mean	18.3	18.9	18.6	18.7	17.7
SD	1.8	1.9	1.7	2.4	1.8
N	15	14	14	15	15
Group 4 – 5000 ppm					
Mean	16.7*	18.1	17.0	17.5	17.2
SD	1.4	0.9	1.1	1.0	1.0
N	14	14	15	15	15

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Males	Mean Feed Consumption Values (grams/animal/day)	Table 6

	Recovery Phase Day			
	8	**15**	**22**	**29**
Group 1 – 0 ppm				
Mean	16.5	20.4	20.2	19.7
SD	4.9	2.7	2.0	1.3
N	5	5	5	5
Group 2 – 500 ppm				
Mean	20.5	22.3	21.9	21.1
SD	1.4	0.6	1.6	1.3
N	5	5	5	5
Group 3 – 1500 ppm				
Mean	20.5	21.2	22.1	20.9
SD	2.0	3.0	2.6	2.4
N	5	5	5	5
Group 4 – 5000 ppm				
Mean	19.4	21.8	22.9	21.5
SD	1.3	1.5	1.2	1.5
N	5	5	5	5

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Females	Mean Feed Consumption Values (grams/animal/day)	Table 6

	Dosing Phase Day								
	1	**8**	**15**	**22**	**29**	**36**	**43**	**50**	**57**
Group 1 – 0 ppm									
Mean	11.3	11.3	11.2	11.1	11.0	11.3	11.9	11.9	12.1
SD	0.8	1.1	0.8	1.2	0.7	0.9	1.0	1.0	0.9
N	10	10	10	10	10	10	10	10	10
Group 2 – 500 ppm									
Mean	11.4	11.6	11.4	10.5	11.3	10.7	11.7	11.6	11.9
SD	0.9	1.5	1.0	1.5	1.8	1.0	1.2	1.3	1.0
N	9	9	9	9	9	9	9	9	9
Group 3 – 1500 ppm									
Mean	11.8	12.1	12.2	11.5	12.0	11.5	13.1	12.4	12.5
SD	1.6	1.0	0.8	0.7	1.2	0.8	1.5	1.4	1.2
N	9	10	10	10	10	10	10	10	10
Group 4 – 5000 ppm									
Mean	11.9	11.3	11.1	10.2	10.9	10.6	11.9	11.6	11.9
SD	0.8	1.3	1.0	0.7	1.3	1.2	1.1	1.1	1.3
N	9	10	10	10	10	10	10	10	10

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Females	Mean Feed Consumption Values (grams/animal/day)	Table 6

	Dosing Phase Day				
	64	**71**	**78**	**85**	**92**
Group 1 – 0 ppm					
Mean	11.7	11.8	11.3	11.7	11.6
SD	1.0	1.1	1.3	1.3	0.6
N	10	10	10	10	10
Group 2 – 500 ppm					
Mean	11.2	11.9	11.5	12.6	12.0
SD	1.1	1.4	1.4	1.2	1.0
N	9	9	9	9	9
Group 3 – 1500 ppm					
Mean	11.5	12.7	12.3	13.0	12.6*
SD	1.4	1.5	1.3	1.6	1.1
N	10	10	10	10	10
Group 4 – 5000 ppm					
Mean	11.4	12.3	11.9	12.4	12.5*
SD	1.4	1.3	1.4	1.1	1.2
N	10	10	9	10	10

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Table 7
Motor Activity Summary Statistics

Sex	Dose (ppm)	n	mean	sd	*p*-value (1)
Males	0	9	30.4	11.0	
	500	10	40.5	8.5	0.0726
	1500	10	37.1	9.9	0.3043
	5000	10	29.1	8.9	0.9807
Females	0	10	25.0	6.2	
	500	10	34.4	8.4	
	1500	10	33.5	9.9	
	5000	10	28.9	12.3	
Combined sexes	0	19	27.6	9.0	
	500	20	37.4	8.8	0.0052 **
	1500	20	35.3	9.8	0.0361 *
	5000	20	29.0	10.4	0.9394

n = number of animals per group.
mean = mean motor activity per group based on animal means over the 12 intervals.
sd = standard deviation based on the animal means over the 12 intervals.
(1) *p*-value for Dunnetts' test following significant ANOVA (*= $p<0.05$, **=$p<0.01$)

Males	Mean Motor Activity Values (number of beam breaks) Week 13	Table 8

	5-Minute Interval												
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Mean**
Group 1 – 0 ppm													
Mean	136	79	54	27	21	13	7	14	2	6	2	5	30
SD	49	38	36	37	32	25	18	26	2	14	5	11	
n	9	9	9	9	9	9	9	9	9	9	9	9	
Group 2 – 500 ppm													
Mean	168	98	75	45	22	10	8	4	14	18	8	16	40
SD	27	34	37	27	30	14	23	6	28	31	14	33	
n	10	10	10	10	10	10	10	10	10	10	10	10	
Group 3 – 1500 ppm													
Mean	154	97	51	42	23	26	18	9	12	6	3	5	37
SD	33	31	31	32	25	36	29	16	23	16	5	10	
n	10	10	10	10	10	10	10	10	10	10	10	10	
Group 4 – 5000 ppm													
Mean	146	90	48	35	11	7	3	2	4	2	0	2	29
SD	40	34	31	25	19	15	7	4	5	5	0	3	
n	10	10	10	10	10	10	10	10	10	10	10	10	

Females	Mean Motor Activity Values (number of beam breaks) Week 13	Table 8

	5-Minute Interval												
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Mean**
Group 1 – 0 ppm													
Mean	104	83	48	28	12	4	7	2	3	3	4	2	25
SD	30	29	25	18	15	6	17	5	5	5	6	3	
n	10	10	10	10	10	10	10	10	10	10	10	10	
Group 2 – 500 ppm													
Mean	117	91	75	47	35	21	15	5	5	1	2	1	34
SD	23	21	15	29	32	25	25	12	8	2	2	2	
n	10	10	10	10	10	10	10	10	10	10	10	10	
Group 3 – 1500													
Mean	116	102	63	51	38	13	6	1	1	2	4	4	33
SD	24	26	22	29	53	18	12	3	2	5	7	7	
n	10	10	10	10	10	10	10	10	10	10	10	10	
Group 4 – 5000 ppm													
Mean	111	75	55	23	35	23	8	5	0	2	2	7	29
SD	26	22	23	21	46	39	14	11	1	3	4	13	
n	10	10	10	10	10	10	10	10	10	10	10	10	

Males	Summary of Functional Observational Battery Evaluations Week 13	Table 9

Exposure Level:		Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Body Weight (g)	Mean	301.1	298.0	298.8	275.1**
	S.D.	17.5	17.6	10.8	16.8
	N	9	10	10	10
Forelimb Grip Strength (g)	Mean	878	910	906	877
	S.D.	154.1	141.4	125.5	78.8
	N	9	10	10	10
Hindlimb Grip Strength (g)	Mean	628	633	642	648
	S.D.	63.8	66.1	56.0	92.3
	N	9	10	10	10
Landing Foot Splay (cm)	Mean	3.4	3.3	3.6	3.4
	S.D.	1.0	0.8	1.1	0.5
	N	9	10	10	10
Body Temperature (°C)	Mean	36.2	36.6	36.6	36.3
	S.D.	1.5	1.3	1.2	1.1
	N	9	10	10	10

*Significantly different from control mean; p≤0.05.
**Significantly different from control mean; p≤0.01.
If no asterisks, no statistically significant differences from control mean.

Males	Summary of Functional Observational Battery Evaluations Week 13	Table 9

	Exposure Level:	Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Number of Animals Examined		9	10	10	10
Home Cage Evaluations					
Posture	Sitting or Standing	9	10	10	10
	Rearing; Standing on Hindlimbs	0	0	0	0
	Asleep; May Be Lying on Side or Curled Up	0	0	0	0
	Lying on Side; Limbs in the Air	0	0	0	0
	Flattened; Limbs May Be Spread	0	0	0	0
	Crouched; Sitting Hunched, Head Hung Down	0	0	0	0
Vocalizations	Not Present	9	10	10	10
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	9	10	10	10
	Eyelids Slightly Drooping	0	0	0	0
	Eyelids Half Closed	0	0	0	0
	Eyelids Completely Closed	0	0	0	0
Motor Movements	No abnormal movements	9	10	10	10
	Tremors	0	0	0	0
	Fasciculations	0	0	0	0
	Convulsions	0	0	0	0
	Stereotypy	0	0	0	0
	Other	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	9	10	10	10
	Easy	0	0	0	0
	Slightly Difficult	0	0	0	0
	Freezes or flinches	0	0	0	0
	Moderately Difficult	0	0	0	0
	Very Difficult	0	0	0	0
Reactivity to Handling	Low	9	10	10	10
	Moderately Low	0	0	0	0
	Moderately High	0	0	0	0
	High	0	0	0	0
Chromodacryorrhea	Not Present	8	10	8	10

Males	Summary of Functional Observational Battery Evaluations Week 13	Table 9

	Present		1	0	2	0
		Exposure Level:	**Group 1 0 ppm**	**Group 2 500 ppm**	**Group 3 1500 ppm**	**Group 4 5000 ppm**
Lacrimation	Not Present		9	10	10	10
	Moderate		0	0	0	0
	Extreme		0	0	0	0
Coat	Normal		9	10	10	10
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		9	10	10	10
	Slight		0	0	0	0
	Moderate		0	0	0	0
	Extreme		0	0	0	0
Open Field Evaluations						
Gait and Posture	Normal		9	10	10	10
	Ataxia					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Hindlimbs Splayed or Drag					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Forelimbs Splayed or Drag					
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Walks on Tiptoes					
		Slight	0	0	0	0
		Severe	0	0	0	0
	Hunched Posture					
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Body Drags or is Flattened					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0

Males	Summary of Functional Observational Battery Evaluations Week 13	Table 9

		Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
	Exposure Level:				
Locomotion	No Impairment	9	10	10	10
	Slightly Impaired	0	0	0	0
	Moderately Impaired	0	0	0	0
	Severly Impaired	0	0	0	0
Arousal	Very Low, Stupor	0	0	0	0
	Moderately Low, Slight Stupor	0	0	0	0
	Slightly Low, Sluggish	0	1	0	2
	Alert	9	9	10	7
	High, Slight Excitement	0	0	0	1
	Very High, Hyper Alert	0	0	0	0
Piloerection	Not Present	9	10	10	10
	Present	0	0	0	0
Exophthalmia	Not Present	9	10	10	10
	Present	0	0	0	0
Feces	Number of Pellets	0	0	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	1	0	0
	Polyuria	0	0	0	0
Motor Movements					
Fasciculations	Not Present	9	10	10	10
	Present	0	0	0	0
Convulsions	Not Present	9	10	10	10
	Present	0	0	0	0
Tremors	Not Present	9	10	10	10
	Present	0	0	0	0
Reflex Assessments					
Visual Approach	No Reaction	0	0	0	0
	Slowly Approaches, Sniffs and/or Turns Away	9	10	10	10
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid	0	0	0	0
	Attacks and/or Bites	0	0	0	0

Males	Summary of Functional Observational Battery Evaluations Week 13	Table 9

	Exposure Level:	Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Audition	No Reaction	0	0	0	0
	Slight Reaction, Some Evidence That Noise Was Heard	0	0	0	0
	Flinches or Flicks Ears	9	10	10	10
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	No Reaction	0	0	1	0
	Turns or Walks Forward, or Vocalizes with Little or No Movement	9	10	9	10
	Fliches; Muscle Contractions Present	0	0	0	0
	Highly Exaggerated, Bizarre Reaction; Attacks, Bites	0	0	0	0
Pupil Response	Pupil Constricts	10	10	10	10
	No Constriction	0	0	0	0
	Miosis	0	0	0	0
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head or Animal Shakes Head	9	10	10	10
	No Response	0	0	0	0
Proprioception	Returns Leg to Original Position	9	10	10	10
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response, Allows Leg to Remain in Pulled Back Position	0	0	0	0
Air Righting Reflex	Lands on All Four Feet	9	10	10	10
	Slightly Uncoordinated	0	0	0	0
	Lands on Side	0	0	0	0
	Lands on Back	0	0	0	0

Females	Summary of Functional Observational Battery Evaluations Week 13	Table 9

Exposure Level:		Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Body Weight	Mean	168.0	168.6	169.5	165.8
(g)	S.D.	6.0	7.5	11.1	11.3
	N	10	10	10	10
Forelimb Grip Strength	Mean	764	717	771	737
(g)	S.D.	109.9	104.1	52.8	67.5
	N	10	10	10	10
Hindlimb Grip Strength	Mean	489	484	503	498
(g)	S.D.	52.9	67.8	79.6	53.4
	N	10	10	10	10
Landing Foot Splay	Mean	2.4	2.3	2.3	2.3
(cm)	S.D.	0.3	0.8	0.7	0.5
	N	10	10	10	10
Body Temperature	Mean	37.1	36.4	37.2	37.1
(°C)	S.D.	1.0	1.6	1.0	1.3
	N	10	10	10	10

*Significantly different from control mean; $p \leq 0.05$.
**Significantly different from control mean; $p \leq 0.01$.
If no asterisks, no statistically significant differences from control mean.

Females	Summary of Functional Observational Battery Evaluations Week 13	Table 9

		Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Exposure Level:					
Number of Animals Examined		10	10	10	10
Home Cage Evaluations					
Posture	Sitting or Standing	10	10	10	10
	Rearing; Standing on Hindlimbs	0	0	0	0
	Asleep; May Be Lying on Side or Curled Up	0	0	0	0
	Lying on Side; Limbs in the Air	0	0	0	0
	Flattened; Limbs May Be Spread	0	0	0	0
	Crouched; Sitting Hunched, Head Hung Down	0	0	0	0
Vocalizations	Not Present	10	10	10	10
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	10	9	10	10
	Eyelids Slightly Drooping	0	0	0	0
	Eyelids Half Closed	0	0	0	0
	Eyelids Completely Closed	0	1	0	0
Motor Movements	No abnormal movements	9	10	10	10
	Tremors	0	0	0	0
	Fasciculations	0	0	0	0
	Convulsions	0	0	0	0
	Stereotypy	0	0	0	0
	Other	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	10	10	10	10
	Easy	0	0	0	0
	Slightly Difficult	0	0	0	0
	Freezes	0	0	0	0
	Moderately Difficult	0	0	0	0
	Very Difficult	0	0	0	0
Reactivity to Handling	Low	10	10	10	10
	Moderately Low	0	0	0	0
	Moderately High	0	0	0	0
	High	0	0	0	0
Chromodacryorrhea	Not Present	5	7	8	9
	Present	5	3	2	1

Females	Summary of Functional Observational Battery Evaluations Week 13	Table 9

			Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
		Exposure Level:				
Lacrimation	Not Present		10	10	10	10
	Moderate		0	0	0	0
	Extreme		0	0	0	0
Coat	Normal		10	10	10	10
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		10	10	10	10
	Slight		0	0	0	0
	Moderate		0	0	0	0
	Extreme		0	0	0	0
Open Field Evaluations						
Gait and Posture	Normal		10	10	10	10
	Ataxia					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Hindlimbs Splayed or Drag					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Forelimbs Splayed or Drag					
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Walks on Tiptoes					
		Slight	0	0	0	0
		Severe	0	0	0	0
	Hunched Posture					
		Moderate	0	0	0	0
		Severe	0	0	0	0
	Body Drags or is Flattened					
		Slight	0	0	0	0
		Moderate	0	0	0	0
		Severe	0	0	0	0

Females	Summary of Functional Observational Battery Evaluations Week 13	Table 9

		Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Exposure Level:					
Locomotion	No Impairment	10	10	10	10
	Slightly Impaired	0	0	0	0
	Moderately Impaired	0	0	0	0
	Severly Impaired	0	0	0	0
Arousal	Very Low, Stupor	0	0	0	0
	Moderately Low, Slight Stupor	0	0	0	0
	Slightly Low, Sluggish	0	0	1	1
	Alert	10	9	9	8
	High, Slight Excitement	0	1	0	1
	Very High, Hyper Alert	0	0	0	0
Piloerection	Not Present	10	10	10	10
	Present	0	0	0	0
Exophthalmia	Not Present	10	10	10	10
	Present	0	0	0	0
Feces	Number of Pellets	0	0	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	0	0	0
	Polyuria	0	0	0	0
Motor Movements					
Fasciculations	Not Present	10	10	10	10
	Present	0	0	0	0
Convulsions	Not Present	10	10	10	10
	Present	0	0	0	0
Tremors	Not Present	10	10	10	10
	Present	0	0	0	0
Reflex Assessments					
Visual Approach	No Reaction	0	0	0	0
	Slowly Approaches, Sniffs and/or Turns Away	10	10	10	10
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid	0	0	0	0
	Attacks and/or Bites	0	0	0	0

Females	Summary of Functional Observational Battery Evaluations Week 13	Table 9

	Exposure Level:	Group 1 0 ppm	Group 2 500 ppm	Group 3 1500 ppm	Group 4 5000 ppm
Audition	No Reaction	0	0	0	0
	Slight Reaction, Some Evidence That Noise Was Heard	0	0	0	0
	Flinches or Flicks Ears	10	10	10	10
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	No Reaction	1	0	0	0
	Turns or Walks Forward, or Vocalizes with Little or No Movement	9	10	10	10
	Fliches; Muscle Contractions Present	0	0	0	0
	Highly Exaggerated, Bizarre Reaction; Attacks, Bites	0	0	0	0
Pupil Response	Pupil Constricts	10	10	10	9
	No Constriction	0	0	0	0
	Miosis	0	0	0	1
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head or Animal Shakes Head	10	10	10	10
	No Response	0	0	0	0
Proprioception	Returns Leg to Original Position	10	10	10	10
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response, Allows Leg to Remain in Pulled Back Position	0	0	0	0
Air Righting Reflex	Lands on All Four Feet	10	10	10	10
	Slightly Uncoordinated	0	0	0	0
	Lands on Side	0	0	0	0
	Lands on Back	0	0	0	0

	Mean Hematology Values Preface	Table 10

Abbreviation	Parameter	Reporting Units
HGB	Hemoglobin Concentration	g/dL
HCT	Hematocrit	percent
RBC	Erythrocyte Count	$10^6/\mu L$
RETIC	Absolute Reticulocyte Count	$10^9/L$
PLT	Platelet Count	$10^3/\mu L$
MPV	Mean Platelet Volume	fL
MCV	Mean Corpuscular Volume	fL
MCH	Mean Corpuscular Hemoglobin	pg
MCHC	Mean Corpuscular Hemoglobin Concentration	g/dL
RDW	Red Cell Distribution Width	%
WBC	Total Leukocyte Count	$10^3/\mu L$
ANEU	Absolute Neutrophils	$10^3/\mu L$
ALYM	Absolute Lymphocytes	$10^3/\mu L$
AMONO	Absolute Monocytes	$10^3/\mu L$
AEOS	Absolute Eosinophils	$10^3/\mu L$
ABASO	Absolute Basophils	$10^3/\mu L$
ALUC	Absolute Large Unstained Cells	$10^3/\mu L$

Key to Statistical Symbols:

*Significantly different from control mean; $p \leq 0.05$.
**Significantly different from control mean; $p \leq 0.01$.
If no asterisks, no statistically significant differences from control mean.

Huntingdon Life Sciences Study No. 04-6154

Table 10

Mean Hematology Values - Termination

Group		HGB	HCT	RBC	RETIC	PLT	MPV	MCV	MCH	MCHC	RDW	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	fL	pg	g/dL	%	x10^3/uL
1M												
0 ppm	Mean	14.7	43.3	8.82	146.7	617	6.7	49.1	16.6	33.8	12.4	4.09
	SD	0.26	0.91	0.231	11.44	35.4	0.11	0.63	0.25	0.38	0.22	0.733
	n	8	8	8	8	8	8	8	8	8	8	8
2M		**										**
500 ppm	Mean	15.1	44.1	9.02	160.8	638	6.7	48.9	16.8	34.3	12.6	5.21
	SD	0.46	1.39	0.229	26.00	57.1	0.33	0.70	0.29	0.45	0.42	0.577
	n	9	9	9	9	9	9	9	9	9	9	9
3M		**	*	*							*	**
1500 ppm	Mean	15.3	44.7	9.17	149.7	618	6.6	48.8	16.7	34.2	12.8	5.26
	SD	0.22	0.96	0.203	13.70	23.1	0.21	0.47	0.27	0.46	0.19	0.333
	n	9	9	9	9	9	9	9	9	9	9	9
4M		**	*	*	**		*				*	
5000 ppm	Mean	15.1	44.3	8.96	173.5	614	7.0	49.5	16.9	34.1	12.8	4.45
	SD	0.22	0.91	0.220	19.39	77.8	0.30	0.77	0.31	0.46	0.34	0.637
	n	10	10	10	10	10	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 10

Mean Hematology Values - Termination

Group		ANEU	ALYM	AMONO	AEOS	ABASO	ALUC
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL
1M							
0 ppm	Mean	0.95	2.89	0.10	0.06	0.06	0.04
	SD	0.265	0.561	0.028	0.018	0.020	0.013
	n	8	8	8	8	8	8
2M			**				
500 ppm	Mean	1.03	3.87	0.11	0.05	0.08	0.06
	SD	0.314	0.574	0.029	0.012	0.024	0.029
	n	9	9	9	9	9	9
3M			**				
1500 ppm	Mean	1.01	3.93	0.12	0.06	0.09	0.05
	SD	0.102	0.307	0.027	0.013	0.023	0.015
	n	9	9	9	9	9	9
4M							
5000 ppm	Mean	1.05	3.12	0.11	0.06	0.07	0.05
	SD	0.196	0.503	0.027	0.014	0.026	0.010
	n	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 10

Mean Hematology Values - Termination

Group		HGB	HCT	RBC	RETIC	PLT	MPV	MCV	MCH	MCHC	RDW	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	fL	pg	g/dL	%	x10^3/uL
1F												
0 ppm	Mean	14.8	43.1	8.39	159.9	581	7.1	51.4	17.6	34.2	11.7	4.42
	SD	0.30	0.79	0.112	18.45	118.9	0.35	0.44	0.18	0.40	0.31	0.691
	n	8	8	8	8	8	8	8	8	8	8	8
2F		*										
500 ppm	Mean	15.1	43.8	8.54	171.0	566	7.3	51.3	17.7	34.5	12.0	4.60
	SD	0.40	1.47	0.260	28.71	131.9	0.32	0.62	0.27	0.41	0.37	1.272
	n	8	8	8	8	8	8	8	8	8	8	8
3F		*										
1500 ppm	Mean	15.1	43.8	8.53	170.3	627	7.1	51.4	17.7	34.4	11.9	4.79
	SD	0.20	0.57	0.097	11.36	57.6	0.40	0.39	0.14	0.37	0.24	0.762
	n	8	8	8	8	8	8	8	8	8	8	8
4F		*										
5000 ppm	Mean	15.1	44.0	8.54	156.3	609	7.3	51.6	17.7	34.4	11.7	4.41
	SD	0.33	1.11	0.237	19.60	54.9	0.51	0.49	0.19	0.41	0.19	0.526
	n	10	10	10	10	10	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 10

Mean Hematology Values - Termination

Group		ANEU	ALYM	AMONO	AEOS	ABASO	ALUC
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL
1F							
0 ppm	Mean	0.66	3.52	0.08	0.06	0.06	0.04
	SD	0.150	0.627	0.008	0.011	0.016	0.006
	n	8	8	8	8	8	8
2F							
500 ppm	Mean	0.74	3.63	0.08	0.06	0.07	0.04
	SD	0.313	1.052	0.028	0.016	0.028	0.018
	n	8	8	8	8	8	8
3F							
1500 ppm	Mean	0.81	3.69	0.10	0.06	0.07	0.05
	SD	0.146	0.577	0.031	0.008	0.031	0.019
	n	8	8	8	8	8	8
4F							
5000 ppm	Mean	0.70	3.46	0.09	0.06	0.06	0.04
	SD	0.106	0.422	0.021	0.016	0.022	0.015
	n	10	10	10	10	10	10

	Mean Coagulation Values Preface	Table 11

Abbreviation	Parameter	Reporting Units
PT	Prothrombin Time	seconds
APTT	Activated Partial Thromboplastin Time	seconds

Key to Statistical Symbols:

*Significantly different from control mean; $p \leq 0.05$.
**Significantly different from controlmean; $p \leq 0.01$.
If no asterisks, no statistically significant differences from control mean.

Huntingdon Life Sciences Study No. 04-6154

Table 11

Mean Coagulation Values - Termination

Group		PT	APTT
		Seconds	Seconds
1M			
0 ppm	Mean	16.4	23.1
	SD	0.33	1.12
	n	8	8
2M		**	
500 ppm	Mean	15.7	23.9
	SD	0.58	3.00
	n	9	9
3M		**	
1500 ppm	Mean	15.5	24.9
	SD	0.41	2.39
	n	8	8
4M		**	
5000 ppm	Mean	15.1	25.5
	SD	0.46	2.73
	n	9	9

Huntingdon Life Sciences Study No. 04-6154

Table 11

Mean Coagulation Values - Termination

Group		PT	APTT
		Seconds	Seconds
1F			
0 ppm	Mean	15.7	21.3
	SD	0.50	2.66
	n	7	7
2F			
500 ppm	Mean	15.7	20.0
	SD	0.78	2.86
	n	6	4
3F			
1500 ppm	Mean	15.2	19.4
	SD	0.34	2.50
	n	7	6
4F			
5000 ppm	Mean	15.7	21.4
	SD	0.55	2.29
	n	8	8

	Mean Clinical Chemistry Values Preface	Table 12

Abbreviation	Parameter	Reporting Units
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
ALKP	Alkaline Phosphatase	U/L
LD	Lactate Dehydrogenase	U/L
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
GLU	Fasting Glucose	mg/dL
CK	Creatine Kinase	U/L
CHOL	Cholesterol (Enzymatic)	mg/dL
TRIG	Triglycerides	mg/dL
TP	Total Protein	g/dL
ALB	Albumin	g/dL
Glob	Globulin (calculated)	g/dL
A/G	Albumin/Globulin Ratio (calculated)	
TBILI	Total Bilirubin	mg/dL
DBILI	Direct Bilirubin	mg/dL
IBILI	Indirect Bilirubin	mg/dL
Na^+	Sodium	mEq/L
K^+	Potassium	mEq/L
Cl^-	Chloride	mEq/L
Ca^{++}	Calcium	mg/dL
PHOS	Inorganic Phosphorus	mg/dL
GGT	Gamma-Glutamyl Transferase	U/L

Key to Statistical Symbols:

*Significantly different from control mean; $p \leq 0.05$.
**Significantly different from control mean; $p \leq 0.01$.
If no asterisks, no statistically significant differences from control mean.

Huntingdon Life Sciences Study No. 04-6154

Table 12

Mean Clinical Chemistry Values - Termination

Group		AST	ALT	ALKP	LD	BUN	CREAT	GLU	CK	CHOL	TRIG	TP
		U/L	U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	U/L	mg/dL	mg/dL	g/dL
1M												
0 ppm	Mean	80	62	163	311	16	0.3	205	498	59	120	6.1
	SD	17.3	10.0	14.4	211.2	1.6	0.06	22.8	853.8	2.9	27.6	0.16
	n	9	9	9	9	9	9	9	9	9	9	9
2M		*	*	**								
500 ppm	Mean	68	52	139	219	15	0.3	191	188	58	137	6.2
	SD	12.4	10.8	18.4	197.8	1.9	0.07	16.1	128.0	4.9	47.9	0.18
	n	10	10	10	10	10	10	10	10	10	10	10
3M		*	*	**				*				
1500 ppm	Mean	67	56	148	163	15	0.2	185	152	56	137	6.2
	SD	8.4	6.5	9.6	145.3	1.2	0.05	15.5	92.4	3.7	25.9	0.11
	n	10	10	10	10	10	10	10	10	10	10	10
4M		**	*	**				**				
5000 ppm	Mean	62	52	128	214	15	0.3	181	184	55	100	6.2
	SD	4.2	4.3	14.0	105.6	1.3	0.05	13.8	70.8	4.2	24.8	0.12
	n	10	10	10	10	10	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 12

Mean Clinical Chemistry Values - Termination

Group		ALB	Glob	A/G	TBILI	DBILI	IBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1M												
0 ppm	Mean	3.7	2.5	1.5	0.09	0.01	0.08	142	4.7	99	10.6	7.6
	SD	0.12	0.10	0.09	0.043	0.007	0.037	1.3	0.54	1.5	0.69	0.73
	n	9	9	9	9	9	9	9	9	9	9	9
2M												*
500 ppm	Mean	3.6	2.5	1.4	0.10	0.00	0.10	142	4.9	99	10.4	8.2
	SD	0.16	0.15	0.13	0.037	0.005	0.036	1.2	0.75	0.8	1.04	0.64
	n	10	10	10	10	10	10	10	10	10	10	10
3M												**
1500 ppm	Mean	3.7	2.5	1.5	0.09	0.01	0.09	142	4.8	100	10.5	8.6
	SD	0.07	0.11	0.10	0.036	0.008	0.035	0.7	0.50	1.1	0.67	0.29
	n	10	10	10	10	10	10	10	10	10	10	10
4M												**
5000 ppm	Mean	3.8	2.5	1.6	0.10	0.01	0.09	142	4.9	99	10.7	8.5
	SD	0.05	0.11	0.07	0.048	0.007	0.045	1.3	0.46	1.1	0.56	0.51
	n	10	10	10	10	10	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 12

Mean Clinical Chemistry Values - Termination

Group		AST	ALT	ALKP	LD	BUN	CREAT	GLU	CK	CHOL	TRIG	TP
		U/L	U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	U/L	mg/dL	mg/dL	g/dL
1F												
0 ppm	Mean	93	74	156	224	15	0.3	172	186	74	43	5.8
	SD	16.6	17.8	20.2	107.6	1.4	0.04	15.2	56.8	6.4	8.5	0.19
	n	9	9	9	9	9	9	9	9	9	9	9
2F		*	**			**	*					
500 ppm	Mean	78	52	140	213	13	0.2	176	191	73	40	5.7
	SD	8.4	4.7	24.0	111.6	1.7	0.04	21.7	70.0	7.6	9.8	0.13
	n	9	9	9	9	9	9	9	9	9	9	9
3F		*	**			**	**					
1500 ppm	Mean	83	55	144	286	13	0.2	170	410	72	37	5.7
	SD	14.7	7.9	18.4	153.1	1.1	0.05	23.1	601.9	5.7	5.9	0.16
	n	10	10	10	10	10	10	10	10	10	10	10
4F		**	**			**	**			**		
5000 ppm	Mean	76	53	145	299	13	0.2	156	240	58	38	5.7
	SD	8.7	5.1	11.5	195.9	1.2	0.04	16.9	128.8	5.7	6.6	0.18
	n	10	10	10	10	10	10	10	10	10	10	10

Huntingdon Life Sciences Study No. 04-6154

Table 12

Mean Clinical Chemistry Values - Termination

Group		ALB	Glob	A/G	TBILI	DBILI	IBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1F												
0 ppm	Mean	3.5	2.3	1.6	0.09	0.00	0.09	142	4.9	102	10.0	7.4
	SD	0.11	0.11	0.07	0.033	0.005	0.036	1.3	0.79	1.3	0.98	0.60
	n	9	9	9	9	9	9	9	9	9	9	9
2F												
500 ppm	Mean	3.5	2.2	1.6	0.09	0.01	0.08	141	4.8	101	10.3	7.9
	SD	0.09	0.07	0.05	0.039	0.007	0.037	0.6	0.50	1.3	0.69	0.54
	n	9	9	9	9	9	9	9	9	9	9	9
3F												**
1500 ppm	Mean	3.5	2.2	1.6	0.11	0.01	0.11	142	4.7	102	10.4	8.1
	SD	0.08	0.11	0.08	0.041	0.010	0.039	0.8	0.32	0.9	0.36	0.33
	n	10	10	10	10	10	10	10	10	10	10	10
4F												**
5000 ppm	Mean	3.5	2.2	1.6	0.09	0.01	0.08	142	4.6	102	10.3	8.2
	SD	0.08	0.11	0.06	0.036	0.014	0.035	1.0	0.40	1.3	0.62	0.39
	n	10	10	10	10	10	10	10	10	10	10	10

	Mean Organ Weights Preface	Table 13

Terminal Sacrifice

Recovery Sacrifice

Key to Abbreviations:

g	=	Grams
wt.	=	Weight
observ.	=	Observed
Thyroid/Para	=	Thyroid/Parathyroid Gland
w/	=	with

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	500 ppm
Group 3	-	1500 ppm
Group 4	-	5000 ppm

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	299.08	0.04788	1.95824	0.97614	0.88044	2.02800	9.38629	1.10008
Standard deviation:	17.07	0.00553	0.04073	0.06519	0.07568	0.07251	0.56650	0.08240
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	0.05368	1.95880	0.97069	0.89982	2.02457	9.17408	1.10134
Standard deviation:	14.80	0.00644	0.10126	0.06698	0.08892	0.11953	0.72974	0.09089
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	0.05876+	1.96162	0.91982	0.90246	2.01133	9.64866	1.11890
Standard deviation:	11.04	0.00437	0.06031	0.06214	0.05500	0.16565	0.65196	0.08854
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	0.05958+	1.90650%	0.89203*	0.85507	1.97877	9.32205	1.01307
Standard deviation:	16.24	0.00552	0.04594	0.06478	0.09672	0.12583	0.64328	0.09362
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate Seminal Vesicles		Spleen	Testes	Thymus	Thyroid/Para
			Male Animals					
1								
Mean:	299.08	0.00794	0.53397	1.23456	0.58592	2.93170	0.22056	0.02724
Standard deviation:	17.07	0.00128	0.09903	0.19957	0.03064	0.13112	0.03901	0.00632
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	0.00795	0.51308	1.22101	0.60124	2.92920	0.20778	0.02964
Standard deviation:	14.80	0.00120	0.09846	0.24000	0.05829	0.15597	0.06242	0.00676
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	0.00796	0.50425	1.21417	0.57971	2.91070	0.21313	0.02761
Standard deviation:	11.04	0.00124	0.13383	0.30461	0.02212	0.15907	0.03340	0.00676
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	0.00796	0.40812*	0.96976*	0.54875%	2.87358	0.17917%	0.02868
Standard deviation:	16.24	0.00183	0.10542	0.11986	0.03763	0.14135	0.01756	0.00730
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
				Female Animals				
1								
Mean:	166.72	0.04755	1.75106	0.56755	1.17155	4.75103	0.79528	0.05702
Standard deviation:	6.35	0.00838	0.05311	0.04367	0.06120	0.27811	0.10630	0.00758
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	166.57	0.05267	1.75454	0.59284	1.22454	4.58930	0.78574	0.06083
Standard deviation:	8.55	0.00567	0.05612	0.05147	0.07346	0.35047	0.02351	0.01001
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	167.31	0.05866+	1.78372	0.59733	1.26315*	4.71926	0.80428	0.06477%
Standard deviation:	10.44	0.00694	0.06059	0.05331	0.09399	0.41241	0.06596	0.00357
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	163.45	0.05872+	1.72553	0.57077	1.26840*	4.94262	0.78381	0.05466
Standard deviation:	10.82	0.00744	0.07751	0.03860	0.08950	0.58573	0.07640	0.00860
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Spleen	Thymus	Thyroid/Para Uterus w/ Cervix	
			F e m a l e A n i m a l s			
1						
M e a n:	166.72	0.00851	0.41279	0.17571	0.01878	0.41304
Standard deviation:	6.35	0.00196	0.02202	0.01757	0.00483	0.07187
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
M e a n:	166.57	0.00823	0.40446	0.17423	0.02042	0.48154
Standard deviation:	8.55	0.00110	0.03068	0.01991	0.00481	0.12377
Number of observ. :	(10)	(10)	(10)	(10)	(9)	(10)
3						
M e a n:	167.31	0.00943	0.42692	0.17811	0.02161	0.54812
Standard deviation:	10.44	0.00085	0.02289	0.02223	0.00225	0.20362
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
M e a n:	163.45	0.00837	0.39804	0.16170	0.02004	0.41566
Standard deviation:	10.82	0.00207	0.03463	0.01574	0.00456	0.13237
Number of observ. :	(10)	(9)	(10)	(10)	(10)	(10)

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%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	299.08	0.01612	0.65656	0.32771	0.29531	0.67899	3.13924	0.36840
Standard deviation:	17.07	0.00258	0.03812	0.03309	0.03165	0.02166	0.10374	0.02860
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	0.01838	0.67142	0.33182	0.30732	0.69124	3.12863	0.37625
Standard deviation:	14.80	0.00256	0.06939	0.02628	0.02855	0.03343	0.15327	0.03133
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	0.01989$	0.66557	0.31194	0.30625	0.68095	3.27106	0.37948
Standard deviation:	11.04	0.00097	0.03619	0.02295	0.02373	0.04468	0.22504	0.03267
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	0.02198$	0.70323	0.32872	0.31401	0.72822+	3.43000+	0.37228
Standard deviation:	16.24	0.00242	0.04039	0.02527	0.02397	0.02833	0.14974	0.02057
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate	Seminal Vesicles	Spleen	Testes	Thymus	Thyroid/Para
				Male Animals				
1								
Mean:	299.08	0.00265	0.17856	0.41161	0.19628	0.98422	0.07405	0.00911
Standard deviation:	17.07	0.00035	0.03161	0.05091	0.01211	0.08639	0.01435	0.00197
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	0.00272	0.17606	0.41844	0.20535	1.00145	0.07056	0.01010
Standard deviation:	14.80	0.00047	0.03900	0.08726	0.01925	0.06949	0.01918	0.00210
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	0.00270	0.17148	0.41258	0.19653	0.98654	0.07220	0.00937
Standard deviation:	11.04	0.00043	0.04760	0.11024	0.00774	0.05060	0.01103	0.00233
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	0.00292	0.15016	0.35764%	0.20202	1.05785%	0.06601	0.01049
Standard deviation:	16.24	0.00064	0.03752	0.04702	0.01122	0.02825	0.00652	0.00244
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
			Female Animals					
1								
Mean:	166.72	0.02847	1.05131	0.34032	0.70264	2.84886	0.47587	0.03420
Standard deviation:	6.35	0.00457	0.04232	0.02108	0.02286	0.10529	0.05117	0.00427
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	166.57	0.03160	1.05557	0.35608	0.73559*	2.75446	0.47239	0.03656
Standard deviation:	8.55	0.00269	0.05896	0.02724	0.03555	0.14605	0.01770	0.00627
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	167.31	0.03507+	1.07041	0.35677	0.75483+	2.82103	0.48172	0.03878%
Standard deviation:	10.44	0.00358	0.08652	0.01795	0.02580	0.18665	0.04118	0.00214
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	163.45	0.03592+	1.05818	0.34938	0.77597+	3.01496	0.47948	0.03340
Standard deviation:	10.82	0.00367	0.05667	0.01245	0.01840	0.18336	0.03235	0.00454
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
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Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Spleen	Thymus	Thyroid/Para Uterus w/ Cervix	
			Female Animals			
1						
Mean:	166.72	0.00511	0.24773	0.10539	0.01131	0.24750
Standard deviation:	6.35	0.00118	0.01256	0.00967	0.00313	0.03957
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	166.57	0.00494	0.24279	0.10444	0.01231	0.28751
Standard deviation:	8.55	0.00060	0.01295	0.00893	0.00296	0.06557
Number of observ. :	(10)	(10)	(10)	(10)	(9)	(10)
3						
Mean:	167.31	0.00564	0.25555	0.10626	0.01300	0.32616
Standard deviation:	10.44	0.00045	0.01202	0.00988	0.00191	0.11779
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
Mean:	163.45	0.00507	0.24345	0.09936	0.01228	0.25647
Standard deviation:	10.82	0.00110	0.01223	0.01217	0.00270	0.09115
Number of observ. :	(10)	(9)	(10)	(10)	(10)	(10)

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%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
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Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	299.08	2.44843	100.0000	49.87150	44.92209	103.5687	479.3420	56.20787
Standard deviation:	17.07	0.30820	0.00000	3.59082	3.15402	3.25829	27.63694	4.51668
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	2.75023	100.0000	49.67707	46.13542	103.7794	470.7367	56.39312
Standard deviation:	14.80	0.38951	0.00000	4.38804	6.25761	9.94493	57.69601	5.71934
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	2.99794+	100.0000	46.90886	46.00050	102.6872	492.4114	57.15741
Standard deviation:	11.04	0.23794	0.00000	3.11759	2.29901	9.47706	38.30017	5.79919
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	3.12732+	100.0000	46.81292	44.84875	103.7686	488.8643	53.14740
Standard deviation:	16.24	0.30892	0.00000	3.57688	4.91242	5.61440	29.81966	4.88976
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
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Huntingdon Life Sciences
Mettlers Road
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Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate Seminal Vesicles		Spleen	Testes	Thymus	Thyroid/Para
				Male Animals				
1								
Mean:	299.08	0.40568	27.22719	63.01220	29.92546	149.7645	11.24439	1.39070
Standard deviation:	17.07	0.06516	4.79900	9.80996	1.52709	7.24430	1.82750	0.31637
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
2								
Mean:	293.06	0.40672	26.12498	62.53035	30.77914	149.9309	10.71987	1.52027
Standard deviation:	14.80	0.06479	4.36637	13.07750	3.48750	11.98826	3.68294	0.36710
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	295.17	0.40638	25.74575	61.75485	29.59873	148.5537	10.87066	1.41310
Standard deviation:	11.04	0.06538	7.04452	14.48718	1.84332	9.96101	1.71215	0.37622
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	271.87+	0.41871	21.41155	50.91581	28.77023	150.7663	9.40095%	1.50173
Standard deviation:	16.24	0.09910	5.56678	6.61963	1.61826	7.39941	0.92918	0.37024
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Huntingdon Life Sciences
Mettlers Road
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Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
			Female Animals					
1								
Mean:	166.72	2.71120	100.0000	32.43054	66.93250	271.5780	45.40373	3.25632
Standard deviation:	6.35	0.44068	0.00000	2.53813	3.47549	18.52115	5.70264	0.42029
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	166.57	3.00070	100.0000	33.84769	69.79238	261.7217	44.82560	3.47265
Standard deviation:	8.55	0.29950	0.00000	3.47930	3.49169	20.24816	1.99424	0.60121
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	167.31	3.29319+	100.0000	33.51747	70.90261	264.7604	45.12715	3.63431%
Standard deviation:	10.44	0.40627	0.00000	3.10221	5.87507	23.94305	3.85507	0.21958
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	163.45	3.40499+	100.0000	33.08973	73.51277+	286.2451	45.40267	3.17100
Standard deviation:	10.82	0.41499	0.00000	1.89905	4.12125	29.56066	3.59348	0.50188
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Spleen	Thymus	Thyroid/Para Uterus w/ Cervix	
			Female Animals			
1						
Mean:	166.72	0.48467	23.60385	10.05150	1.07162	23.63572
Standard deviation:	6.35	0.10384	1.61768	1.13856	0.27526	4.33913
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	166.57	0.46880	23.06214	9.92300	1.16421	27.47844
Standard deviation:	8.55	0.05984	1.73886	1.00522	0.29186	7.14592
Number of observ. :	(10)	(10)	(10)	(10)	(9)	(10)
3						
Mean:	167.31	0.52898	23.97000	10.01497	1.21240	30.91815
Standard deviation:	10.44	0.04758	1.69366	1.42548	0.12838	12.26834
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
Mean:	163.45	0.48370	23.06546	9.37410	1.16359	24.11009
Standard deviation:	10.82	0.11287	1.67170	0.84148	0.26543	7.74873
Number of observ. :	(10)	(9)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	328.76	0.04370	1.98562	1.06848	0.92314	2.14766	10.43288	1.27052
Standard deviation:	15.64	0.00930	0.06305	0.04218	0.09963	0.13269	0.91128	0.11766
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2								
Mean:	340.98	0.04384	1.95984	1.04270	0.93138	2.16160	11.05290	1.34562
Standard deviation:	22.66	0.00534	0.05944	0.16392	0.02670	0.16485	0.97832	0.31415
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3								
Mean:	327.98	0.05136	2.00632	1.02908	0.98786	2.18818	10.48676	1.22604
Standard deviation:	17.77	0.00212	0.07688	0.11057	0.06768	0.13648	0.56885	0.10259
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4								
Mean:	323.98	0.05096	1.95484	1.04162	0.95546	2.15438	10.75250	1.17454
Standard deviation:	15.54	0.00223	0.05732	0.06532	0.04420	0.08297	0.42588	0.05059
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
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Rat/Fischer

Summary statistics for absolute organ weights (g)
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate Seminal Vesicles		Spleen	Testes	Thymus	Thyroid/Para
				Male Animals				
1								
Mean:	328.76	0.00960	0.41716	1.20676	0.58824	3.09136	0.16898	0.02708
Standard deviation:	15.64	0.00144	0.17260	0.41315	0.07207	0.06911	0.01643	0.00096
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2								
Mean:	340.98	0.00788	0.55742	1.46656	0.64466	2.89256	0.20848%	0.03124$
Standard deviation:	22.66	0.00099	0.12238	0.16999	0.04912	0.43152	0.01634	0.00168
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3								
Mean:	327.98	0.00934	0.70098*	1.68142	0.64572	3.01130	0.21668	0.03006
Standard deviation:	17.77	0.00214	0.23455	0.36294	0.07205	0.29951	0.05715	0.00557
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4								
Mean:	323.98	0.00928	0.48816	1.55680	0.65586	3.10906	0.20792	0.03002%
Standard deviation:	15.54	0.00141	0.11165	0.25401	0.02705	0.03845	0.03425	0.00210
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
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Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	328.76	0.01331	0.60499	0.32571	0.28057	0.65326	3.16875	0.38749
Standard deviation:	15.64	0.00287	0.03262	0.02189	0.02502	0.02578	0.13595	0.04451
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2								
Mean:	340.98	0.01285	0.57591	0.30492	0.27397	0.63402	3.23833	0.39260
Standard deviation:	22.66	0.00136	0.02218	0.03778	0.01710	0.02481	0.09133	0.07294
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3								
Mean:	327.98	0.01568	0.61265	0.31322	0.30126	0.66716	3.19746	0.37393
Standard deviation:	17.77	0.00065	0.02904	0.01978	0.01422	0.02017	0.03063	0.02626
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4								
Mean:	323.98	0.01577	0.60493	0.32237	0.29568	0.66627	3.32044*	0.36344
Standard deviation:	15.54	0.00123	0.04342	0.03044	0.02367	0.04242	0.07219	0.02804
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Body Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate Seminal Vesicles	Spleen	Testes	Thymus	Thyroid/Para
			Male Animals				
1							
Mean:	328.76	0.00293	0.12713	0.36589	0.17849	0.94177	0.05151	0.00825
Standard deviation:	15.64	0.00049	0.05358	0.12325	0.01591	0.04256	0.00570	0.00042
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2							
Mean:	340.98	0.00231	0.16335	0.43019	0.18915	0.84624	0.06111%	0.00917%
Standard deviation:	22.66	0.00025	0.03417	0.04472	0.00926	0.09981	0.00127	0.00039
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3							
Mean:	327.98	0.00284	0.21157*	0.50912	0.19664	0.91738	0.06607	0.00916
Standard deviation:	17.77	0.00057	0.06460	0.08247	0.01605	0.06427	0.01689	0.00168
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4							
Mean:	323.98	0.00287	0.15043	0.48375	0.20267*	0.96134	0.06449	0.00929
Standard deviation:	15.54	0.00048	0.03188	0.09871	0.00978	0.04613	0.01288	0.00087
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	328.76	2.19265	100.0000	53.86806	46.56651	108.1361	525.4652	63.90799
Standard deviation:	15.64	0.42342	0.00000	3.10924	5.74359	5.16332	43.82209	4.40882
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2								
Mean:	340.98	2.23594	100.0000	53.12375	47.54019	110.1824	563.1910	68.38714
Standard deviation:	22.66	0.25937	0.00000	7.69538	1.33115	5.13500	32.40360	13.98988
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3								
Mean:	327.98	2.56209	100.0000	51.25554	49.20844	109.0251	522.8256	61.04210
Standard deviation:	17.77	0.12406	0.00000	4.72366	2.05498	4.32448	24.65673	3.23015
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4								
Mean:	323.98	2.60893	100.0000	53.25058	48.87238	110.2359	550.8254	60.07536
Standard deviation:	15.54	0.14446	0.00000	2.02672	1.62945	3.99048	35.13577	1.56861
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Summary Statistics for % Organ to Brain Weight
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

Group	Final Body wt. (g)	Pituitary Gland	Prostate Seminal Vesicles		Spleen	Testes	Thymus	Thyroid/Para
			M a l e	A n i m a l s				
1								
M e a n:	328.76	0.48497	20.94092	60.56212	29.63777	155.7534	8.50636	1.36470
Standard deviation:	15.64	0.08439	8.71529	19.73854	3.67673	3.70432	0.70754	0.05937
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
2								
M e a n:	340.98	0.40161	28.39994	74.78847	32.86667	147.3772	10.62576$	1.59362$
Standard deviation:	22.66	0.04393	5.98013	8.07859	1.71527	20.09700	0.51385	0.06060
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
3								
M e a n:	327.98	0.46302	34.72562*	83.63820	32.12788	150.0009	10.73710	1.49712
Standard deviation:	17.77	0.08808	11.00524	17.00308	2.59180	12.59273	2.40220	0.27049
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
4								
M e a n:	323.98	0.47508	24.97178	79.47727	33.55893	159.1257	10.60419%	1.53585%
Standard deviation:	15.54	0.07476	5.69360	11.28201	1.30330	3.83056	1.42987	0.10146
Number of observ. :	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

	Incidence Summary Report for Gross Necropsy Observations Preface	Table 14

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Key to Abbreviations

w/ = with

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 500 ppm
Group 3 - 1500 ppm
Group 4 - 5000 ppm

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Incidence Summary Report for Gross Necropsy Observations by Animal
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	9	10	10	10	10	10	10	10
Within Normal Limits	6	7	9	10	8	8	7	8
Eyes								
Exophthalmia	0	0	0	0	0	0	1	0
Kidneys								
Cyst	1	0	0	0	0	0	0	0
Liver								
Mass	0	0	0	0	0	0	0	1
Ovaries								
Cyst	0	0	0	0	0	1	0	0
Prostate								
Discolored	0	1	0	0	0	0	0	0
Spleen								
Nodule	0	0	0	0	1	0	0	0
Testes								
Discolored	0	1	0	0	0	0	0	0
Uterus w/ Cervix								
Distended	0	0	0	0	0	2	3	1
Thymus								
Discolored	2	1	1	0	0	0	0	0
Lymph Node other								
Discolored	0	0	0	0	1	1	0	0
Skin (other)								
Hair Thin/Absent	0	0	0	0	0	0	0	1

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Incidence Summary Report for Gross Necropsy Observations by Animal
Study number: 04-6154
Scheduled Sacrifices FS
Study start date: 08-Dec-05

Subchronic/Inhalation

	-- Males --			
Group:	1	2	3	4
Number in group:	5	5	5	5
Within Normal Limits	2	3	5	5
Epididymides				
Small	0	1	0	0
Testes				
Small	0	1	0	0
Soft	0	1	0	0
Discolored	0	1	0	0
Thymus				
Discolored	3	1	0	0
Tail				
Gloved	1	0	0	0

Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
Rat/Fischer

Incidence Summary Report for Gross Necropsy Observations by Animal
Study number: 04-6154
All Unscheduled Sacrifices
Study start date: 08-Dec-05

Subchronic/Inhalation

	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	1	0	0	0	0	0	0	0
Within Normal Limits	1	0	0	0	0	0	0	0

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Key to Abbreviations

Ctls	=	Controls (Group 1)
LN	=	Lymph Node
Nose/Turb Sec 1	=	Nose/Turbinates Section 1
Nose/Turb Sec 2	=	Nose/Turbinates Section 2
Nose/Turb Sec 3	=	Nose/Turbinates Section 3
Nose/Turb Sec 4	=	Nose/Turbinates Section 4
SC	=	Spinal Cord
Submandib/Max	=	Submandibular/Submaxillary
V-DVTC	=	Ventral Diverticulum
V-SM-G	=	Ventral Seromucous Glands
w/	=	with
-	=	Finding not present or observed

Histopathology grading:

Grade 1: MINIMAL = the change is barely discernible and/or very few/very small foci or areas are affected

Grade 2: SLIGHT = the change is more noticeable but only evident as few/small foci or areas affected

Grade 3: MODERATE = the change is obviously present, and of appreciable size and/or number

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	500 ppm
Group 3	-	1500 ppm
Group 4	-	5000 ppm

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1

Tissues With Diagnoses	Animal sex:	-- Animals Affected -- Males -- Ctls	2	3	4	-- Females -- Ctls	2	3	4
	Dosage group:								
	No. in group:	9	10	10	10	10	10	10	10
Adrenal Glands	Number examined:	9	0	0	10	10	0	0	10
Aorta	Number examined:	9	0	0	10	10	1	0	10
Brain	Number examined:	9	0	0	10	10	0	0	10
Cecum	Number examined:	9	0	0	10	10	0	0	10
Cervical SC	Number examined:	9	0	0	10	10	0	0	10
Colon	Number examined:	9	0	0	10	10	0	0	10
Duodenum	Number examined:	9	0	0	10	10	0	0	10
Epididymides	Number examined:	9	0	0	10				
Esophagus	Number examined:	9	0	0	10	10	0	0	10
Femoral Marrow	Number examined:	9	0	0	10	10	0	0	10
Femur w/ Joint	Number examined:	9	0	0	10	10	0	0	7
Heart	Number examined:	9	0	0	10	10	0	0	10
INFLAMMATORY FOCI WITH OR WITHOUT MYOCARDIAL DEGENERATION	->	2	0	0	4	4	0	0	5
	1>	2	0	0	6	6	0	0	5
	2>	5	0	0	0	0	0	0	0
	Total Incidence of Finding Observed:	7	0	0	6	6	0	0	5
Ileum	Number examined:	9	0	0	10	10	0	0	10

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Ileum ..... Number examined:		9	0	0	10	10	0	0	10
MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	->	8	0	0	10	10	0	0	10
	2>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
Jejunum ..... Number examined:		9	0	0	10	10	0	0	10
Kidneys ..... Number examined:		9	0	0	10	10	0	0	10
CORTICO-MEDULLARY JUNCTION: MINERAL DEPOSIT(S)									
	->	9	0	0	9	0	0	0	0
	1>	0	0	0	1	10	0	0	10
..... Total Incidence of Finding Observed:		0	0	0	1	10	0	0	10
BASOPHILIC TUBULES									
	->	7	0	0	6	10	0	0	9
	1>	2	0	0	4	0	0	0	1
..... Total Incidence of Finding Observed:		2	0	0	4	0	0	0	1
INTERSTITIAL SUBACUTE/CHRONIC INFLAMMATORY FOCI									
	->	7	0	0	9	8	0	0	10
	1>	2	0	0	1	2	0	0	0
..... Total Incidence of Finding Observed:		2	0	0	1	2	0	0	0
DILATED TUBULES									
	->	8	0	0	9	9	0	0	10
	1>	0	0	0	1	1	0	0	0
	3>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		1	0	0	1	1	0	0	0

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Kidneys .....Number examined:		9	0	0	10	10	0	0	10
MEDULLA: MINERAL DEPOSIT(S)									
	->	2	0	0	1	1	0	0	1
	1>	7	0	0	9	9	0	0	9
.....Total Incidence of Finding Observed:		7	0	0	9	9	0	0	9
Larynx: V-DVTC .....Number examined:		9	0	0	10	7	0	0	9
MUCOSA: SERO-MUCOUS GLANDS DILATED									
	->	4	0	0	5	5	0	0	7
	1>	4	0	0	1	2	0	0	2
	2>	1	0	0	4	0	0	0	0
.....Total Incidence of Finding Observed:		5	0	0	5	2	0	0	2
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)									
	->	7	0	0	7	4	0	0	8
	1>	1	0	0	2	3	0	0	1
	2>	1	0	0	1	0	0	0	0
.....Total Incidence of Finding Observed:		2	0	0	3	3	0	0	1
MUCOSA: LYMPHOID CELL AGGREGATE(S)									
	->	8	0	0	6	7	0	0	9
	1>	1	0	0	4	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	4	0	0	0	0
Larynx: V-SM-G .....Number examined:		4	0	0	9	3	0	0	2
MUCOSA: SERO-MUCOUS GLANDS DILATED									
	->	4	0	0	9	3	0	0	2
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Larynx: V-SM-G .....Number examined:		4	0	0	9	3	0	0	2
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)									
	->	0	0	0	3	0	0	0	0
	1>	3	0	0	4	1	0	0	2
	2>	1	0	0	2	2	0	0	0
.....Total Incidence of Finding Observed:		4	0	0	6	3	0	0	2
MUCOSA: LYMPHOID CELL AGGREGATE(S)									
	->	3	0	0	4	1	0	0	2
	1>	1	0	0	4	2	0	0	0
	2>	0	0	0	1	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	5	2	0	0	0
MUCOSA: EPITHELIUM-SQUAMOUS/SQUAMOID METAPLASIA									
	->	4	0	0	8	3	0	0	2
	1>	0	0	0	1	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	1	0	0	0	0
MUCOSA: STRATIFIED SQUAMOUS EPITHELIUM (NORMAL)-HYPERPLASIA									
	->	4	0	0	8	3	0	0	2
	1>	0	0	0	1	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	1	0	0	0	0
Liver .....Number examined:		9	0	0	10	10	0	0	10
INFLAMMATORY FOCI									
	->	6	0	0	7	3	0	0	5
	1>	3	0	0	3	7	0	0	5
.....Total Incidence of Finding Observed:		3	0	0	3	7	0	0	5

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Liver	Number examined:	9	0	0	10	10	0	0	10
MEDIAL LOBE ANOMALY									
	->	9	0	0	10	10	0	0	9
	2>	0	0	0	0	0	0	0	1
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	1
Lumbar SC	Number examined:	9	0	0	10	10	0	0	10
Lungs	Number examined:	9	10	10	10	10	10	10	10
ALVEOLAR/INTRAALVEOLAR MACROPHAGES									
	->	0	0	1	0	1	0	0	0
	1>	9	10	9	10	8	10	10	10
	2>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	9	10	9	10	9	10	10	10
SUBPLEURAL/PERIVASCULAR LYMPHOID AGGREGATES WITH OR WITHOUT -VARIABLE NUMBERS OF NEUTROPHILS									
	->	4	6	5	7	5	4	8	4
	1>	5	4	5	3	5	6	2	6
.....	Total Incidence of Finding Observed:	5	4	5	3	5	6	2	6
AGONAL HEMORRHAGE(S)									
	->	7	8	9	8	9	10	10	10
	1>	2	2	1	2	1	0	0	0
.....	Total Incidence of Finding Observed:	2	2	1	2	1	0	0	0
VESSEL(S): MINERAL DEPOSIT(S)									
	->	3	6	8	8	6	5	6	6
	1>	6	4	2	2	4	5	4	4
.....	Total Incidence of Finding Observed:	6	4	2	2	4	5	4	4

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Lungs	Number examined:	9	10	10	10	10	10	10	10
SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	->	9	9	10	10	10	10	10	10
	1>	0	1	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	1	0	0	0	0	0	0
Lymph Node other	Number examined:	0	0	0	0	0	0	0	0
Mediastinal LN	Number examined:	8	0	0	10	10	0	0	9
PARACORTICAL HYPERPLASIA									
	1>	1	0	0	0	3	0	0	0
	2>	2	0	0	6	2	0	0	4
	3>	5	0	0	4	5	0	0	5
.....	Total Incidence of Finding Observed:	8	0	0	10	10	0	0	9
SINUSES: FREE ERYTHROCYTES									
	->	4	0	0	4	9	0	0	7
	1>	3	0	0	3	1	0	0	1
	2>	1	0	0	1	0	0	0	1
	3>	0	0	0	2	0	0	0	0
.....	Total Incidence of Finding Observed:	4	0	0	6	1	0	0	2
SINUSOIDAL HISTIOCYTES									
	->	6	0	0	8	9	0	0	8
	1>	1	0	0	1	1	0	0	1
	2>	1	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	2	0	0	2	1	0	0	1
Mesenteric LN	Number examined:	9	0	0	10	10	0	0	10
SINUSOIDAL HISTIOCYTES									
	->	1	0	0	1	0	0	0	1
	1>	4	0	0	3	2	0	0	4
	2>	4	0	0	6	8	0	0	5
.....	Total Incidence of Finding Observed:	8	0	0	9	10	0	0	9

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Mesenteric LN ..... Number examined:		9	0	0	10	10	0	0	10
PARACORTICAL HYPERPLASIA									
	->	0	0	0	0	1	0	0	0
	2>	8	0	0	9	8	0	0	10
	3>	1	0	0	1	1	0	0	0
..... Total Incidence of Finding Observed:		9	0	0	10	9	0	0	10
SINUSES: FREE ERYTHROCYTES									
	->	7	0	0	8	7	0	0	9
	1>	1	0	0	2	2	0	0	1
	2>	1	0	0	0	1	0	0	0
..... Total Incidence of Finding Observed:		2	0	0	2	3	0	0	1
HISTIOCYTIC AGGREGATES									
	->	7	0	0	7	3	0	0	7
	1>	1	0	0	3	5	0	0	2
	2>	0	0	0	0	2	0	0	1
	3>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		2	0	0	3	7	0	0	3
Nerve Sciatic ..... Number examined:		9	0	0	10	10	0	0	10
Nose/Turb Sec 1 ..... Number examined:		9	0	0	10	10	0	0	10
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA									
	->	3	0	0	8	3	0	0	8
	1>	1	0	0	1	3	0	0	1
	2>	5	0	0	1	4	0	0	1
..... Total Incidence of Finding Observed:		6	0	0	2	7	0	0	2

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Nose/Turb Sec 1 .....Number examined:		9	0	0	10	10	0	0	10
NASAL MUCOSA (RESPIRATORY): BASOPHILIC MATERIAL									
	->	9	0	0	1	9	0	0	10
	1>	0	0	0	9	1	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	9	1	0	0	0
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	->	9	0	0	9	9	0	0	10
	1>	0	0	0	1	1	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	1	1	0	0	0
NASAL MUCOSA (RESPIRATORY): GLANDS DILATED									
	->	9	0	0	10	10	0	0	6
	1>	0	0	0	0	0	0	0	3
	2>	0	0	0	0	0	0	0	1
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	4
Nose/Turb Sec 2 .....Number examined:		9	0	0	10	10	0	0	10
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA									
	->	3	0	0	8	5	0	0	6
	1>	5	0	0	2	5	0	0	4
	2>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		6	0	0	2	5	0	0	4
NASAL MUCOSA (RESPIRATORY/OLFACTORY): BASOPHILIC MATERIAL									
	->	6	0	0	7	7	0	0	10
	1>	3	0	0	3	3	0	0	0
.....Total Incidence of Finding Observed:		3	0	0	3	3	0	0	0

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Nose/Turb Sec 2 .....Number examined:		9	0	0	10	10	0	0	10
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	->	5	0	0	6	9	0	0	7
	1>	4	0	0	4	1	0	0	3
.....Total Incidence of Finding Observed:		4	0	0	4	1	0	0	3
NASAL MUCOSA (RESPIRATORY): GLANDS DILATED									
	->	8	0	0	9	9	0	0	10
	1>	0	0	0	1	1	0	0	0
	2>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	1	1	0	0	0
NASAL MUCOSA (RESPIRATORY): SUBACUTE (CHRONIC ACTIVE)/ -CHRONIC INFLAMMATION									
	->	9	0	0	10	10	0	0	9
	2>	0	0	0	0	0	0	0	1
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	1
Nose/Turb Sec 3 .....Number examined:		9	0	0	10	10	0	0	10
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA									
	->	9	0	0	10	10	0	0	9
	2>	0	0	0	0	0	0	0	1
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	1
NASAL MUCOSA (OLFACTORY/RESPIRATORY): BASOPHILIC MATERIAL									
	->	1	0	0	0	3	0	0	2
	1>	7	0	0	8	7	0	0	8
	2>	1	0	0	2	0	0	0	0
.....Total Incidence of Finding Observed:		8	0	0	10	7	0	0	8

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Nose/Turb Sec 3 .....Number examined:		9	0	0	10	10	0	0	10
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	->	0	0	0	0	0	0	0	1
	1>	8	0	0	9	10	0	0	8
	2>	1	0	0	1	0	0	0	1
.....Total Incidence of Finding Observed:		9	0	0	10	10	0	0	9
NASAL MUCOSA (OLFACTORY): GLANDS DILATED									
	->	8	0	0	10	9	0	0	8
	1>	1	0	0	0	1	0	0	2
.....Total Incidence of Finding Observed:		1	0	0	0	1	0	0	2
Nose/Turb Sec 4 .....Number examined:		9	0	0	10	10	0	0	10
NASAL MUCOSA (OLFACTORY/RESPIRATORY): BASOPHILIC MATERIAL									
	->	0	0	0	0	2	0	0	3
	1>	9	0	0	10	8	0	0	7
.....Total Incidence of Finding Observed:		9	0	0	10	8	0	0	7
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	1>	6	0	0	7	10	0	0	8
	2>	3	0	0	3	0	0	0	2
.....Total Incidence of Finding Observed:		9	0	0	10	10	0	0	10
Ovaries .....Number examined:						10	0	0	10
Pancreas .....Number examined:		9	0	0	10	10	0	0	10
ACINAR CELL ATROPHY WITH OR WITHOUT CHRONIC INFLAMMATION									
	->	9	0	0	9	10	0	0	10
	2>	0	0	0	1	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	1	0	0	0	0
Parathyroid .....Number examined:		9	9	7	9	10	8	9	9

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Prostate	Number examined:	9	0	0	10				
LYMPHOID CELL AGGREGATE(S)									
	->	8	0	0	7				
	1>	1	0	0	3				
.....	Total Incidence of Finding Observed:	1	0	0	3				
Rectum/Low Colon	Number examined:	9	0	0	10	10	0	0	10
Salivary Glands	Number examined:	9	0	0	10	10	0	0	10
Seminal Vesicles	Number examined:	9	0	0	10				
Spleen	Number examined:	9	0	0	10	10	0	0	10
ACCESSORY SPLENIC TISSUE									
	->	9	0	0	10	9	0	0	10
	1>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Sternal Marrow	Number examined:	9	0	0	10	10	0	0	10
Sternum	Number examined:	9	0	0	10	10	0	0	10
Stomach	Number examined:	9	0	0	10	10	0	0	10
GLANDULAR MUCOSA: DILATED GLANDS									
	->	5	0	0	6	7	0	0	9
	1>	4	0	0	4	3	0	0	1
.....	Total Incidence of Finding Observed:	4	0	0	4	3	0	0	1
Submandib/Max LN	Number examined:	9	0	0	10	9	0	0	10
PARACORTICAL HYPERPLASIA									
	->	0	0	0	1	1	0	0	0
	1>	1	0	0	0	1	0	0	1
	2>	5	0	0	3	1	0	0	2
	3>	3	0	0	6	6	0	0	7
.....	Total Incidence of Finding Observed:	9	0	0	9	8	0	0	10

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Submandib/Max LN ..... Number examined:		9	0	0	10	9	0	0	10
SINUSOIDAL HISTIOCYTES									
	->	2	0	0	3	2	0	0	3
	1>	4	0	0	7	2	0	0	2
	2>	3	0	0	0	4	0	0	5
	3>	0	0	0	0	1	0	0	0
..... Total Incidence of Finding Observed:		7	0	0	7	7	0	0	7
SINUSES: FREE ERYTHROCYTES									
	->	7	0	0	10	7	0	0	9
	1>	1	0	0	0	2	0	0	1
	3>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		2	0	0	0	2	0	0	1
SINUSOIDAL PLASMA CELLS									
	->	9	0	0	9	9	0	0	10
	3>	0	0	0	1	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	1	0	0	0	0
Testes ..... Number examined:		9	0	0	10				
GERMINAL EPITHELIUM: DEGENERATION/ATROPHY									
	->	7	0	0	8				
	1>	2	0	0	2				
..... Total Incidence of Finding Observed:		2	0	0	2				
Thoracic SC ..... Number examined:		9	0	0	10	10	0	0	10
Thymus ..... Number examined:		9	0	0	10	10	0	0	10
HEMORRHAGE(S)									
	->	2	0	0	5	8	0	0	8
	1>	5	0	0	5	2	0	0	2
	2>	2	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		7	0	0	5	2	0	0	2

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Thyroid .....Number examined:		9	10	10	10	10	10	10	10
FOLLICULAR CELL HYPERTROPHY WITH OR WITHOUT MINIMAL -HYPERPLASIA									
	->	9	4	3	3	10	10	10	9
	1>	0	6	7	7	0	0	0	1
.....Total Incidence of Finding Observed:		0	6	7	7	0	0	0	1
CYSTIC FOLLICULAR HYPERPLASIA									
	->	9	10	10	10	10	10	10	10
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
LYMPHOID CELL AGGREGATE(S)									
	->	7	9	9	10	9	10	10	10
	1>	2	1	1	0	1	0	0	0
.....Total Incidence of Finding Observed:		2	1	1	0	1	0	0	0
MINERAL DEPOSIT(S)									
	->	6	7	9	10	10	7	8	7
	1>	3	3	1	0	0	3	2	3
.....Total Incidence of Finding Observed:		3	3	1	0	0	3	2	3
Trachea .....Number examined:		9	0	0	10	10	0	0	10
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)									
	->	5	0	0	7	7	0	0	4
	1>	2	0	0	3	0	0	0	4
	2>	2	0	0	0	3	0	0	2
.....Total Incidence of Finding Observed:		4	0	0	3	3	0	0	6

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Terminal Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	9	10	10	10	10	10	10	10
Trachea	Number examined:	9	0	0	10	10	0	0	10
MUCOSA: GLANDS DILATED									
	->	9	0	0	9	10	0	0	10
	2>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	1	0	0	0	0
MUCOSA: LYMPHOID CELL AGGREGATE(S)									
	->	8	0	0	10	10	0	0	9
	1>	1	0	0	0	0	0	0	1
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	1
Urinary Bladder	Number examined:	9	0	0	9	10	0	0	10
Uterus w/ Cervix	Number examined:					10	0	0	10
LUMEN: DILATED									
	->					7	0	0	8
	1>					2	0	0	0
	2>					1	0	0	1
	3>					0	0	0	1
.....	Total Incidence of Finding Observed:					3	0	0	2

All Diagnoses; Phases: P3; Death types: Scheduled FS; Date of death range: 24-Mar-06 To 27-Mar-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Recovery Sacrifice

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	5	5	5	5	0	0	0	0
Parathyroid ..... Number examined:		5	5	5	4	0	0	0	0
Thyroid ..... Number examined:		5	5	5	5	0	0	0	0
FOLLICULAR CELL HYPERTROPHY WITH OR WITHOUT MINIMAL -HYPERPLASIA									
	->	5	5	5	5	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
CYSTIC FOLLICULAR HYPERPLASIA									
	->	5	5	5	4	0	0	0	0
	2>	0	0	0	1	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	1	0	0	0	0
LYMPHOID CELL AGGREGATE(S)									
	->	5	5	5	5	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MINERAL DEPOSIT(S)									
	->	3	1	0	2	0	0	0	0
	1>	2	4	5	3	0	0	0	0
..... Total Incidence of Finding Observed:		2	4	5	3	0	0	0	0

All Diagnoses; Phases: P4; Death types: Scheduled FS; Date of death range: 21-Apr-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Adrenal Glands	Number examined:	1	0	0	0	0	0	0	0
Aorta	Number examined:	1	0	0	0	0	0	0	0
Brain	Number examined:	1	0	0	0	0	0	0	0
Cecum	Number examined:	1	0	0	0	0	0	0	0
Cervical SC	Number examined:	1	0	0	0	0	0	0	0
Colon	Number examined:	1	0	0	0	0	0	0	0
Duodenum	Number examined:	1	0	0	0	0	0	0	0
Epididymides	Number examined:	1	0	0	0				
Esophagus	Number examined:	1	0	0	0	0	0	0	0
Femoral Marrow	Number examined:	1	0	0	0	0	0	0	0
Femur w/ Joint	Number examined:	1	0	0	0	0	0	0	0
Heart	Number examined:	1	0	0	0	0	0	0	0
INFLAMMATORY FOCI WITH OR WITHOUT MYOCARDIAL DEGENERATION	->	1	0	0	0	0	0	0	0
	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Ileum	Number examined:	0	0	0	0	0	0	0	0
MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Jejunum	Number examined:	0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Kidneys .....Number examined:		1	0	0	0	0	0	0	0
CORTICO-MEDULLARY JUNCTION: MINERAL DEPOSIT(S)	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
BASOPHILIC TUBULES	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
INTERSTITIAL SUBACUTE/CHRONIC INFLAMMATORY FOCI	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
DILATED TUBULES	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MEDULLA: MINERAL DEPOSIT(S)	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Larynx: V-DVTC .....Number examined:		0	0	0	0	0	0	0	0
MUCOSA: SERO-MUCOUS GLANDS DILATED									
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)									
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Larynx: V-DVTC	Number examined:	0	0	0	0	0	0	0	0
MUCOSA: LYMPHOID CELL AGGREGATE(S)	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Larynx: V-SM-G	Number examined:	0	0	0	0	0	0	0	0
MUCOSA: SERO-MUCOUS GLANDS DILATED	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
MUCOSA: LYMPHOID CELL AGGREGATE(S)	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
MUCOSA: EPITHELIUM-SQUAMOUS/SQUAMOID METAPLASIA	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
MUCOSA: STRATIFIED SQUAMOUS EPITHELIUM (NORMAL)-HYPERPLASIA	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Liver	Number examined:	1	0	0	0	0	0	0	0
INFLAMMATORY FOCI	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
MEDIAL LOBE ANOMALY	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Lumbar SC	Number examined:	1	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1		-- Animals Affected --							
	Animal sex:	-- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Lungs	Number examined:	1	0	0	0	0	0	0	0
ALVEOLAR/INTRAALVEOLAR MACROPHAGES									
	1>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
SUBPLEURAL/PERIVASCULAR LYMPHOID AGGREGATES WITH OR WITHOUT -VARIABLE NUMBERS OF NEUTROPHILS									
	1>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
AGONAL HEMORRHAGE(S)									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
VESSEL(S): MINERAL DEPOSIT(S)									
	1>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Lymph Node other	Number examined:	0	0	0	0	0	0	0	0
Mediastinal LN	Number examined:	1	0	0	0	0	0	0	0
PARACORTICAL HYPERPLASIA									
	3>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
SINUSES: FREE ERYTHROCYTES									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Mediastinal LN ..... Number examined:		1	0	0	0	0	0	0	0
SINUSOIDAL HISTIOCYTES									
	1>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
Mesenteric LN ..... Number examined:		1	0	0	0	0	0	0	0
SINUSOIDAL HISTIOCYTES									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
PARACORTICAL HYPERPLASIA									
	2>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
SINUSES: FREE ERYTHROCYTES									
	2>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
HISTIOCYTIC AGGREGATES									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Nerve Sciatic ..... Number examined:		1	0	0	0	0	0	0	0
Nose/Turb Sec 1 ..... Number examined:		1	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Nose/Turb Sec 1 .....Number examined:		1	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): BASOPHILIC MATERIAL	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
NASAL LUMEN: EOSINOPHILIC MATERIAL	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): GLANDS DILATED	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Nose/Turb Sec 2 .....Number examined:		1	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY/OLFACTORY): BASOPHILIC MATERIAL	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
NASAL LUMEN: EOSINOPHILIC MATERIAL	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): GLANDS DILATED	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Nose/Turb Sec 2	Number examined:	1	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): SUBACUTE (CHRONIC ACTIVE)/ -CHRONIC INFLAMMATION									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Nose/Turb Sec 3	Number examined:	1	0	0	0	0	0	0	0
NASAL MUCOSA (RESPIRATORY): EPITHELIUM- GOBLET CELL -HYPERTROPHY/HYPERPLASIA									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
NASAL MUCOSA (OLFACTORY/RESPIRATORY): BASOPHILIC MATERIAL									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	1>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
NASAL MUCOSA (OLFACTORY): GLANDS DILATED									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Nose/Turb Sec 4	Number examined:	1	0	0	0	0	0	0	0
NASAL MUCOSA (OLFACTORY/RESPIRATORY): BASOPHILIC MATERIAL									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
NASAL LUMEN: EOSINOPHILIC MATERIAL									
	->	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	0
Ovaries	Number examined:					0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Pancreas ..... Number examined:		1	0	0	0	0	0	0	0
ACINAR CELL ATROPHY WITH OR WITHOUT CHRONIC INFLAMMATION	->	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Parathyroid ..... Number examined:		0	0	0	0	0	0	0	0
Prostate ..... Number examined:		1	0	0	0				
LYMPHOID CELL AGGREGATE(S)	->	1	0	0	0				
..... Total Incidence of Finding Observed:		0	0	0	0				
Rectum/Low Colon ..... Number examined:		1	0	0	0	0	0	0	0
Salivary Glands ..... Number examined:		1	0	0	0	0	0	0	0
Seminal Vesicles ..... Number examined:		1	0	0	0				
Spleen ..... Number examined:		1	0	0	0	0	0	0	0
ACCESSORY SPLENIC TISSUE	->	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Sternal Marrow ..... Number examined:		1	0	0	0	0	0	0	0
Sternum ..... Number examined:		1	0	0	0	0	0	0	0
Stomach ..... Number examined:		1	0	0	0	0	0	0	0
GLANDULAR MUCOSA: DILATED GLANDS	->	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Submandib/Max LN ..... Number examined:		1	0	0	0	0	0	0	0
PARACORTICAL HYPERPLASIA									
	1>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
SINUSOIDAL HISTIOCYTES									
	->	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
SINUSES: FREE ERYTHROCYTES									
	3>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
SINUSOIDAL PLASMA CELLS									
	->	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Testes ..... Number examined:		1	0	0	0				
GERMINAL EPITHELIUM: DEGENERATION/ATROPHY									
	->	1	0	0	0				
..... Total Incidence of Finding Observed:		0	0	0	0				
Thoracic SC ..... Number examined:		1	0	0	0	0	0	0	0
Thymus ..... Number examined:		1	0	0	0	0	0	0	0
HEMORRHAGE(S)									
	2>	1	0	0	0	0	0	0	0
..... Total Incidence of Finding Observed:		1	0	0	0	0	0	0	0
Thyroid ..... Number examined:		1	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

Perfluoro-n-butyl iodide (PFBI): A 13-Week Nose-Only Inhalation Toxicity Study in Rats with a 4-Week Recovery Period

Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Thyroid .....Number examined:		1	0	0	0	0	0	0	0
FOLLICULAR CELL HYPERTROPHY WITH OR WITHOUT MINIMAL -HYPERPLASIA									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
CYSTIC FOLLICULAR HYPERPLASIA									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
LYMPHOID CELL AGGREGATE(S)									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MINERAL DEPOSIT(S)									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Trachea .....Number examined:		1	0	0	0	0	0	0	0
MUCOSA: MIXED INFLAMMATORY CELLS (PRIMARILY LYMPHOID CELLS -ADMIXED WITH A SMALL AND VARIABLE NUMBER OF NEUTROPHILS -AND/OR EOSINOPHILS)									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MUCOSA: GLANDS DILATED									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MUCOSA: LYMPHOID CELL AGGREGATE(S)									
	->	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
Urinary Bladder .....Number examined:		1	0	0	0	0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06

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Incidence Summary of Microscopic Findings with Severity Levels
Unscheduled Deaths

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	1	0	0	0	0	0	0	0
Uterus w/ Cervix	Number examined:					0	0	0	0
LUMEN: DILATED	Total Incidence of Finding Observed:					0	0	0	0

All Diagnoses; Phases: P3, P4; Death types: Unscheduled U3; Date of death range: 18-Jan-06 To 21-Apr-06