Data Requirement

EPA OPPTS 870.3650
OECD 422

STUDY NO. 03-4244

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

Final Report

VOLUME I of III

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Submitted to: American Petroleum Institute (API)
1220 L Street, Northwest
Washington, D.C. 20005-4070

Attn: [redacted]

Date: 16 April 2010

STATEMENT OF COMPLIANCE

This study was conducted in compliance with the United States Environmental Protection Agency's Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and the Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM/(98)17, with the following exceptions that did not effect the integrity of the study:

1. A lot number for the test substance was not available.
2. The actual location for the synthesis documentation of the test substance was not provided by the supplier.

[redacted]

[redacted]

Date

[redacted]

[redacted]

3/29/18

Date

SIGNATURE PAGE

SCIENTISTS

The following scientists were responsible for the overall conduct of this study. Departmental supervisory personnel are listed on the personnel page of this report (Appendix MM).

[redacted]

16 April 2010
Date

[redacted]

16th April 2010
Date

SCIENTIFIC REVIEW

The following scientist has reviewed and approved this report:

[redacted]

14 APR 2010
Date

[1] Wanda B. High was the Study Pathologist for this study and for submission of the draft report and is no longer employed at the Testing Facility. Dianne Creasy is assuming responsibility for finalization of the pathology evaluation of this report.

[2] Keith P. Hazelden was the original scientific reviewer of this report and is no longer employed at the Testing Facility. Robert M. Parker is assuming responsibility for final review of this report.

QUALITY ASSURANCE STATEMENT

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management.

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
CATO Research Facility Inspection	14 May 03	30 Jan 04
GLP Protocol Review	14 Nov 03	18 Nov 03
Exposure, Monitoring & Equipment Records	15 Dec 03	16 Dec 03
Functional Observational Battery Evaluations, Motor Activity and Training Records	9 Jan 04	13 Jan 04
Clinical Pathology Blood Collection, Main Study Necropsy and Training Records	14 Jan 04	14 Jan 04
Pup Body Weights and Training Records	23 Jan 04	23 Jan 04
Satellite Female & Pup Lactation Day 4 Sacrifices	26 Jan 04	27 Jan 04
Post Study Test Substance Stability Analysis	6 Feb 04	13 Feb 04
Draft Final Report and Data	8-11, 13-18 & 21 Jun 04	21 Jun 04
Isobutane Post-Study Characterization & Stability Analytical Report and Data	23 Jul 04	23 Jul 04
Final Report Review & Protocol Amendments No. 1	5-7, 20 Nov 08	20 Nov 08
Protocol Amendment No. 2	7 Apr 10	7 Apr 10

[redacted]

16 Apr 10
Date

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY

This study was designed to screen the potential toxicity, including neurotoxicity and reproductive performance in male and female rats when isobutane was administered by whole-body inhalation exposure. It also was designed to permit detection of effects in both sexes on mating behavior and on gonadal function that may not be evident from histological examination of the reproductive organs. In addition, for female rats, this study design can detect effects on conception, development of the conceptus and parturition and pup survival to postnatal Day 4.

The test substance was administered as a gas to Sprague Dawley CD rats (12/sex/main study group and 12 females/satellite group) at target concentrations of 900, 3000 and 9000 ppm (note: highest dose is 50% of the lower explosive limit) for 6 hours/day, 7 days/week for 2 weeks prior to mating initiation. Exposure levels were determined using an infrared spectrophotometer (IR) 4 times per chamber per day. Main study male rats were exposed during the mating and post-mating periods until euthanized for a minimum exposure of 28 days. Main study female rats (12/group) were exposed once daily (6 hours/day), 7 days/week for 4 weeks (minimum of 28 days). Satellite female rats were exposed once daily (6 hours/day), 7 days/week for at least two weeks prior to mating initiation. Satellite female rats continued to be treated once daily (6 hours/day) during mating. Once mated, satellite female rats were treated once daily (6 hours/day) during gestation days 0-19. Main study females were evaluated for subchronic effects and satellite females for reproductive effects only. The following parameters were evaluated in all animals: viability, clinical observations, body weights, feed consumption, functional observational battery (FOB), motor activity, clinical pathology (termination), organ weights, and macroscopic observations. Microscopic pathology was conducted in the main study control and high-exposure groups only).

The test substance, purchased from MG Industries, was assayed by GC versus an analytical standard before and after the study to demonstrate the purity and stability of the test substance. The test substance was determined to be 99.84% isobutane before the study and 99.53% isobutane after the study demonstrating the purity and the stability of the test substance. Chamber distribution analyses showed that the test substance was evenly distributed within each chamber. The mean (± standard deviation) analytical (IR) concentrations for the control and the respective exposure groups were as follows: 0 ± 0, 930.0 ± 27.8, 3122 ± 83 and 9148 ± 201 ppm. Chamber environmental conditions averaged 24°C temperature and 55% relative humidity. Mean particle size distribution measurements for the exposures indicated that the atmospheres were gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chambers.

SUMMARY

There was no effect of treatment on survival. All animals survived until the termination of the study. The test animals were generally unremarkable during the exposure periods (in-chamber) and during the non-exposure periods. There were no exposure-related differences in body weights or weight changes or feed consumption in the test substance exposed animals compared to the air control animals. There was no apparent exposure-related effect on FOB or motor activity parameters for either sex in this study. There were no exposure-related differences in hematology or coagulation values or clinical chemistry values in test substance exposed animals compared to the air control animals at the terminal interval. There were no exposure-related differences in macroscopic postmortem evaluations or organ weights in the test substance exposed animals compared to the air control animals. There were no microscopic findings considered to be related to exposure to isobutane.

Almost all mated female animals were found pregnant and delivered live pups. In the 9000 ppm group, 25% of the mated females did not become pregnant, and this reduction in the male and fertility indices (75%) was considered exposure-related. Mating index for the male rats treated with the test substance were comparable to the air control group. Mating and gestation indices for the female rats treated with the test substance were comparable to the air control group. Almost all females in each group mated at the first opportunity. There were also no treatment-related differences in the other reproductive parameters up to the time of parturition including the percent of females completing delivery and the duration of gestation, when compared to the air control group. An exposure-related increase in post-implantation loss was also observed for the 9000 ppm group of exposed female rats. Otherwise, there were no exposure-related differences in any of the parturition parameters including pre-implantation loss, the total number of pups delivered, the number of pups dying, the viability (4 day survival) index, the pup sex ratio and the number of live pups/litter, when compared to the air control group. There were no exposure-related differences in body weights or weight gains in the pups feeding from females exposed to test substance during gestation compared to the pups feeding from air control animals. There were no exposure-related differences in macroscopic postmortem evaluations in the pups feeding from females exposed to test substance during gestation as compared to the pups feeding from air control animals.

In conclusion, exposure of male and female rats to target concentrations of 900, 3000 or 9000 ppm of isobutane by whole-body inhalation for 4-6 weeks resulted in no general systemic/neurotoxic effects. A no-observed-adverse effect level (NOAEL) of 9000 ppm was determined for all general systemic/neurotoxic endpoints in this study. Based on decreased male and female fertility and increased post-implantation loss in the 9000 ppm group, the fertility and reproductive/developmental endpoints NOAEL was determined to be 3000 ppm. The NOAEL for pup endpoints was 9000 ppm based on no effects in offspring survival, body weight and development up to post-natal day 4.

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1. INTRODUCTION

This study was designed to screen the potential toxicity, including neurotoxicity and reproductive performance in male and female rats when isobutane, an industrial gas, is administered by whole-body inhalation exposure. It also was designed to permit detection of effects in both sexes on mating behavior and on gonadal function that may not be evident from histological examination of the reproductive organs. In addition, for female rats this study can detect effects on conception, development of the conceptus and parturition and pup survival to lactation day 4.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

American Petroleum Institute (API)
1220 L Street, Northwest
Washington, D.C. 20005-4070

2.1.2. SPONSOR REPRESENTATIVE

[redacted]

2.1.3. TESTING FACILITY

Huntingdon Life Sciences (HLS)
100 Mettlers Road
East Millstone, New Jersey 08875-2360

2.1.4. STUDY DIRECTOR

[redacted]

2.2. STUDY DATES

2.2.1. STUDY INITIATION

26 November 2003 (date study director signed the Protocol)

2.2.2. DATE OF ANIMAL RECEIPT

2 December 2003 (experimental start date, per OECD GLP's)

2.2.3. EXPOSURE INITIATION

15 December 2003 (experimental start date, per EPA GLP's)

2.2.4. MATING INITIATION

29 December 2003

2.2.5. MATING TERMINATION

12 January 2004

2.2.6. EXPOSURE TERMINATIONS

14 January 2004 (main study)
31 January 2004 (satellite female)

2.2.7. TERMINAL SACRIFICES

14-16 January 2004 (main study)
24-27, 29, 30 January and 6 February 2004 (satellite female)

2.2.8. EXPERIMENTAL TERMINATION

14 April 2010 (date of last data collection = Date final report is signed by the pathologist)

2.2.9. STUDY COMPLETION

16 April 2010 (date final report is signed by the study director)

2.3. EXPERIMENTAL OUTLINE

Group	Group Designation	Exposure Levels (ppm)	Treatment Schedule Pre-mating Period		Number of Animals	
			Main Study Male Rats[b]	Main Study and Satellite Female Rats[b,c]	Main Study Male Rats	Main Study and Satellite Female Rats*
1	Air Control[a]	0	2 weeks	2 weeks	12	24
2	Low	900	2 weeks	2 weeks	12	24
3	Mid	3000	2 weeks	2 weeks	12	24
4	High	9000	2 weeks	2 weeks	12	24

*12/group = main study animals for subchronic evaluations only

*12/group = satellite animals for reproductive/developmental evaluations only

[a]Control animals were treated with air only with the same treatment regimen as the treated groups.

[b]Main study male rats (12/group) were exposed once daily (6 hours/day), 7 days/week for 2 weeks prior to mating initiation. Exposure of main study male rats continued during the mating and post-mating periods for a minimum exposure of 28 days. Main study female rats (12/group) were exposed once daily (6 hours/day), 7 days/week for 4 weeks for a minimum of 28 days.

[c]Satellite female rats (12/group) for the reproductive/developmental study were exposed once daily (6 hours/day), 7 days/week for at least two weeks prior to mating initiation. Satellite female rats continued to be treated once daily (6 hours/day) during mating. Once mated, satellite female rats were treated once daily (6 hours/day) during gestation days 0-19.

The first day of exposure was designated day 0 of the study.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY OF ADMINISTRATION

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures were recommended in the referenced guidelines.

2.4.2. EXPOSURE LEVEL SELECTION

The exposure levels were based on results of a 2-week range-finding study (HLS Study No. 03-6145, see Appendix LL, range finding Study) which showed no toxicity at exposure levels of 90, 900 and 9000 ppm. Therefore, the high exposure level was established (for safety reasons) at 9000 ppm since it was 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

2.4.3. TEST ANIMAL SELECTION

The rat is a rodent animal model acceptable under OECD and EPA testing guidelines for reproductive/developmental toxicity and neurotoxicity studies. In addition, historical data is available in the testing facility for comparative evaluation with this strain of rat.

2.4.4. NUMBER OF ANIMALS

The number of animals in this study was considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD and EPA guidelines. Ten pregnancies per group were considered an adequate number for screening for developmental toxicities. The reference guideline indicated 8-10 litters per group provide the necessary degree of consistency between studies. With the group size of 12 used in this study, and with recent pregnancy rates of 80-90%, this was anticipated to provide between 8-10 litters/group for evaluation. On this basis, group sizes of 12 paired main study male and satellite female rats were considered appropriate for this study and provided a sufficient number of litters in each group to meet guideline requirements. Group sizes of 12 main study female rats were considered appropriate for providing comparable data to the main study male rats.

2.5. TEST SUBSTANCE

Isobutane

2.5.1. TEST SUBSTANCE CATEGORY

Industrial gas

2.5.2. SUPPLIER

MG Industries
3 Great Valley Parkway
Malvern, Pennsylvania 19355

2.5.3. LOT NUMBER

Not available

2.5.4. PURITY AND STABILITY

99.0% per supplier. The testing facility also determined the purity and stability by assaying by gas chromatography (GC) before and after the study (see Appendix JJ).

2.5.5. DESCRIPTION

Colorless gas

2.5.6. DATE RECEIVED

6 May 2003

2.5.7. EXPIRATION DATE

Not available, stable per MSDS and per stability assessment performed as part of this study.

2.5.8. ANALYSIS

Documentation of the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the batch of the test substance and the maintenance of these records was the responsibility of the supplier. Documentation of the identity, strength, composition and stability were also confirmed by the testing facility.

Note that the actual location for the synthesis of the test substance has not been provided by the supplier.

2.5.9. STORAGE

Ambient (in an outside solvent shed) when not in use in the inhalation laboratory.

2.5.10. ARCHIVAL SAMPLE

An archival sample of the test substance was taken and stored in the archives of the sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, Virginia 20166). One cylinder (a common archival for this and the preceding range-finding study) was initially shipped to ChevronTexaco on 13 August 2003 and then was delivered to EPL archives for storage.

2.5.11. DISPOSITION

The unused portion of the test substance as well as any empty test substance containers will be returned to the supplier following submission of the final study report with this test substance.

2.6. TEST ANIMALS

2.6.1. SPECIES

Albino Rats (Outbred) VAF/Plus®
Sprague-Dawley Derived (CD®)
Crl:CD® (SD) IGS BR

2.6.2. SUPPLIER

Charles River Laboratories
Raleigh, North Carolina 27610

2.6.3. NUMBER OF ANIMALS

Received:
160 total (54 males, 106 females)

Placed on test:
144 total (48 males, 96 females)

Females were nulliparous and non-pregnant and were from a separate colony area than the males.

2.6.4. AGE AT RECEIPT

Approximately 6 weeks

2.6.5. AGE AT INITIATION OF EXPOSURES

Approximately 8 weeks

2.6.6. WEIGHT AT INITIATION OF EXPOSURES (GRAMS)

	Mean	Range
Male:	277	249 - 301
Female (Main/Satellite):	194	171 - 216

Individual weights of animals placed on test were within ±20% of the mean weight for each sex at randomization.

2.6.7. ACCLIMATION PERIOD

Animals were acclimated for approximately 2 weeks. All animals were checked for viability twice daily. Prior to assignment to study, all animals were examined to ascertain suitability for study.

2.7. ANIMAL ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations and body weight data were randomly assigned by a computerized random sort program, by sex, to control or treated groups in an attempt to equalize mean group body weights. Female animals were randomly assigned to 4 main/satellite study groups (12/group) and the male animals (12/group) to 4 main study groups. Disposition of all animals not utilized in the study is maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon arrival. After selection, each animal was identified with a metal ear tag 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.

2.9. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

2.10. ANIMAL HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.10.2. HOUSING

Animals were housed individually in stainless-steel suspended cages with wire mesh floors and fronts, except for the mating period when one main study male and one satellite female rat were housed together. During cohabitation (when satellite female rats were brought to the main study male rat's cages), male and female rats were housed in stainless steel cages of appropriate size for group housing animals. Each cage was fitted to secure a glass feeder jar with a stainless steel lid. From gestation day 18 and during lactation, the dam was housed with her litter in plastic "shoebox" cages with bedding.

2.10.3. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly. During periods that feed consumption was not recorded, fresh feed was presented at least weekly.

2.10.4. FEED ANALYSIS

Analysis of each feed lot used during this study was performed by the manufacturer. Results can be found in Appendix PP. There

were no known contaminants in the feed that were expected to interfere with the results of this study.

2.10.5. WATER

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction via an automated watering system.

2.10.6. WATER ANALYSIS

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 can be found in Appendix PP. There were no known contaminants in the water that were expected to interfere with the results of this study.

2.10.7. BEDDING SUBSTANCE

Ground corncob bedding (Bed-O'-Cobs® ¼ inch irradiated, The Andersons, Maumee, Ohio) was provided for each mated female rat on day 18 of gestation. Fresh bedding was provided weekly or as needed throughout lactation.

2.10.8. BEDDING ANALYSIS

Analyses for each batch of bedding used on study can be found in Appendix PP. There were no known contaminants in the bedding that were expected to interfere with the results of this study.

2.10.9. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve-hour light/dark cycle controlled via an automatic timer was provided.

Temperature

Temperature was monitored in accordance with testing facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:	18 to 26°C
Actual Range:	20 to 22°C
Daily Average Range:	21 to 22°C

Relative Humidity

Relative humidity was monitored in accordance with testing facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:	30 to 70%
Actual Range:	42 to 63%
Daily Average Range:	35 to 55%

2.11. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

See Appendix II, Inhalation Report.

2.12. MATING PROCEDURE

Within each treatment group, the main study male and satellite female rats were co-housed continuously (1:1) until evidence of mating was seen, or for 2 consecutive weeks. Pairing of male and female littermates was prevented by ordering males and females sourced from different parts of the supplying facility. Satellite female rats were observed at approximately the same time each morning for the presence of a vaginal plug or sperm in the vaginal smear. If not mated, the stage of the estrous cycle was recorded instead. The day on which evidence of mating was observed was defined as day 0 of gestation. Once mated, the satellite female rats were removed from the mating cages and housed individually for the remainder of the study.

2.13. EXPERIMENTAL EVALUATIONS

2.13.1. VIABILITY CHECKS (CAGESIDE)

Observations for mortality and general condition were made at least twice daily (once in the morning and once in the afternoon).

2.13.2. DETAILED PHYSICAL EXAMINATIONS

Each animal was removed from its cage and a detailed physical observation performed prior to randomization. Main study male rats were observed once weekly beginning during the pre-mating period and throughout the study. Main study female rats were observed weekly after randomization and throughout the study. Satellite female rats were observed weekly during the pre-mating period and on gestation days 0, 7, 14, 20 and lactation days 0 (except if parturition didn't complete on the same day as it initiated), 1 and 4.

All animals were observed as a group at least once during each exposure. This was routinely performed near the middle of each exposure.

Examinations during non-exposure periods included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) were recorded.

2.13.3. BODY WEIGHTS

Body weights of the main study male and female rats were recorded at the time of randomization into test groups, on the first day of treatment and weekly thereafter throughout the study. Satellite female rats for the reproduction study were weighed at the time of randomization into test groups, on the first day of treatment and twice weekly until evidence of copulation was observed. Mated satellite female rats were weighed on gestation days 0, 7, 14 and 20, and satellite female rats that delivered litters were weighed

on lactation days 1 and 4. Terminal body weights for main study animals were recorded after fasting. Satellite females were not fasted prior to recording of terminal body weights.

2.13.4. FEED CONSUMPTION

Feed consumption for the main study male rats was recorded pretest and weekly during the pre-mating treatment period. Feed consumption for the main study female rats was recorded pretest and weekly during the treatment period. Feed consumption for satellite female rats was recorded pretest and weekly during the pre-mating period, and if not mated, during the post-mating period until delivery. Feed consumption was not recorded during the mating period when main study male rats were co-housed with satellite female rats. For pregnant or confirmed mated satellite female rats, feed consumption was recorded on gestation days 0-7, 7-14 and 14-20 and on lactation days 1-4.

Feed was available without restriction, except during exposures and at terminal fasting for the main study animals. Animals were presented with full feeders of known weight. After 7 days (pre-mating), 6 or 7 days (gestation) or 3 days (lactation), the feeders were reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal over the 7, 6 or 3-day period. Feed consumption was measured (weighed) weekly, beginning one week prior to treatment.

Calculation

Feed Consumption (g/kg/day) =

$$\frac{\text{grams of feed consumed}}{\text{body weight (kg)}^{a}} \div \text{7, 6 or 3 days}$$

[a]The average of the current and first weight of the week was used.

2.13.5. PARTURITION AND LACTATION

On gestation day 18, several days prior to expected parturition, satellite female rats were transferred to solid, plastic cages with bedding provided. Thereafter, examinations for signs of parturition were made twice daily (morning and afternoon). The duration of

gestation was documented. When parturition began on one day and ended the next, the lactation day 0 observations were actually recorded on lactation day 1, after all pups had been delivered. Evidence of difficult or prolonged parturition or unusual behavior, if observed, was recorded. The day on which parturition initiated was defined as lactation day 0. Litters were observed as soon as possible after parturition completion for the number of live and dead pups, pup abnormalities and pup sex. Thereafter, litters were observed twice daily (morning and afternoon). All pups in the litter were uniquely identified by toe tattoo after parturition completion. The presence of dead pups was recorded, and dead pups were removed from the litter as found. Any unusual behaviors/observations and absence of milk in the stomach were noted.

2.13.6. F_1 PUP EVALUATIONS

Physical Examinations

Each F_1 pup was examined on lactation days 0 and 4. Pups were also observed for any abnormal behavior.

Body Weights

Individual F_1 pup weights were recorded on lactation days 1 and 4.

Sexing

Pups were sexed on lactation day 0 and sex was verified on lactation day 4.

Where parturition occurred over a two day period, these evaluations were performed on lactation day 1 after all pups had been delivered (lactation day 0 being defined as the day that parturition initiated).

2.14. NEUROBEHAVIORAL EXAMINATIONS

Observations on all main study male and female rats from all exposure groups were recorded as outlined below. Observations were assessed during the last week of exposure. Animals were not exposed on the day of

evaluations. Testing was staggered over several sessions. Each session consisted of approximately equal numbers of animals per sex per exposure level. 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 FOB was performed for all animals before evaluation of motor activity. Positive historical control data demonstrating the sensitivity of the procedure is documented in Appendix KK.

2.14.1. FUNCTIONAL OBSERVATIONAL BATTERY

The time of testing was balanced across treatment groups. All observations during the treatment period were performed 'blind', *i.e.*, the observer was unaware of the animals' treatment. The following evaluations were performed as part of the functional observational battery:

Sensory Observations
startle response to auditory stimuli
tail pinch response

Neuromuscular Observations
grip strength – hindlimb and forelimb

Physiological Observations
rectal temperature

Temperature

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. Excursions outside the specified range were considered not to have affected the integrity of the study.

Desired:	18 to 26°C
Actual:	17 to 20°C

Relative Humidity

Relative humidity was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Excursions below the specified range (approximately half of the measures) were considered not to have affected the integrity of the study because the FOB measure period was of brief duration.

Desired: 30 to 70%
Actual: 12 to 36%

Noise Level

Noise level was monitored using a Digital Sound Level Meter, Model 840029 (Sper Scientific, Ltd., Scottsdale, Arizona) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 55 to 65 dB
Actual: 57.6 to 61.5 dB

Illumination

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, New York) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: <80 footcandles
Actual: 40.5 to 45.7 footcandles

2.14.2. MOTOR ACTIVITY

Activity was monitored using an automated Photobeam Activity System (San Diego Instruments, Inc.). Sessions were 60 minutes in length; each session was divided into 12 five-minute intervals. The time of testing was balanced across treatment groups.

Temperature

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 18 to 26°C
Actual: 18 to 20°C

Relative Humidity

Relative humidity was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation. Excursions below the specified range (approximately half of the measures) were considered not to have affected the integrity of the study because the motor activity measure period was of brief duration.

Desired: 30 to 70%
Actual: 8 to 37%

Noise Level

Noise level was monitored using a Digital Sound Level Meter, Model 840029 (Sper Scientific, Ltd., Scottsdale, Arizona) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 55 to 65 dB
Actual: 57.3 to 62.8 dB

Illumination

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, New York) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: <80 footcandles
Actual: 44.1 to 52.3 footcandles

2.15. CLINICAL PATHOLOGY

Clinical pathology procedures and parameters were based on those recommended in published guidelines (Joint Scientific Committee, 1996).

Blood samples for hematology, coagulation and clinical chemistry studies were obtained from lightly anesthetized (CO_2/O_2) main study animals (12/sex/group) via puncture of the orbital sinus (retrobulbar) at study termination. Animals were fasted overnight prior to blood collection.

Blood was collected and studies performed as follows:

2.15.1. HEMATOLOGY

Blood for hematology studies was collected (approximately 0.25 mL) into tubes containing EDTA anticoagulant.

Blood samples were analyzed as follows:

ADVIA 120 HematologyAnalyzer, Bayer Corporation.

Hemoglobin concentration
Hematocrit
Erythrocyte count
Platelet count
Mean corpuscular volume
Mean corpuscular hemoglobin
Mean corpuscular hemoglobin concentration
Total leukocyte count
Reticulocyte count
Differential leukocyte count[1]

Other

Erythrocyte and platelet morphology (from peripheral blood smear) *(Henry, 1991)*

2.15.2. COAGULATION

Blood for coagulation studies was collected (approximately 0.75 mL) into tubes containing sodium citrate anticoagulant.

[1]When questionable values were obtained, manual differential leukocyte counts (Henry, 1991) and absolute value calculations were performed for verification.

Blood samples were analyzed as follows:

Mechanical clot detection system, STA Compact®, Diagnostica Stago Products

Prothrombin time
Activated partial thromboplastin time

2.15.3. CLINICAL CHEMISTRY

Blood for clinical chemistry studies (approximately 1.0 mL) was collected into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum.

Blood samples were analyzed as follows:

Hitachi 717, Roche Corporation Automatic Analyzer

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

Other

Globulin (*calculated value; total protein - albumin*)
Albumin/globulin ratio (*calculated value; albumin ÷ globulin*)

2.15.4. RETENTION/STORAGE OF SPECIMENS

Any remaining (frozen) serum, which may have limited storage stability, was stored for up to six months after completion of assays and then discarded. Peripheral blood smears were retained and archived with the study.

2.16. POSTMORTEM EVALUATIONS

2.16.1. METHOD OF EUTHANASIA

All animals (except lactation days 4 or 5 pups) were euthanized by exsanguination following an overexposure of carbon dioxide inhalation. Lactation days 4 or 5 pups were euthanized using an intraperitoneal injection of sodium pentobarbital.

2.16.2. EUTHANASIA SCHEDULE

Main Study Male and Female Rats

Main study male and female rats were euthanized after at least 28 days of exposure.

Satellite Female Rats in the Reproduction Study

Mated satellite female rats were euthanized on postpartum days 4 or 5. Satellite female rats in which evidence of mating was detected but failed to deliver were sacrificed 26 or 27 days after evidence of mating.

2.16.3. MACROSCOPIC EXAMINATION – MAIN STUDY MALE RATS

Macroscopic postmortem examinations were performed on all main study male rats. Postmortem examinations included examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain.

2.16.4. MACROSCOPIC EXAMINATIONS – FEMALE RATS

Macroscopic postmortem examinations were performed on all main study and satellite female rats. Postmortem examinations included examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. The number of implantation sites and corpora lutea were recorded for each satellite female rat.

2.16.5. ORGAN WEIGHTS

Organs indicated in Table I (page 31) were taken at the scheduled necropsy, recorded and organ/body and organ/brain weight ratios calculated. Prior to weighing, all organs were carefully dissected and properly trimmed to remove fat and other contiguous tissue in a uniform manner. Organs were weighed as soon as possible after dissection to avoid drying. Paired reproductive organs were weighed separately. All other paired organs were weighed together.

2.16.6. TISSUES PRESERVED AND EXAMINED HISTOLOGICALLY

The tissues listed in Table I (page 31) were obtained at necropsy for all main study male and female rats, as well as all satellite females. Slides of the indicated tissues were prepared and examined microscopically for control and high exposure main study animals. During the microscopic examination of the testes, special emphasis was placed on the stages of spermatogenesis and the histopathology of interstitial testicular cell structure. Any abnormalities not noted during macroscopic postmortem examinations, which were seen during histological processing were recorded.

TABLE I

ORGAN NAME	WEIGHED	PRESERVED Main and Satellite Study	EXAMINED MICROSCOPICALLY Main Study (Groups 1 and 4)
Adrenal glands	X	X	X
Bone (sternum/femur)[a]		X	X
Bone marrow (rib)		X	[b]
Brain (medulla/pons, cerebrum and cerebellum)	X	X	X
Epididymides	X	X	X
Heart	X	X	X
Kidneys	X	X	X
Large intestine (cecum, colon and rectum)		X	X
Larynx		X	
Liver	X	X	X
Lungs (with mainstem bronchi)	X	X	X
Lymph node (mesenteric and mediastinal)		X	X
Mammary glands (with adjacent skin)		X	X
Nasopharynx		X	
Ovaries (with oviducts)	X	X	X
Prostate		X	X
Seminal vesicles		X	X
Small intestine (duodenum, ileum and Jejunum)		X	X
Spinal cord (cervical, thoracic and lumbar)		X	X
Spleen	X	X	X
Stomach		X	X
Testes	X	X	X
Thymus	X	X	X
Thyroid with parathyroids		X	X
Tibial nerve		X	X
Trachea		X	X
Urinary bladder		X	X
Uterus with vagina	X	X	X
All macroscopic lesions and tissue masses		X	X

[a]Qualitative examination (no differential count).

[b]Bone marrow smears were prepared but not examined.

Preservatives

All tissues - 10% neutral buffered formalin (NBF).
Testes and epididymides were placed in Modified Davidson's solution for at least 24 hours and then retained in NBF. Lungs and urinary bladder were infused with NBF for optimal preservation.

Smear preparations of the marrow from the rib were air dried and fixed in absolute methanol.

Processing

After fixation, the tissues and organs from Groups 1 and 4 main study animals were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides and stained with hematoxylin and eosin.

2.16.7. MACROSCOPIC POSTMORTEM EXAMINATION - F_1 PUPS

Macroscopic postmortem examinations (internal and external) were performed on all F_1 pups found dead during lactation.

All F_1 pups found dead at birth were initially identified as stillborn. Unless prevented by an extreme autolytic or cannibalized condition, a lung floatation test was used to reclassify pups as stillborn or alive but found dead. Pups that could not be tested remained classified as stillborn.

Macroscopic postmortem examinations (external only) were performed on all F_1 pups on lactation day 4 or 5 for pups surviving to that interval. Unusual observations, including gross abnormalities and the absence of milk in the stomach, were noted and then the carcasses discarded.

2.17. STATISTICAL ANALYSIS

2.17.1. CONTINUOUS DATA

The following parameters were analyzed statistically:

Body weights
Body weight changes
Feed consumption values
Rectal temperature
Grip Strength measurements
Hematology
Coagulation
Clinical Chemistry
Gestation length
Corpora lutea and implantation sites, pre and post implantation loss
F_1 pup weights (each weighing interval during lactation)
Number of pups (F_1 litters) per pregnant female rats
Number of male and females pups
Pup weight distinguished by sex and as a composite for both sexes (litter as experimental unit)
Organ weights
Organ weight to body weight ratios
Organ weight to brain weight ratios

Method of Analysis

Mean values of all exposure groups were compared to the mean value for the control group at each time interval.

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 FOB and clinical pathology parameters, if the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. All other 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; Dunlap and Duffy, 1975). If significant differences among the means were indicated, additional tests were used to determine which means were significantly

different from the control: Dunnett's (Dunlap et al., 1981; 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.

Exceptions

Statistical evaluations were not performed when the standard deviation for the control group was 0.

When 75% of the values for a clinical pathology parameter were the same, Fisher's Exact Test (Fisher, 1973) was performed followed by Mantel's test (Mantel, 1963).

Motor Activity Counts

The data was 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. Analyses were conducted by CATO Research, 200 Westpark Corporate Center, 4364 South Alston Avenue, Durham, NC 27713-2280. The testing facility was responsible for the GLP compliance of this subcontractor.

2.17.2. INCIDENCE DATA

The following parameters were analyzed statistically:

Mortality rate
Mating indices, pregnancy rates, male fertility indices
Litter survival indices
Gestation indices
Incidence of dams with no viable pups
Mean pup survival indices (lactation days 0 and 4)

Incidence Data Analysis

A Fisher Exact Test with Bonferonni correction was performed to identify differences between the control and treatment groups (Siegel, 1956). All statistical tests were conducted at the 5% and 1%, two-sided risk levels.

2.18. DATA STORAGE

All raw data, preserved specimens and retained samples, as well as the original study protocol (and any amendments) and the original final report are to be maintained in the archives of the testing facility (including those generated by the statistical subcontractor) upon completion of the study. The sponsor will determine the final disposition of these materials.

2.19. REGULATORY REFERENCES

2.19.1. TEST GUIDELINE

This study complied with the Organization for Economic Cooperation and Development (March 22, 1996). OECD Guidelines for Testing of Chemicals; OECD Guideline 422: Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, pp. 1-14 and US EPA OPPTS Health Effects Test Guidelines 870.3650, Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, July 2000.

2.19.2. GOOD LABORATORY PRACTICES

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

2.19.3. ANIMAL WELFARE ACT COMPLIANCE

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.

2.20. PROTOCOL DEVIATIONS

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

1. Due to snowfall and the absence of staff on study day 31 (15 January 2004), the following protocol deviation occurred:

   a) Necropsy on all main study animals could not be completed as scheduled on study days 30 and 31. Instead, necropsy was performed on the first three animals in each sex as per protocol on study day 31 and the rest performed the next day on study day 32.

   b) All remaining main study animals were fasted overnight prior to blood sampling procedures on study day 31. However, since not all animals could be sacrificed on study day 31, these animals were provided with feeders for the maximum period possible during study day 31, which was then removed and they were fasted prior to their sacrifice on study day 32. The following animals were euthanized and postmortem examination performed on study day 32. The following animals did not receive an exposure on the day before their sacrifice as required by protocol because further inhalation exposure would result in excessive fasting period: Males - 1040, 1041, 1042, 2040, 2041,

2042, 3040, 3041, 3042, 4040, 4041, 4042. Females - 1540, 1541, 1542, 2540, 2541, 2542, 3540, 3541, 3542, 4540, 4541, 4542.

2. Due to a labeling error, the testes and epididymides for animal nos. 2032, 3034 and 4032 were not clearly labeled; therefore, the tissues could not be identified when processed for histopathology, but all tissues were determined to be within normal limits.

3. Due to technician error, the in-chamber observations were not performed on study day 32.

4. Due to an inadequate number of prosectors because of snow on study day 44 (28 January 2004), the lactation Day 4 dams and litters (animal nos. 1548, 1550, 1554, 2546, 2549, 3552, 3553, 3554, 4547 and 4548) and the gestation day 26 (animal no. 3551) were not sacrificed as scheduled. The dams and litters were sacrificed on lactation day 5 and the female that did not deliver was sacrificed on gestation day 27.

5. Due to technician error, the organs were weighed for the satellite females that did not deliver pups.

6. Examination of external surface, orifices, all tissues, organs, cavities and carcass was not checked on the manually recorded necropsy record sheets for Animal Nos. 1545, 2553, 3546, 3547-1, 3547-2 and 3547-3.

3. RESULTS AND DISCUSSION

3.1. TEST SUBSTANCE ANALYSIS

(Appendix JJ)

Pre-study GC analysis of the test substance showed a purity of 99.84% for isobutane. This value compared closely to the purity of 99.51% for the analytical standard of isobutane and the 99.0% purity as guaranteed by the supplier of the test substance. Post-study GC analysis of the test substance showed a purity of 99.53% for isobutane. This value compared closely to the purity of 99.50% for the analytical standard of isobutane and the 99.0% pre-study purity demonstrating stability of the test substance over the period of this study.

3.2. CHAMBER MONITORING

(Appendix II)

Chamber distribution analyses showed that the test substance was evenly distributed within each chamber. Samples of air in the testing room showed no test substance before or during the study.

The target and mean (± standard deviation) analytical (IR) and nominal concentrations (based on gas flows) are summarized as follows:

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0 ± 0	0 ± 0
2	Isobutane	900	930.0 ± 27.8	882 ± 14
3	Isobutane	3000	3122 ± 83	2950 ± 0
4	Isobutane	9000	9148 ± 201	8730 ± 0

The analytically measured exposure levels of the airborne test substance were reasonably close, in the opinion of the study director, to the targeted exposure levels and nominal concentrations (both based on gas flows, as summarized above and defined in Appendix II, and based on weight of test substance consumed, as summarized and defined in Appendix II).

Chamber environmental conditions averaged 24°C temperature and 55% relative humidity.

Mean particle size distribution measurements for the exposures are summarized as follows:

Group	Test Substance	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m^3)
1	air control	2.532	2.127	2.42×10^{-3}
2	isobutane	2.486	2.022	2.23×10^{-3}
3	isobutane	1.999	2.027	2.12×10^{-3}
4	isobutane	1.541	2.031	1.52×10^{-3}

These results indicated that the atmospheres were gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

3.3. MAIN STUDY ANIMALS

3.3.1. MORTALITY

(Appendix A)

There was no effect of treatment on survival. All animals survived until the termination of the study.

3.3.2. PHYSICAL OBSERVATION DATA

(Table 1; Appendices B and II)

The test animals were generally unremarkable during the exposure periods (in-chamber) and during non-exposure periods. There was a low incidence of transient red nasal discharge between test days 8 and 29 in all groups including the control animals. These findings were only slightly more prevalent among test substance exposed animals.

3.3.3. BODY WEIGHTS

(Tables 2 and 3; Appendices C and D)

There were no exposure-related differences in body weights or weight changes in the test substance exposed animals as compared to the air control animals.

3.3.4. FEED CONSUMPTION

(Table 4; Appendix E)

There were no meaningful differences in feed consumption in the test substance exposed animals as compared to the air control animals. The statistical significance in increased feed consumption that occurred in females at 9000 ppm occurred pre-study.

3.3.5. NEUROBEHAVIORAL STUDIES

3.3.5.1. FUNCTIONAL OBSERVATIONAL BATTERY

(Table 5; Appendix F)

There was no exposure-related effect on functional observational battery parameters for either sex in this study.

3.3.5.2.MOTOR ACTIVITY

(Figures 1 and 2; Table 6; Appendix G)

There was no exposure-related effect on motor activity for either sex in this study.

3.3.6. CLINICAL PATHOLOGY

3.3.6.1. HEMATOLOGY

(Table 7; Appendix H)

There were no meaningful differences in hematology values in test substance exposed animals as compared to the air control animals at termination. Statistically significant increases in hemoglobin and mean corpuscular hemoglobin concentration in the 9000 ppm test substance exposed

males, decreases in platelets in 3000 and 9000 ppm test substance exposed males and decreases in monocytes in 3000 and 9000 ppm test substance exposed females were seen in exposure-related patterns but there were no accompanying changes in the other hematology parameters, nor were there any similar differences in the other sex. In isolation, these minor inter-group differences were not considered to indicate an effect of the exposures and were generally within the normal range of these values for a rat.

3.3.6.2. COAGULATION

(Table 8; Appendix I)

There were no exposure-related differences in coagulation values in test substance exposed animals as compared to the air control animals at termination.

3.3.6.3. CLINICAL CHEMISTRY

(Table 9; Appendix J)

There were no meaningful differences in clinical chemistry values in the test substance exposed animals as compared to the air control animals at termination. Statistically significant increases in sodium concentration in the 9000 ppm test substance exposed males and decreases in phosphorus concentration in all test substance exposed females were seen but the absolute differences were relatively small, were not in an exposure level related pattern and there were no similar differences in the other sex. In isolation, these minor inter-group differences were not considered to indicate an effect of the exposures.

3.3.7. ORGAN WEIGHTS

(Table 10; Appendix K)

There were no meaningful inter-group differences in organ weights in the test substance exposed animals as compared with air control animals. The 900 and 3000 ppm exposed males showed an

increase in spleen weights (absolute and/or relative to body or brain weight) but no similar difference was seen in the 9000 ppm exposed males or any of the exposed females. In isolation, this minor inter-group difference was not considered to indicate an effect of the exposures.

3.3.8. MACROSCOPIC POSTMORTEM EVALUATIONS

(Table 11; Appendix L)

All macroscopic findings occurred at a similar incidence in control and test substance treated animals or occurred sporadically, and thus were considered incidental findings and not related to the exposure to the test substance.

3.3.9. HISTOPATHOLOGICAL EVALUATIONS

(Table 12; Appendix L)

There were no exposure-related differences in microscopic postmortem evaluations in the 9000 ppm test substance exposed animals as compared to the air control animals. Changes were observed randomly in individual animals and were thus considered incidental findings and not related to the exposure to the test substance.

The testes were examined qualitatively with an awareness of the stages of the spermatogenic cycle to detect any disturbances in spermatogenesis, and with emphasis on the interstitial (Leydig) cells to detect any changes in cellular size or structure:

Testes - Stages of Spermatogenesis: No abnormalities were evident in test substance exposed or air control rats.
Testicular Interstitial Cells: No abnormalities were observed in testicular interstitial cells in test substance exposed or air control rats.

3.4. SATELLITE STUDY FEMALE ANIMALS

3.4.1. MORTALITY AND PREGNANCY

(Table 13; Appendix M)

There was no effect of treatment on survival. All animals survived until the termination of the study. All mated female animals (except one each in the 900 and 3000 ppm groups and three in the 9000 ppm group) were found pregnant and delivered live pups.

3.4.2. PHYSICAL OBSERVATION DATA – PREMATING, MATING, GESTATION AND LACTATION PERIODS

(Tables 14, 15 and 16; Appendices N, O and P)

The test animals were generally unremarkable during the exposure periods (in-chamber) and during the non-exposure periods. There were only the usual low and sporadic incidences of findings that are common to this strain of rat: predominantly localized patchy alopecia or staining, chromodacryorrhea and maloccluded incisors.

3.4.3. BODY WEIGHTS - PREMATING, MATING, GESTATION AND LACTATION PERIODS

(Tables 17 to 22; Appendices Q to V)

There were no exposure-related differences in body weights or weight changes in the test substance exposed animals as compared to the air control animals.

3.4.4. FEED CONSUMPTION – PREMATING, GESTATION AND LACTATION PERIODS

(Tables 23, 24, 25; Appendices W, X and Y)

There were no exposure-related differences in feed consumption in the test substance exposed animals as compared to the air control animals.

3.4.5. MATING, FERTILITY AND GESTATION PARAMETERS

(Tables 26 and 27; Appendices Z and AA)

Mating and gestation indices for both sexes were considered to have been unaffected by the exposures. All but one or two of the pairings in each of the test substance exposed groups mated at the first opportunity (first available estrus). There were 3 non-pregnant females in the 9000 ppm group, and the male and female fertility indices were reduced (75%), which was outside the historical control range of the testing facility (87.5%-100%, mean 93.7%; based on nine studies conducted between 2001 and 2002), therefore this finding was considered exposure related. There were no exposure-related inter-group differences for the delivery parameters, including the number of females successfully completing delivery, the duration of gestation and the proportion with live litters and/or with stillborn pups.

3.4.6. PARTURITION AND LITTER SURVIVAL DATA

(Table 27; Appendices BB and CC)

An exposure related and statistically significant increase in post-implantation loss (as defined by the difference between the number of live pups born and the number of implantations, including any stillborn pups) was seen for the 9000 ppm exposed female rats. Lung floatation tests were performed at macroscopic examinations on dead pups on either PND 0 or 1 to determine stillborn or found dead status, and deaths thereafter were all determined to be found dead. Otherwise, there were no exposure-related differences in any of the parturition parameters including pre-implantation loss (as defined by the difference between the number of corpora lutea and the number of implantations detected in the uterus), the total number of pups delivered, the number of pups dying, the viability

(4 day survival) index, the pup sex ratio and the number of live pups/litter, when compared to the air control group.

The lung floatation test was performed on tissue from pup 1549/07. This pup is listed as found dead on lactation day 1; however, the pup was found dead during the first observations after parturition was completed.

3.4.7. MACROSCOPIC POSTMORTEM EVALUATIONS

(Table 28; Appendix DD)

There were no exposure-related differences in the incidence of macroscopic postmortem findings in the test substance exposed animals as compared to the air control animals. There were sporadic incidences of findings in both the control and exposed animals (such as discolored lungs [2 of 12 in the control group and 1 of 11 in the 900 ppm group] and thymus [1 of 12 in the control group]) that were not considered related to treatment with the test substance.

3.4.8. ORGAN WEIGHTS

(Table 29; Appendix EE)

There were no exposure-related differences in organ weights in the test substance exposed animals as compared to the air control animals. A statistically significant increase in heart to brain weight ratio in 9000 ppm exposed females was seen but, in the absence of any macroscopic and microscopic abnormalities in the main study animals, this difference was considered to have been incidental.

3.5. PUP DATA

3.5.1. PHYSICAL OBSERVATION DATA

(Table 30; Appendix FF)

The pups were unremarkable during the early lactation period until termination at postnatal day 4.

3.5.2. BODY WEIGHT DATA

(Tables 31 and 32; Appendix GG)

There were no exposure-related differences in body weights or weight gains, up to postnatal day 4, in the pups from test substance exposed animals as compared to the pups from air control animals.

3.5.3. MACROSCOPIC POSTMORTEM EVALUATIONS

(Table 33; Appendix HH)

There were no exposure-related differences in the incidence of macroscopic postmortem evaluations in the pups from test substance exposed animals as compared to the pups from air control animals.

4. CONCLUSION

Exposure of male and female rats to target concentrations of 900, 3000 or 9000 ppm of isobutane by whole-body inhalation for 4-6 weeks resulted in no general systemic/neurotoxic effects. A no-observed-adverse effect level (NOAEL) of 9000 ppm was determined for all general systemic/neurotoxic endpoints in this study. There were decreases in male and female fertility and an exposure related increase in post-implantation loss in the 9000 ppm exposed female rats, therefore, the fertility and reproductive/developmental endpoints NOAEL was determined to be 3000 ppm. There was no effect on offspring survival, body weight and development up to postnatal day 4, therefore, the NOAEL for pup endpoints was 9000 ppm.

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CALCULATIONS

Female Mating Index:

no. of females with confirmed mating (sperm and/or vaginal plug) plus no. of pregnant females without evidence of mating (no sperm or vaginal plug)/no. of females placed with males

Female Fertility Index:

no. of females pregnant/no. of females confirmed mating or pregnancy for females without evidence of mating

Male Mating Index:

no. of males with confirmed mating with a female or pregnancy for females without evidence of mating/no. of males placed with females

Male Fertility Index:

no. of males mating and impregnating a female plus the no. of males with a pregnant female without evidence of mating/no. of males with confirmed mating plus no. of males with a pregnant female without evidence of mating

Gestation Index:

no. of females with liveborn/no. of females with confirmed pregnancy

Viability Index:

no. of pups alive Day 4/no. of liveborn pups

Live Birth Index:

total no. of liveborn pups/total no. of pups born

Pregnancy Index:

total no. of females pregnant/total no. of females mated

Pre-implantation Loss:

No. of corpora lutea – no. of implantation sites

Post-implantation Loss:

total no. of implantation sites – no. of live pups

	General Preface	

General Notes

Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

Key to Abbreviations

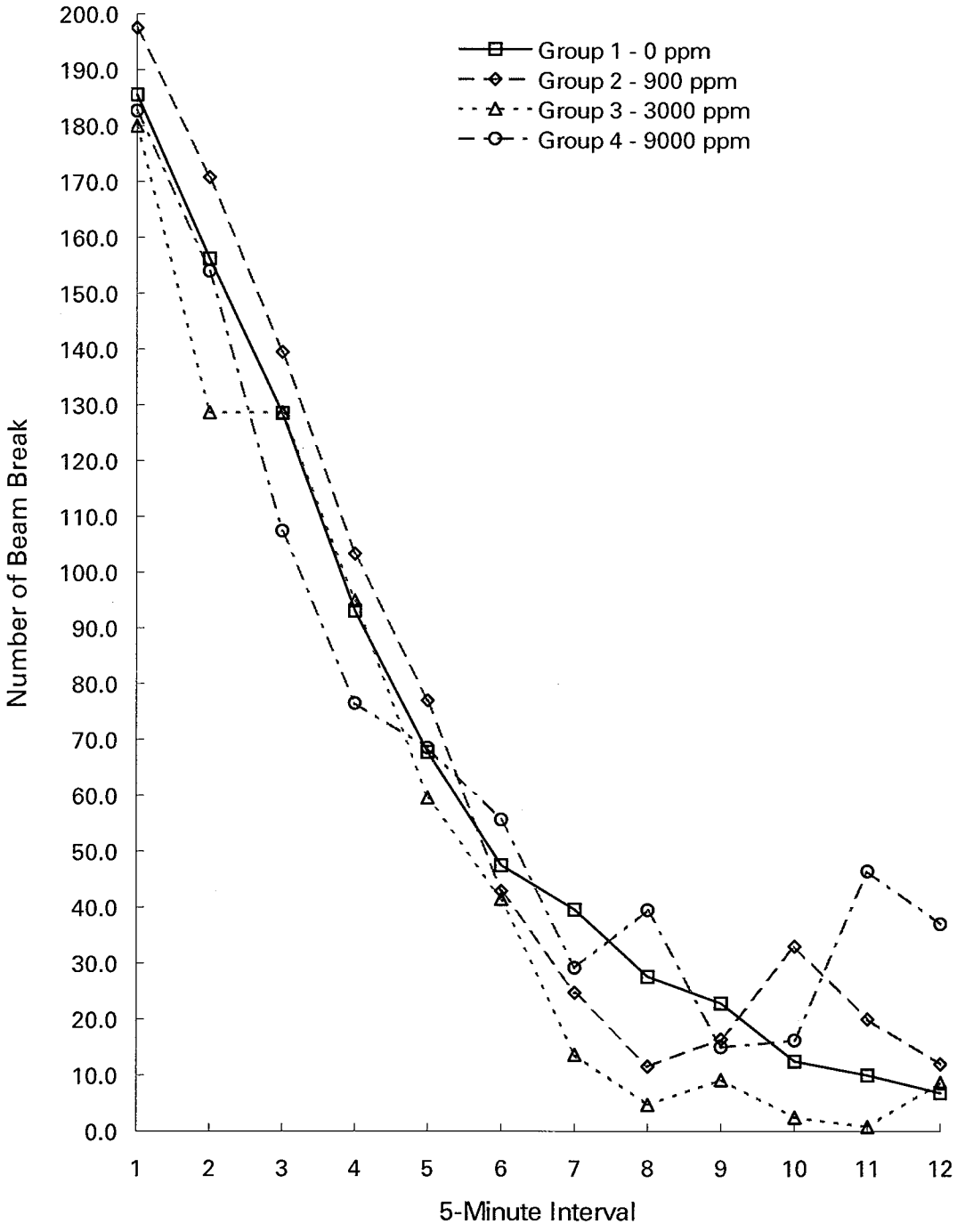
M	=	Male
F	=	Female
Gen.	=	General
PG	=	Pregnant
S	=	Satellite

Notes

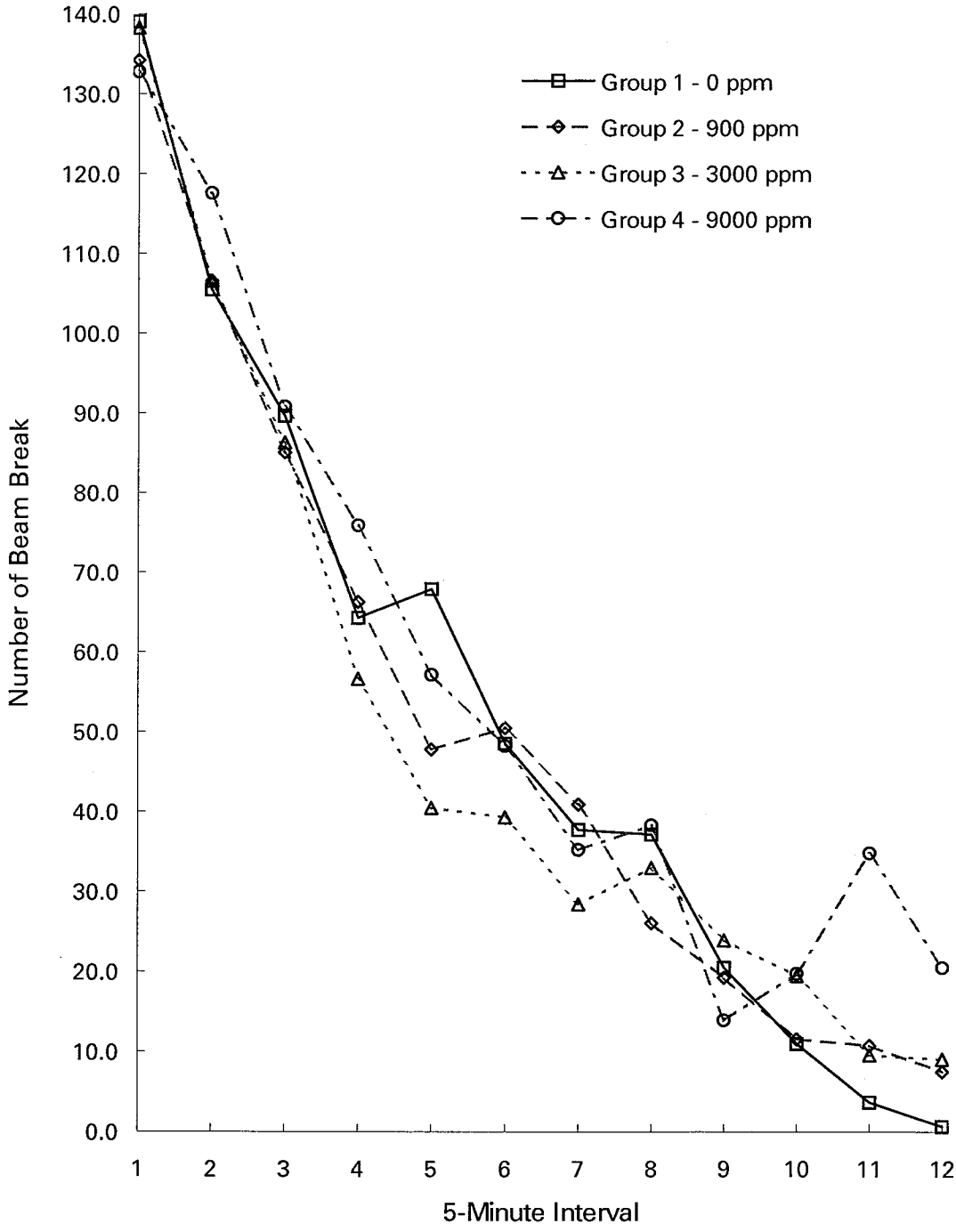
1. Days 0-14 – Pre-mating; Days 14-28 – Mating; After Day 28 – Post-mating

2. The study title was revised to "Isobutane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures" effective 16 November 2009. Only the cover page and summary of the report were revised to reflect this change since all other pages were computer generated based on the original study title.

Males	Mean Motor Activity 4th Week of Exposure	Figure 1



Females	Mean Motor Activity 4th Week of Exposure	Figure 2



	Summary of Clinical Observations Main Study Preface	Table 1

Number of animals examined represents the total number of animals observed and animals which were killed at a scheduled sacrifice for a given interval.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

TABLE 1

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

MALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY									
	GROUP#	-7	0	8	15	22	29	30	31	32	TOTAL
# OF ANIMALS EXAMINED	1	12	12	12	12	12	12	6	3	3	
	2	12	12	12	12	12	12	6	3	3	
	3	12	12	12	12	12	12	6	3	3	
	4	12	12	12	12	12	12	6	3	3	
Normal											
WITHIN NORMAL LIMITS	1	12	12	12	12	12	12	0	0	0	12
	2	12	12	11	8	8	7	0	0	0	12
	3	12	12	11	11	10	9	0	0	0	12
	4	12	12	12	12	9	8	0	0	0	12
Dead											
TERMINAL SACRIFICE	1	0	0	0	0	0	0	6	3	3	12
	2	0	0	0	0	0	0	6	3	3	12
	3	0	0	0	0	0	0	6	3	3	12
	4	0	0	0	0	0	0	6	3	3	12
Dermal-General											
ALOPECIA -	1	0	0	0	0	0	0	0	0	0	0
EXTREMITIES/SNOUT	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	1	1	0	0	0	1
NECROSIS{TIPOF TAIL}	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	1	1	0	0	0	1
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0
Ocular											
CHROMODACRYORRHEA -	1	0	0	0	0	0	0	0	0	0	0
BILATERAL	2	0	0	0	3	3	3	0	0	0	3
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0

TABLE 1

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

MALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY									
	GROUP#	-7	0	8	15	22	29	30	31	32	TOTAL
# OF ANIMALS EXAMINED	1	12	12	12	12	12	12	6	3	3	
	2	12	12	12	12	12	12	6	3	3	
	3	12	12	12	12	12	12	6	3	3	
	4	12	12	12	12	12	12	6	3	3	
Oral/Buccal											
INCISORS MALOCCLUDED	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	2	2	2	0	0	0	2
	3	0	0	1	1	0	0	0	0	0	1
	4	0	0	0	0	0	0	0	0	0	0
NASAL DISCHARGE - RED	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	1	1	0	1	0	0	0	2
	3	0	0	0	0	1	2	0	0	0	2
	4	0	0	0	0	2	3	0	0	0	4
INCISORS BROKEN/MISSING	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	1	1	0	0	0	1
	4	0	0	0	0	0	0	0	0	0	0

TABLE 1

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY									
	GROUP#	-7	0	8	15	22	29	30	31	32	TOTAL
# OF ANIMALS EXAMINED	1	12	12	12	12	12	12	6	3	3	
	2	12	12	12	12	12	12	6	3	3	
	3	12	12	12	12	12	12	6	3	3	
	4	12	12	12	12	12	12	6	3	3	
Normal											
WITHIN NORMAL LIMITS	1	12	12	12	12	11	9	0	0	0	12
	2	12	12	12	12	12	12	0	0	0	12
	3	12	12	11	11	11	11	0	0	0	12
	4	12	12	10	10	10	9	0	0	0	12
Dead											
TERMINAL SACRIFICE	1	0	0	0	0	0	0	6	3	3	12
	2	0	0	0	0	0	0	6	3	3	12
	3	0	0	0	0	0	0	6	3	3	12
	4	0	0	0	0	0	0	6	3	3	12
Dermal-General											
ALOPECIA - EXTREMITIES/SNOUT	1	0	0	0	0	1	1	0	0	0	1
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	1	1	1	1	0	0	0	1
	4	0	0	0	0	0	0	0	0	0	0
ALOPECIA - GENERAL	1	0	0	0	0	0	1	0	0	0	1
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	1	1	0	0	0	1
SCABS	1	0	0	0	0	0	1	0	0	0	1
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0

TABLE 1

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY									
	GROUP#	-7	0	8	15	22	29	30	31	32	TOTAL
# OF ANIMALS EXAMINED	1	12	12	12	12	12	12	6	3	3	
	2	12	12	12	12	12	12	6	3	3	
	3	12	12	12	12	12	12	6	3	3	
	4	12	12	12	12	12	12	6	3	3	
Ocular											
CHROMODACRYORRHEA - UNILATERAL	1	0	0	0	0	0	1	0	0	0	1
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0
Oral/Buccal											
INCISORS MALOCCLUDED	1	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	1	1	1	1	0	0	0	1
NASAL DISCHARGE - RED	1	0	0	0	0	0	1	0	0	0	1
	2	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0
	4	0	0	1	1	0	1	0	0	0	2

TABLE 2

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

MALES — MEAN BODY WEIGHT VALUES (GRAMS)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY -7	MEAN	212	212	210	211
	S.D.	9.6	9.0	10.7	9.3
	N	12	12	12	12
DAY 0	MEAN	277	282	273	275
	S.D.	13.9	10.3	12.9	12.5
	N	12	12	12	12
DAY 7	MEAN	318	322	309	312
	S.D.	19.5	14.6	15.2	22.0
	N	12	12	12	12
DAY 14	MEAN	352	349	345	345
	S.D.	25.7	16.9	17.0	27.4
	N	12	12	12	12
DAY 21	MEAN	387	386	377	374
	S.D.	28.4	19.3	22.4	31.0
	N	12	12	12	12
DAY 28	MEAN	408	411	400	398
	S.D.	31.1	24.5	24.0	35.2
	N	12	12	12	12

No statistically significant differences

TABLE 2

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN BODY WEIGHT VALUES (GRAMS)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY -7	MEAN	168	168	168	167
	S.D.	7.2	6.9	7.3	7.9
	N	12	12	12	12
DAY 0	MEAN	193	197	195	195
	S.D.	8.9	11.4	8.2	11.0
	N	12	12	12	12
DAY 7	MEAN	211	212	212	209
	S.D.	8.5	12.3	8.7	12.9
	N	12	12	12	12
DAY 14	MEAN	230	231	228	226
	S.D.	10.1	14.6	12.0	16.9
	N	12	12	12	12
DAY 21	MEAN	242	246	242	241
	S.D.	10.7	14.4	15.7	16.3
	N	12	12	12	12
DAY 28	MEAN	251	256	251	254
	S.D.	15.8	17.8	15.8	19.5
	N	12	12	12	12

No statistically significant differences

TABLE 3

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

MALES — MEAN BODY WEIGHT GAIN (GRAMS)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY -7 TO 0	MEAN	66	70	63	64
	S.D.	5.4	5.6	6.0	8.2
	N	12	12	12	12
DAY 0 TO 7	MEAN	40	40	36	37
	S.D.	7.8	7.5	8.5	10.0
	N	12	12	12	12
DAY 7 TO 14	MEAN	34	27	37	33
	S.D.	7.7	14.2	8.0	7.8
	N	12	12	12	12
DAY 14 TO 21	MEAN	35	37	32	29
	S.D.	5.9	11.2	7.7	6.2
	N	12	12	12	12
DAY 21 TO 28	MEAN	21	25	23	25
	S.D.	8.4	11.5	8.0	8.3
	N	12	12	12	12
DAY 0 TO 28	MEAN	130	129	127	124
	S.D.	21.9	21.4	21.9	23.5
	N	12	12	12	12

No statistically significant differences

TABLE 3

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN BODY WEIGHT GAIN (GRAMS)

		DOSE GROUP	1	2	3	4
		DOSE LEVEL (PPM)	0	900	3000	9000
DAY	-7 TO 0	MEAN	26	29	27	27
		S.D.	7.6	5.6	5.9	6.0
		N	12	12	12	12
DAY	0 TO 7	MEAN	18	15	17	15
		S.D.	5.4	3.3	5.7	6.2
		N	12	12	12	12
DAY	7 TO 14	MEAN	19	19	16	17
		S.D.	6.6	7.9	5.4	7.6
		N	12	12	12	12
DAY	14 TO 21	MEAN	12	15	14	15
		S.D.	4.5	5.6	6.9	4.3
		N	12	12	12	12
DAY	21 TO 28	MEAN	9	9	9	13
		S.D.	12.6	4.5	7.6	8.4
		N	12	12	12	12
DAY	0 TO 28	MEAN	57	59	56	59
		S.D.	15.2	11.4	11.0	12.7
		N	12	12	12	12

No statistically significant differences

TABLE 4

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

MALES — MEAN FEED CONSUMPTION (GRAMS/KG/DAY)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0	MEAN	106	107	105	107
	S.D.	3.0	4.4	4.8	4.7
	N	12	12	12	11
DAY 7	MEAN	87	88	85	87
	S.D.	2.9	3.4	6.0	4.4
	N	12	12	12	12
DAY 14	MEAN	73	73	73	73
	S.D.	2.9	4.2	4.1	3.5
	N	12	12	12	12

No statistically significant differences

TABLE 4

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN FEED CONSUMPTION (GRAMS/KG/DAY)

		DOSE GROUP	1	2	3	4
		DOSE LEVEL (PPM)	0	900	3000	9000
DAY	0	MEAN	95	98	100	106**
		S.D.	4.6	5.9	5.8	8.0
		N	10	9	10	11
DAY	7	MEAN	85	87	85	88
		S.D.	4.0	4.8	5.1	4.0
		N	12	11	12	12
DAY	14	MEAN	81	83	82	83
		S.D.	2.6	6.0	3.8	4.1
		N	12	11	12	12
DAY	21	MEAN	75	74	76	78
		S.D.	4.0	6.3	4.3	3.4
		N	12	11	11	12
DAY	28	MEAN	69	71	72	72
		S.D.	5.1	5.7	4.5	3.9
		N	12	11	12	12

Statistical key: ** = p<0.01

Males	Summary of Functional Observational Battery Evaluations Main Study 4th Week of Exposure	Table 5

Exposure Level (ppm):		Group 1 0	Group 2 900	Group 3 3000	Group 4 9000
Forelimb Grip Strength (grams of force)[1]					
	Mean	995.4	1045.6	1035.6	1015.0
	S.D.	138.2	167.7	200.2	135.5
	N	12	12	12	12
Hindlimb Grip Strength (grams of force)[1]					
	Mean	788.1	739.6	790.2	770.8
	S.D.	104.7	73.8	85.0	88.0
	N	12	12	12	12
Rectal Temperature (°C)					
	Mean	37.2	36.8	38.0	37.7
	S.D.	1.7	1.2	1.2	1.2
	N	12	12	12	12
Reflex Assessments					
Number of Animals Examined		12	12	12	12
Audition Assessment					
Normal		12	12	12	12
No Reaction		0	0	0	0
Exaggerated, Jumps, Flips, Bites		0	0	0	0
Pain Perception					
Normal		12	11	12	10
No Reaction		0	1	0	1
Increased Pain		0	0	0	1

[1] The means of Trials 1 and 2 were calculated and statistically evaluated.
*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	Summary of Functional Observational Battery Evaluations Main Study 4th Week of Exposure	Table 5

Exposure Level (ppm):		Group 1 0	Group 2 900	Group 3 3000	Group 4 9000
Forelimb Grip Strength (grams of force)[1]					
	Mean	837.3	820.8	780.4	852.5
	S.D.	114.7	143.1	147.6	84.3
	N	12	12	12	12
Hindlimb Grip Strength (grams of force)[1]					
	Mean	684.2	689.6	666.0	724.4
	S.D.	100.5	78.8	94.6	100.7
	N	12	12	12	12
Rectal Temperature (°C)					
	Mean	38.3	38.2	38.3	38.0
	S.D.	1.1	0.7	0.8	1.4
	N	12	12	12	12
Reflex Assessments					
Number of Animals Examined		12	12	12	12
Audition Assessment					
Normal		12	12	12	12
No Reaction		0	0	0	0
Exaggerated, Jumps, Flips, Bites		0	0	0	0
Pain Perception					
Normal		11	12	12	12
No Reaction		0	0	0	0
Increased Pain		1	0	0	0

[1] The means of Trials 1 and 2 were calculated and statistically evaluated.
*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.

	Mean Motor Activity Values Main Study 4th Week of Exposure	Table 6

Overview

The following is a brief summary of the statistical analysis of the motor activity data for Study 03-4244. Main study male and female rats were exposed to the test substance once daily (six hours/day), seven days/week for a minimum of 28 days; male rats were exposed for at least 2 weeks prior to mating. Inhalation exposure levels to the test substance, Isobutane, were 0 (air control), 900, 3000 and 9000 ppm. Motor activity data were collected for twelve rats/sex/group in the 4th week of exposure. Motor activity data were analyzed using split-plot repeated measures analysis of variance, comparing active-treatment groups with the control.

Methods

Motor activity counts (the number of beam breaks in an automated Photobeam Activity System) were collected in twelve consecutive five-minute intervals during the 4th week of exposure. The details of the experimental procedures for motor activity are given in the study protocol.

Motor activity data were analyzed using split-plot repeated measures analysis of variance (ANOVA) with model terms for group, animal within group, interval and group by interval interaction. If the group by interval interaction was statistically significant, 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 with respect to 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. No investigation of model fit was requested or performed. 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.

Results

The analysis results for motor activity data are summarized in Table 6-1. The parallel hypothesis, as indicated by no significant group by interval interaction, was accepted for males, females, and combined sexes. When the level hypothesis was tested for the males, females, and combined sexes, no significant difference was found between different exposure groups. No pairwise comparison of exposure groups was required.

	Mean Motor Activity Values Main Study 4th Week of Exposure	Table 6

Table 6-1. Summary of Statistical Results (p-values) for Motor Activity Data

Period	Sex	Parallel Hypothesis (p-value)	Level Hypothesis (p-value)	Significant Pairwise Results
4th Week of Exposure	Male	0.6508	0.6114	NA
	Female	0.9779	0.6462	NA
	Combined	0.6586	0.4866	NA

NA: not applicable

Discussion

There were no apparent exposure-related effects on motor activity for either sex in this study.

Analysis Performed By:

[redacted]

Cato Research Ltd.

26 April 2006
Date

Males	Mean Motor Activity Values[a] Main Study 4th Week of Exposure	Table 6

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group 1 – 0 ppm												
Mean	185.6	156.3	128.5	93.1	67.8	47.5	39.6	27.6	22.8	12.5	10.0	6.8
SD	33.15	46.14	36.67	51.37	54.24	52.52	55.49	42.29	47.68	36.85	27.32	17.90
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 2 – 900 ppm												
Mean	197.5	170.8	139.5	103.3	77.0	42.9	24.8	11.6	16.4	33.0	20.0	12.0
SD	55.73	44.81	67.84	67.07	88.89	65.72	56.35	22.83	40.37	78.34	43.13	29.59
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 3 – 3000 ppm												
Mean	180.0	128.7	128.7	94.9	59.6	41.5	13.7	4.8	9.2	2.5	0.8	8.7
SD	52.70	58.30	54.96	56.12	64.49	53.34	26.97	14.01	19.71	7.74	2.33	13.32
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 4 – 9000 ppm												
Mean	182.7	154.0	107.4	76.5	68.5	55.7	29.2	39.5	15.0	16.3	46.4	37.0
SD	40.09	38.53	44.59	53.05	59.91	57.25	41.51	50.58	33.98	43.02	81.98	53.32
N	12	12	12	12	12	12	12	12	12	12	12	12

[a]Number of beam breaks per interval.

Females	Mean Motor Activity Values[a] Main Study 4th Week of Exposure	Table 6

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group 1 – 0 ppm												
Mean	139.0	105.5	89.7	64.3	67.9	48.6	37.8	37.2	20.5	11.0	3.7	0.7
SD	26.07	26.18	52.90	37.08	41.24	39.25	47.45	44.33	32.44	35.00	6.29	1.78
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 2 – 900 ppm												
Mean	134.2	106.6	85.1	66.3	47.8	50.5	40.9	26.1	19.3	11.6	10.8	7.5
SD	24.42	24.49	24.28	29.31	39.73	40.20	43.21	38.40	31.05	22.89	19.62	16.77
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 3 – 3000 ppm												
Mean	138.3	106.6	86.3	56.7	40.5	39.3	28.4	33.0	23.9	19.5	9.6	9.1
SD	39.70	24.73	22.58	22.61	36.07	45.52	29.30	34.37	42.42	34.92	25.35	13.34
N	12	12	12	12	12	12	12	12	12	12	12	12
Group 4 – 9000 ppm												
Mean	132.8	117.6	90.8	75.9	57.2	48.3	35.3	38.3	13.9	19.8	34.8	20.5
SD	35.50	27.28	30.08	32.90	34.09	35.55	36.35	46.78	24.96	32.52	50.13	33.17
N	12	12	12	12	12	12	12	12	12	12	12	12

[a]Number of beam breaks per interval.

	Mean Hematology Values Main Study Preface	Table 7

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

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. 03-4244
Table 7 - Main Study
Mean Hematology Values - Termination

Group		HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
1M										
0 ppm	Mean	15.6	46.4	8.18	197.9	898	56.7	19.1	33.7	12.25
	SD	0.57	2.06	0.441	39.26	214.3	1.75	0.67	0.46	2.712
	n	12	12	12	12	12	12	12	12	12
2M										
900 ppm	Mean	15.6	46.2	8.09	207.0	770	57.1	19.2	33.6	*15.07
	SD	0.56	1.70	0.391	78.37	162.9	1.77	0.62	0.33	2.962
	n	12	12	12	12	12	12	12	12	12
3M										
3000 ppm	Mean	15.9	46.9	8.08	187.7	*721	58.1	19.8	34.0	12.11
	SD	0.68	2.58	0.550	31.48	103.3	1.62	0.74	0.61	2.159
	n	12	12	12	12	12	12	12	12	12
4M										
9000 ppm	Mean	*16.1	47.2	8.23	189.3	*767	57.4	19.6	*34.2	12.85
	SD	0.55	1.73	0.382	21.43	161.1	1.23	0.59	0.47	2.202
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 7 - Main Study
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	1.87	9.81	0.23	0.12	0.15	0.07
	SD	0.525	2.502	0.090	0.056	0.061	0.022
	n	12	12	12	12	12	12
2M							
900 ppm	Mean	2.33	12.00	0.30	0.15	0.18	0.11
	SD	0.708	2.756	0.070	0.064	0.062	0.090
	n	12	12	12	12	12	12
3M							
3000 ppm	Mean	1.84	9.71	0.22	0.13	0.13	0.07
	SD	0.457	2.144	0.058	0.075	0.038	0.026
	n	12	12	12	12	12	12
4M							
9000 ppm	Mean	1.88	10.44	0.20	0.12	0.14	0.08
	SD	0.584	2.023	0.080	0.065	0.038	0.034
	n	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 7 - Main Study
Mean Hematology Values - Termination

Group		HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
1F										
0 ppm	Mean	15.5	44.3	7.99	187.3	734	55.4	19.4	35.1	11.41
	SD	1.05	2.70	0.431	65.61	210.8	1.20	0.45	0.54	1.914
	n	12	12	12	12	12	12	12	12	12
2F										
900 ppm	Mean	15.7	44.8	8.00	199.4	768	56.0	19.6	35.0	12.32
	SD	0.48	1.60	0.319	38.45	73.2	1.81	0.47	0.79	2.407
	n	12	12	12	12	12	12	12	12	12
3F										
3000 ppm	Mean	15.6	44.5	7.96	187.4	755	55.9	19.6	35.1	10.42
	SD	0.55	1.57	0.312	41.75	153.2	0.83	0.44	0.67	2.282
	n	12	12	12	12	12	12	12	12	12
4F										
9000 ppm	Mean	15.7	44.9	8.16	187.9	724	55.0	19.2	34.9	11.35
	SD	0.51	1.07	0.201	29.92	163.9	1.24	0.48	0.69	3.351
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 7 - Main Study
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	2.42	8.31	0.25	0.25	0.12	0.06
	SD	1.275	1.949	0.116	0.196	0.074	0.038
	n	12	12	12	12	12	12
2F							
900 ppm	Mean	2.24	9.47	0.22	0.20	0.13	0.07
	SD	1.125	1.635	0.079	0.115	0.041	0.018
	n	12	12	12	12	12	12
3F							
3000 ppm	Mean	1.50	8.36	0.17*	0.23	0.10	0.06
	SD	0.335	1.981	0.070	0.103	0.042	0.033
	n	12	12	12	12	12	12
4F							
9000 ppm	Mean	1.73	9.05	0.17*	0.21	0.13	0.07
	SD	0.679	2.845	0.070	0.130	0.064	0.035
	n	12	12	12	12	12	12

	Mean Coagulation Values Main Study Preface	Table 8

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

Huntingdon Life Sciences Study No. 03-4244
Table 8 - Main Study
Mean Coagulation Values - Termination

Group		PT	APTT
		Seconds	Seconds
1M			
0 ppm	Mean	14.2	22.6
	SD	1.20	2.10
	n	12	12
2M			
900 ppm	Mean	14.0	23.3
	SD	0.97	2.39
	n	12	12
3M			
3000 ppm	Mean	13.5	22.4
	SD	0.90	2.04
	n	12	12
4M			
9000 ppm	Mean	13.4	22.7
	SD	1.33	1.43
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 8 - Main Study
Mean Coagulation Values - Termination

Group		PT	APTT
		Seconds	Seconds
1F			
0 ppm	Mean	11.9	22.0
	SD	0.46	1.88
	n	12	12
2F			
900 ppm	Mean	12.0	21.8
	SD	0.62	1.18
	n	12	12
3F			
3000 ppm	Mean	11.8	21.7
	SD	0.61	1.49
	n	12	12
4F			
9000 ppm	Mean	11.8	21.5
	SD	0.53	1.52
	n	12	12

	Mean Clinical Chemistry Values Main Study Preface	Table 9

Abbreviation	Parameter	Reporting Units
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
ALKP	Alkaline Phosphatase	U/L
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
GLU	Fasting Glucose	mg/dL
CHOL	Total 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
Na^+	Sodium	mEq/L
K^+	Potassium	mEq/L
Cl^-	Chloride	mEq/L
Ca^{++}	Calcium	mg/dL
PHOS	Inorganic Phosphorus	mg/dL
GGT	Gamma-Glutamyl Transpeptidase	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. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
1M										
0 ppm	Mean	79	38	157	12.5	0.3	100	56	49	6.5
	SD	11.9	6.9	28.3	1.70	0.00	7.4	8.8	10.8	0.21
	n	12	12	12	12	12	12	12	12	12
2M										
900 ppm	Mean	82	42	140	12.3	0.3	105	63	66	6.5
	SD	12.7	16.2	18.7	1.75	0.05	15.7	8.8	26.8	0.31
	n	12	12	12	12	12	12	12	12	12
3M										
3000 ppm	Mean	76	37	151	12.7	0.3	98	58	54	6.5
	SD	5.3	4.1	39.4	0.89	0.05	4.9	11.1	16.5	0.28
	n	12	12	12	12	12	12	12	12	12
4M										
9000 ppm	Mean	79	40	172	12.8	0.3	99	58	45	6.4
	SD	7.8	6.8	43.3	1.58	0.05	4.1	12.7	12.1	0.34
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1M										
0 ppm	Mean	4.4	2.2	2.0	0.12	147	6.0	102	11.0	9.1
	SD	0.11	0.21	0.22	0.015	1.6	0.37	1.6	0.19	0.80
	n	12	12	12	12	12	12	12	12	12
2M										
900 ppm	Mean	4.4	2.2	2.1	0.13	147	5.9	102	11.0	9.0
	SD	0.16	0.21	0.19	0.024	1.6	0.43	2.5	0.27	0.77
	n	12	12	12	12	12	12	12	12	12
3M										
3000 ppm	Mean	4.4	2.1	2.1	0.13	148	5.9	102	11.0	9.0
	SD	0.11	0.23	0.22	0.022	1.4	0.28	1.9	0.32	0.51
	n	12	12	12	12	12	12	12	12	12
4M										
9000 ppm	Mean	4.4	2.0	2.2	0.12	149 *	6.0	102	10.9	8.8
	SD	0.13	0.26	0.27	0.017	1.5	0.24	2.6	0.24	0.53
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		GGT
		U/L
1M		
0 ppm	Mean	0
	SD	0.0
	n	12
2M		
900 ppm	Mean	0
	SD	0.0
	n	12
3M		
3000 ppm	Mean	0
	SD	0.0
	n	12
4M		
9000 ppm	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
1F										
0 ppm	Mean	96	38	117	18.3	0.5	97	63	65	7.0
	SD	60.1	12.3	28.4	13.78	0.25	8.0	9.3	120.4	0.61
	n	12	12	12	12	12	12	12	12	12
2F										
900 ppm	Mean	73	31	106	13.8	0.4	100	63	31	7.1
	SD	8.6	3.4	25.6	1.48	0.05	7.1	9.5	6.4	0.20
	n	12	12	12	12	12	12	12	12	12
3F										
3000 ppm	Mean	78	35	93	13.6	0.4	102	63	32	7.1
	SD	9.5	8.4	25.5	1.89	0.07	9.7	14.7	4.9	0.42
	n	12	12	12	12	12	12	12	12	12
4F										
9000 ppm	Mean	72	34	101	14.0	0.3	101	69	32	7.1
	SD	8.7	5.4	24.0	1.96	0.05	6.4	15.7	6.9	0.18
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1F										
0 ppm	Mean	4.7	2.3	2.1	0.15	148	5.7	103	11.3	9.0
	SD	0.73	0.36	0.50	0.032	1.9	0.60	2.7	0.57	1.54
	n	12	12	12	12	12	12	12	12	12
2F										
900 ppm	Mean	4.9	2.2	2.3	0.14	149	5.6	103	11.2	8.1*
	SD	0.19	0.15	0.21	0.016	2.0	0.32	2.7	0.37	0.50
	n	12	12	12	12	12	12	12	12	12
3F										
3000 ppm	Mean	5.0	2.1	2.4	0.15	148	5.6	104	11.2	7.8*
	SD	0.41	0.19	0.32	0.021	1.8	0.31	2.7	0.47	0.69
	n	12	12	12	12	12	12	12	12	12
4F										
9000 ppm	Mean	4.9	2.2	2.2	0.15	148	5.8	103	11.2	8.0*
	SD	0.19	0.20	0.27	0.024	1.9	0.41	2.6	0.27	0.62
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Table 9 - Main Study
Mean Clinical Chemistry Values - Termination

Group		GGT
		U/L
1F		
0 ppm	Mean	0
	SD	0.0
	n	12
2F		
900 ppm	Mean	0
	SD	0.0
	n	12
3F		
3000 ppm	Mean	0
	SD	0.0
	n	12
4F		
9000 ppm	Mean	0
	SD	0.0
	n	12

	Mean Organ Weights Main Study Preface	Table 10

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% Organ to Brain Weight Ratios 94

Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observation

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Note: Ovaries were weighed with oviducts.

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice - Main Study

Summary statistics for absolute organ weights (g)
Study number: 034244

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys	Liver
			M a l e A n i m a l s					
1								
M e a n:	380.1	0.0753	2.1202	0.6227	0.6323	1.2967	3.3975	12.0207
Standard deviation:	33.0	0.0150	0.0721	0.0775	0.0715	0.1320	0.2700	1.1024
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
M e a n:	385.8	0.0732	2.1283	0.6498	0.6420	1.3667	3.5078	13.1141
Standard deviation:	21.4	0.0143	0.1089	0.0875	0.0827	0.1412	0.3174	1.3603
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
M e a n:	373.8	0.0747	2.1078	0.6230	0.6272	1.3657	3.4834	12.1528
Standard deviation:	22.3	0.0123	0.1196	0.0433	0.0574	0.1065	0.3408	1.0248
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
M e a n:	371.4	0.0718	2.0779	0.6023	0.6254	1.3280	3.3786	12.1645
Standard deviation:	30.2	0.0096	0.0947	0.0502	0.0474	0.1555	0.3612	1.6131
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice - Main Study

Summary statistics for absolute organ weights (g)
Study number: 034244

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Group	Terminal Body wt. (g)	Lungs	Spleen	Testis Left	Testis Right	Thymus
			M a l e A n i m a l s			
1						
M e a n:	380.1	1.8272	0.6875	1.6352	1.6344	0.4763
Standard deviation:	33.0	0.2403	0.1111	0.1426	0.1460	0.1289
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
2						
M e a n:	385.8	2.0065	0.8450%	1.6452	1.6284	0.5197
Standard deviation:	21.4	0.2583	0.2140	0.1215	0.1155	0.1307
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
3						
M e a n:	373.8	1.9305	0.7609	1.6046	1.6109	0.4829
Standard deviation:	22.3	0.2279	0.0954	0.1681	0.1728	0.1347
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
4						
M e a n:	371.4	1.8943	0.7011	1.5593	1.5552	0.4992
Standard deviation:	30.2	0.4327	0.0782	0.0791	0.0725	0.0991
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Summary statistics for absolute organ weights (g)
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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
				Female Animals				
1								
Mean:	228.5	0.0799	1.9224	0.9087	2.5815	8.8007	1.4893	0.0703
Standard deviation:	17.7	0.0136	0.1184	0.0702	2.1663	2.7077	0.3673	0.0108
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	234.0	0.0775	1.9628	0.9048	2.0956	8.7429	1.3923	0.0680
Standard deviation:	13.1	0.0151	0.0707	0.0700	0.1624	0.8950	0.1521	0.0171
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
Mean:	229.9	0.0723	1.9459	0.8999	2.0470	8.0863	1.3565	0.0688
Standard deviation:	15.8	0.0111	0.0989	0.0708	0.1509	0.9510	0.1589	0.0072
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
Mean:	231.3	0.0783	1.9229	0.8912	2.0909	8.2062	1.4425	0.0719
Standard deviation:	18.5	0.0091	0.0705	0.0890	0.1708	1.0846	0.3544	0.0171
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Group	Terminal Body wt. (g)	Ovary Right	Spleen	Thymus	Uterus w/vagina
			Female Animals		
1					
Mean:	228.5	0.0722	0.5447	0.4283	0.7791
Standard deviation:	17.7	0.0131	0.1913	0.1115	0.1939
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
Mean:	234.0	0.0729	0.5936	0.4659	0.9094
Standard deviation:	13.1	0.0106	0.0673	0.0926	0.2166
Number of observ. :	(12)	(12)	(12)	(12)	(12)
3					
Mean:	229.9	0.0643	0.5119	0.4364	0.9528
Standard deviation:	15.8	0.0115	0.0631	0.0847	0.2995
Number of observ. :	(12)	(12)	(12)	(12)	(12)
4					
Mean:	231.3	0.0717	0.5082	0.4511	0.9122
Standard deviation:	18.5	0.0188	0.0735	0.1239	0.2351
Number of observ. :	(12)	(12)	(12)	(12)	(12)

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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

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Summary Statistics for % Organ to Body Weight
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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Right	Epididymis Left	Heart	Kidneys	Liver
				M a l e A n i m a l s				
1								
M e a n:	380.1	0.0199	0.5608	0.1643	0.1674	0.3420	0.8965	3.1711
Standard deviation:	33.0	0.0038	0.0412	0.0198	0.0232	0.0291	0.0666	0.2685
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
M e a n:	385.8	0.0190	0.5535	0.1686	0.1667	0.3544	0.9096	3.4021
Standard deviation:	21.4	0.0036	0.0475	0.0223	0.0226	0.0326	0.0696	0.3338
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
M e a n:	373.8	0.0200	0.5653	0.1671	0.1688	0.3654	0.9324	3.2517
Standard deviation:	22.3	0.0034	0.0401	0.0148	0.0233	0.0191	0.0806	0.2050
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
M e a n:	371.4	0.0194	0.5619	0.1630	0.1693	0.3579	0.9094	3.2664
Standard deviation:	30.2	0.0024	0.0390	0.0175	0.0170	0.0330	0.0584	0.2212
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Group	Terminal Body wt. (g)	Lungs	Spleen	Testis Left	Testis Right	Thymus
			Male Animals			
1						
Mean:	380.1	0.4805	0.1807	0.4330	0.4323	0.1241
Standard deviation:	33.0	0.0420	0.0231	0.0523	0.0481	0.0259
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
2						
Mean:	385.8	0.5194	0.2199	0.4273	0.4228	0.1343
Standard deviation:	21.4	0.0507	0.0607	0.0360	0.0331	0.0307
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
3						
Mean:	373.8	0.5164	0.2039%	0.4314	0.4330	0.1286
Standard deviation:	22.3	0.0514	0.0263	0.0581	0.0589	0.0328
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
4						
Mean:	371.4	0.5076	0.1888	0.4224	0.4211	0.1341
Standard deviation:	30.2	0.0877	0.0153	0.0398	0.0368	0.0219
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
				Female Animals				
1								
Mean:	228.5	0.0351	0.8461	0.3991	1.1132	3.8373	0.6492	0.0310
Standard deviation:	17.7	0.0058	0.0864	0.0343	0.8573	1.0197	0.1311	0.0055
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	234.0	0.0332	0.8406	0.3869	0.8965	3.7389	0.5941	0.0290
Standard deviation:	13.1	0.0065	0.0464	0.0264	0.0694	0.3602	0.0464	0.0071
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
Mean:	229.9	0.0315	0.8489	0.3921	0.8908	3.5150	0.5904	0.0300
Standard deviation:	15.8	0.0047	0.0542	0.0272	0.0370	0.3173	0.0619	0.0037
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
Mean:	231.3	0.0341	0.8360	0.3855	0.9058	3.5435	0.6291	0.0310
Standard deviation:	18.5	0.0056	0.0713	0.0249	0.0624	0.2902	0.1805	0.0064
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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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Group	Terminal Body wt. (g)	Ovary Right	Spleen	Thymus	Uterus w/vagina
			Female Animals		
1					
Mean:	228.5	0.0316	0.2359	0.1864	0.3411
Standard deviation:	17.7	0.0054	0.0709	0.0452	0.0817
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
Mean:	234.0	0.0312	0.2536	0.1990	0.3916
Standard deviation:	13.1	0.0050	0.0240	0.0370	0.1046
Number of observ. :	(12)	(12)	(12)	(12)	(12)
3					
Mean:	229.9	0.0280	0.2225	0.1909	0.4132
Standard deviation:	15.8	0.0053	0.0219	0.0425	0.1211
Number of observ. :	(12)	(12)	(12)	(12)	(12)
4					
Mean:	231.3	0.0309	0.2194	0.1943	0.3933
Standard deviation:	18.5	0.0071	0.0213	0.0474	0.0901
Number of observ. :	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys	Liver
			M a l e A n i m a l s					
1								
M e a n:	380.1	3.5551	100.0000	29.3875	29.8584	61.1880	160.1603	567.2712
Standard deviation:	33.0	0.6927	0.0000	3.6233	3.5462	6.1400	10.2940	52.1017
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
M e a n:	385.8	3.4320	100.0000	30.5822	30.2122	64.2020	165.0941	616.7012
Standard deviation:	21.4	0.6090	0.0000	4.2630	4.0579	5.6801	15.7050	59.1922
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
M e a n:	373.8	3.5594	100.0000	29.6912	29.8557	64.9656	165.6183	577.1867
Standard deviation:	22.3	0.6433	0.0000	3.2194	3.3189	6.1883	17.4361	45.2004
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
M e a n:	371.4	3.4588	100.0000	29.0357	30.1360	63.8891	162.5543	584.5827
Standard deviation:	30.2	0.4749	0.0000	2.7447	2.4538	6.6418	15.4723	64.6293
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Summary Statistics for % Organ to Brain Weight
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Group	Terminal Body wt. (g)	Lungs	Spleen	Testis Left	Testis Right	Thymus
			Male Animals			
1						
Mean:	380.1	86.1810	32.3909	77.2503	77.1870	22.3910
Standard deviation:	33.0	10.8774	4.8648	7.6532	7.5076	5.7090
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
2						
Mean:	385.8	94.4099	39.7507%	77.4114	76.6327	24.4156
Standard deviation:	21.4	12.1908	10.3031	6.0832	6.0033	5.9632
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
3						
Mean:	373.8	91.8336	36.1281	76.4094	76.6980	23.0714
Standard deviation:	22.3	11.9325	4.3305	9.6806	9.6844	7.0209
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)
4						
Mean:	371.4	90.8940	33.7762	75.1614	74.9395	23.9925
Standard deviation:	30.2	18.5110	3.7792	4.7253	4.0335	4.4450
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
			Female Animals					
1								
Mean:	228.5	4.1730	100.0000	47.4671	136.7384	462.8098	77.8425	3.6783
Standard deviation:	17.7	0.7686	0.0000	5.0901	122.8556	162.7199	21.1441	0.6653
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	234.0	3.9676	100.0000	46.1056	106.9606	446.0310	70.9102	3.4704
Standard deviation:	13.1	0.8723	0.0000	3.3331	10.0677	49.0315	7.1541	0.9035
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
3								
Mean:	229.9	3.7385	100.0000	46.3104	105.2403	415.4348	69.7293	3.5443
Standard deviation:	15.8	0.6949	0.0000	3.8486	6.5347	43.4347	7.8633	0.4234
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
4								
Mean:	231.3	4.0789	100.0000	46.3602	108.8175	426.8266	74.7529	3.7386
Standard deviation:	18.5	0.5393	0.0000	4.3149	8.7853	52.8588	16.4121	0.8439
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

*(+) = 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

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Summary Statistics for % Organ to Brain Weight
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Group	Terminal Body wt. (g)	Ovary Right	Spleen	Uterus w/vagina Thymus	
			F e m a l e A n i m a l s		
1					
M e a n:	228.5	3.7696	28.6632	22.4504	40.5562
Standard deviation:	17.7	0.7232	11.2424	6.3006	9.8753
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
M e a n:	234.0	3.7227	30.2513	23.7895	46.5125
Standard deviation:	13.1	0.5980	3.4144	4.9075	11.7309
Number of observ. :	(12)	(12)	(12)	(12)	(12)
3					
M e a n:	229.9	3.3180	26.3402	22.5770	48.9431
Standard deviation:	15.8	0.6630	3.2829	5.0553	15.2180
Number of observ. :	(12)	(12)	(12)	(12)	(12)
4					
M e a n:	231.3	3.7292	26.4098	23.4356	47.4969
Standard deviation:	18.5	0.9449	3.4466	6.2353	12.1707
Number of observ. :	(12)	(12)	(12)	(12)	(12)

*(+) = 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 Main Study Preface	Table 11

Key to Abbreviation

LN = Lymph Node

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

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	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	12	12	12	12	12	12	12	12
Within normal limits	9	10	11	9	9	11	11	10
Kidneys								
Enlarged	0	0	0	0	1	0	0	0
Irregular Shape	0	0	0	0	1	0	0	0
Discolored	0	0	0	0	1	0	0	0
Liver								
Enlarged	0	0	0	0	1	0	0	0
Lungs								
Discolored	2	1	1	3	0	1	1	0
Mediastinal LN								
Enlarged	0	0	0	0	1	0	0	0
Skin-protocol								
Hair Thin/Absent	0	0	0	0	0	0	0	1
Spleen								
Enlarged	0	0	0	0	1	0	0	0
Thymus								
Discolored	1	1	0	0	0	0	0	0
Uterus								
Distended	0	0	0	0	0	0	0	1
Lymph Node,other								
Enlarged	0	0	0	0	1	0	0	0
Skin (other)								
Scab	0	0	0	0	1	0	0	0
Extremity								
Hair Thin/Absent	0	0	0	0	1	0	0	0

	Incidence Summary of Microscopic Findings with Severity Levels Main Study Preface	Table 12

Key to Abbreviations

Ctls	=	Controls
LN	=	Lymph Node
Lymph/Retic Sys	=	Lymphoreticular System
M	=	Malignant
Mesentery/Perito	=	Mesentery/Peritoneal
N-	=	Metastatic
NAD	=	No abnormal diagnosis
No.	=	Number
Oviducts/Fallop	=	Oviducts/Fallopian Tubes
SC	=	Spinal Cord

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Adrenal Glands	Number examined:	12	0	0	12	12	0	0	12
EXTRACAPSULAR CORTICAL EPITHELIAL HYPERPLASIA									
	Nad>	11	0	0	12	12	0	0	12
	Slight>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
N-METASTATIC/INVASIVE NEOPLASM									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Brain	Number examined:	12	0	0	12	12	0	0	12
Cecum	Number examined:	12	0	0	12	12	0	0	12
Cervical SC	Number examined:	12	0	0	12	12	0	0	11
Colon	Number examined:	12	0	0	12	12	0	0	12
Duodenum	Number examined:	12	0	0	12	12	0	0	12
Epididymides	Number examined:	12	1	1	12				
MONONUCLEAR CELL AGGREGATES									
	Nad>	10	1	1	11				
	Minimal>	2	0	0	1				
.....	Total Incidence of Finding Observed:	2	0	0	1				
SEMINIFEROUS TUBULES: TUBULAR DILATATION									
	Nad>	12	1	1	11				
	Slight>	0	0	0	1				
.....	Total Incidence of Finding Observed:	0	0	0	1				

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1

Tissues With Diagnoses	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
	No. in group:	12	12	12	12	12	12	12	12
Extremity	Number examined:	0	0	0	0	1	0	0	0
HAIR FOLLICLES/SKIN, FOREPAW, RIGHT AND LEFT: ABSENT HAIR -SHAFT									
	Minimal>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	1	0	0	0
Femoral Marrow	Number examined:	12	0	0	11	12	0	0	12
Femur	Number examined:	12	0	0	11	12	0	0	12
Heart	Number examined:	12	0	0	12	12	0	0	12
MYOCARDIUM: ACUTE/SUBACUTE INFLAMMATION									
	Nad>	12	0	0	12	12	0	0	12
.....Total Incidence of Finding Observed:		0	0	0	0	0	0	0	0
MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	Nad>	9	0	0	5	7	0	0	8
	Minimal>	2	0	0	7	5	0	0	4
	Slight>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding Observed:		3	0	0	7	5	0	0	4
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding Observed:		0	0	0	0	1	0	0	0
Ileum	Number examined:	12	0	0	12	12	0	0	12
Jejunum	Number examined:	12	0	0	12	12	0	0	12

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Kidneys	Number examined:	12	0	0	12	12	0	0	12
MEDULLARY TUBULES: EOSINOPHILIC CASTS									
	Nad>	12	0	0	11	12	0	0	12
	Minimal>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	1	0	0	0	0
CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC									
	Nad>	10	0	0	8	11	0	0	12
	Minimal>	2	0	0	3	1	0	0	0
	Slight>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	2	0	0	4	1	0	0	0
CORTEX/CORTICO-MEDULLARY JUNCTION: TUBULE(S) DILATED									
	Nad>	11	0	0	12	12	0	0	12
	Moderate>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
CORTEX: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	Nad>	12	0	0	9	12	0	0	12
	Minimal>	0	0	0	3	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	3	0	0	0	0
INFARCT									
	Nad>	12	0	0	12	11	0	0	12
	Moderate>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Kidneys .....Number examined:		12	0	0	12	12	0	0	12
MEDULLA: MINERAL DEPOSIT(S)									
	Nad>	12	0	0	11	11	0	0	9
	Minimal>	0	0	0	1	1	0	0	3
.....Total Incidence of Finding Observed:		0	0	0	1	1	0	0	3
INTERSTITIAL MONONUCLEAR CELL AGGREGATES									
	Nad>	10	0	0	8	9	0	0	12
	Minimal>	2	0	0	4	3	0	0	0
.....Total Incidence of Finding Observed:		2	0	0	4	3	0	0	0
Larynx .....Number examined:		0	0	0	0	0	0	0	0
Liver .....Number examined:		12	0	0	12	12	0	0	12
CONGESTION									
	Nad>	12	0	0	12	10	0	0	11
	Slight>	0	0	0	0	2	0	0	1
.....Total Incidence of Finding Observed:		0	0	0	0	2	0	0	1
CENTRILOBULAR HEPATOCELLULAR NECROSIS (INDIVIDUAL CELL)									
	Nad>	11	0	0	11	11	0	0	12
	Minimal>	1	0	0	1	1	0	0	0
.....Total Incidence of Finding Observed:		1	0	0	1	1	0	0	0
SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI									
	Nad>	7	0	0	5	7	0	0	10
	Minimal>	5	0	0	6	5	0	0	1
	Slight>	0	0	0	1	0	0	0	1
.....Total Incidence of Finding Observed:		5	0	0	7	5	0	0	2

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Liver	Number examined:	12	0	0	12	12	0	0	12
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Lumbar SC	Number examined:	12	0	0	12	12	0	0	11
Lungs	Number examined:	12	0	0	12	12	0	0	12
PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES									
	Nad>	0	0	0	0	1	0	0	0
	Minimal>	3	0	0	4	4	0	0	7
	Slight>	9	0	0	7	7	0	0	5
	Moderate>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	12	0	0	12	11	0	0	12
PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY -CELL INFILTRATE									
	Nad>	4	0	0	7	8	0	0	9
	Minimal>	8	0	0	5	4	0	0	3
.....	Total Incidence of Finding Observed:	8	0	0	5	4	0	0	3
ALVEOLAR ACUTE INFLAMMATORY CELL INFILTRATE									
	Nad>	12	0	0	12	12	0	0	11
	Slight>	0	0	0	0	0	0	0	1
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	1
ALVEOLAR/INTRAALVEOLAR MACROPHAGES									
	Nad>	1	0	0	0	1	0	0	0
	Minimal>	11	0	0	12	9	0	0	12
	Slight>	0	0	0	0	2	0	0	0
.....	Total Incidence of Finding Observed:	11	0	0	12	11	0	0	12

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

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:	12	12	12	12	12	12	12	12
Lungs	Number examined:	12	0	0	12	12	0	0	12
VESSEL(S): MINERAL DEPOSIT(S)									
	Nad>	6	0	0	1	6	0	0	5
	Minimal>	6	0	0	11	6	0	0	7
.....Total Incidence of Finding	Observed:	6	0	0	11	6	0	0	7
HEMORRHAGE(S)									
	Nad>	11	0	0	7	12	0	0	12
	Minimal>	1	0	0	4	0	0	0	0
	Slight>	0	0	0	1	0	0	0	0
.....Total Incidence of Finding	Observed:	1	0	0	5	0	0	0	0
INTERSTITIUM: OSSEOUS METAPLASIA									
	Nad>	12	0	0	11	12	0	0	11
	Minimal>	0	0	0	1	0	0	0	1
.....Total Incidence of Finding	Observed:	0	0	0	1	0	0	0	1
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding	Observed:	0	0	0	0	1	0	0	0
Lymph Node,other	Number examined:	0	0	0	0	1	0	0	0
CORTICAL LYMPHOID DEVELOPMENT									
	Moderate>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding	Observed:	0	0	0	0	1	0	0	0
PARACORTICAL LYMPHOID DEVELOPMENT									
	Slight>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding	Observed:	0	0	0	0	1	0	0	0

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Lymph Node,other	Number examined:	0	0	0	0	1	0	0	0
FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS									
	Minimal>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
INCREASED HISTIOCYTES									
	Moderate>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
LYMPHOID CELL DEPLETION/ATROPHY									
	Moderate>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
N-MALIGNANT LYMPHOMA									
	Tumor present>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Lymph/Retic Sys	Number examined:	0	0	0	0	1	0	0	0
M-MALIGNANT LYMPHOMA									
	Incidental>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Mammary-protocol	Number examined:	12	0	0	11	12	0	0	12
MALE TYPE: (UNDIFFRENTIATED TYPE)									
	Nad>	0	0	0	0	12	0	0	12
	Present>	12	0	0	11	0	0	0	0
.....	Total Incidence of Finding Observed:	12	0	0	11	0	0	0	0
FEMALE TYPE (DIFFERENTIATED TYPE)									
	Nad>	12	0	0	11	0	0	0	0
	Present>	0	0	0	0	12	0	0	12
.....	Total Incidence of Finding Observed:	0	0	0	0	12	0	0	12

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Mediastinal LN	Number examined:	12	0	0	12	12	0	0	12
RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA									
	Nad>	0	0	0	0	1	0	0	0
	Minimal>	4	0	0	6	3	0	0	4
	Slight>	7	0	0	4	6	0	0	7
	Moderate>	1	0	0	2	2	0	0	1
.....Total Incidence of Finding	Observed:	12	0	0	12	11	0	0	12
RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE -AREA									
	Nad>	0	0	0	0	1	0	0	0
	Minimal>	0	0	0	1	1	0	0	0
	Slight>	2	0	0	4	4	0	0	1
	Moderate>	7	0	0	6	6	0	0	9
	Marked>	2	0	0	1	0	0	0	2
	Severe>	1	0	0	0	0	0	0	0
.....Total Incidence of Finding	Observed:	12	0	0	12	11	0	0	12
FOLLICULAR GERMINAL CENTER DEVELOPMENT									
	Nad>	8	0	0	6	5	0	0	5
	Present>	4	0	0	6	7	0	0	7
.....Total Incidence of Finding	Observed:	4	0	0	6	7	0	0	7
FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS									
	Nad>	3	0	0	2	2	0	0	1
	Minimal>	3	0	0	6	3	0	0	6
	Slight>	6	0	0	4	7	0	0	5
.....Total Incidence of Finding	Observed:	9	0	0	10	10	0	0	11
RETICULOENDOTHELIAL CELLS: BROWN PIGMENT									
	Nad>	11	0	0	11	9	0	0	9
	Minimal>	1	0	0	1	0	0	0	1
	Slight>	0	0	0	0	3	0	0	2
.....Total Incidence of Finding	Observed:	1	0	0	1	3	0	0	3

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Mediastinal LN	Number examined:	12	0	0	12	12	0	0	12
PROMINENT SINUS HISTIOCYTES									
	Nad>	10	0	0	7	9	0	0	10
	Present>	2	0	0	5	3	0	0	2
.....Total Incidence of Finding	Observed:	2	0	0	5	3	0	0	2
PROMINENT PLASMA CELL POPULATION									
	Nad>	9	0	0	7	10	0	0	12
	Minimal>	0	0	0	2	0	0	0	0
	Slight>	3	0	0	3	2	0	0	0
.....Total Incidence of Finding	Observed:	3	0	0	5	2	0	0	0
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding	Observed:	0	0	0	0	1	0	0	0
Mesenteric LN	Number examined:	12	0	0	12	12	0	0	12
RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA									
	Minimal>	0	0	0	2	0	0	0	1
	Slight>	12	0	0	9	8	0	0	10
	Moderate>	0	0	0	1	4	0	0	1
.....Total Incidence of Finding	Observed:	12	0	0	12	12	0	0	12
RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE -AREA									
	Minimal>	0	0	0	1	1	0	0	0
	Slight>	0	0	0	1	1	0	0	1
	Moderate>	10	0	0	7	9	0	0	11
	Marked>	2	0	0	3	1	0	0	0
.....Total Incidence of Finding	Observed:	12	0	0	12	12	0	0	12
FOLLICULAR GERMINAL CENTER DEVELOPMENT									
	Nad>	3	0	0	3	1	0	0	1
	Present>	9	0	0	9	11	0	0	11
.....Total Incidence of Finding	Observed:	9	0	0	9	11	0	0	11

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Mesenteric LN	Number examined:	12	0	0	12	12	0	0	12
FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS									
	Nad>	10	0	0	11	12	0	0	12
	Minimal>	1	0	0	1	0	0	0	0
	Slight>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	2	0	0	1	0	0	0	0
PROMINENT SINUS/PARACORTICAL HISTIOCYTES									
	Nad>	2	0	0	1	0	0	0	1
	Present>	10	0	0	11	12	0	0	11
.....	Total Incidence of Finding Observed:	10	0	0	11	12	0	0	11
FOAMY HISTIOCYTES									
	Nad>	11	0	0	12	12	0	0	12
	Minimal>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
PROMINENT PLASMA CELLS									
	Nad>	12	0	0	10	10	0	0	12
	Minimal>	0	0	0	0	1	0	0	0
	Slight>	0	0	0	2	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	2	2	0	0	0
Mesentery/Perito	Number examined:	0	0	0	0	1	0	0	0
RENAL MESENTERY: MONONUCLEAR CELL AGGREGATES									
	Slight>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Nose/Turbinates	Number examined:	0	0	0	0	0	0	0	0

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Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Ovaries	Number examined:					12	0	0	12
SERTOLIFORM CELLS									
	Nad>					10	0	0	11
	Present>					2	0	0	1
.....Total Incidence of Finding	Observed:					2	0	0	1
MINERAL DEPOSIT(S)									
	Nad>					11	0	0	12
	Minimal>					1	0	0	0
.....Total Incidence of Finding	Observed:					1	0	0	0
N-METASTATIC/INVASIVE NEOPLASM									
	Nad>					11	0	0	12
	Tumor present>					1	0	0	0
.....Total Incidence of Finding	Observed:					1	0	0	0
Oviducts/Fallop	Number examined:					12	0	0	12
Parathyroid	Number examined:	10	0	0	9	6	0	0	9
Prostate	Number examined:	12	0	0	12				
INTERSTITAL MONONUCLEAR CELL AGGREGATES									
	Nad>	7	0	0	7				
	Minimal>	3	0	0	2				
	Slight>	2	0	0	2				
	Moderate>	0	0	0	1				
.....Total Incidence of Finding	Observed:	5	0	0	5				
INTRALUMINAL CELLULAR/INFLAMMATORY DEBRIS									
	Nad>	12	0	0	11				
	Moderate>	0	0	0	1				
.....Total Incidence of Finding	Observed:	0	0	0	1				

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

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Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Prostate	Number examined:	12	0	0	12				
GLANDULAR DILATATION									
	Nad>	12	0	0	11				
	Marked>	0	0	0	1				
.....	Total Incidence of Finding Observed:	0	0	0	1				
Rectum/Low Colon	Number examined:	12	0	0	12	12	0	0	12
Seminal vesicles	Number examined:	12	0	0	12				
Skin (other)	Number examined:	0	0	0	0	1	0	0	0
ACANTHOSIS WITH SUPERIFICIAL ENCRUSTATION									
	Minimal>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Skin-protocol	Number examined:	12	0	0	11	12	0	0	12
SUBCUTANEOUS MUSCLE: SUBACUTE/CHRONIC INFLAMMATORY FOCI -WITH DEGENERATION/NECROSIS									
	Nad>	12	0	0	10	12	0	0	11
	Minimal>	0	0	0	1	0	0	0	0
	Slight>	0	0	0	0	0	0	0	1
.....	Total Incidence of Finding Observed:	0	0	0	1	0	0	0	1
HAIR FOLLICLES: EMPTY/WITHOUT HAIR SHAFT									
	Nad>	12	0	0	11	12	0	0	11
	Slight>	0	0	0	0	0	0	0	1
.....	Total Incidence of Finding Observed:	0	0	0	0	0	0	0	1
Spleen	Number examined:	12	0	0	12	12	0	0	12
N-MALIGNANT LYMPHOMA									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	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:	11	0	0	12	12	0	0	12
Sternum	Number examined:	11	0	0	12	12	0	0	12

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

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:	12	12	12	12	12	12	12	12
Stomach	Number examined:	12	0	0	12	12	0	0	12
Testes	Number examined:	12	1	1	12				
GERM CELL DEGENERATION/MULTINUCLEATE CELLS									
	Nad>	11	1	1	11				
	Minimal>	0	0	0	1				
	Slight>	1	0	0	0				
.....	Total Incidence of Finding Observed:	1	0	0	1				
Thoracic SC	Number examined:	12	0	0	12	12	0	0	10
Thymus	Number examined:	12	0	0	12	12	0	0	12
LYMPHOCYTOLYSIS/INVOLUTION									
	Nad>	0	0	0	1	1	0	0	1
	Minimal>	12	0	0	11	11	0	0	11
.....	Total Incidence of Finding Observed:	12	0	0	11	11	0	0	11
HEMORRHAGE									
	Nad>	5	0	0	3	9	0	0	9
	Minimal>	7	0	0	8	3	0	0	3
	Slight>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	7	0	0	9	3	0	0	3
LYMPHOID HYPERPLASIA									
	Nad>	12	0	0	11	11	0	0	11
	Minimal>	0	0	0	0	1	0	0	1
	Slight>	0	0	0	1	0	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	1	1	0	0	1
CYST(S)									
	Nad>	12	0	0	12	11	0	0	12
	Slight>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

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:	12	12	12	12	12	12	12	12
Thymus	Number examined:	12	0	0	12	12	0	0	12
EPITHELIUM: HYPERPLASIA									
	Nad>	11	0	0	12	12	0	0	12
	Slight>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
ULTIMOBRACHIAL REST(S)									
	Nad>	11	0	0	12	12	0	0	12
	Slight>	1	0	0	0	0	0	0	0
.....	Total Incidence of Finding Observed:	1	0	0	0	0	0	0	0
N-METASTATIC/INVASIVE NEOPLASM									
	Nad>	12	0	0	12	11	0	0	12
	Tumor present>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
ATROPHY WITH EOSINOPHILIC GRANULOMATOUS INFLAMMATORY CELL -INFILTRATE									
	Nad>	12	0	0	12	11	0	0	12
	Moderate>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
Thyroid	Number examined:	12	0	0	12	10	0	0	12
LYMPHOID CELL AGGREGATE(S)									
	Nad>	12	0	0	12	9	0	0	12
	Minimal>	0	0	0	0	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	0	1	0	0	0
ECTOPIC THYMIC TISSUE									
	Nad>	12	0	0	8	9	0	0	12
	Present>	0	0	0	4	1	0	0	0
.....	Total Incidence of Finding Observed:	0	0	0	4	1	0	0	0
ULTIMOBRANCHIAL REST(S)									
	Nad>	11	0	0	12	9	0	0	10
	Present>	1	0	0	0	1	0	0	2
.....	Total Incidence of Finding Observed:	1	0	0	0	1	0	0	2

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures

Incidence Summary of Microscopic Findings with Severity Levels
Main Study Animals

Controls from group(s): 1	Animal sex:	-- Animals Affected -- Males --				-- Animals Affected -- Females --			
	Dosage group:	Ctls	2	3	4	Ctls	2	3	4
Tissues With Diagnoses	No. in group:	12	12	12	12	12	12	12	12
Thyroid	Number examined:	12	0	0	12	10	0	0	12
FOLLICULAR DILATATION									
	Nad>	12	0	0	11	8	0	0	11
	Minimal>	0	0	0	1	0	0	0	0
	Slight>	0	0	0	0	1	0	0	1
	Moderate>	0	0	0	0	1	0	0	0
.....Total Incidence of Finding	Observed:	0	0	0	1	2	0	0	1
Tibial Nerve	Number examined:	12	0	0	12	12	0	0	12
Trachea	Number examined:	12	0	0	12	12	0	0	12
MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION									
	Nad>	10	0	0	11	9	0	0	11
	Minimal>	2	0	0	1	2	0	0	0
	Slight>	0	0	0	0	1	0	0	1
.....Total Incidence of Finding	Observed:	2	0	0	1	3	0	0	1
Urinary bladder	Number examined:	12	0	0	12	11	0	0	11
Uterus	Number examined:					12	0	0	12
LUMEN: DILATED									
	Nad>					6	0	0	7
	Slight>					4	0	0	1
	Moderate>					2	0	0	4
.....Total Incidence of Finding	Observed:					6	0	0	5
Vagina	Number examined:					12	0	0	12

All Diagnoses; Phases: P2; Death types: Scheduled FS; Date of death range: 14-Jan-04 To 16-Jan-04

TABLE 13

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF SURVIVAL AND PREGNANCY

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
No. of females cohabitated	N	12	12	12	12
Pregnant	N	12	11	11	9
- Died/sacrificed	N	0	0	0	0
- Died delivering	N	0	0	0	0
- Died/sacrificed post partum	N	0	0	0	0
- Aborted died/sacrificed	N	0	0	0	0
Nonpregnant	N	0	1	1	3
- Died/sacrificed	N	0	0	0	0
Total females died/sacrificed	N	0	0	0	0
	%	0.0	0.0	0.0	0.0
Dams delivering	N	12	11	11	9
- With liveborn pups	N	12	11	11	9
	%	100.0	100.0	100.0	100.0
- With all pups stillborn	N	0	0	0	0
	%	0.0	0.0	0.0	0.0

No statistically significant differences

	Summary of Clinical Observations Satellite Study Preface	Table 14

Number of animals examined represents the total number of animals observed. After Day 15, observations of pregnant animals are reported on Table 15.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

TABLE 14

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY					
	GROUP#	-7	0	8	15	22	TOTAL
# OF ANIMALS EXAMINED	1	12	12	12	11	0	
	2	12	12	12	6	0	
	3	12	12	12	10	1	
	4	12	12	12	10	0	
Normal							
WITHIN NORMAL LIMITS	1	12	12	12	11	0	12
	2	12	12	11	5	0	12
	3	12	12	12	10	1	12
	4	12	12	12	10	0	12
Dermal-General							
ALOPECIA - EXTREMITIES/SNOUT	1	0	0	0	0	0	0
	2	0	0	1	1	0	1
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0

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TABLE 15

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP	1	2	3	4
DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0 to 20				
Normal				
WITHIN NORMAL LIMITS	45/12	40/11	47/12	46/12
Dermal-General				
ALOPECIA - EXTREMITIES/SNOUT	3/ 1	6/ 2	1/ 1	2/ 1
Ocular				
CHROMODACRYORRHEA - UNILATERAL	0/ 0	2/ 1	0/ 0	0/ 0
Oral/Buccal				
INCISORS MALOCCLUDED	0/ 0	2/ 1	0/ 0	0/ 0

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TABLE 16

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF MATERNAL CLINICAL OBSERVATIONS DURING LACTATION - (frequency/animals)

DOSE GROUP	1	2	3	4
DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0 to 5				
Normal				
WITHIN NORMAL LIMITS	29/10	24/ 9	26/ 9	21/ 8
TERMINAL SACRIFICE	12/12	11/11	11/11	9/ 9
Dermal-General				
ALOPECIA - EXTREMITIES/SNOUT	6/ 2	5/ 2	6/ 2	3/ 1
ALOPECIA - GENERAL	1/ 1	1/ 1	0/ 0	0/ 0

TABLE 17

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN BODY WEIGHT VALUES (GRAMS)

		DOSE GROUP	1	2	3	4
		DOSE LEVEL (PPM)	0	900	3000	9000
DAY	-7	MEAN	169	168	168	169
		S.D.	6.7	6.6	7.5	7.4
		N	12	12	12	12
DAY	0	MEAN	191	194	194	196
		S.D.	9.4	8.7	7.4	12.7
		N	12	12	12	12
DAY	4	MEAN	200	202	202	206
		S.D.	10.3	8.4	7.4	15.6
		N	12	12	12	12
DAY	7	MEAN	210	207	212	216
		S.D.	13.4	9.0	9.4	16.1
		N	12	12	12	12
DAY	11	MEAN	219	215	220	225
		S.D.	11.8	9.6	11.5	17.6
		N	12	12	12	12
DAY	14	MEAN	225	223	226	231
		S.D.	11.4	12.1	13.6	18.8
		N	12	12	12	12

No statistically significant differences

TABLE 18

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN BODY WEIGHT GAIN (GRAMS)

		DOSE GROUP	1	2	3	4
		DOSE LEVEL (PPM)	0	900	3000	9000
DAY -7 TO 0		MEAN	22	25	26	27
		S.D.	6.8	5.3	5.3	6.4
		N	12	12	12	12
DAY 0 TO 4		MEAN	9	8	8	10
		S.D.	4.2	3.8	3.1	5.7
		N	12	12	12	12
DAY 4 TO 7		MEAN	10	5	9	10
		S.D.	4.4	4.9	5.6	4.3
		N	12	12	12	12
DAY 7 TO 11		MEAN	9	8	8	10
		S.D.	2.5	6.1	4.0	3.1
		N	12	12	12	12
DAY 11 TO 14		MEAN	6	8	6	6
		S.D.	5.6	7.7	7.1	6.0
		N	12	12	12	12
DAY 0 TO 14		MEAN	34	29	32	35
		S.D.	7.8	11.5	7.1	9.2
		N	12	12	12	12

No statistically significant differences

TABLE 19

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0	MEAN	232	226	235	236
	S.D.	12.9	9.1	17.2	19.8
	N	12	11	11	9
DAY 7	MEAN	269	260	271	272
	S.D.	11.9	11.2	17.7	25.6
	N	12	11	11	9
DAY 14	MEAN	306	294	303	306
	S.D.	14.8	14.8	20.6	28.5
	N	12	11	11	9
DAY 20	MEAN	372	354	371	376
	S.D.	22.8	19.0	21.6	31.5
	N	12	11	11	9

No statistically significant differences

TABLE 20

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
DAYS 0 TO 7	MEAN	37	34	36	36
	S.D.	4.6	5.8	4.9	9.8
	N	12	11	11	9
DAYS 7 TO 14	MEAN	38	34	32	35
	S.D.	5.1	4.5	5.3	5.3
	N	12	11	11	9
DAYS 14 TO 20	MEAN	66	60	68	69
	S.D.	10.9	17.5	9.6	7.4
	N	12	11	11	9
DAYS 0 TO 20	MEAN	140	128	136	140
	S.D.	12.8	18.0	10.8	14.9
	N	12	11	11	9

No statistically significant differences

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TABLE 21

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF MATERNAL LACTATION BODY WEIGHTS (GRAMS)

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
DAY 1	MEAN	280	267	276	281
	S.D.	13.3	15.1	22.2	33.9
	N	12	11	11	9
DAY 4	MEAN	292	282	290	290
	S.D.	16.0	16.5	23.3	36.6
	N	12	11	11	9

No statistically significant differences

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TABLE 22

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
DAYS 1 TO 4	MEAN	12	16	13	9
	S.D.	6.9	5.9	13.1	9.8
	N	12	11	11	9

No statistically significant differences

TABLE 23

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES — MEAN FEED CONSUMPTION (GRAMS/KG/DAY)

	DOSE GROUP	1	2	3	4
	DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0	MEAN	96	98	99	100
	S.D.	3.1	5.2	5.1	5.2
	N	12	10	10	9
DAY 7	MEAN	84	85	87	87
	S.D.	4.4	3.6	3.8	4.0
	N	12	12	12	12
DAY 14	MEAN	81	81	84	82
	S.D.	4.1	4.0	3.9	2.8
	N	12	11	11	12

No statistically significant differences

TABLE 24

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF GESTATION FEED CONSUMPTION (GRAMS/KG/DAY)

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
DAYS 0 TO 7	MEAN	86	84	88	83
	S.D.	4.7	4.5	5.2	4.4
	N	12	11	11	9
DAYS 7 TO 14	MEAN	81	79	80	79
	S.D.	3.8	3.6	4.9	3.7
	N	12	11	11	9
DAYS 14 TO 20	MEAN	70	70	71	71
	S.D.	3.7	4.2	4.6	3.1
	N	12	11	11	9

No statistically significant differences

TABLE 25

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF LACTATION FEED CONSUMPTION (GRAMS/KG/DAY)

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
DAYS 1 TO 4	MEAN	120	136	112	112
	S.D.	18.0	39.6	19.4	14.3
	N	12	10	11	8

No statistically significant differences

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TABLE 26

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF COHABITATION DATA

DOSE GROUP DOSE LEVEL (PPM)		1 0	2 900	3 3000	4 9000
Females paired with males	N	12	12	12	12
Total number mated	N	12	12	12	12
female mating index	%	100.0	100.0	100.0	100.0
pregnant	N	12	11	11	9
female fertility index	%	100.0	91.7	91.7	75.0
pregnancy index	%	100.0	91.7	91.7	75.0
Males placed with females	N	12	12	12	12
Total number mated	N	12	12	12	12
male mating index	%	100.0	100.0	100.0	100.0
with females pregnant	N	12	11	11	9
male fertility index	%	100.0	91.7	91.7	75.0
Females with defined day 0 of Gestation	N	12	12	12	12
No. of days until Mating	MEAN	2.8	2.4	4.1	2.9
	S.D.	0.97	1.73	3.34	1.38
Day 1 to 4	N	12	11	10	11
	%	100.0	91.7	83.3	91.7
Day 5 to 8	N	0	1	1	1
	%	0.0	8.3	8.3	8.3
Day 9 to 14	N	0	0	1	0
	%	0.0	0.0	8.3	0.0

No statistically significant differences

TABLE 27

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF DELIVERY AND LITTER DATA

DOSE GROUP DOSE LEVEL (PPM)		1 0	2 900	3 3000	4 9000
Females on Study	N	12	12	12	12
Females Mated	N	12	12	12	12
Mating Index	%	100.0	100.0	100.0	100.0
Females Pregnant	N	12	11	11	9
Female Fertility Index	%	100.0	91.7	91.7	75.0
Females with Liveborn	N	12	11	11	9
Gestation Index	%	100.0	100.0	100.0	100.0
Females Completing Delivery	N	12	11	11	9
	%	100.0	100.0	100.0	100.0
with Stillborn Pups	N	0	0	1	0
	%	0.0	0.0	9.1	0.0
with all Stillborn	N	0	0	0	0
	%	0.0	0.0	0.0	0.0
Litters with Liveborn, but no Pups Alive					
day 4	N	0	0	0	0
	%	0.0	0.0	0.0	0.0
Duration of Gestation	MEAN	21.8	21.7	21.8	21.7
	S.D.	0.45	0.47	0.40	0.50
	N	12	11	11	9

No statistically significant differences

TABLE 27

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF DELIVERY AND LITTER DATA

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
Litters with Liveborn Pups	N	12	11	11	9
Pups Delivered (total)	N	165	148	147	121
	MEAN	13.8	13.5	13.4	13.4
	S.D.	1.60	1.44	2.73	1.59
Liveborn	N	165	148	145	121
Live Birth Index	%	100.0	100.0	98.6	100.0
Stillborn	N	0	0	2	0
	%	0.0	0.0	1.4	0.0
Liveborn, not culled prior to day 4	N	165	148	145	121
Pups Dying, Missing, and/or Cannibalized					
day 0	N	1	0	0	0
	%	0.6	0.0	0.0	0.0
days 1-4	N	4	3	2	1
	%	2.4	2.0	1.4	0.8
Pups Surviving 4 days	N	160	145	143	120
Viability Index	%	97.0	98.0	98.6	99.2

No statistically significant differences

TABLE 27

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF DELIVERY AND LITTER DATA

DOSE GROUP DOSE LEVEL (PPM)		1 0	2 900	3 3000	4 9000
Implantation Sites per Litter	N	175	155	153	136
	MEAN	14.6	14.1	13.9	15.1
	S.D.	1.38	1.58	2.55	1.62
Corpora Lutea	TOTAL	196	166	164	148
	MEAN	16.3	15.1	14.9	16.4
	S.D.	1.87	2.12	2.07	2.13
Preimplantation Loss	MEAN	1.8	1.0	1.0	1.3
	S.D.	1.8	1.2	1.0	0.9
Postimplantation Loss	MEAN	0.8	0.6	0.7	* 1.8
	S.D.	0.9	1.2	0.8	0.8
Live Pups/Litter					
day 0	MEAN	13.8	13.5	13.2	13.4
	S.D.	1.60	1.44	2.75	1.59
	N	12	11	11	9
day 1	MEAN	13.6	13.4	13.0	13.4
	S.D.	1.62	1.43	2.83	1.59
	N	12	11	11	9
day 4	MEAN	13.3	13.2	13.0	13.3
	S.D.	1.92	1.33	2.83	1.80
	N	12	11	11	9
Sex Ratio - Male Pups:Total Pups					
day 0	N	96	75	74	62
	%	58.2	50.7	51.4	51.2
day 4	N	92	73	74	61
	%	57.5	50.3	51.7	50.8

Statistical key: * = p<0.05

	Incidence Summary Report for Gross Necropsy Observations Satellite Study Preface	Table 28

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Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

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Terminal Sacrifice - Satellite

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	-- Females --			
Group:	1	2	3	4
Number in group:	12	11	11	9
Within normal limits	8	8	11	9
Kidneys				
Dilated Pelvis	0	1	0	0
Lungs				
Discolored	2	1	0	0
Thymus				
Discolored	1	0	0	0
Skin (other)				
Hair Thin/Absent	1	1	0	0

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Terminal Sacrifice - Non-pregnant

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	-- Females --			
Group:	1	2	3	4
Number in group:	0	1	1	3
Within normal limits	0	1	1	3

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Terminal Sacrifice – Non-pregnant
Absolute Organ Weights 144

Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observed

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

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Parental Organ Weights - Satellite

Summary statistics for absolute organ weights (g)
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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
				Female Animals				
1								
Mean:	294.7	0.0921	2.0473	0.9968	2.4016	13.1901	1.5280	0.0761
Standard deviation:	18.2	0.0130	0.0786	0.0875	0.2383	1.5408	0.1297	0.0158
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	283.4	0.0979	2.0134	1.0298	2.5297	13.8646	1.5531	0.0768
Standard deviation:	16.1	0.0177	0.0793	0.1142	0.2728	1.5778	0.1928	0.0118
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
3								
Mean:	289.5	0.0895	1.9711	1.0233	2.3857	12.8847	1.5165	0.0689
Standard deviation:	23.9	0.0193	0.0769	0.0866	0.1958	1.6637	0.1872	0.0096
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
4								
Mean:	291.7	0.1029	1.9783	1.0678	2.5095	13.2951	1.6476	0.0824
Standard deviation:	37.8	0.0114	0.1053	0.0743	0.3129	2.3431	0.2170	0.0169
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Parental Organ Weights - Satellite

Summary statistics for absolute organ weights (g)
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Group	Terminal Body wt. (g)	Ovary Right	Spleen	Thymus	Uterus w/vagina
			Female Animals		
1					
Mean:	294.7	0.0771	0.6511	0.3199	1.0935
Standard deviation:	18.2	0.0091	0.1113	0.0740	0.1895
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
Mean:	283.4	0.0807	0.6111	0.2724	1.0502
Standard deviation:	16.1	0.0147	0.0927	0.0519	0.1666
Number of observ. :	(11)	(11)	(11)	(11)	(11)
3					
Mean:	289.5	0.0825	0.6197	0.2660	1.0177
Standard deviation:	23.9	0.0119	0.0991	0.0702	0.1325
Number of observ. :	(11)	(11)	(11)	(11)	(11)
4					
Mean:	291.7	0.0804	0.6447	0.3149	1.0138
Standard deviation:	37.8	0.0142	0.1243	0.1103	0.0756
Number of observ. :	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Summary Statistics for % Organ to Body Weight
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Parental Organ Weights - Satellite

Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
				Female Animals				
1								
Mean:	294.7	0.0312	0.6971	0.3388	0.8153	4.4749	0.5189	0.0258
Standard deviation:	18.2	0.0037	0.0488	0.0271	0.0668	0.4311	0.0352	0.0051
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	283.4	0.0346	0.7121	0.3630	0.8953	4.8950	0.5480	0.0271
Standard deviation:	16.1	0.0062	0.0437	0.0309	0.1118	0.5063	0.0601	0.0037
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
3								
Mean:	289.5	0.0312	0.6841	0.3546	0.8278	4.4588	0.5247	0.0241
Standard deviation:	23.9	0.0075	0.0473	0.0291	0.0803	0.5207	0.0543	0.0044
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
4								
Mean:	291.7	0.0359	0.6857	0.3704	0.8640	4.5553	0.5691	0.0282
Standard deviation:	37.8	0.0062	0.0729	0.0455	0.0778	0.4826	0.0795	0.0036
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Parental Organ Weights - Satellite

Summary Statistics for % Organ to Body Weight
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Group	Terminal Body wt. (g)	Ovary Right	Spleen	Thymus	Uterus w/vagina
			Female Animals		
1					
Mean:	294.7	0.0262	0.2214	0.1097	0.3730
Standard deviation:	18.2	0.0026	0.0371	0.0289	0.0698
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
Mean:	283.4	0.0285	0.2154	0.0959	0.3721
Standard deviation:	16.1	0.0055	0.0300	0.0165	0.0665
Number of observ. :	(11)	(11)	(11)	(11)	(11)
3					
Mean:	289.5	0.0287	0.2130	0.0912	0.3546
Standard deviation:	23.9	0.0049	0.0198	0.0200	0.0603
Number of observ. :	(11)	(11)	(11)	(11)	(11)
4					
Mean:	291.7	0.0280	0.2203	0.1069	0.3520
Standard deviation:	37.8	0.0064	0.0215	0.0281	0.0479
Number of observ. :	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Parental Organ Weights - Satellite

Summary Statistics for % Organ to Brain Weight
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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovary Left
				Female Animals				
1								
Mean:	294.7	4.5030	100.0000	48.7676	117.2887	645.7914	74.7192	3.7255
Standard deviation:	18.2	0.6459	0.0000	4.7109	10.6277	85.7038	6.8520	0.8234
Number of observ. :	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)
2								
Mean:	283.4	4.8505	100.0000	51.1018	125.5179	687.2154	77.0722	3.8136
Standard deviation:	16.1	0.7917	0.0000	4.8021	11.4101	56.8401	8.3467	0.5685
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
3								
Mean:	289.5	4.5329	100.0000	51.9073	120.9577	653.2299	76.7808	3.5048
Standard deviation:	23.9	0.9061	0.0000	3.6977	7.4519	76.4552	7.2633	0.5243
Number of observ. :	(11)	(11)	(11)	(11)	(11)	(11)	(11)	(11)
4								
Mean:	291.7	5.2232	100.0000	54.0032*	126.6499	671.0273	83.2826	4.1619
Standard deviation:	37.8	0.7084	0.0000	3.0504	11.9752	104.4646	10.0582	0.7894
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Summary Statistics for % Organ to Brain Weight
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Parental Organ Weights - Satellite

Group	Terminal Body wt. (g)	Ovary Right	Spleen	Thymus	Uterus w/vagina
			F e m a l e A n i m a l s		
1					
M e a n:	294.7	3.7724	31.8212	15.6370	53.4982
Standard deviation:	18.2	0.4993	5.4826	3.5314	9.5939
Number of observ. :	(12)	(12)	(12)	(12)	(12)
2					
M e a n:	283.4	3.9935	30.3582	13.5256	52.0606
Standard deviation:	16.1	0.6138	4.5894	2.5312	7.3363
Number of observ. :	(11)	(11)	(11)	(11)	(11)
3					
M e a n:	289.5	4.1848	31.3535	13.4176	51.6566
Standard deviation:	23.9	0.5834	4.2021	3.1949	6.6358
Number of observ. :	(11)	(11)	(11)	(11)	(11)
4					
M e a n:	291.7	4.0769	32.4351	15.7333	51.3638
Standard deviation:	37.8	0.7789	4.7137	4.6921	4.5964
Number of observ. :	(9)	(9)	(9)	(9)	(9)

*(+) = 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

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Summary statistics for absolute organ weights (g)
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Terminal Sacrifice - Non-pregnant

Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
			Female Animals				
2							
Mean:	247.6	0.0915	1.9169	1.0163	2.3842	12.4708	1.5540
Standard deviation:	0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :	(1)	(1)	(1)	(1)	(1)	(1)	(1)
3							
Mean:	254.6	0.0650	1.9557	0.9282	2.1161	10.4723	1.6344
Standard deviation:	0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :	(1)	(1)	(1)	(1)	(1)	(1)	(1)
4							
Mean:	256.4	0.0918	1.8446	0.9425	2.2416	10.0551	1.5555
Standard deviation:	24.2	0.0188	0.0998	0.0901	0.1991	0.9866	0.0483
Number of observ. :	(3)	(3)	(3)	(3)	(3)	(3)	(3)

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Summary statistics for absolute organ weights (g)
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Terminal Sacrifice - Non-pregnant

Group	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
			Female Animals			
2						
Mean:	247.6	0.0742	0.0914	0.4749	0.2940	0.7765
Standard deviation:	0	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :	(1)	(1)	(1)	(1)	(1)	(1)
3						
Mean:	254.6	0.0675	0.0668	0.5945	0.2600	0.9016
Standard deviation:	0	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :	(1)	(1)	(1)	(1)	(1)	(1)
4						
Mean:	256.4	0.0901	0.0839	0.5806	0.3847	0.9248
Standard deviation:	24.2	0.0034	0.0017	0.0637	0.0658	0.0455
Number of observ. :	(3)	(3)	(3)	(3)	(3)	(3)

TABLE 30

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF PUP CLINICAL OBSERVATIONS DURING LACTATION - (frequency/animals)

DOSE GROUP	1	2	3	4
DOSE LEVEL (PPM)	0	900	3000	9000
DAY 0 to 4				
Normal				
WITHIN NORMAL LIMITS	324/12	293/11	287/11	241/ 9

TABLE 31

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

	DOSE GROUP		1	2	3	4
	DOSE LEVEL (PPM)		0	900	3000	9000
day 1	males	MEAN	7.1	7.2	7.3	7.0
		S.D.	0.51	0.58	0.76	0.63
		N	12	11	11	9
1	females	MEAN	6.8	6.7	7.0	6.6
		S.D.	0.48	0.69	0.71	0.40
		N	12	11	11	9
1	males+females	MEAN	7.0	6.9	7.1	6.8
		S.D.	0.52	0.61	0.70	0.52
		N	12	11	11	9
day 4	males	MEAN	10.3	10.2	10.4	10.1
		S.D.	1.08	0.92	1.29	1.29
		N	12	11	11	9
4	females	MEAN	9.9	9.5	10.1	9.4
		S.D.	1.03	0.99	1.13	0.95
		N	12	11	11	9
4	males+females	MEAN	10.1	9.9	10.2	9.7
		S.D.	1.06	0.97	1.17	1.14
		N	12	11	11	9

No statistically significant differences

TABLE 32

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF PUP BODY WEIGHT GAIN -- GRAMS

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
day 1- 4 males	MEAN	3.1	3.0	3.2	3.0
	S.D.	0.69	0.54	0.64	0.85
	N	12	11	11	9
females	MEAN	3.1	2.9	3.1	2.8
	S.D.	0.64	0.45	0.56	0.69
	N	12	11	11	9
males+females	MEAN	3.1	3.0	3.1	2.9
	S.D.	0.66	0.52	0.59	0.77
	N	12	11	11	9

No statistically significant differences

TABLE 33

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF PUP NECROPSY OBSERVATIONS

DOSE GROUP DOSE LEVEL (PPM)		1 0	2 900	3 3000	4 9000
Litters Evaluated	N	12	11	11	9
Pups Evaluated	N	165	147	146	121
Live	N	165	147	144	121
Stillborn	N	0	0	2	0
GROSS EXAM					
Litter Incidence	N	1	0	1	1
Pup Incidence	N	2	0	1	1
AUTOLYSIS					
Pup Incidence	N	2	0	1	1
	%	1.2	0.0	0.7	0.8
Litter Incidence	N	1	0	1	1
	%	8.3	0.0	9.1	11.1
LUNGS					
Litter Incidence	N	2	0	1	0
Pup Incidence	N	2	0	2	0
LUNG FLOATAION TEST - LUNGS FLOAT					
Pup Incidence	N	2	0	0	0
	%	1.2	0.0	0.0	0.0
Litter Incidence	N	2	0	0	0
	%	16.7	0.0	0.0	0.0
LUNG FLOATATION TEST - LUNGS DO NOT FLOAT					
Pup Incidence	N	0	0	2	0
	%	0.0	0.0	1.4	0.0
Litter Incidence	N	0	0	1	0
	%	0.0	0.0	9.1	0.0

No statistically significant differences

TABLE 33

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

SUMMARY OF PUP NECROPSY OBSERVATIONS

DOSE GROUP		1	2	3	4
DOSE LEVEL (PPM)		0	900	3000	9000
Litters Evaluated	N	12	11	11	9
Pups Evaluated	N	165	147	146	121
Live	N	165	147	144	121
Stillborn	N	0	0	2	0
STOMACH					
Litter Incidence	N	2	0	1	0
Pup Incidence	N	2	0	2	0
NO MILK IN STOMACH					
Pup Incidence	N	1	0	2	0
	%	0.6	0.0	1.4	0.0
Litter Incidence	N	1	0	1	0
	%	8.3	0.0	9.1	0.0
MILK IN STOMACH					
Pup Incidence	N	1	0	0	0
	%	0.6	0.0	0.0	0.0
Litter Incidence	N	1	0	0	0
	%	8.3	0.0	0.0	0.0

No statistically significant differences

APPENDIX A

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
1031	TERMINAL SACRIFICE	14-JAN-04	30
1032	TERMINAL SACRIFICE	14-JAN-04	30
1033	TERMINAL SACRIFICE	14-JAN-04	30
1034	TERMINAL SACRIFICE	14-JAN-04	30
1035	TERMINAL SACRIFICE	14-JAN-04	30
1036	TERMINAL SACRIFICE	14-JAN-04	30
1037	TERMINAL SACRIFICE	15-JAN-04	31
1038	TERMINAL SACRIFICE	15-JAN-04	31
1039	TERMINAL SACRIFICE	15-JAN-04	31
1040	TERMINAL SACRIFICE	16-JAN-04	32
1041	TERMINAL SACRIFICE	16-JAN-04	32
1042	TERMINAL SACRIFICE	16-JAN-04	32

APPENDIX A

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 2 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
2031	TERMINAL SACRIFICE	14-JAN-04	30
2032	TERMINAL SACRIFICE	14-JAN-04	30
2033	TERMINAL SACRIFICE	14-JAN-04	30
2034	TERMINAL SACRIFICE	14-JAN-04	30
2035	TERMINAL SACRIFICE	14-JAN-04	30
2036	TERMINAL SACRIFICE	14-JAN-04	30
2037	TERMINAL SACRIFICE	15-JAN-04	31
2038	TERMINAL SACRIFICE	15-JAN-04	31
2039	TERMINAL SACRIFICE	15-JAN-04	31
2040	TERMINAL SACRIFICE	16-JAN-04	32
2041	TERMINAL SACRIFICE	16-JAN-04	32
2042	TERMINAL SACRIFICE	16-JAN-04	32

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 3 3000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
3031	TERMINAL SACRIFICE	14-JAN-04	30
3032	TERMINAL SACRIFICE	14-JAN-04	30
3033	TERMINAL SACRIFICE	14-JAN-04	30
3034	TERMINAL SACRIFICE	14-JAN-04	30
3035	TERMINAL SACRIFICE	14-JAN-04	30
3036	TERMINAL SACRIFICE	14-JAN-04	30
3037	TERMINAL SACRIFICE	15-JAN-04	31
3038	TERMINAL SACRIFICE	15-JAN-04	31
3043	TERMINAL SACRIFICE	15-JAN-04	31
3040	TERMINAL SACRIFICE	16-JAN-04	32
3041	TERMINAL SACRIFICE	16-JAN-04	32
3042	TERMINAL SACRIFICE	16-JAN-04	32

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
4031	TERMINAL SACRIFICE	14-JAN-04	30
4032	TERMINAL SACRIFICE	14-JAN-04	30
4033	TERMINAL SACRIFICE	14-JAN-04	30
4034	TERMINAL SACRIFICE	14-JAN-04	30
4035	TERMINAL SACRIFICE	14-JAN-04	30
4036	TERMINAL SACRIFICE	14-JAN-04	30
4037	TERMINAL SACRIFICE	15-JAN-04	31
4038	TERMINAL SACRIFICE	15-JAN-04	31
4039	TERMINAL SACRIFICE	15-JAN-04	31
4040	TERMINAL SACRIFICE	16-JAN-04	32
4041	TERMINAL SACRIFICE	16-JAN-04	32
4042	TERMINAL SACRIFICE	16-JAN-04	32

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
1531	TERMINAL SACRIFICE	14-JAN-04	30
1532	TERMINAL SACRIFICE	14-JAN-04	30
1533	TERMINAL SACRIFICE	14-JAN-04	30
1534	TERMINAL SACRIFICE	14-JAN-04	30
1535	TERMINAL SACRIFICE	14-JAN-04	30
1536	TERMINAL SACRIFICE	14-JAN-04	30
1537	TERMINAL SACRIFICE	15-JAN-04	31
1538	TERMINAL SACRIFICE	15-JAN-04	31
1539	TERMINAL SACRIFICE	15-JAN-04	31
1540	TERMINAL SACRIFICE	16-JAN-04	32
1541	TERMINAL SACRIFICE	16-JAN-04	32
1542	TERMINAL SACRIFICE	16-JAN-04	32

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
2531	TERMINAL SACRIFICE	14-JAN-04	30
2532	TERMINAL SACRIFICE	14-JAN-04	30
2533	TERMINAL SACRIFICE	14-JAN-04	30
2534	TERMINAL SACRIFICE	14-JAN-04	30
2535	TERMINAL SACRIFICE	14-JAN-04	30
2536	TERMINAL SACRIFICE	14-JAN-04	30
2537	TERMINAL SACRIFICE	15-JAN-04	31
2538	TERMINAL SACRIFICE	15-JAN-04	31
2539	TERMINAL SACRIFICE	15-JAN-04	31
2540	TERMINAL SACRIFICE	16-JAN-04	32
2541	TERMINAL SACRIFICE	16-JAN-04	32
2542	TERMINAL SACRIFICE	16-JAN-04	32

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 3000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
3531	TERMINAL SACRIFICE	14-JAN-04	30
3532	TERMINAL SACRIFICE	14-JAN-04	30
3533	TERMINAL SACRIFICE	14-JAN-04	30
3534	TERMINAL SACRIFICE	14-JAN-04	30
3535	TERMINAL SACRIFICE	14-JAN-04	30
3536	TERMINAL SACRIFICE	14-JAN-04	30
3537	TERMINAL SACRIFICE	15-JAN-04	31
3538	TERMINAL SACRIFICE	15-JAN-04	31
3539	TERMINAL SACRIFICE	15-JAN-04	31
3540	TERMINAL SACRIFICE	16-JAN-04	32
3541	TERMINAL SACRIFICE	16-JAN-04	32
3542	TERMINAL SACRIFICE	16-JAN-04	32

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY
4531	TERMINAL SACRIFICE	14-JAN-04	30
4532	TERMINAL SACRIFICE	14-JAN-04	30
4533	TERMINAL SACRIFICE	14-JAN-04	30
4534	TERMINAL SACRIFICE	14-JAN-04	30
4535	TERMINAL SACRIFICE	14-JAN-04	30
4536	TERMINAL SACRIFICE	14-JAN-04	30
4537	TERMINAL SACRIFICE	15-JAN-04	31
4538	TERMINAL SACRIFICE	15-JAN-04	31
4539	TERMINAL SACRIFICE	15-JAN-04	31
4540	TERMINAL SACRIFICE	16-JAN-04	32
4541	TERMINAL SACRIFICE	16-JAN-04	32
4542	TERMINAL SACRIFICE	16-JAN-04	32

	Individual Clinical Observations Main Study Preface	Appendix B

For summarization purposes, descriptive comments [i.e., location of scab(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

APPENDIX B

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
1031	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1032	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1033	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1034	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1035	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1036	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1037	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
1038	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
1039	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
1040	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
1041	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
1042	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
2031	WITHIN NORMAL LIMITS	P	P	P						
	TERMINAL SACRIFICE							P		
	CHROMODACRYORRHEA - BILATERAL				P	P	P			
	INCISORS MALOCCLUDED				P	P	P			
2032	WITHIN NORMAL LIMITS	P	P	P						
	TERMINAL SACRIFICE							P		
	CHROMODACRYORRHEA - BILATERAL				P	P	P			
2033	WITHIN NORMAL LIMITS	P	P	P						
	TERMINAL SACRIFICE							P		
	CHROMODACRYORRHEA - BILATERAL				P	P	P			
	INCISORS MALOCCLUDED				P	P	P			
2034	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2035	WITHIN NORMAL LIMITS	P	P	P	P					
	TERMINAL SACRIFICE							P		
	NECROSIS{TIPOF TAIL}					P	P			
2036	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2037	WITHIN NORMAL LIMITS	P	P	P	P	P				
	TERMINAL SACRIFICE								P	
	NASAL DISCHARGE - RED						P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	2	9	0	1	2
2038	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2039	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2040	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
2041	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
2042	WITHIN NORMAL LIMITS	P	P			P	P			
	TERMINAL SACRIFICE								P	
	NASAL DISCHARGE - RED			P	P					

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
3031	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3032	WITHIN NORMAL LIMITS	P	P	P	P					
	TERMINAL SACRIFICE							P		
	NASAL DISCHARGE - RED					P	P			
3033	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3034	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3035	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3036	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3037	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
3038	WITHIN NORMAL LIMITS	P	P	P	P	P				
	TERMINAL SACRIFICE								P	
	NASAL DISCHARGE - RED						P			
3043	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
3040	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
3041	WITHIN NORMAL LIMITS	P	P							
	TERMINAL SACRIFICE									P
	INCISORS MALOCCLUDED				P	P				
	INCISORS BROKEN/MISSING						P	P		
3042	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2 2 9	3 0	3 1	3 2
4031	WITHIN NORMAL LIMITS	P	P	P	P	P			
	TERMINAL SACRIFICE						P		
	NASAL DISCHARGE - RED					P			
4032	WITHIN NORMAL LIMITS	P	P	P	P	P	P		
	TERMINAL SACRIFICE						P		
4033	WITHIN NORMAL LIMITS	P	P	P	P	P			
	TERMINAL SACRIFICE						P		
	NASAL DISCHARGE - RED					P			
4034	WITHIN NORMAL LIMITS	P	P	P	P	P	P		
	TERMINAL SACRIFICE						P		
4035	WITHIN NORMAL LIMITS	P	P	P	P	P	P		
	TERMINAL SACRIFICE						P		
4036	WITHIN NORMAL LIMITS	P	P	P	P				
	TERMINAL SACRIFICE						P		
	ALOPECIA - EXTREMITIES/SNOUT					2	2		
4037	WITHIN NORMAL LIMITS	P	P	P	P	P	P		
	TERMINAL SACRIFICE							P	
4038	WITHIN NORMAL LIMITS	P	P	P	P	P			
	TERMINAL SACRIFICE							P	
	NASAL DISCHARGE - RED					P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
4039	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
4040	WITHIN NORMAL LIMITS	P	P	P	P					
	TERMINAL SACRIFICE									P
	NASAL DISCHARGE - RED						P	P		
4041	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
4042	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 2 5	2	2 9	3 0	3 1	3 2
1531	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1532	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1533	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1534	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1535	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1536	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
1537	WITHIN NORMAL LIMITS	P	P	P	P	P				
	TERMINAL SACRIFICE								P	
	CHROMODACRYORRHEA - UNILATERAL						P			
	NASAL DISCHARGE - RED						P			
1538	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
1539	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
1540	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
1541	WITHIN NORMAL LIMITS	P	P	P	P	P				
	TERMINAL SACRIFICE									P
	ALOPECIA - GENERAL						2			
	SCABS						P			
	DORSAL									
1542	WITHIN NORMAL LIMITS	P	P	P	P					
	TERMINAL SACRIFICE									P
	ALOPECIA - EXTREMITIES/SNOUT					3	3			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2 2	2 9	3 0	3 1	3 2
2531	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2532	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2533	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2534	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2535	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2536	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
2537	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
2538	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
2539	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
2540	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
2541	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
2542	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
3531	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3532	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3533	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3534	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3535	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3536	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
3537	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
3538	WITHIN NORMAL LIMITS	P	P							
	TERMINAL SACRIFICE								P	
	ALOPECIA - EXTREMITIES/SNOUT				3	3	3	3		
3539	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

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ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	2	9	0	1	2
3540	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
3541	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P
3542	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE									P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX B

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2	2 9	3 0	3 1	3 2
4531	WITHIN NORMAL LIMITS	P	P	P	P	P				
	TERMINAL SACRIFICE							P		
	NASAL DISCHARGE - RED						P			
4532	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
4533	WITHIN NORMAL LIMITS	P	P			P	P			
	TERMINAL SACRIFICE							P		
	NASAL DISCHARGE - RED			P	P					
4534	WITHIN NORMAL LIMITS	P	P	P	P					
	TERMINAL SACRIFICE							P		
	ALOPECIA - GENERAL					2	2			
4535	WITHIN NORMAL LIMITS	P	P							
	TERMINAL SACRIFICE							P		
	INCISORS MALOCCLUDED			P	P	P	P			
4536	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
4537	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
4538	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX B

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	2	9	0	1	2
4539	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE							P		
4540	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
4541	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	
4542	WITHIN NORMAL LIMITS	P	P	P	P	P	P			
	TERMINAL SACRIFICE								P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
1031	203	265	311	356	395	422
1032	216	287	327	359	396	407
1033	191	249	280	305	340	360
1034	227	301	354	399	441	479
1035	219	285	330	368	407	425
1036	214	278	314	345	367	386
1037	221	292	336	379	410	429
1038	207	274	309	336	374	383
1039	218	284	317	346	381	403
1040	212	276	326	364	396	410
1041	205	274	318	353	392	418
1042	208	264	292	316	343	373
MEAN	212	277	318	352	387	408
S.D.	9.6	13.9	19.5	25.7	28.4	31.1
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 2 900 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
2031	221	290	331	336	379	409
2032	215	296	351	351	412	452
2033	199	273	316	341	373	411
2034	212	277	321	362	403	412
2035	208	271	311	348	389	413
2036	196	266	305	327	374	379
2037	216	279	309	330	351	379
2038	217	286	315	346	379	404
2039	204	275	309	348	384	417
2040	226	301	344	380	404	428
2041	212	284	318	346	372	381
2042	219	283	333	379	417	450
MEAN	212	282	322	349	386	411
S.D.	9.0	10.3	14.6	16.9	19.3	24.5
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 3 3000 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
3031	211	272	311	331	370	389
3032	212	279	309	345	373	391
3033	216	266	285	315	328	348
3034	197	262	292	333	364	390
3035	206	272	307	350	387	419
3036	203	272	316	354	395	426
3037	215	276	319	357	394	400
3038	225	290	331	365	392	404
3043	191	255	300	352	386	413
3040	222	292	334	373	410	441
3041	219	287	310	341	372	398
3042	198	253	290	326	351	377
MEAN	210	273	309	345	377	400
S.D.	10.7	12.9	15.2	17.0	22.4	24.0
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 4 9000 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
4031	219	287	330	368	390	421
4032	206	273	310	351	374	384
4033	208	256	285	300	318	331
4034	213	285	335	380	417	440
4035	217	282	325	358	385	414
4036	205	272	306	345	380	404
4037	199	269	299	333	361	397
4038	221	288	336	370	406	441
4039	192	255	274	303	332	348
4040	215	280	329	360	389	411
4041	213	260	284	310	337	366
4042	222	288	329	362	399	426
MEAN	211	275	312	345	374	398
S.D.	9.3	12.5	22.0	27.4	31.0	35.2
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
1531	168	206	224	239	244	269
1532	176	205	213	234	246	252
1533	162	198	216	228	236	236
1534	168	193	218	243	251	260
1535	178	206	223	243	257	264
1536	163	191	212	242	261	271
1537	165	191	207	229	241	217
1538	175	197	209	229	240	251
1539	169	185	208	222	227	246
1540	159	180	196	223	235	244
1541	155	185	199	211	226	237
1542	174	185	213	221	239	261
MEAN	168	193	211	230	242	251
S.D.	7.2	8.9	8.5	10.1	10.7	15.8
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
2531	167	202	222	239	254	267
2532	171	205	224	233	258	274
2533	168	201	215	237	243	250
2534	163	188	203	212	226	236
2535	175	206	227	246	259	271
2536	176	208	222	250	257	269
2537	160	191	203	207	221	221
2538	164	192	205	233	247	258
2539	157	171	186	209	226	232
2540	179	211	220	246	263	276
2541	163	186	201	226	251	255
2542	173	203	216	232	249	260
MEAN	168	197	212	231	246	256
S.D.	6.9	11.4	12.3	14.6	14.4	17.8
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
3531	163	188	207	218	239	257
3532	157	183	193	207	213	215
3533	172	200	214	223	243	248
3534	169	196	209	216	232	245
3535	164	197	219	235	249	257
3536	175	206	226	245	268	274
3537	171	189	215	237	251	255
3538	166	198	215	234	251	247
3539	181	212	221	246	257	276
3540	160	196	208	227	235	247
3541	177	193	217	231	250	257
3542	162	187	205	219	219	240
MEAN	168	195	212	228	242	251
S.D.	7.3	8.2	8.7	12.0	15.7	15.8
N	12	12	12	12	12	12

APPENDIX C

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY					
ANIMAL#	-7	0	7	14	21	28
4531	167	204	218	230	242	258
4532	170	201	206	235	244	247
4533	176	207	225	242	255	268
4534	161	192	210	235	250	262
4535	174	200	206	229	238	262
4536	163	198	210	232	246	262
4537	157	177	185	199	217	229
4538	181	207	231	253	274	298
4539	174	196	219	233	254	249
4540	154	173	193	201	219	229
4541	165	189	201	205	226	230
4542	168	192	209	219	235	255
MEAN	167	195	209	226	241	254
S.D.	7.9	11.0	12.9	16.9	16.3	19.5
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
1031	63	45	46	38	28	157
1032	71	39	32	37	11	119
1033	58	31	25	35	21	111
1034	74	53	45	42	38	178
1035	66	45	38	39	18	139
1036	63	36	32	21	20	109
1037	72	43	43	31	19	137
1038	67	35	27	38	9	109
1039	66	34	29	35	22	119
1040	64	50	38	32	14	134
1041	69	45	35	39	26	145
1042	56	28	24	27	30	109
MEAN	66	40	34	35	21	130
S.D.	5.4	7.8	7.7	5.9	8.4	21.9
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 2 900 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
2031	69	41	5	43	30	119
2032	82	55	-1	61	40	156
2033	75	43	25	33	38	138
2034	65	44	41	41	9	135
2035	63	40	37	41	24	142
2036	70	40	21	48	4	113
2037	63	30	21	20	28	99
2038	69	30	31	33	24	118
2039	71	35	39	36	33	142
2040	75	43	36	24	24	127
2041	72	34	28	26	10	97
2042	64	50	46	38	33	168
MEAN	70	40	27	37	25	129
S.D.	5.6	7.5	14.2	11.2	11.5	21.4
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 3 3000 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
3031	62	39	20	39	20	117
3032	67	30	36	28	19	112
3033	49	20	30	13	21	82
3034	65	30	41	31	27	129
3035	65	35	43	36	32	147
3036	69	45	38	41	30	154
3037	61	43	39	37	6	124
3038	65	41	34	27	11	113
3043	64	45	53	34	26	158
3040	70	42	39	37	30	148
3041	68	22	31	31	26	111
3042	55	38	35	25	26	125
MEAN	63	36	37	32	23	127
S.D.	6.0	8.5	8.0	7.7	8.0	21.9
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

MALES GROUP 4 9000 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
4031	69	43	38	22	31	134
4032	67	37	42	23	10	111
4033	47	29	15	18	13	75
4034	72	50	45	37	23	154
4035	65	43	33	27	28	132
4036	67	34	40	34	25	133
4037	70	30	34	28	36	128
4038	67	48	34	36	36	153
4039	63	19	29	29	16	93
4040	65	48	32	29	22	131
4041	47	24	26	26	29	106
4042	66	41	33	37	27	138
MEAN	64	37	33	29	25	124
S.D.	8.2	10.0	7.8	6.2	8.3	23.5
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
1531	37	19	15	5	25	64
1532	29	9	21	12	6	47
1533	36	18	13	7	1	39
1534	26	24	26	8	9	67
1535	28	18	20	14	7	58
1536	27	22	30	19	11	81
1537	26	16	22	13	-25	26
1538	22	12	21	11	11	54
1539	15	23	14	5	19	62
1540	21	16	27	12	9	64
1541	30	14	12	16	10	51
1542	11	28	9	18	22	76
MEAN	26	18	19	12	9	57
S.D.	7.6	5.4	6.6	4.5	12.6	15.2
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
2531	35	20	18	15	13	65
2532	34	19	9	25	16	69
2533	32	15	22	6	7	49
2534	25	15	9	14	10	48
2535	30	21	19	14	12	65
2536	32	14	28	8	12	62
2537	31	12	4	14	-1	30
2538	28	13	27	15	10	66
2539	14	15	23	17	6	61
2540	31	10	26	17	13	65
2541	23	15	25	25	4	69
2542	30	13	15	18	11	57
MEAN	29	15	19	15	9	59
S.D.	5.6	3.3	7.9	5.6	4.5	11.4
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
3531	26	18	11	21	18	68
3532	27	10	14	6	2	32
3533	28	14	9	20	5	48
3534	27	14	6	17	13	49
3535	33	23	16	14	8	60
3536	31	20	19	23	6	68
3537	17	27	21	14	4	67
3538	31	18	19	17	-5	49
3539	32	8	26	11	19	64
3540	36	13	19	8	13	52
3541	16	24	13	19	7	64
3542	25	17	14	0	22	53
MEAN	27	17	16	14	9	56
S.D.	5.9	5.7	5.4	6.9	7.6	11.0
N	12	12	12	12	12	12

APPENDIX D

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY					
ANIMAL#	-7-0	0-7	7-14	14-21	21-28	0-28
4531	38	14	11	12	16	54
4532	32	5	29	9	3	46
4533	31	18	17	13	13	61
4534	31	18	24	16	12	70
4535	26	6	24	9	25	62
4536	34	12	22	15	16	65
4537	19	9	13	18	12	52
4538	26	24	22	21	23	90
4539	22	23	15	20	-5	53
4540	19	20	8	19	10	56
4541	25	12	4	20	5	41
4542	24	17	10	16	20	63
MEAN	27	15	17	15	13	59
S.D.	6.0	6.2	7.6	4.3	8.4	12.7
N	12	12	12	12	12	12

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

MALES GROUP 1 0 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
1031	109	87	72
1032	105	85	70
1033	110	85	70
1034	106	90	77
1035	105	89	73
1036	106	85	74
1037	98	83	72
1038	106	84	69
1039	108	88	76
1040	106	93	78
1041	106	88	73
1042	103	85	70
MEAN	106	87	73
S.D.	3.0	2.9	2.9
N	12	12	12

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

MALES GROUP 2 900 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
2031	112	93	66
2032	107	86	69
2033	105	89	75
2034	109	85	72
2035	109	87	78
2036	114	93	81
2037	102	88	71
2038	105	83	73
2039	111	90	74
2040	98	85	70
2041	109	90	72
2042	104	91	77
MEAN	107	88	73
S.D.	4.4	3.4	4.2
N	12	12	12

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

MALES GROUP 3 3000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
3031	110	93	74
3032	100	80	72
3033	98	76	66
3034	102	82	70
3035	99	81	69
3036	110	93	75
3037	109	90	77
3038	107	86	72
3043	113	93	82
3040	107	87	75
3041	105	78	73
3042	101	85	72
MEAN	105	85	73
S.D.	4.8	6.0	4.1
N	12	12	12

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

MALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
4031	111	94	78
4032	108	87	75
4033	104	84	68
4034	108	87	75
4035	108	89	75
4036	102	82	70
4037	116	92	76
4038	104	89	72
4039	113	87	75
4040	105	94	71
4041	SF	82	72
4042	100	82	67
MEAN	107	87	73
S.D.	4.7	4.4	3.5
N	11	12	12

SF=Spilled Feeder

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY				
ANIMAL#	0	7	14	21	28
1531	98	81	79	75	73
1532	94	78	79	75	68
1533	SF	87	80	78	70
1534	94	83	84	68	61
1535	88	84	76	70	62
1536	SF	86	83	75	71
1537	95	91	80	76	67
1538	88	79	78	69	67
1539	94	89	83	82	80
1540	94	86	84	74	69
1541	104	89	83	79	72
1542	96	87	80	77	74
MEAN	95	85	81	75	69
S.D.	4.6	4.0	2.6	4.0	5.1
N	10	12	12	12	12

SF=Spilled Feeder

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY				
ANIMAL#	0	7	14	21	28
2531	96	81	76	71	72
2532	97	81	79	79	74
2533	92	82	77	64	62
2534	91	86	76	70	69
2535	CF	CF	CF	CF	CF
2536	SF	88	86	67	70
2537	107	96	95	87	84
2538	101	91	89	75	75
2539	91	91	84	75	67
2540	103	90	84	74	71
2541	SF	87	84	77	67
2542	101	88	82	78	72
MEAN	98	87	83	74	71
S.D.	5.9	4.8	6.0	6.3	5.7
N	9	11	11	11	11

CF=Contaminated Feeder SF=Spilled Feeder

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY				
ANIMAL#	0	7	14	21	28
3531	96	84	81	SF	73
3532	97	84	77	70	64
3533	93	81	81	76	65
3534	107	83	80	78	73
3535	105	88	83	78	74
3536	100	84	80	75	68
3537	111	96	91	83	79
3538	100	88	81	75	74
3539	94	76	82	73	75
3540	SF	81	84	74	71
3541	99	89	85	84	76
3542	SF	82	76	72	74
MEAN	100	85	82	76	72
S.D.	5.8	5.1	3.8	4.3	4.5
N	10	12	12	11	12

SF=Spilled Feeder

APPENDIX E

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY				
ANIMAL#	0	7	14	21	28
4531	104	85	81	77	72
4532	102	90	83	74	71
4533	98	92	79	74	69
4534	100	88	82	74	67
4535	121	86	81	77	75
4536	113	88	88	78	71
4537	101	91	87	85	76
4538	109	91	88	78	77
4539	SF	86	86	80	69
4540	117	92	87	82	77
4541	98	82	75	75	65
4542	103	80	81	78	74
MEAN	106	88	83	78	72
S.D.	8.0	4.0	4.1	3.4	3.9
N	11	12	12	12	12

SF=Spilled Feeder

	Individual Functional Observational Battery Evaluations Main Study Preface	Appendix F

Key:

REFLEX ASSESSMENTS

Audition Assessment: (Sound)	1 - Normal; flinches and/or flicks ears 2 - No reaction 3 - Exaggerated; jumps, flips, bites
Pain Perception: (Pain)	1 - Normal; turns and bites at the site or walks forward, away from the stimulus 2 - No reaction 3 - Increased pain; jumps forward, with or without vocalization, or exhibits highly exaggerated bizarre reaction, attacks, bites

GRIP STRENGTH[1]

Forelimb and hindlimb grip strength measured in grams of force.

RECTAL TEMPERATURE

Measured in centigrade.

[1]The means of Trials 1 and 2 were calculated and statistically evaluated in Table 5.

Males	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 1 – 0 ppm									
1031	1	1	1100	1020	**1060**	840	1000	**920**	38.3
1032	1	1	610	1080	**845**	705	835	**770**	38.9
1033	1	1	900	1070	**985**	775	925	**850**	36.8
1034	1	1	1085	1175	**1130**	990	840	**915**	36.6
1035	1	1	1200	1085	**1143**	895	935	**915**	37.0
1036	1	1	990	1200	**1095**	740	770	**755**	38.4
1037	1	1	1065	1180	**1123**	670	785	**728**	37.8
1038	1	1	870	1020	**945**	850	865	**858**	38.8
1039	1	1	805	915	**860**	805	635	**720**	33.4
1040	1	1	645	735	**690**	630	630	**630**	37.4
1041	1	1	1115	935	**1025**	715	530	**623**	34.5
1042	1	1	1175	915	**1045**	810	740	**775**	38.4

Males	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 2 - 900 ppm									
2031	1	2	940	1050	**995**	745	685	**715**	36.2
2032	1	1	750	720	**735**	610	755	**683**	36.3
2033	1	1	1090	1100	**1095**	655	705	**680**	38.4
2034	1	1	1300	900	**1100**	850	600	**725**	38.4
2035	1	1	1020	700	**860**	680	840	**760**	37.7
2036	1	1	1120	1245	**1183**	705	740	**723**	35.8
2037	1	1	935	975	**955**	670	690	**680**	35.7
2038	1	1	1035	1195	**1115**	505	755	**630**	34.6
2039	1	1	1300	1195	**1248**	755	760	**758**	37.6
2040	1	1	935	775	**855**	780	805	**793**	36.6
2041	1	1	1305	1255	**1280**	900	885	**893**	37.9
2042	1	1	1365	890	**1128**	755	920	**838**	36.7

Males	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 3 – 3000 ppm									
3031	1	1	1100	995	**1048**	895	935	**915**	37.6
3032	1	1	490	720	**605**	685	660	**673**	38.8
3033	1	1	925	880	**903**	960	680	**820**	38.2
3034	1	1	1060	1280	**1170**	815	965	**890**	36.3
3035	1	1	715	1100	**908**	710	805	**758**	38.9
3036	1	1	1095	1360	**1228**	695	640	**668**	38.2
3037	1	1	1230	1000	**1115**	835	820	**828**	34.9
3038	1	1	1015	1200	**1108**	750	1060	**905**	38.7
3040	1	1	845	890	**868**	855	755	**805**	38.4
3041	1	1	1500	1195	**1348**	660	870	**765**	38.6
3042	1	1	1210	1155	**1183**	710	760	**735**	38.7
3043	1	1	1040	855	**948**	685	760	**723**	38.9

Males	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 4 – 9000 ppm									
4031	1	1	1085	1100	**1093**	770	660	**715**	38.4
4032	1	2	1055	1025	**1040**	800	685	**743**	38.0
4033	1	1	805	895	**850**	625	775	**700**	36.4
4034	1	1	965	1200	**1083**	665	750	**708**	37.4
4035	1	1	965	940	**953**	615	755	**685**	38.3
4036	1	1	1205	1055	**1130**	660	685	**673**	37.8
4037	1	1	1185	1065	**1125**	1000	875	**938**	38.8
4038	1	1	950	855	**903**	860	675	**768**	35.6
4039	1	1	930	855	**893**	845	680	**763**	38.0
4040	1	1	790	845	**818**	800	915	**858**	35.6
4041	1	1	990	1050	**1020**	815	770	**793**	39.0
4042	1	3	1270	1280	**1275**	905	915	**910**	38.6

Females	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 1 – 0 ppm									
1531	1	1	695	815	**755**	595	755	**675**	39.0
1532	1	1	985	1015	**1000**	760	730	**745**	37.3
1533	1	1	690	740	**715**	660	735	**698**	37.9
1534	1	1	565	730	**648**	510	525	**518**	38.5
1535	1	1	825	835	**830**	575	650	**613**	38.1
1536	1	1	795	725	**760**	720	420	**570**	39.1
1537	1	1	1000	895	**948**	765	655	**710**	38.6
1538	1	1	790	805	**798**	680	750	**715**	35.4
1539	1	1	1040	1010	**1025**	855	885	**870**	38.9
1540	1	1	705	900	**803**	735	690	**713**	37.8
1541	1	1	890	870	**880**	815	790	**803**	39.1
1542	1	3	935	840	**888**	625	540	**583**	39.3

Females	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
	Sound	Pain	Forelimb Trial 1	Forelimb Trial 2	Forelimb Mean	Hindlimb Trial 1	Hindlimb Trial 2	Hindlimb Mean	
Group 2 – 900 ppm									
2531	1	1	560	640	**600**	600	610	**605**	38.3
2532	1	1	885	940	**913**	700	705	**703**	38.7
2533	1	1	1135	965	**1050**	830	785	**808**	38.5
2534	1	1	695	635	**665**	675	535	**605**	37.4
2535	1	1	955	915	**935**	875	640	**758**	37.3
2536	1	1	775	610	**693**	610	585	**598**	37.2
2537	1	1	825	925	**875**	675	585	**630**	38.3
2538	1	1	890	950	**920**	855	510	**683**	39.7
2539	1	1	855	925	**890**	900	600	**750**	38.1
2540	1	1	690	580	**635**	715	565	**640**	38.3
2541	1	1	675	865	**770**	805	835	**820**	38.3
2542	1	1	845	965	**905**	610	745	**678**	38.8

Females	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 3 – 3000 ppm									
3531	1	1	375	840	**608**	515	610	**563**	38.3
3532	1	1	650	775	**713**	590	530	**560**	39.0
3533	1	1	960	1000	**980**	635	765	**700**	36.1
3534	1	1	1030	750	**890**	655	580	**618**	37.5
3535	1	1	660	750	**705**	530	555	**543**	38.3
3536	1	1	775	530	**653**	705	800	**753**	38.5
3537	1	1	1100	895	**998**	755	745	**750**	38.2
3538	1	1	550	635	**593**	735	660	**698**	39.1
3539	1	1	640	660	**650**	780	615	**698**	38.7
3540	1	1	700	940	**820**	895	755	**825**	38.4
3541	1	1	925	980	**953**	505	610	**558**	38.2
3542	1	1	760	850	**805**	775	685	**730**	38.8

Females	Individual Functional Observational Battery Evaluations 4th Week of Exposure	Appendix F

Animal Number	Reflex Assessments		Grip Strength (grams)						Rectal Temperature (°C)
			Forelimb			Hindlimb			
	Sound	Pain	Trial 1	Trial 2	Mean	Trial 1	Trial 2	Mean	
Group 4 – 9000 ppm									
4531	1	1	790	1040	**915**	830	865	**848**	34.1
4532	1	1	550	960	**755**	720	650	**685**	37.9
4533	1	1	850	990	**920**	665	525	**595**	37.7
4534	1	1	610	890	**750**	645	705	**675**	37.7
4535	1	1	855	890	**873**	560	665	**613**	39.3
4536	1	1	790	890	**840**	720	635	**678**	37.6
4537	1	1	875	710	**793**	560	625	**593**	38.5
4538	1	1	1000	885	**943**	835	705	**770**	39.0
4539	1	1	940	750	**845**	855	920	**888**	38.6
4540	1	1	790	700	**745**	770	775	**773**	38.3
4541	1	1	785	895	**840**	780	705	**743**	38.4
4542	1	1	1030	995	**1013**	730	940	**835**	39.4

Males	Individual Motor Activity Values[a] Main Study 4th Week of Exposure	Appendix G

Animal Number	Interval 1	2	3	4	5	6	7	8	9	10	11	12
Group 1 – 0 ppm												
1031	196	127	166	174	170	137	190	142	23	0	5	1
1032	142	111	80	81	60	27	5	0	0	0	0	0
1033	230	216	130	83	3	9	0	0	3	2	12	0
1034	222	191	117	27	72	21	17	0	1	0	0	0
1035	193	193	163	157	125	125	57	23	113	12	3	0
1036	175	239	158	120	91	55	32	21	0	4	0	0
1037	175	153	168	136	91	65	34	5	0	0	0	0
1038	134	141	64	42	0	0	0	71	134	129	96	61
1039	233	130	166	48	11	0	0	0	0	3	4	19
1040	205	123	96	20	4	0	96	24	0	0	0	1
1041	159	168	131	127	85	120	40	0	0	0	0	0
1042	163	83	103	102	101	11	4	45	0	0	0	0
Mean	**185.6**	**156.3**	**128.5**	**93.1**	**67.8**	**47.5**	**39.6**	**27.6**	**22.8**	**12.5**	**10.0**	**6.8**
SD	**33.15**	**46.14**	**36.67**	**51.37**	**54.24**	**52.52**	**55.49**	**42.29**	**47.68**	**36.85**	**27.32**	**17.90**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**
Group 2 – 900 ppm												
2031	239	185	132	174	29	0	0	0	0	0	0	4
2032	181	101	1	0	0	3	0	0	0	0	0	0
2033	175	187	174	12	1	0	0	0	0	9	2	4
2034	217	204	167	137	19	0	1	0	1	0	1	0
2035	218	163	187	141	72	17	1	0	0	2	0	0
2036	267	233	170	154	157	173	155	50	51	249	83	16
2037	280	224	246	186	272	180	135	66	0	0	10	16
2038	138	168	133	68	17	0	0	0	8	0	0	0
2039	232	214	206	147	193	49	0	0	0	0	0	0
2040	84	120	72	2	0	0	5	1	1	0	5	0
2041	165	136	65	107	50	58	0	0	0	0	4	0
2042	174	114	121	112	114	35	0	22	136	136	135	104
Mean	**197.5**	**170.8**	**139.5**	**103.3**	**77.0**	**42.9**	**24.8**	**11.6**	**16.4**	**33.0**	**20.0**	**12.0**
SD	**55.73**	**44.81**	**67.84**	**67.07**	**88.89**	**65.72**	**56.35**	**22.83**	**40.37**	**78.34**	**43.13**	**29.59**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

[a]Number of beam breaks per interval.

Males	Individual Motor Activity Values[a] Main Study 4th Week of Exposure	Appendix G

Animal Number	Interval 1	2	3	4	5	6	7	8	9	10	11	12
Group 3 – 3000 ppm												
3031	243	173	132	156	82	136	93	0	0	2	2	0
3032	200	122	164	98	7	1	0	5	1	0	0	4
3033	128	93	98	24	0	0	0	0	0	0	0	15
3034	223	128	177	91	118	134	27	49	35	0	0	0
3035	92	31	67	73	0	0	0	0	2	0	0	0
3036	230	233	180	115	69	60	28	1	0	0	0	1
3037	199	103	65	1	0	0	4	1	9	0	0	0
3038	169	162	63	111	6	0	0	0	63	27	0	23
3043	218	182	151	178	136	78	0	0	0	0	0	9
3040	211	161	194	174	127	14	1	0	0	0	0	44
3041	91	40	194	68	2	0	4	0	0	0	8	8
3042	156	116	59	50	168	75	7	1	0	1	0	0
Mean	**180.0**	**128.7**	**128.7**	**94.9**	**59.6**	**41.5**	**13.7**	**4.8**	**9.2**	**2.5**	**0.8**	**8.7**
SD	**52.70**	**58.30**	**54.96**	**56.12**	**64.49**	**53.34**	**26.97**	**14.01**	**19.71**	**7.74**	**2.33**	**13.32**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**
Group 4 – 9000 ppm												
4031	132	145	63	0	0	0	0	38	1	0	3	8
4032	159	119	104	107	121	110	13	0	0	4	4	1
4033	132	85	67	8	40	38	0	100	20	0	0	0
4034	223	144	15	0	59	67	62	119	7	1	0	0
4035	255	176	91	168	168	90	54	133	118	149	200	33
4036	175	160	157	93	92	39	82	5	0	0	1	30
4037	175	134	167	85	134	149	124	56	32	2	51	88
4038	222	144	130	39	5	0	3	0	0	0	13	5
4039	159	204	126	93	0	0	0	3	0	1	0	1
4040	178	192	129	98	139	152	11	0	0	0	0	3
4041	154	125	90	118	28	9	1	20	2	2	52	132
4042	228	220	150	109	36	14	0	0	0	36	233	143
Mean	**182.7**	**154.0**	**107.4**	**76.5**	**68.5**	**55.7**	**29.2**	**39.5**	**15.0**	**16.3**	**46.4**	**37.0**
SD	**40.09**	**38.53**	**44.59**	**53.05**	**59.91**	**57.25**	**41.51**	**50.58**	**33.98**	**43.02**	**81.98**	**53.32**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

[a]Number of beam breaks per interval

Females	Individual Motor Activity Values[a] Main Study 4th Week of Exposure	Appendix G

Animal Number	Interval 1	2	3	4	5	6	7	8	9	10	11	12
Group 1 – 0 ppm												
1531	130	103	88	33	81	0	38	40	40	0	13	0
1532	139	156	77	77	51	66	11	8	0	0	0	0
1533	154	97	56	19	43	0	0	0	3	0	1	0
1534	83	78	0	30	108	66	2	0	0	0	0	0
1535	168	121	166	119	59	0	5	0	2	2	0	0
1536	130	125	149	104	155	87	86	73	25	0	0	0
1537	159	112	132	102	58	29	134	124	52	2	7	0
1538	111	120	128	71	103	71	8	2	0	0	0	0
1539	170	92	68	73	22	7	4	0	2	6	4	6
1540	159	50	1	0	0	71	114	96	15	0	0	2
1541	117	109	104	86	80	74	42	26	0	0	0	0
1542	148	103	107	58	55	112	9	77	107	122	19	0
Mean	**139.0**	**105.5**	**89.7**	**64.3**	**67.9**	**48.6**	**37.8**	**37.2**	**20.5**	**11.0**	**3.7**	**0.7**
SD	**26.07**	**26.18**	**52.90**	**37.08**	**41.24**	**39.25**	**47.45**	**44.33**	**32.44**	**35.00**	**6.29**	**1.78**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**
Group 2 – 900 ppm												
2531	165	118	105	119	103	78	30	0	0	0	0	0
2532	99	87	80	43	54	113	25	7	0	0	1	1
2533	107	71	75	66	6	0	3	0	5	0	31	57
2534	153	132	61	80	3	22	0	0	0	0	0	0
2535	184	122	120	49	68	54	32	4	3	3	0	1
2536	130	133	102	101	88	102	100	92	15	0	0	0
2537	150	109	68	94	100	64	33	0	0	0	0	5
2538	123	105	101	72	61	82	50	47	62	21	0	1
2539	128	84	63	21	1	0	0	0	0	0	2	0
2540	125	133	108	27	1	0	0	0	0	0	0	0
2541	127	121	99	64	20	26	90	95	85	45	39	3
2542	119	64	39	60	69	65	128	68	61	70	56	22
Mean	**134.2**	**106.6**	**85.1**	**66.3**	**47.8**	**50.5**	**40.9**	**26.1**	**19.3**	**11.6**	**10.8**	**7.5**
SD	**24.42**	**24.49**	**24.28**	**29.31**	**39.73**	**40.20**	**43.21**	**38.40**	**31.05**	**22.89**	**19.62**	**16.77**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

[a]Number of beam breaks per interval

Females	Individual Motor Activity Values[a] Main Study 4th Week of Exposure	Appendix G

Animal Number	Interval 1	2	3	4	5	6	7	8	9	10	11	12
Group 3 – 3000 ppm												
3531	161	128	105	66	70	67	19	114	102	67	14	39
3532	146	125	63	81	126	126	64	25	0	0	0	0
3533	133	102	53	67	49	25	0	0	0	0	0	15
3534	132	80	88	96	57	98	61	54	0	0	0	0
3535	137	75	67	38	11	2	1	63	79	94	6	20
3536	206	131	89	18	0	0	4	8	3	5	0	0
3537	186	125	106	73	29	0	49	23	0	0	0	0
3554	172	111	53	52	2	4	7	2	0	0	4	1
3539	109	77	85	52	29	6	6	7	1	0	2	3
3540	124	148	103	23	6	0	0	1	0	0	0	3
3541	76	90	120	58	55	59	65	52	100	68	89	28
3542	77	87	104	56	52	85	65	47	2	0	0	0
Mean	**138.3**	**106.6**	**86.3**	**56.7**	**40.5**	**39.3**	**28.4**	**33.0**	**23.9**	**19.5**	**9.6**	**9.1**
SD	**39.70**	**24.73**	**22.58**	**22.61**	**36.07**	**45.52**	**29.30**	**34.37**	**42.42**	**34.92**	**25.35**	**13.34**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**
Group 4 – 9000 ppm												
4531	120	87	113	127	9	6	0	3	1	0	5	0
4532	132	109	99	41	95	103	49	17	8	0	0	3
4533	160	120	88	67	31	72	86	11	3	67	118	75
4534	127	60	103	83	79	68	33	49	0	0	0	0
4535	164	117	127	98	76	87	61	66	4	0	9	0
4536	153	140	71	107	101	78	103	87	39	25	80	62
4537	83	155	90	91	92	5	0	0	0	0	0	0
4538	213	152	119	95	38	39	56	89	1	0	0	0
4539	122	105	47	58	75	49	1	0	0	0	0	0
4540	112	115	88	65	55	61	0	0	0	0	4	0
4541	90	141	118	77	34	5	1	0	29	91	127	85
4542	117	110	27	2	1	6	33	138	82	54	75	21
Mean	**132.8**	**117.6**	**90.8**	**75.9**	**57.2**	**48.3**	**35.3**	**38.3**	**13.9**	**19.8**	**34.8**	**20.5**
SD	**35.50**	**27.28**	**30.08**	**32.90**	**34.09**	**35.55**	**36.35**	**46.78**	**24.96**	**32.52**	**50.13**	**33.17**
N	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

[a]Number of beam breaks per interval

	Individual Hematology Values Main Study Preface	Appendix H

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

ERYTHROCYTE MORPHOLOGY

Abbreviation	Cell Morphology	Range
Poly	Polychromasia	1+ = few
Poik	Poikilocytosis	2+ = slight

PLATELET MORPHOLOGY (PLT MORPH)

Abbreviation	Definition
CLSL	Slight Platelet Clumping Noted
LPO	Occasional Large Platelets Noted
NAN	No abnormalities noted

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Individual Hematology Values - Termination

Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
1M	1031	15.8	47.2	7.78	293.5	1259	60.7	20.3	33.5	17.87
0 ppm	1032	16.7	49.5	8.75	184.1	642	56.5	19.1	33.7	9.52
	1033	14.8	43.4	7.93	198.4	994	54.7	18.7	34.1	8.87
	1034	15.5	45.1	7.84	225.9	848	57.5	19.7	34.3	14.58
	1035	15.2	45.1	8.06	181.5	1048	56.0	18.9	33.7	11.09
	1036	15.2	44.5	7.65	150.6	1014	58.2	19.9	34.2	10.53
	1037	15.1	45.5	8.04	158.1	683	56.6	18.8	33.2	13.25
	1038	15.6	46.4	8.44	150.7	882	55.0	18.5	33.7	12.04
	1039	15.3	45.1	8.09	206.7	1195	55.7	19.0	34.0	10.28
	1040	16.3	49.4	9.06	216.2	911	54.6	18.0	33.0	9.93
	1041	15.7	45.7	7.88	201.0	685	58.1	19.9	34.3	14.63
	1042	16.3	49.3	8.65	207.8	613	57.0	18.9	33.1	14.43
	Mean	15.6	46.4	8.18	197.9	898	56.7	19.1	33.7	12.25
	SD	0.57	2.06	0.441	39.26	214.3	1.75	0.67	0.46	2.712
	n	12	12	12	12	12	12	12	12	12

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Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
1M	1031	1.61	15.65	0.18	0.12	0.22	0.08	1+	1+	NAN
0 ppm	1032	1.80	7.16	0.17	0.22	0.13	0.04	1+	1+	CLSL
	1033	1.05	7.42	0.20	0.05	0.09	0.06	1+	1+	LPO
	1034	2.22	11.35	0.49	0.15	0.29	0.09	1+	1+	NAN
	1035	2.72	7.94	0.16	0.06	0.15	0.06	1+	1+	NAN
	1036	1.32	8.77	0.21	0.05	0.08	0.10	1+	1+	NAN
	1037	1.41	11.33	0.22	0.09	0.13	0.06	1+	1+	NAN
	1038	1.94	9.60	0.20	0.08	0.12	0.10	1+	1+	NAN
	1039	1.88	8.03	0.18	0.08	0.08	0.04	1+	1+	LPO
	1040	1.61	7.72	0.21	0.16	0.13	0.09	1+	1+	NAN
	1041	2.19	11.77	0.26	0.15	0.15	0.10	1+	1+	CLSL
	1042	2.74	10.96	0.29	0.18	0.18	0.07	1+	1+	NAN
	Mean	1.87	9.81	0.23	0.12	0.15	0.07			
	SD	0.525	2.502	0.090	0.056	0.061	0.022			
	n	12	12	12	12	12	12			

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Individual Hematology Values - Termination

Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
2M	2031	15.2	45.3	7.88	220.1	858	57.5	19.3	33.6	15.01
900 ppm	2032	14.5	43.0	7.53	433.1	965	57.1	19.3	33.7	16.74
	2033	15.5	45.9	7.67	239.5	749	59.8	20.1	33.7	18.41
	2034	14.9	44.6	7.82	110.8	705	57.0	19.1	33.5	16.02
	2035	15.7	47.1	8.27	156.8	1058	56.9	18.9	33.3	16.83
	2036	16.3	48.9	8.75	171.0	613	55.8	18.6	33.3	13.15
	2037	16.2	47.9	8.67	175.2	708	55.3	18.7	33.9	13.09
	2038	16.0	46.2	8.07	207.6	830	57.3	19.8	34.5	9.27
	2039	15.5	45.9	7.69	186.4	573	59.7	20.1	33.7	11.48
	2040	15.9	47.8	8.33	183.2	495	57.4	19.1	33.3	14.91
	2041	15.0	44.4	8.32	204.7	863	53.4	18.0	33.7	19.93
	2042	15.9	47.3	8.13	195.7	828	58.3	19.5	33.5	15.94
	Mean	15.6	46.2	8.09	207.0	770	57.1	19.2	33.6	15.07
	SD	0.56	1.70	0.391	78.37	162.9	1.77	0.62	0.33	2.962
	n	12	12	12	12	12	12	12	12	12

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Individual Hematology Values - Termination

Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
2M	2031	2.12	12.17	0.31	0.17	0.15	0.09	1+	1+	NAN
900 ppm	2032	2.83	13.14	0.38	0.10	0.20	0.10	1+	1+	NAN
	2033	1.94	15.72	0.28	0.13	0.24	0.09	1+	1+	NAN
	2034	3.33	11.90	0.36	0.16	0.19	0.08	1+	1+	CLSL
	2035	2.42	13.60	0.37	0.08	0.25	0.12	1+	1+	NAN
	2036	2.56	9.84	0.35	0.17	0.16	0.07	1+	1+	CLSL
	2037	2.44	9.87	0.26	0.27	0.19	0.06	1+	1+	CLSL
	2038	1.11	7.78	0.16	0.11	0.08	0.04	1+	1+	LPO
	2039	1.75	9.20	0.20	0.20	0.10	0.04	1+	1+	CLSL
	2040	3.57	10.61	0.28	0.22	0.16	0.08	1+	1+	CLSL
	2041	1.53	17.32	0.36	0.04	0.30	0.38	1+	1+	NAN
	2042	2.33	12.85	0.34	0.12	0.17	0.13	1+	1+	LPO
	Mean	2.33	12.00	0.30	0.15	0.18	0.11			
	SD	0.708	2.756	0.070	0.064	0.062	0.090			
	n	12	12	12	12	12	12			

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Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
3M	3031	15.7	46.7	8.22	183.6	714	56.8	19.1	33.7	15.18
3000 ppm	3032	15.7	45.1	7.85	185.4	716	57.4	20.0	34.8	10.55
	3033	15.6	45.3	7.82	155.6	802	58.0	20.0	34.4	10.44
	3034	16.1	46.8	7.99	198.0	723	58.6	20.2	34.5	10.47
	3035	17.2	51.2	8.73	214.9	672	58.6	19.7	33.6	11.74
	3036	15.0	42.7	7.29	192.4	619	58.5	20.5	35.1	11.29
	3037	15.7	47.3	8.43	140.1	840	56.1	18.6	33.2	17.41
	3038	16.2	47.9	8.50	145.5	626	56.4	19.0	33.7	13.17
	3040	16.5	48.9	8.47	207.0	611	57.7	19.5	33.7	11.87
	3041	14.8	43.3	6.94	251.8	605	62.4	21.3	34.2	10.65
	3042	16.1	47.0	7.98	173.7	930	58.9	20.2	34.3	10.90
	3043	16.7	50.5	8.69	203.8	795	58.1	19.3	33.2	11.62
	Mean	15.9	46.9	8.08	187.7	721	58.1	19.8	34.0	12.11
	SD	0.68	2.58	0.550	31.48	103.3	1.62	0.74	0.61	2.159
	n	12	12	12	12	12	12	12	12	12

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Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
3M	3031	2.29	12.21	0.32	0.13	0.15	0.08	1+	1+	CLSL
3000 ppm	3032	1.52	8.45	0.25	0.10	0.15	0.08	1+	1+	NAN
	3033	1.30	8.72	0.16	0.10	0.10	0.07	1+	1+	NAN
	3034	2.15	7.90	0.18	0.06	0.13	0.05	1+	1+	NAN
	3035	1.31	9.87	0.20	0.06	0.23	0.07	1+	1+	NAN
	3036	1.84	8.90	0.18	0.20	0.10	0.07	1+	1+	CLSL
	3037	1.49	15.36	0.15	0.11	0.16	0.14	1+	1+	NAN
	3038	2.46	9.98	0.28	0.24	0.14	0.06	1+	1+	CLSL
	3040	2.28	8.90	0.21	0.29	0.12	0.06	1+	1+	CLSL
	3041	2.41	7.67	0.28	0.14	0.09	0.06	1+	1+	CLSL
	3042	1.78	8.72	0.16	0.08	0.11	0.03	1+	1+	CLSL
	3043	1.30	9.80	0.28	0.06	0.12	0.06	1+	1+	NAN
	Mean	1.84	9.71	0.22	0.13	0.13	0.07			
	SD	0.457	2.144	0.058	0.075	0.038	0.026			
	n	12	12	12	12	12	12			

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Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
4M	4031	16.0	47.0	7.94	179.5	852	59.2	20.2	34.0	12.57
9000 ppm	4032	17.1	49.5	8.40	154.4	717	59.0	20.4	34.6	17.51
	4033	16.0	45.8	7.98	154.8	834	57.4	20.0	34.9	14.41
	4034	15.4	44.5	7.70	196.8	1081	57.8	20.0	34.7	11.65
	4035	16.1	47.5	8.30	193.1	498	57.2	19.3	33.8	15.60
	4036	16.3	47.8	8.24	188.5	897	58.0	19.8	34.2	11.97
	4037	15.7	45.6	8.13	204.2	545	56.2	19.3	34.3	10.83
	4038	16.3	47.7	8.16	192.2	802	58.4	20.0	34.2	13.29
	4039	15.8	47.8	8.53	214.0	691	56.0	18.5	33.1	9.48
	4040	15.5	45.1	7.81	190.1	863	57.8	19.8	34.3	13.63
	4041	16.4	47.7	8.45	227.7	636	56.5	19.4	34.4	11.99
	4042	17.1	50.4	9.13	176.6	791	55.2	18.7	33.9	11.32
	Mean	16.1	47.2	8.23	189.3	767	57.4	19.6	34.2	12.85
	SD	0.55	1.73	0.382	21.43	161.1	1.23	0.59	0.47	2.202
	n	12	12	12	12	12	12	12	12	12

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Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
4M	4031	1.44	10.65	0.21	0.07	0.15	0.05	1+	1+	CLSL
9000 ppm	4032	1.72	15.09	0.17	0.19	0.19	0.13	1+	1+	CLSL
	4033	1.69	12.28	0.15	0.09	0.14	0.06	1+	1+	CLSL
	4034	1.13	10.12	0.18	0.04	0.09	0.09	1+	1+	CLSL
	4035	2.84	11.79	0.42	0.24	0.21	0.10	1+	1+	CLSL
	4036	1.23	10.30	0.16	0.05	0.14	0.10	1+	1+	NAN
	4037	2.62	7.75	0.16	0.13	0.11	0.05	1+	1+	NAN
	4038	2.29	10.31	0.25	0.15	0.15	0.13	1+	1+	CLSL
	4039	1.65	7.48	0.09	0.12	0.10	0.04	1+	1+	NAN
	4040	2.61	10.59	0.18	0.06	0.10	0.09	1+	1+	NAN
	4041	1.95	9.38	0.22	0.21	0.18	0.05	1+	1+	CLSL
	4042	1.35	9.51	0.20	0.10	0.12	0.03	1+	1+	CLSL
	Mean	1.88	10.44	0.20	0.12	0.14	0.08			
	SD	0.584	2.023	0.080	0.065	0.038	0.034			
	n	12	12	12	12	12	12			

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Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
1F	1531	15.4	42.8	8.05	188.6	715	53.1	19.2	36.1	8.75
0 ppm	1532	15.6	44.3	8.04	146.9	1078	55.1	19.4	35.2	11.63
	1533	15.1	43.6	8.11	116.6	1043	53.8	18.7	34.7	9.38
	1534	13.1	38.1	7.02	197.6	824	54.2	18.6	34.4	11.62
	1535	16.0	45.1	8.17	131.1	445	55.2	19.6	35.4	13.33
	1536	17.6	49.3	8.76	191.8	692	56.3	20.1	35.7	14.63
	1537	15.9	46.1	8.17	180.1	423	56.5	19.5	34.6	11.10
	1538	15.7	45.4	8.03	162.5	536	56.6	19.5	34.5	10.08
	1539	16.4	46.1	8.24	169.5	596	55.9	19.9	35.7	10.48
	1540	15.0	42.8	7.67	176.9	763	55.8	19.5	35.0	13.51
	1541	15.7	45.3	8.15	208.9	827	55.6	19.3	34.7	9.25
	1542	15.0	42.8	7.51	376.7	864	57.0	19.9	35.0	13.19
	Mean	15.5	44.3	7.99	187.3	734	55.4	19.4	35.1	11.41
	SD	1.05	2.70	0.431	65.61	210.8	1.20	0.45	0.54	1.914
	n	12	12	12	12	12	12	12	12	12

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Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
1F	1531	1.92	6.17	0.14	0.33	0.14	0.05	1+	1+	NAN
0 ppm	1532	0.80	10.41	0.13	0.03	0.15	0.11	1+	1+	CLSL
	1533	1.07	7.93	0.13	0.10	0.10	0.06	1+	1+	CLSL
	1534	3.25	7.67	0.46	0.23	0.00	0.00	1+	1+	LPO
	1535	1.89	10.74	0.20	0.22	0.18	0.09	1+	1+	CLSL
	1536	3.94	9.70	0.37	0.21	0.31	0.11	1+	1+	CLSL
	1537	5.21	4.70	0.29	0.80	0.08	0.02	1+	1+	CLSL
	1538	1.57	7.84	0.18	0.36	0.10	0.03	1+	1+	CLSL
	1539	2.63	7.27	0.24	0.19	0.11	0.03	1+	1+	CLSL
	1540	1.73	10.97	0.40	0.18	0.12	0.11	1+	1+	NAN
	1541	1.88	6.95	0.14	0.14	0.08	0.05	1+	1+	NAN
	1542	3.18	9.37	0.32	0.17	0.09	0.06	1+	1+	NAN
	Mean	2.42	8.31	0.25	0.25	0.12	0.06			
	SD	1.275	1.949	0.116	0.196	0.074	0.038			
	n	12	12	12	12	12	12			

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
2F	2531	15.2	44.7	7.69	219.5	832	58.1	19.8	34.1	10.52
900 ppm	2532	16.1	45.6	8.05	212.8	787	56.7	19.9	35.2	14.50
	2533	16.0	45.3	8.27	153.4	707	54.7	19.4	35.4	11.22
	2534	15.8	44.8	8.53	159.2	759	52.6	18.5	35.2	9.01
	2535	16.2	45.1	8.27	183.6	803	54.5	19.5	35.9	12.57
	2536	15.5	42.7	7.84	155.9	583	54.4	19.7	36.2	16.05
	2537	14.6	41.6	7.47	192.1	846	55.6	19.5	35.0	8.90
	2538	15.9	45.6	8.07	195.0	833	56.5	19.7	34.9	11.11
	2539	16.0	47.3	8.39	238.0	724	56.4	19.1	33.8	13.58
	2540	15.9	46.9	7.89	286.4	744	59.4	20.2	34.0	16.11
	2541	15.1	43.9	7.70	179.9	811	57.0	19.7	34.5	12.62
	2542	15.9	44.2	7.84	216.4	792	56.3	20.2	35.9	11.70
	Mean	15.7	44.8	8.00	199.4	768	56.0	19.6	35.0	12.32
	SD	0.48	1.60	0.319	38.45	73.2	1.81	0.47	0.79	2.407
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
2F	2531	1.84	8.18	0.21	0.11	0.12	0.05	1+	1+	NAN
900 ppm	2532	3.31	10.49	0.33	0.10	0.18	0.08	1+	1+	NAN
	2533	2.11	8.44	0.21	0.27	0.12	0.06	1+	1+	CLSL
	2534	1.42	7.04	0.22	0.12	0.14	0.06	1+	1+	CLSL
	2535	1.56	10.30	0.31	0.21	0.11	0.06	1+	1+	CLSL
	2536	5.35	9.88	0.25	0.25	0.22	0.10	1+	1+	CLSL
	2537	1.38	7.21	0.09	0.09	0.08	0.05	1+	1+	NAN
	2538	1.56	9.17	0.12	0.08	0.09	0.09	1+	1+	NAN
	2539	2.06	10.77	0.17	0.40	0.11	0.08	1+	1+	CLSL
	2540	2.46	12.93	0.30	0.19	0.16	0.07	1+	1+	LPO
	2541	2.31	9.61	0.12	0.41	0.09	0.09	2+	1+	CLSL
	2542	1.53	9.57	0.27	0.15	0.12	0.05	1+	1+	NAN
	Mean	2.24	9.47	0.22	0.20	0.13	0.07			
	SD	1.125	1.635	0.079	0.115	0.041	0.018			
	n	12	12	12	12	12	12			

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
3F	3531	16.0	45.1	8.03	225.5	734	56.2	20.0	35.6	8.97
3000 ppm	3532	15.9	45.0	7.99	211.8	942	56.4	19.9	35.4	9.03
	3533	14.9	42.7	7.90	177.7	810	54.1	18.9	35.0	9.62
	3534	16.0	44.4	8.11	189.4	585	54.8	19.8	36.1	9.17
	3535	16.6	47.7	8.59	143.6	494	55.6	19.3	34.8	13.36
	3536	15.1	42.0	7.43	128.6	856	56.5	20.3	35.9	14.79
	3537	15.0	43.5	7.68	280.9	623	56.6	19.5	34.5	8.06
	3538	14.8	43.6	7.69	199.9	822	56.7	19.2	33.9	9.23
	3539	15.5	43.4	7.69	193.6	826	56.4	20.1	35.6	11.67
	3540	15.6	44.9	8.16	194.1	751	55.1	19.1	34.7	7.40
	3541	15.7	45.3	8.02	160.7	1006	56.5	19.5	34.6	11.04
	3542	16.0	46.2	8.27	143.2	605	55.9	19.3	34.5	12.71
	Mean	15.6	44.5	7.96	187.4	755	55.9	19.6	35.1	10.42
	SD	0.55	1.57	0.312	41.75	153.2	0.83	0.44	0.67	2.282
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
3F	3531	1.65	6.79	0.18	0.22	0.10	0.04	1+	1+	CLSL
3000 ppm	3532	1.15	7.45	0.15	0.11	0.11	0.06	1+	1+	CLSL
	3533	1.13	8.04	0.16	0.12	0.08	0.07	1+	1+	CLSL
	3534	1.93	6.71	0.11	0.28	0.10	0.04	1+	1+	CLSL
	3535	1.80	10.80	0.33	0.14	0.18	0.10	1+	1+	CLSL
	3536	1.90	12.07	0.23	0.28	0.17	0.14	1+	1+	CLSL
	3537	1.60	5.90	0.10	0.37	0.06	0.04	2+	1+	CLSL
	3538	1.19	7.60	0.09	0.25	0.07	0.04	2+	1+	CLSL
	3539	1.69	9.19	0.18	0.44	0.10	0.07	2+	1+	CLSL
	3540	0.90	6.12	0.12	0.18	0.04	0.02	2+	1+	CLSL
	3541	1.44	9.21	0.14	0.13	0.07	0.04	1+	1+	NAN
	3542	1.61	10.43	0.25	0.25	0.12	0.06	2+	1+	CLSL
	Mean	1.50	8.36	0.17	0.23	0.10	0.06			
	SD	0.335	1.981	0.070	0.103	0.042	0.033			
	n	12	12	12	12	12	12			

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	HGB	HCT	RBC	RETIC	PLT	MCV	MCH	MCHC	WBC
		g/dL	%	x10^6/uL	x10^9/L	x10^3/uL	fL	pg	g/dL	x10^3/uL
4F	4531	15.9	45.8	8.22	182.4	631	55.7	19.4	34.8	12.94
9000 ppm	4532	16.0	45.5	8.23	200.2	478	55.3	19.4	35.1	11.72
	4533	16.1	46.2	8.51	185.6	591	54.3	18.9	34.8	14.42
	4534	16.1	44.7	8.35	165.9	709	53.5	19.3	36.0	15.23
	4535	15.8	44.2	8.14	233.5	566	54.3	19.4	35.6	16.42
	4536	16.3	46.2	8.31	222.8	853	55.6	19.6	35.3	12.37
	4537	15.3	44.2	7.72	203.4	936	57.2	19.8	34.7	8.83
	4538	15.5	45.9	8.08	211.4	603	56.8	19.2	33.8	11.89
	4539	14.5	42.7	7.98	150.5	990	53.5	18.1	33.9	5.40
	4540	15.3	44.6	8.02	138.8	643	55.6	19.1	34.4	11.45
	4541	15.2	44.0	8.19	156.0	845	53.7	18.5	34.5	8.73
	4542	15.8	44.4	8.16	204.1	848	54.4	19.4	35.7	6.80
	Mean	15.7	44.9	8.16	187.9	724	55.0	19.2	34.9	11.35
	SD	0.51	1.07	0.201	29.92	163.9	1.24	0.48	0.69	3.351
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix H - Main Study
Individual Hematology Values - Termination

Group	Animal Number	ANEU	ALYM	AMONO	AEOS	ABASO	ALUC	Poik	Poly	PLT MORPH
		x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL	x10^3/uL			
4F	4531	2.03	10.25	0.13	0.27	0.16	0.10	1+	1+	CLSL
9000 ppm	4532	2.93	8.07	0.21	0.27	0.17	0.07	1+	1+	CLSL
	4533	1.54	12.31	0.19	0.13	0.18	0.08	1+	1+	CLSL
	4534	2.05	12.53	0.22	0.16	0.18	0.09	1+	1+	LPO
	4535	2.59	12.86	0.19	0.46	0.23	0.10	1+	1+	CLSL
	4536	1.50	10.42	0.13	0.10	0.17	0.05	1+	1+	CLSL
	4537	0.97	7.53	0.17	0.07	0.06	0.03	2+	1+	NAN
	4538	2.48	8.46	0.33	0.35	0.14	0.13	2+	1+	CLSL
	4539	1.03	4.17	0.06	0.08	0.03	0.02	2+	1+	CLSL
	4540	0.89	9.93	0.12	0.36	0.09	0.06	2+	1+	CLSL
	4541	1.35	7.07	0.13	0.08	0.06	0.04	2+	1+	NAN
	4542	1.37	5.01	0.11	0.23	0.06	0.02	2+	1+	CLSL
	Mean	1.73	9.05	0.17	0.21	0.13	0.07			
	SD	0.679	2.845	0.070	0.130	0.064	0.035			
	n	12	12	12	12	12	12			

	Individual Coagulation Values Main Study Preface	Appendix I

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

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
1M	1031	13.5	21.1
0 ppm	1032	16.1	25.4
	1033	16.3	26.7
	1034	13.8	20.5
	1035	13.3	20.1
	1036	14.8	22.7
	1037	12.8	22.2
	1038	13.0	22.0
	1039	15.1	23.8
	1040	14.6	22.5
	1041	13.0	19.9
	1042	13.9	23.9
	Mean	14.2	22.6
	SD	1.20	2.10
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
2M	2031	13.7	21.5
900 ppm	2032	14.6	23.9
	2033	13.6	21.9
	2034	14.1	21.3
	2035	14.6	24.6
	2036	15.4	26.8
	2037	15.1	28.8
	2038	12.4	20.9
	2039	15.0	23.5
	2040	13.8	22.3
	2041	13.1	22.6
	2042	12.7	21.9
	Mean	14.0	23.3
	SD	0.97	2.39
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
3M	3031	13.3	19.3
3000 ppm	3032	14.3	22.2
	3033	14.3	20.9
	3034	15.6	24.3
	3035	13.1	22.7
	3036	13.5	22.0
	3037	12.8	23.1
	3038	13.3	21.9
	3040	13.9	24.4
	3041	12.9	23.5
	3042	12.2	18.6
	3043	13.0	25.5
	Mean	13.5	22.4
	SD	0.90	2.04
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
4M	4031	14.4	22.7
9000 ppm	4032	17.2	25.4
	4033	13.6	22.4
	4034	12.7	22.0
	4035	13.0	21.5
	4036	13.0	23.7
	4037	13.5	24.7
	4038	12.5	23.6
	4039	12.7	21.7
	4040	12.2	20.4
	4041	13.5	22.3
	4042	12.7	21.8
	Mean	13.4	22.7
	SD	1.33	1.43
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
1F	1531	12.0	21.4
0 ppm	1532	12.2	20.5
	1533	11.3	21.1
	1534	12.1	24.4
	1535	11.9	19.8
	1536	12.6	22.3
	1537	12.5	23.2
	1538	11.5	22.3
	1539	12.1	24.1
	1540	11.2	24.3
	1541	12.1	22.0
	1542	11.4	18.3
	Mean	11.9	22.0
	SD	0.46	1.88
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
2F	2531	12.0	23.4
900 ppm	2532	12.2	21.4
	2533	12.8	22.4
	2534	11.5	21.9
	2535	12.6	24.0
	2536	13.0	22.7
	2537	11.3	21.9
	2538	11.2	21.1
	2539	11.9	20.7
	2540	12.1	21.1
	2541	11.1	19.9
	2542	11.9	21.0
	Mean	12.0	21.8
	SD	0.62	1.18
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
3F	3531	11.1	19.9
3000 ppm	3532	12.1	20.4
	3533	11.3	24.2
	3534	11.5	23.3
	3535	11.8	23.9
	3536	11.3	21.1
	3537	13.0	23.0
	3538	11.4	21.6
	3539	12.0	21.5
	3540	11.4	20.8
	3541	12.2	20.1
	3542	12.8	21.1
	Mean	11.8	21.7
	SD	0.61	1.49
	n	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix I - Main Study
Individual Coagulation Values - Termination

Group	Animal Number	PT	APTT
		Seconds	Seconds
4F	4531	12.1	20.9
9000 ppm	4532	11.8	23.2
	4533	11.7	19.0
	4534	12.6	22.4
	4535	11.8	21.2
	4536	11.7	22.3
	4537	11.4	20.2
	4538	11.3	20.3
	4539	11.2	23.0
	4540	12.8	24.1
	4541	12.2	20.8
	4542	11.2	20.2
	Mean	11.8	21.5
	SD	0.53	1.52
	n	12	12

	Individual Clinical Chemistry Values Main Study Preface	Appendix J

Abbreviation	Parameter	Reporting Units
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
ALKP	Alkaline Phosphatase	U/L
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
GLU	Fasting Glucose	mg/dL
CHOL	Total 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
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

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
1M	1031	70	34	160	14.5	0.3	93	51	59	6.4
0 ppm	1032	91	44	153	12.1	0.3	92	56	50	6.4
	1033	56	23	189	10.4	0.3	96	37	31	6.3
	1034	79	36	148	11.7	0.3	108	61	56	6.6
	1035	75	33	116	12.6	0.3	106	54	32	6.5
	1036	68	37	134	13.5	0.3	102	64	64	6.4
	1037	99	52	170	12.4	0.3	100	58	53	6.5
	1038	76	41	157	11.2	0.3	93	69	42	6.6
	1039	83	35	113	11.4	0.3	115	50	49	6.4
	1040	94	36	211	10.9	0.3	106	64	59	6.9
	1041	81	40	178	13.0	0.3	92	59	54	6.5
	1042	76	39	153	16.5	0.3	100	46	39	7.0
	Mean	79	38	157	12.5	0.3	100	56	49	6.5
	SD	11.9	6.9	28.3	1.70	0.00	7.4	8.8	10.8	0.21
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1M	1031	4.3	2.1	2.0	0.13	147	6.2	104	11.3	9.3
0 ppm	1032	4.3	2.1	2.0	0.10	148	6.2	103	10.9	8.2
	1033	4.5	1.8	2.5	0.12	147	5.8	103	10.8	9.4
	1034	4.4	2.2	2.0	0.13	148	5.6	103	11.1	9.5
	1035	4.4	2.1	2.1	0.15	146	5.9	103	10.9	9.2
	1036	4.5	1.9	2.4	0.11	146	5.8	104	10.8	9.6
	1037	4.2	2.3	1.8	0.12	146	6.3	100	10.9	9.0
	1038	4.4	2.2	2.0	0.13	148	5.5	101	10.7	7.6
	1039	4.2	2.2	1.9	0.13	145	6.5	100	10.7	10.4
	1040	4.4	2.5	1.8	0.13	148	6.5	100	11.1	10.0
	1041	4.4	2.1	2.1	0.11	149	5.6	101	11.1	8.5
	1042	4.5	2.5	1.8	0.10	151	5.6	100	11.1	8.4
	Mean	4.4	2.2	2.0	0.12	147	6.0	102	11.0	9.1
	SD	0.11	0.21	0.22	0.015	1.6	0.37	1.6	0.19	0.80
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
1M	1031	0
0 ppm	1032	0
	1033	0
	1034	0
	1035	0
	1036	0
	1037	0
	1038	0
	1039	0
	1040	0
	1041	0
	1042	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
2M	2031	79	43	136	12.3	0.3	99	62	55	6.5
900 ppm	2032	97	34	131	10.1	0.4	143	64	58	6.6
	2033	79	36	144	15.9	0.3	94	45	28	6.3
	2034	75	31	129	10.6	0.3	93	54	50	5.9
	2035	85	43	167	10.6	0.3	104	63	56	6.5
	2036	82	37	150	13.3	0.3	91	75	83	6.8
	2037	83	40	168	13.8	0.4	92	70	69	7.2
	2038	71	35	108	11.0	0.3	103	54	32	6.5
	2039	73	34	133	12.3	0.3	128	67	65	6.5
	2040	74	37	112	11.5	0.3	109	60	81	6.4
	2041	116	92	148	11.9	0.2	98	61	97	6.3
	2042	75	39	148	14.4	0.3	103	75	123	6.7
	Mean	82	42	140	12.3	0.3	105	63	66	6.5
	SD	12.7	16.2	18.7	1.75	0.05	15.7	8.8	26.8	0.31
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
2M	2031	4.5	2.0	2.3	0.13	146	5.9	100	11.1	8.9
900 ppm	2032	4.3	2.3	1.9	0.16	144	6.1	102	11.1	10.5
	2033	4.2	2.1	2.0	0.14	145	5.7	102	10.8	7.9
	2034	4.2	1.7	2.5	0.09	148	5.7	107	10.8	9.0
	2035	4.4	2.1	2.1	0.16	147	5.2	103	11.1	9.1
	2036	4.6	2.2	2.1	0.11	149	5.9	105	11.3	8.4
	2037	4.6	2.6	1.8	0.12	148	6.3	99	10.8	8.5
	2038	4.3	2.2	2.0	0.11	147	6.1	100	10.7	9.0
	2039	4.4	2.1	2.1	0.10	146	6.9	101	11.0	10.2
	2040	4.3	2.1	2.0	0.12	149	5.5	102	11.0	8.3
	2041	4.1	2.2	1.9	0.16	148	5.8	101	10.9	8.4
	2042	4.5	2.2	2.0	0.13	148	5.8	98	11.7	9.4
	Mean	4.4	2.2	2.1	0.13	147	5.9	102	11.0	9.0
	SD	0.16	0.21	0.19	0.024	1.6	0.43	2.5	0.27	0.77
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
2M	2031	0
900 ppm	2032	0
	2033	0
	2034	0
	2035	0
	2036	0
	2037	0
	2038	0
	2039	0
	2040	0
	2041	0
	2042	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
3M	3031	80	37	148	13.5	0.4	96	51	64	6.4
3000 ppm	3032	82	40	214	14.3	0.3	99	42	42	6.1
	3033	77	35	183	12.5	0.4	93	45	33	6.1
	3034	75	34	133	12.1	0.3	99	44	33	6.5
	3035	84	42	228	12.6	0.4	90	61	71	6.6
	3036	69	36	153	12.9	0.3	103	66	52	6.4
	3037	68	40	154	13.3	0.3	105	68	86	6.4
	3038	77	42	121	12.0	0.3	96	50	44	6.6
	3040	83	32	114	12.4	0.4	104	73	66	6.8
	3041	73	31	112	10.9	0.3	91	57	66	6.7
	3042	71	31	108	12.6	0.3	98	60	42	7.0
	3043	76	40	138	13.6	0.3	96	73	52	6.9
	Mean	76	37	151	12.7	0.3	98	58	54	6.5
	SD	5.3	4.1	39.4	0.89	0.05	4.9	11.1	16.5	0.28
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
3M	3031	4.4	2.0	2.2	0.15	147	6.4	103	11.0	8.0
3000 ppm	3032	4.2	1.9	2.2	0.15	147	5.5	104	10.9	9.0
	3033	4.4	1.7	2.6	0.15	148	5.9	106	10.3	8.3
	3034	4.5	2.0	2.3	0.12	145	5.8	102	10.9	9.0
	3035	4.6	2.0	2.3	0.12	150	6.1	104	11.3	9.0
	3036	4.3	2.1	2.0	0.10	147	5.9	102	11.2	9.8
	3037	4.4	2.0	2.2	0.11	147	5.9	100	10.6	8.5
	3038	4.4	2.2	2.0	0.11	149	5.7	103	10.7	9.1
	3040	4.5	2.3	2.0	0.11	149	6.3	101	10.8	9.1
	3041	4.4	2.3	1.9	0.11	148	6.1	102	11.1	9.5
	3042	4.5	2.5	1.8	0.16	150	5.5	102	11.2	8.9
	3043	4.5	2.4	1.9	0.15	148	5.8	99	11.4	9.4
	Mean	4.4	2.1	2.1	0.13	148	5.9	102	11.0	9.0
	SD	0.11	0.23	0.22	0.022	1.4	0.28	1.9	0.32	0.51
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
3M	3031	0
3000 ppm	3032	0
	3033	0
	3034	0
	3035	0
	3036	0
	3037	0
	3038	0
	3040	0
	3041	0
	3042	0
	3043	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
4M	4031	75	33	121	13.0	0.3	103	59	32	6.4
9000 ppm	4032	90	38	210	12.3	0.4	95	47	37	6.6
	4033	67	32	177	15.8	0.3	100	47	21	5.9
	4034	76	35	113	12.2	0.3	93	54	46	6.0
	4035	69	36	128	13.4	0.3	101	70	55	6.6
	4036	73	44	188	14.5	0.3	101	51	61	6.3
	4037	84	40	147	12.1	0.3	107	71	41	6.6
	4038	81	50	180	9.8	0.4	94	86	58	6.6
	4039	93	39	206	11.7	0.3	101	51	38	6.2
	4040	76	41	133	11.7	0.3	96	63	55	6.3
	4041	82	55	240	14.3	0.4	101	54	39	6.6
	4042	77	39	226	13.3	0.3	97	41	54	7.2
	Mean	79	40	172	12.8	0.3	99	58	45	6.4
	SD	7.8	6.8	43.3	1.58	0.05	4.1	12.7	12.1	0.34
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
4M	4031	4.3	2.1	2.0	0.11	149	6.0	105	10.6	8.8
9000 ppm	4032	4.5	2.1	2.1	0.14	149	6.2	103	11.0	8.4
	4033	4.4	1.5	2.9	0.12	148	6.1	106	10.6	8.6
	4034	4.1	1.9	2.2	0.15	146	6.1	104	10.7	9.0
	4035	4.4	2.2	2.0	0.11	150	5.9	104	11.0	8.9
	4036	4.4	1.9	2.3	0.12	149	5.5	104	11.2	8.7
	4037	4.5	2.1	2.1	0.09	149	5.7	99	10.6	7.9
	4038	4.5	2.1	2.1	0.11	148	6.1	99	11.1	8.5
	4039	4.4	1.8	2.4	0.11	150	6.1	103	10.9	9.1
	4040	4.3	2.0	2.2	0.12	151	5.7	102	10.8	9.5
	4041	4.5	2.1	2.1	0.14	147	6.3	99	10.8	9.9
	4042	4.6	2.6	1.8	0.12	151	6.1	99	11.3	8.5
	Mean	4.4	2.0	2.2	0.12	149	6.0	102	10.9	8.8
	SD	0.13	0.26	0.27	0.017	1.5	0.24	2.6	0.24	0.53
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
4M	4031	0
9000 ppm	4032	0
	4033	0
	4034	0
	4035	0
	4036	0
	4037	0
	4038	0
	4039	0
	4040	0
	4041	0
	4042	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
1F	1531	96	33	108	15.7	0.5	89	62	25	6.5
0 ppm	1532	79	31	135	13.7	0.4	96	48	34	6.7
	1533	79	37	112	15.2	0.3	103	71	28	7.5
	1534	285	74	75	61.5	1.2	86	55	447	5.5
	1535	69	30	119	11.7	0.4	111	56	35	6.8
	1536	84	32	178	18.7	0.5	101	55	28	7.6
	1537	65	39	71	17.2	0.3	99	72	32	7.7
	1538	69	29	122	11.4	0.3	107	66	33	7.0
	1539	95	41	123	15.3	0.4	91	82	36	7.1
	1540	80	45	97	14.5	0.4	102	61	29	7.5
	1541	75	33	131	11.0	0.3	94	61	27	6.8
	1542	81	33	131	14.2	0.4	87	67	26	6.7
	Mean	96	38	117	18.3	0.5	97	63	65	7.0
	SD	60.1	12.3	28.4	13.78	0.25	8.0	9.3	120.4	0.61
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
1F	1531	4.6	1.9	2.4	0.17	149	5.6	107	10.3	6.9
0 ppm	1532	4.9	1.8	2.7	0.17	149	5.4	105	11.4	8.0
	1533	5.2	2.3	2.3	0.18	147	5.8	106	11.8	9.1
	1534	2.5	3.0	0.8	0.10	148	4.3	101	12.4	13.2
	1535	4.6	2.2	2.1	0.16	151	5.7	108	11.3	9.7
	1536	5.0	2.6	1.9	0.20	148	6.5	102	11.8	9.3
	1537	4.9	2.8	1.8	0.10	151	6.3	102	11.4	9.6
	1538	5.0	2.0	2.5	0.12	147	5.2	103	11.2	8.2
	1539	4.7	2.4	2.0	0.16	145	6.2	100	11.1	8.7
	1540	5.3	2.2	2.4	0.17	147	5.9	100	11.3	8.6
	1541	4.4	2.4	1.8	0.12	148	5.5	102	10.7	7.9
	1542	4.7	2.0	2.4	0.15	145	6.3	101	10.6	9.2
	Mean	4.7	2.3	2.1	0.15	148	5.7	103	11.3	9.0
	SD	0.73	0.36	0.50	0.032	1.9	0.60	2.7	0.57	1.54
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
1F	1531	0
0 ppm	1532	0
	1533	0
	1534	0
	1535	0
	1536	0
	1537	0
	1538	0
	1539	0
	1540	0
	1541	0
	1542	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
2F	2531	78	28	101	16.5	0.4	94	57	26	7.2
900 ppm	2532	76	28	153	13.2	0.4	106	57	24	7.1
	2533	94	39	113	13.5	0.3	107	81	29	6.8
	2534	63	32	73	14.3	0.4	116	72	30	7.2
	2535	73	27	116	13.7	0.4	95	57	34	7.2
	2536	75	33	112	12.1	0.3	103	60	33	6.9
	2537	62	32	87	11.7	0.3	98	57	23	6.8
	2538	64	28	115	14.8	0.4	99	81	42	7.0
	2539	73	31	89	13.4	0.4	91	63	30	7.2
	2540	75	30	102	14.6	0.4	97	62	43	7.5
	2541	71	34	143	15.9	0.4	93	55	35	7.1
	2542	69	33	66	12.2	0.3	100	56	27	7.0
	Mean	73	31	106	13.8	0.4	100	63	31	7.1
	SD	8.6	3.4	25.6	1.48	0.05	7.1	9.5	6.4	0.20
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
2F	2531	4.8	2.4	2.0	0.17	151	6.0	106	11.1	8.1
900 ppm	2532	5.0	2.1	2.4	0.15	151	5.5	106	11.3	8.1
	2533	4.7	2.1	2.2	0.15	152	5.2	106	11.2	8.7
	2534	5.2	2.0	2.6	0.15	151	5.3	104	11.8	7.7
	2535	5.0	2.2	2.3	0.16	151	5.1	105	11.8	9.1
	2536	4.6	2.3	2.0	0.14	148	5.7	103	11.2	7.7
	2537	4.7	2.1	2.2	0.11	146	5.9	102	10.4	7.8
	2538	4.8	2.2	2.2	0.12	147	5.5	100	11.1	7.6
	2539	5.2	2.0	2.6	0.14	148	5.7	101	11.4	8.0
	2540	5.0	2.5	2.0	0.15	148	5.7	99	11.4	7.8
	2541	5.0	2.1	2.4	0.14	148	6.1	104	11.1	7.6
	2542	4.9	2.1	2.3	0.14	148	5.3	99	11.1	8.7
	Mean	4.9	2.2	2.3	0.14	149	5.6	103	11.2	8.1
	SD	0.19	0.15	0.21	0.016	2.0	0.32	2.7	0.37	0.50
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
2F	2531	0
900 ppm	2532	0
	2533	0
	2534	0
	2535	0
	2536	0
	2537	0
	2538	0
	2539	0
	2540	0
	2541	0
	2542	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
3F	3531	69	31	126	14.5	0.5	110	76	37	7.6
3000 ppm	3532	91	35	94	15.9	0.4	99	45	29	6.8
	3533	68	25	53	16.0	0.5	108	48	30	7.3
	3534	70	33	89	12.7	0.4	118	67	32	7.4
	3535	90	55	89	14.8	0.4	106	84	41	8.0
	3536	67	34	64	11.6	0.3	106	58	35	7.3
	3537	93	48	74	11.1	0.3	105	63	23	6.9
	3538	69	29	87	11.8	0.4	109	91	29	7.3
	3539	81	32	99	16.4	0.4	95	49	32	6.5
	3540	79	31	87	14.1	0.4	96	61	34	6.7
	3541	76	30	146	12.0	0.4	88	49	30	6.9
	3542	79	35	111	12.5	0.3	85	64	26	7.0
	Mean	78	35	93	13.6	0.4	102	63	32	7.1
	SD	9.5	8.4	25.5	1.89	0.07	9.7	14.7	4.9	0.42
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
3F	3531	5.5	2.1	2.6	0.18	148	5.5	106	11.7	6.8
3000 ppm	3532	5.1	1.7	3.0	0.16	150	6.2	107	11.3	9.0
	3533	5.2	2.1	2.5	0.14	147	5.3	105	11.1	7.3
	3534	5.1	2.3	2.2	0.13	150	6.2	106	11.9	8.8
	3535	5.8	2.2	2.6	0.18	151	5.3	106	11.9	8.4
	3536	5.1	2.2	2.3	0.16	151	5.4	107	11.6	7.5
	3537	4.7	2.2	2.1	0.15	148	5.7	102	10.6	7.5
	3538	5.2	2.1	2.5	0.14	146	5.8	100	11.0	7.2
	3539	4.2	2.3	1.8	0.12	148	5.7	101	10.6	8.3
	3540	4.7	2.0	2.4	0.13	146	5.5	101	10.7	7.4
	3541	5.1	1.8	2.8	0.13	147	5.4	102	11.1	7.3
	3542	4.8	2.2	2.2	0.12	147	5.7	101	11.0	7.8
	Mean	5.0	2.1	2.4	0.15	148	5.6	104	11.2	7.8
	SD	0.41	0.19	0.32	0.021	1.8	0.31	2.7	0.47	0.69
	n	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
3F	3531	0
3000 ppm	3532	0
	3533	0
	3534	0
	3535	0
	3536	0
	3537	0
	3538	0
	3539	0
	3540	0
	3541	0
	3542	0
	Mean	0
	SD	0.0
	n	12

Huntingdon Life Sciences Study No. 03-4244
Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	AST	ALT	ALKP	BUN	CREAT	GLU	CHOL	TRIG	TP
		U/L	U/L	U/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL
4F	4531	83	36	75	16.0	0.4	102	51	18	7.1
9000 ppm	4532	80	34	76	15.0	0.3	102	54	23	7.0
	4533	74	28	82	14.6	0.4	107	66	33	7.2
	4534	82	38	120	13.4	0.4	107	67	34	7.3
	4535	67	40	114	10.1	0.3	94	80	33	7.4
	4536	66	29	121	11.9	0.4	114	78	38	7.2
	4537	65	33	63	15.7	0.3	95	57	32	7.2
	4538	81	42	117	13.0	0.4	98	89	45	7.1
	4539	58	32	85	11.8	0.3	108	99	33	7.4
	4540	79	42	114	16.5	0.3	96	71	34	6.9
	4541	62	26	106	15.3	0.3	99	47	27	7.1
	4542	69	31	141	14.6	0.3	95	74	35	6.8
	Mean	72	34	101	14.0	0.3	101	69	32	7.1
	SD	8.7	5.4	24.0	1.96	0.05	6.4	15.7	6.9	0.18
	n	12	12	12	12	12	12	12	12	12

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Appendix J - Main Study
Individual Clinical Chemistry Values - Termination

Group	Animal Number	ALB	Glob	A/G	TBILI	Na+	K+	Cl-	Ca++	PHOS
		g/dL	g/dL		mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
4F	4531	4.9	2.2	2.2	0.13	152	5.1	107	11.1	7.9
9000 ppm	4532	5.0	2.0	2.5	0.18	149	6.1	104	11.1	8.9
	4533	4.8	2.4	2.0	0.16	149	6.1	104	11.5	8.7
	4534	5.0	2.3	2.2	0.15	151	6.5	105	11.3	8.1
	4535	4.9	2.5	2.0	0.14	148	6.0	105	11.6	8.3
	4536	4.8	2.4	2.0	0.16	149	6.1	104	11.4	8.6
	4537	5.2	2.0	2.6	0.14	147	5.7	101	11.4	8.1
	4538	4.6	2.5	1.8	0.11	146	5.5	99	11.2	7.2
	4539	5.3	2.1	2.5	0.19	147	5.5	100	11.1	7.3
	4540	4.7	2.2	2.1	0.12	146	6.1	100	10.9	8.2
	4541	4.9	2.2	2.2	0.13	148	5.3	103	10.7	8.1
	4542	4.9	1.9	2.6	0.14	147	6.0	100	10.9	6.9
	Mean	4.9	2.2	2.2	0.15	148	5.8	103	11.2	8.0
	SD	0.19	0.20	0.27	0.024	1.9	0.41	2.6	0.27	0.62
	n	12	12	12	12	12	12	12	12	12

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Individual Clinical Chemistry Values - Termination

Group	Animal Number	GGT
		U/L
4F	4531	0
9000 ppm	4532	0
	4533	0
	4534	0
	4535	0
	4536	0
	4537	0
	4538	0
	4539	0
	4540	0
	4541	0
	4542	0
	Mean	0
	SD	0.0
	n	12

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Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observations

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Note: Ovaries were weighed with oviducts.

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
				M a l e A n i m a l s				
1031/M	1/1	389.5	0.0776	2.1553	0.5059	0.5046	1.2415	3.3887
1032/M	1/1	381.6	0.0700	2.0627	0.5454	0.5574	1.1634	3.3332
1033/M	1/1	334.4	0.0716	2.0331	0.6173	0.6201	1.2879	3.3421
1034/M	1/1	447.6	0.0956	2.1502	0.7094	0.6511	1.6761	3.7783
1035/M	1/1	399.9	0.0899	2.1664	0.7517	0.6741	1.2913	3.7361
1036/M	1/1	362.1	0.0568	2.0344	0.6784	0.7272	1.1962	3.0088
1037/M	1/1	414.7	0.0631	2.2668	0.6979	0.7295	1.2878	3.5302
1038/M	1/1	364.1	0.0493	2.1884	0.5450	0.5810	1.2855	3.6405
1039/M	1/1	375.3	0.1003	2.1643	0.5632	0.5594	1.2124	3.4667
1040/M	1/1	381.2	0.0770	2.0677	0.5843	0.6179	1.3828	3.5111
1041/M	1/1	385.7	0.0755	2.0730	0.6685	0.6976	1.2787	3.0124
1042/M	1/1	325.3	0.0774	2.0803	0.6057	0.6680	1.2569	3.0218
M e a n:		380.1	0.0753	2.1202	0.6227	0.6323	1.2967	3.3975
Standard deviation:		33.0	0.0150	0.0721	0.0775	0.0715	0.1320	0.2700
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	0.0653	1.9413	0.5349	0.5332	1.1146	3.6266
2032/M	2/1	418.2	0.1058	2.1531	0.7673	0.6759	1.5477	4.1534
2033/M	2/1	377.5	0.0939	2.3370	0.5560	0.5865	1.5457	3.8161
2034/M	2/1	394.8	0.0598	2.1092	0.6812	0.6018	1.3975	3.2035
2035/M	2/1	389.8	0.0822	2.1459	0.6294	0.6756	1.3820	3.7388
2036/M	2/1	363.4	0.0670	2.0678	0.5477	0.5423	1.2414	3.0969
2037/M	2/1	352.0	0.0701	2.3131	0.7069	0.6760	1.2694	3.1652
2038/M	2/1	384.1	0.0703	2.0822	0.6136	0.5562	1.1885	3.6015
2039/M	2/1	394.8	0.0655	2.1598	0.6423	0.6872	1.5129	3.6595
2040/M	2/1	393.5	0.0560	2.1095	0.5899	0.6208	1.3830	3.4985
2041/M	2/1	354.5	0.0742	2.0549	0.7309	0.7611	1.3464	3.2975
2042/M	2/1	417.7	0.0677	2.0656	0.7971	0.7876	1.4708	3.2365
M e a n:		385.8	0.0732	2.1283	0.6498	0.6420	1.3667	3.5078
Standard deviation:		21.4	0.0143	0.1089	0.0875	0.0827	0.1412	0.3174
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	0.0897	2.0268	0.5890	0.6453	1.2937	3.1277
3032/M	3/1	373.9	0.0886	2.2337	0.5276	0.5164	1.2613	3.1693
3033/M	3/1	334.8	0.0534	2.1044	0.5771	0.7379	1.2711	2.9683
3034/M	3/1	358.7	0.0755	2.0984	0.6501	0.6113	1.3450	3.4819
3035/M	3/1	383.6	0.0903	2.1865	0.6160	0.6471	1.3197	4.0036
3036/M	3/1	402.9	0.0566	2.1993	0.6391	0.6228	1.4505	3.3694
3037/M	3/1	383.7	0.0740	1.9905	0.6453	0.5657	1.3287	3.2525
3038/M	3/1	382.2	0.0613	2.3338	0.6467	0.6658	1.4171	3.5923
3040/M	3/1	404.8	0.0803	1.9795	0.6529	0.6227	1.6093	3.8714
3041/M	3/1	359.4	0.0785	2.1254	0.6128	0.6472	1.4187	3.9154
3042/M	3/1	343.5	0.0748	1.9110	0.6946	0.6716	1.2318	3.3028
3043/M	3/1	394.0	0.0731	2.1047	0.6248	0.5725	1.4418	3.7458
M e a n:		373.8	0.0747	2.1078	0.6230	0.6272	1.3657	3.4834

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
Standard deviation:		22.3	0.0123	0.1196	0.0433	0.0574	0.1065	0.3408
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	0.0872	1.9905	0.5678	0.5853	1.1385	3.2969
4032/M	4/1	363.3	0.0592	2.0320	0.5972	0.6031	1.2386	3.3086
4033/M	4/1	310.9	0.0718	1.9794	0.5353	0.5760	1.2373	2.7785
4034/M	4/1	412.8	0.0841	2.1562	0.6681	0.6146	1.3900	3.6095
4035/M	4/1	386.9	0.0653	2.1390	0.5830	0.6343	1.4164	3.3103
4036/M	4/1	384.2	0.0797	2.2321	0.6443	0.6604	1.3533	3.5290
4037/M	4/1	371.9	0.0723	2.0075	0.6297	0.6327	1.4878	3.9459
4038/M	4/1	409.1	0.0810	2.1609	0.6227	0.7267	1.6607	3.9238
4039/M	4/1	336.1	0.0608	2.1267	0.6007	0.6339	1.1803	3.0338
4040/M	4/1	376.2	0.0611	2.0471	0.5288	0.5941	1.4199	3.2432
4041/M	4/1	337.4	0.0725	1.9173	0.6883	0.6824	1.1532	2.9598
4042/M	4/1	381.6	0.0662	2.1456	0.5622	0.5608	1.2600	3.6039
M e a n:		371.4	0.0718	2.0779	0.6023	0.6254	1.3280	3.3786
Standard deviation:		30.2	0.0096	0.0947	0.0502	0.0474	0.1555	0.3612
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
				Male Animals				
1031/M	1/1	389.5	11.4751	1.9638	0.7619	1.5544	1.5727	0.7172
1032/M	1/1	381.6	10.9257	1.9183	0.6017	1.7365	1.7304	0.4527
1033/M	1/1	334.4	12.5400	1.7631	0.7726	1.7317	1.6779	0.2911
1034/M	1/1	447.6	14.2178	2.4354	0.9106	1.6668	1.6799	0.6938
1035/M	1/1	399.9	12.7123	1.8248	0.6959	1.8649	1.8586	0.3987
1036/M	1/1	362.1	12.7329	1.5249	0.6050	1.7406	1.7641	0.4066
1037/M	1/1	414.7	12.5703	1.8669	0.8160	1.6709	1.7624	0.5853
1038/M	1/1	364.1	10.6112	1.5403	0.6563	1.5828	1.5017	0.4443
1039/M	1/1	375.3	12.7746	1.8476	0.6086	1.2836	1.3038	0.4318
1040/M	1/1	381.2	11.8672	1.6544	0.5663	1.5828	1.5917	0.4657
1041/M	1/1	385.7	11.3812	1.9081	0.7097	1.5883	1.5703	0.4814
1042/M	1/1	325.3	10.4399	1.6792	0.5456	1.6195	1.5994	0.3469
Mean:		380.1	12.0207	1.8272	0.6875	1.6352	1.6344	0.4763
Standard deviation:		33.0	1.1024	0.2403	0.1111	0.1426	0.1460	0.1289
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	12.6769	1.8809	0.6924	1.5093	1.5324	0.5568
2032/M	2/1	418.2	15.0123	2.7171	1.1276	1.6783	1.6209	0.8045
2033/M	2/1	377.5	15.6125	2.1113	0.8559	1.6440	1.6411	0.6580
2034/M	2/1	394.8	12.8042	1.9927	0.8653	1.6609	1.7325	0.5007
2035/M	2/1	389.8	12.1200	1.8556	0.8406	1.5732	1.6473	0.5882
2036/M	2/1	363.4	13.2067	1.7521	0.5978	1.4105	1.3517	0.2864
2037/M	2/1	352.0	11.4420	1.8241	0.8561	1.7417	1.6582	0.4165
2038/M	2/1	384.1	12.4856	2.1140	0.6188	1.5790	1.5185	0.4610
2039/M	2/1	394.8	15.0314	2.0268	0.7020	1.5905	1.6285	0.4953
2040/M	2/1	393.5	11.8746	1.8069	0.7817	1.8027	1.7394	0.5488
2041/M	2/1	354.5	12.2447	1.8775	1.3579	1.7185	1.7061	0.5066
2042/M	2/1	417.7	12.8586	2.1185	0.8442	1.8336	1.7636	0.4139
Mean:		385.8	13.1141	2.0065	0.8450	1.6452	1.6284	0.5197
Standard deviation:		21.4	1.3603	0.2583	0.2140	0.1215	0.1155	0.1307
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	11.5924	2.0643	0.7226	1.7520	1.7120	0.4031
3032/M	3/1	373.9	10.7117	1.7800	0.8446	1.2901	1.2431	0.3080
3033/M	3/1	334.8	11.6616	1.5863	0.5586	1.5190	1.5876	0.3440
3034/M	3/1	358.7	12.1814	1.6519	0.6994	1.5288	1.5305	0.3156
3035/M	3/1	383.6	12.1159	1.8593	0.7783	1.8238	1.8526	0.4943
3036/M	3/1	402.9	13.1288	2.0011	0.7494	1.5370	1.5836	0.5782
3037/M	3/1	383.7	12.3550	2.2293	0.8127	1.5672	1.5367	0.7893
3038/M	3/1	382.2	14.0196	2.0867	0.8603	1.7389	1.7717	0.4711
3040/M	3/1	404.8	12.8749	1.7739	0.6447	1.4449	1.4860	0.5651
3041/M	3/1	359.4	11.6415	1.9489	0.9010	1.7193	1.6781	0.5545
3042/M	3/1	343.5	10.4771	1.8330	0.7840	1.8380	1.8435	0.4735
3043/M	3/1	394.0	13.0740	2.3510	0.7756	1.4958	1.5056	0.4976
Mean:		373.8	12.1528	1.9305	0.7609	1.6046	1.6109	0.4829

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
Standard deviation:		22.3	1.0248	0.2279	0.0954	0.1681	0.1728	0.1347
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	12.5357	1.8898	0.7676	1.6595	1.6314	0.4332
4032/M	4/1	363.3	11.3509	1.8185	0.7515	1.5415	1.5314	0.5947
4033/M	4/1	310.9	9.9672	1.5286	0.6372	1.4303	1.4059	0.3378
4034/M	4/1	412.8	13.1839	2.0818	0.8113	1.5506	1.4982	0.6507
4035/M	4/1	386.9	12.4494	2.0047	0.7110	1.5028	1.5736	0.3875
4036/M	4/1	384.2	13.2712	2.0635	0.7417	1.6596	1.6468	0.4989
4037/M	4/1	371.9	12.6192	1.7855	0.7339	1.5987	1.5560	0.4640
4038/M	4/1	409.1	15.7436	3.1177	0.7553	1.4747	1.5179	0.6544
4039/M	4/1	336.1	10.3622	1.6827	0.5706	1.6867	1.6753	0.4734
4040/M	4/1	376.2	12.1250	1.5350	0.7300	1.5008	1.5194	0.4339
4041/M	4/1	337.4	10.0750	1.5808	0.6181	1.5573	1.5459	0.5114
4042/M	4/1	381.6	12.2910	1.6430	0.5845	1.5490	1.5602	0.5502
M e a n:		371.4	12.1645	1.8943	0.7011	1.5593	1.5552	0.4992
Standard deviation:		30.2	1.6131	0.4327	0.0782	0.0791	0.0725	0.0991
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1531/F	1/1	244.4	0.0968	1.9560	0.8510	2.0297	8.9718	1.3020
1532/F	1/1	227.5	0.0700	1.9704	0.9006	1.9657	7.0613	1.5161
1533/F	1/1	226.4	0.0716	1.8764	1.0725	2.0064	8.8391	1.1472
1534/F	1/1	247.0	0.0960	1.7947	1.0003	9.4461	16.9297	2.5330
1535/F	1/1	243.0	0.0659	1.9847	0.8958	2.0659	7.4327	1.5414
1536/F	1/1	253.9	0.0911	2.1020	0.9311	1.9199	7.9153	1.6675
1537/F	1/1	190.4	0.0807	2.0480	0.8507	1.9529	6.9995	1.1789
1538/F	1/1	229.8	0.1010	1.9037	0.9407	2.2093	8.9410	1.4007
1539/F	1/1	226.5	0.0657	2.0602	0.8645	2.0844	8.5294	1.5696
1540/F	1/1	218.9	0.0624	1.8640	0.8820	1.7658	6.9534	1.4725
1541/F	1/1	207.4	0.0830	1.7782	0.8212	1.8062	7.5318	1.2462
1542/F	1/1	226.4	0.0745	1.7304	0.8938	1.7261	9.5030	1.2965
Mean:		228.5	0.0799	1.9224	0.9087	2.5815	8.8007	1.4893
Standard deviation:		17.7	0.0136	0.1184	0.0702	2.1663	2.7077	0.3673
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	0.0777	2.0208	1.0004	2.2629	9.8551	1.6064
2532/F	2/1	245.6	0.1043	1.9044	0.9432	2.2466	9.0908	1.3963
2533/F	2/1	232.2	0.0753	2.0670	0.8715	1.9431	7.8727	1.2816
2534/F	2/1	219.0	0.0764	1.8788	0.7353	1.8960	7.4473	1.0909
2535/F	2/1	242.7	0.0856	1.9363	0.8705	2.2277	8.9784	1.5173
2536/F	2/1	247.5	0.0683	1.9900	0.9080	2.2364	10.4312	1.3638
2537/F	2/1	213.5	0.0922	1.8627	0.8832	2.3303	9.6756	1.2186
2538/F	2/1	236.2	0.0928	1.8717	0.9183	2.0785	8.3981	1.4890
2539/F	2/1	212.8	0.0502	1.9685	0.9173	1.8324	8.1938	1.2819
2540/F	2/1	250.3	0.0572	2.0326	0.9947	2.0492	8.5717	1.5635
2541/F	2/1	230.2	0.0720	2.0336	0.8671	1.9958	7.8812	1.4786
2542/F	2/1	233.4	0.0778	1.9877	0.9481	2.0479	8.5186	1.4197
Mean:		234.0	0.0775	1.9628	0.9048	2.0956	8.7429	1.3923
Standard deviation:		13.1	0.0151	0.0707	0.0700	0.1624	0.8950	0.1521
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	0.0647	1.9887	0.9424	1.9499	7.5950	1.2793
3532/F	3/1	197.4	0.0692	1.8114	0.8266	1.7573	6.6715	1.0368
3533/F	3/1	228.8	0.0906	1.8085	0.7975	1.9107	9.0775	1.1125
3534/F	3/1	219.4	0.0622	1.8860	0.8412	2.0702	6.9267	1.5268
3535/F	3/1	241.0	0.0630	1.9401	1.0040	2.0241	8.1288	1.4879
3536/F	3/1	252.4	0.0683	2.0858	0.9467	2.3038	8.8106	1.2785
3537/F	3/1	234.3	0.0901	1.8103	0.9952	2.1035	7.6965	1.4603
3538/F	3/1	234.5	0.0768	2.0575	0.9383	2.1841	9.5113	1.5261
3539/F	3/1	252.8	0.0839	2.0122	0.8591	2.1967	8.8034	1.4533
3540/F	3/1	223.5	0.0569	2.0397	0.9126	1.9644	9.0185	1.3888
3541/F	3/1	232.9	0.0759	1.9299	0.9254	2.1505	7.8093	1.4259
3542/F	3/1	211.8	0.0665	1.9809	0.8102	1.9485	6.9862	1.3013
Mean:		229.9	0.0723	1.9459	0.8999	2.0470	8.0863	1.3565

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		15.8	0.0111	0.0989	0.0708	0.1509	0.9510	0.1589
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	0.0767	1.9727	0.9372	1.9983	7.3682	1.2540
4532/F	4/1	228.5	0.0784	1.8079	0.8377	2.1014	8.5267	1.0783
4533/F	4/1	245.1	0.0724	1.8157	0.9102	1.9398	7.5958	1.4152
4534/F	4/1	237.5	0.0609	1.9441	0.8575	2.2091	8.4154	1.4002
4535/F	4/1	240.9	0.0811	1.9639	0.9604	2.1288	9.0624	1.4184
4536/F	4/1	238.8	0.0904	1.8722	0.8485	2.1657	7.9490	1.4157
4537/F	4/1	206.6	0.0866	1.9490	0.8697	2.1186	7.8534	1.4665
4538/F	4/1	271.3	0.0778	2.0130	1.1105	2.4651	11.1126	1.6406
4539/F	4/1	238.0	0.0700	1.9501	0.8724	2.1882	7.8717	1.2927
4540/F	4/1	210.9	0.0709	2.0197	0.7488	1.7852	6.9806	2.4603
4541/F	4/1	206.2	0.0934	1.8647	0.8263	2.0512	7.3659	1.3441
4542/F	4/1	225.1	0.0804	1.9019	0.9149	1.9395	8.3731	1.1238
M e a n:		231.3	0.0783	1.9229	0.8912	2.0909	8.2062	1.4425
Standard deviation:		18.5	0.0091	0.0705	0.0890	0.1708	1.0846	0.3544
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
1531/F	1/1	244.4	0.0879	0.0855	0.5025	0.4574	0.7219
1532/F	1/1	227.5	0.0761	0.0692	0.4898	0.3406	1.2509
1533/F	1/1	226.4	0.0573	0.0572	0.4713	0.4414	0.7443
1534/F	1/1	247.0	0.0695	0.0749	1.0948	0.3856	0.8595
1535/F	1/1	243.0	0.0663	0.0794	0.5442	0.4894	0.8537
1536/F	1/1	253.9	0.0661	0.0897	0.5546	0.4782	0.8031
1537/F	1/1	190.4	0.0631	0.0542	0.2831	0.1841	0.6288
1538/F	1/1	229.8	0.0753	0.0720	0.5572	0.6090	0.9619
1539/F	1/1	226.5	0.0623	0.0677	0.5048	0.4280	0.6350
1540/F	1/1	218.9	0.0635	0.0579	0.5087	0.3284	0.6291
1541/F	1/1	207.4	0.0930	0.0946	0.4226	0.4361	0.7539
1542/F	1/1	226.4	0.0636	0.0644	0.6028	0.5610	0.5071
Mean:		228.5	0.0703	0.0722	0.5447	0.4283	0.7791
Standard deviation:		17.7	0.0108	0.0131	0.1913	0.1115	0.1939
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	0.0977	0.0829	0.5942	0.4206	0.8552
2532/F	2/1	245.6	0.0684	0.0707	0.7040	0.4933	0.9037
2533/F	2/1	232.2	0.0745	0.0626	0.5778	0.4285	1.1810
2534/F	2/1	219.0	0.0481	0.0572	0.5123	0.4961	1.2072
2535/F	2/1	242.7	0.0563	0.0739	0.5753	0.5314	0.7639
2536/F	2/1	247.5	0.0706	0.0757	0.7151	0.6801	1.1336
2537/F	2/1	213.5	0.0749	0.0825	0.6123	0.3591	1.1887
2538/F	2/1	236.2	0.1006	0.0912	0.4933	0.5202	0.8780
2539/F	2/1	212.8	0.0524	0.0746	0.5446	0.5021	0.8187
2540/F	2/1	250.3	0.0533	0.0613	0.6410	0.4401	0.6002
2541/F	2/1	230.2	0.0649	0.0812	0.5753	0.3529	0.7140
2542/F	2/1	233.4	0.0542	0.0609	0.5776	0.3661	0.6682
Mean:		234.0	0.0680	0.0729	0.5936	0.4659	0.9094
Standard deviation:		13.1	0.0171	0.0106	0.0673	0.0926	0.2166
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	0.0788	0.0562	0.5769	0.3225	0.8695
3532/F	3/1	197.4	0.0771	0.0747	0.4814	0.5747	0.6465
3533/F	3/1	228.8	0.0741	0.0638	0.5146	0.4348	0.7868
3534/F	3/1	219.4	0.0605	0.0457	0.3827	0.3683	0.8289
3535/F	3/1	241.0	0.0651	0.0727	0.5564	0.4198	0.5462
3536/F	3/1	252.4	0.0695	0.0782	0.5830	0.4914	0.9331
3537/F	3/1	234.3	0.0626	0.0791	0.5369	0.5222	1.3935
3538/F	3/1	234.5	0.0644	0.0449	0.5148	0.3289	1.3903
3539/F	3/1	252.8	0.0812	0.0615	0.5460	0.4846	1.3719
3540/F	3/1	223.5	0.0649	0.0598	0.4264	0.3409	0.6625
3541/F	3/1	232.9	0.0666	0.0704	0.5656	0.5273	0.8853
3542/F	3/1	211.8	0.0607	0.0640	0.4575	0.4212	1.1188
Mean:		229.9	0.0688	0.0643	0.5119	0.4364	0.9528

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		15.8	0.0072	0.0115	0.0631	0.0847	0.2995
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	0.0836	0.1005	0.5022	0.4268	0.9614
4532/F	4/1	228.5	0.0711	0.0632	0.4642	0.4279	0.8355
4533/F	4/1	245.1	0.0597	0.0696	0.5068	0.4644	1.0317
4534/F	4/1	237.5	0.0657	0.0532	0.5973	0.7540	1.2750
4535/F	4/1	240.9	0.0702	0.0751	0.5797	0.5371	0.5341
4536/F	4/1	238.8	0.0647	0.0811	0.4680	0.4512	0.8624
4537/F	4/1	206.6	0.0567	0.0515	0.4641	0.3966	0.7106
4538/F	4/1	271.3	0.1151	0.1071	0.6751	0.5591	1.0428
4539/F	4/1	238.0	0.0724	0.0600	0.4944	0.3209	1.3434
4540/F	4/1	210.9	0.0537	0.0459	0.4537	0.4441	0.7023
4541/F	4/1	206.2	0.0890	0.0788	0.4802	0.3224	0.7746
4542/F	4/1	225.1	0.0613	0.0741	0.4130	0.3092	0.8727
M e a n:		231.3	0.0719	0.0717	0.5082	0.4511	0.9122
Standard deviation:		18.5	0.0171	0.0188	0.0735	0.1239	0.2351
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
				M a l e	A n i m a l s			
1031/M	1/1	389.5	0.0199	0.5534	0.1299	0.1296	0.3187	0.8700
1032/M	1/1	381.6	0.0183	0.5405	0.1429	0.1461	0.3049	0.8735
1033/M	1/1	334.4	0.0214	0.6080	0.1846	0.1854	0.3851	0.9994
1034/M	1/1	447.6	0.0214	0.4804	0.1585	0.1455	0.3745	0.8441
1035/M	1/1	399.9	0.0225	0.5417	0.1880	0.1686	0.3229	0.9343
1036/M	1/1	362.1	0.0157	0.5618	0.1874	0.2008	0.3304	0.8309
1037/M	1/1	414.7	0.0152	0.5466	0.1683	0.1759	0.3105	0.8513
1038/M	1/1	364.1	0.0135	0.6010	0.1497	0.1596	0.3531	0.9999
1039/M	1/1	375.3	0.0267	0.5767	0.1501	0.1491	0.3230	0.9237
1040/M	1/1	381.2	0.0202	0.5424	0.1533	0.1621	0.3627	0.9211
1041/M	1/1	385.7	0.0196	0.5375	0.1733	0.1809	0.3315	0.7810
1042/M	1/1	325.3	0.0238	0.6395	0.1862	0.2053	0.3864	0.9289
M e a n:		380.1	0.0199	0.5608	0.1643	0.1674	0.3420	0.8965
Standard deviation:		33.0	0.0038	0.0412	0.0198	0.0232	0.0291	0.0666
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	0.0168	0.4983	0.1373	0.1369	0.2861	0.9309
2032/M	2/1	418.2	0.0253	0.5148	0.1835	0.1616	0.3701	0.9932
2033/M	2/1	377.5	0.0249	0.6191	0.1473	0.1554	0.4095	1.0109
2034/M	2/1	394.8	0.0151	0.5342	0.1725	0.1524	0.3540	0.8114
2035/M	2/1	389.8	0.0211	0.5505	0.1615	0.1733	0.3545	0.9592
2036/M	2/1	363.4	0.0184	0.5690	0.1507	0.1492	0.3416	0.8522
2037/M	2/1	352.0	0.0199	0.6571	0.2008	0.1920	0.3606	0.8992
2038/M	2/1	384.1	0.0183	0.5421	0.1598	0.1448	0.3094	0.9376
2039/M	2/1	394.8	0.0166	0.5471	0.1627	0.1741	0.3832	0.9269
2040/M	2/1	393.5	0.0142	0.5361	0.1499	0.1578	0.3515	0.8891
2041/M	2/1	354.5	0.0209	0.5797	0.2062	0.2147	0.3798	0.9302
2042/M	2/1	417.7	0.0162	0.4945	0.1908	0.1886	0.3521	0.7748
M e a n:		385.8	0.0190	0.5535	0.1686	0.1667	0.3544	0.9096
Standard deviation:		21.4	0.0036	0.0475	0.0223	0.0226	0.0326	0.0696
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	0.0246	0.5565	0.1617	0.1772	0.3552	0.8588
3032/M	3/1	373.9	0.0237	0.5974	0.1411	0.1381	0.3373	0.8476
3033/M	3/1	334.8	0.0159	0.6286	0.1724	0.2204	0.3797	0.8866
3034/M	3/1	358.7	0.0210	0.5850	0.1812	0.1704	0.3750	0.9707
3035/M	3/1	383.6	0.0235	0.5700	0.1606	0.1687	0.3440	1.0437
3036/M	3/1	402.9	0.0140	0.5459	0.1586	0.1546	0.3600	0.8363
3037/M	3/1	383.7	0.0193	0.5188	0.1682	0.1474	0.3463	0.8477
3038/M	3/1	382.2	0.0160	0.6106	0.1692	0.1742	0.3708	0.9399
3040/M	3/1	404.8	0.0198	0.4890	0.1613	0.1538	0.3976	0.9564
3041/M	3/1	359.4	0.0218	0.5914	0.1705	0.1801	0.3947	1.0894
3042/M	3/1	343.5	0.0218	0.5563	0.2022	0.1955	0.3586	0.9615
3043/M	3/1	394.0	0.0186	0.5342	0.1586	0.1453	0.3659	0.9507
M e a n:		373.8	0.0200	0.5653	0.1671	0.1688	0.3654	0.9324

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
Standard deviation:		22.3	0.0034	0.0401	0.0148	0.0233	0.0191	0.0806
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	0.0226	0.5154	0.1470	0.1516	0.2948	0.8537
4032/M	4/1	363.3	0.0163	0.5593	0.1644	0.1660	0.3409	0.9107
4033/M	4/1	310.9	0.0231	0.6367	0.1722	0.1853	0.3980	0.8937
4034/M	4/1	412.8	0.0204	0.5223	0.1618	0.1489	0.3367	0.8744
4035/M	4/1	386.9	0.0169	0.5529	0.1507	0.1639	0.3661	0.8556
4036/M	4/1	384.2	0.0207	0.5810	0.1677	0.1719	0.3522	0.9185
4037/M	4/1	371.9	0.0194	0.5398	0.1693	0.1701	0.4001	1.0610
4038/M	4/1	409.1	0.0198	0.5282	0.1522	0.1776	0.4059	0.9591
4039/M	4/1	336.1	0.0181	0.6328	0.1787	0.1886	0.3512	0.9026
4040/M	4/1	376.2	0.0162	0.5442	0.1406	0.1579	0.3774	0.8621
4041/M	4/1	337.4	0.0215	0.5683	0.2040	0.2023	0.3418	0.8772
4042/M	4/1	381.6	0.0173	0.5623	0.1473	0.1470	0.3302	0.9444
M e a n:		371.4	0.0194	0.5619	0.1630	0.1693	0.3579	0.9094
Standard deviation:		30.2	0.0024	0.0390	0.0175	0.0170	0.0330	0.0584
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
				Male Animals				
1031/M	1/1	389.5	2.9461	0.5042	0.1956	0.3991	0.4038	0.1841
1032/M	1/1	381.6	2.8631	0.5027	0.1577	0.4551	0.4535	0.1186
1033/M	1/1	334.4	3.7500	0.5272	0.2310	0.5179	0.5018	0.0871
1034/M	1/1	447.6	3.1765	0.5441	0.2034	0.3724	0.3753	0.1550
1035/M	1/1	399.9	3.1789	0.4563	0.1740	0.4663	0.4648	0.0997
1036/M	1/1	362.1	3.5164	0.4211	0.1671	0.4807	0.4872	0.1123
1037/M	1/1	414.7	3.0312	0.4502	0.1968	0.4029	0.4250	0.1411
1038/M	1/1	364.1	2.9144	0.4230	0.1803	0.4347	0.4124	0.1220
1039/M	1/1	375.3	3.4038	0.4923	0.1622	0.3420	0.3474	0.1151
1040/M	1/1	381.2	3.1131	0.4340	0.1486	0.4152	0.4175	0.1222
1041/M	1/1	385.7	2.9508	0.4947	0.1840	0.4118	0.4071	0.1248
1042/M	1/1	325.3	3.2093	0.5162	0.1677	0.4978	0.4917	0.1066
Mean:		380.1	3.1711	0.4805	0.1807	0.4330	0.4323	0.1241
Standard deviation:		33.0	0.2685	0.0420	0.0231	0.0523	0.0481	0.0259
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	3.2538	0.4828	0.1777	0.3874	0.3933	0.1429
2032/M	2/1	418.2	3.5897	0.6497	0.2696	0.4013	0.3876	0.1924
2033/M	2/1	377.5	4.1358	0.5593	0.2267	0.4355	0.4347	0.1743
2034/M	2/1	394.8	3.2432	0.5047	0.2192	0.4207	0.4388	0.1268
2035/M	2/1	389.8	3.1093	0.4760	0.2156	0.4036	0.4226	0.1509
2036/M	2/1	363.4	3.6342	0.4821	0.1645	0.3881	0.3720	0.0788
2037/M	2/1	352.0	3.2506	0.5182	0.2432	0.4948	0.4711	0.1183
2038/M	2/1	384.1	3.2506	0.5504	0.1611	0.4111	0.3953	0.1200
2039/M	2/1	394.8	3.8073	0.5134	0.1778	0.4029	0.4125	0.1255
2040/M	2/1	393.5	3.0177	0.4592	0.1987	0.4581	0.4420	0.1395
2041/M	2/1	354.5	3.4541	0.5296	0.3830	0.4848	0.4813	0.1429
2042/M	2/1	417.7	3.0784	0.5072	0.2021	0.4390	0.4222	0.0991
Mean:		385.8	3.4021	0.5194	0.2199	0.4273	0.4228	0.1343
Standard deviation:		21.4	0.3338	0.0507	0.0607	0.0360	0.0331	0.0307
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	3.1830	0.5668	0.1984	0.4811	0.4701	0.1107
3032/M	3/1	373.9	2.8649	0.4761	0.2259	0.3450	0.3325	0.0824
3033/M	3/1	334.8	3.4832	0.4738	0.1668	0.4537	0.4742	0.1027
3034/M	3/1	358.7	3.3960	0.4605	0.1950	0.4262	0.4267	0.0880
3035/M	3/1	383.6	3.1585	0.4847	0.2029	0.4754	0.4830	0.1289
3036/M	3/1	402.9	3.2586	0.4967	0.1860	0.3815	0.3931	0.1435
3037/M	3/1	383.7	3.2200	0.5810	0.2118	0.4084	0.4005	0.2057
3038/M	3/1	382.2	3.6681	0.5460	0.2251	0.4550	0.4636	0.1233
3040/M	3/1	404.8	3.1806	0.4382	0.1593	0.3569	0.3671	0.1396
3041/M	3/1	359.4	3.2391	0.5423	0.2507	0.4784	0.4669	0.1543
3042/M	3/1	343.5	3.0501	0.5336	0.2282	0.5351	0.5367	0.1378
3043/M	3/1	394.0	3.3183	0.5967	0.1969	0.3796	0.3821	0.1263
Mean:		373.8	3.2517	0.5164	0.2039	0.4314	0.4330	0.1286

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
Standard deviation:		22.3	0.2050	0.0514	0.0263	0.0581	0.0589	0.0328
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	3.2459	0.4893	0.1988	0.4297	0.4224	0.1122
4032/M	4/1	363.3	3.1244	0.5006	0.2069	0.4243	0.4215	0.1637
4033/M	4/1	310.9	3.2059	0.4917	0.2050	0.4601	0.4522	0.1087
4034/M	4/1	412.8	3.1938	0.5043	0.1965	0.3756	0.3629	0.1576
4035/M	4/1	386.9	3.2177	0.5181	0.1838	0.3884	0.4067	0.1002
4036/M	4/1	384.2	3.4542	0.5371	0.1931	0.4320	0.4286	0.1299
4037/M	4/1	371.9	3.3932	0.4801	0.1973	0.4299	0.4184	0.1248
4038/M	4/1	409.1	3.8484	0.7621	0.1846	0.3605	0.3710	0.1600
4039/M	4/1	336.1	3.0831	0.5007	0.1698	0.5018	0.4985	0.1409
4040/M	4/1	376.2	3.2230	0.4080	0.1940	0.3989	0.4039	0.1153
4041/M	4/1	337.4	2.9861	0.4685	0.1832	0.4616	0.4582	0.1516
4042/M	4/1	381.6	3.2209	0.4306	0.1532	0.4059	0.4089	0.1442
M e a n:		371.4	3.2664	0.5076	0.1888	0.4224	0.4211	0.1341
Standard deviation:		30.2	0.2212	0.0877	0.0153	0.0398	0.0368	0.0219
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1531/F	1/1	244.4	0.0396	0.8003	0.3482	0.8305	3.6709	0.5327
1532/F	1/1	227.5	0.0308	0.8661	0.3959	0.8640	3.1039	0.6664
1533/F	1/1	226.4	0.0316	0.8288	0.4737	0.8862	3.9042	0.5067
1534/F	1/1	247.0	0.0389	0.7266	0.4050	3.8243	6.8541	1.0255
1535/F	1/1	243.0	0.0271	0.8167	0.3686	0.8502	3.0587	0.6343
1536/F	1/1	253.9	0.0359	0.8279	0.3667	0.7562	3.1175	0.6568
1537/F	1/1	190.4	0.0424	1.0756	0.4468	1.0257	3.6762	0.6192
1538/F	1/1	229.8	0.0440	0.8284	0.4094	0.9614	3.8908	0.6095
1539/F	1/1	226.5	0.0290	0.9096	0.3817	0.9203	3.7657	0.6930
1540/F	1/1	218.9	0.0285	0.8515	0.4029	0.8067	3.1765	0.6727
1541/F	1/1	207.4	0.0400	0.8574	0.3959	0.8709	3.6315	0.6009
1542/F	1/1	226.4	0.0329	0.7643	0.3948	0.7624	4.1974	0.5727
	Mean:	228.5	0.0351	0.8461	0.3991	1.1132	3.8373	0.6492
Standard deviation:		17.7	0.0058	0.0864	0.0343	0.8573	1.0197	0.1311
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	0.0317	0.8252	0.4085	0.9240	4.0241	0.6559
2532/F	2/1	245.6	0.0425	0.7754	0.3840	0.9147	3.7015	0.5685
2533/F	2/1	232.2	0.0324	0.8902	0.3753	0.8368	3.3905	0.5519
2534/F	2/1	219.0	0.0349	0.8579	0.3358	0.8658	3.4006	0.4981
2535/F	2/1	242.7	0.0353	0.7978	0.3587	0.9179	3.6994	0.6252
2536/F	2/1	247.5	0.0276	0.8040	0.3669	0.9036	4.2146	0.5510
2537/F	2/1	213.5	0.0432	0.8725	0.4137	1.0915	4.5319	0.5708
2538/F	2/1	236.2	0.0393	0.7924	0.3888	0.8800	3.5555	0.6304
2539/F	2/1	212.8	0.0236	0.9250	0.4311	0.8611	3.8505	0.6024
2540/F	2/1	250.3	0.0229	0.8121	0.3974	0.8187	3.4246	0.6247
2541/F	2/1	230.2	0.0313	0.8834	0.3767	0.8670	3.4236	0.6423
2542/F	2/1	233.4	0.0333	0.8516	0.4062	0.8774	3.6498	0.6083
	Mean:	234.0	0.0332	0.8406	0.3869	0.8965	3.7389	0.5941
Standard deviation:		13.1	0.0065	0.0464	0.0264	0.0694	0.3602	0.0464
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	0.0281	0.8647	0.4097	0.8478	3.3022	0.5562
3532/F	3/1	197.4	0.0351	0.9176	0.4187	0.8902	3.3797	0.5252
3533/F	3/1	228.8	0.0396	0.7904	0.3486	0.8351	3.9674	0.4862
3534/F	3/1	219.4	0.0284	0.8596	0.3834	0.9436	3.1571	0.6959
3535/F	3/1	241.0	0.0261	0.8050	0.4166	0.8399	3.3729	0.6174
3536/F	3/1	252.4	0.0271	0.8264	0.3751	0.9128	3.4907	0.5065
3537/F	3/1	234.3	0.0385	0.7726	0.4248	0.8978	3.2849	0.6233
3538/F	3/1	234.5	0.0328	0.8774	0.4001	0.9314	4.0560	0.6508
3539/F	3/1	252.8	0.0332	0.7960	0.3398	0.8689	3.4824	0.5749
3540/F	3/1	223.5	0.0255	0.9126	0.4083	0.8789	4.0351	0.6214
3541/F	3/1	232.9	0.0326	0.8286	0.3973	0.9234	3.3531	0.6122
3542/F	3/1	211.8	0.0314	0.9353	0.3825	0.9200	3.2985	0.6144
	Mean:	229.9	0.0315	0.8489	0.3921	0.8908	3.5150	0.5904

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		15.8	0.0047	0.0542	0.0272	0.0370	0.3173	0.0619
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	0.0338	0.8702	0.4134	0.8815	3.2502	0.5532
4532/F	4/1	228.5	0.0343	0.7912	0.3666	0.9196	3.7316	0.4719
4533/F	4/1	245.1	0.0295	0.7408	0.3714	0.7914	3.0991	0.5774
4534/F	4/1	237.5	0.0256	0.8186	0.3611	0.9301	3.5433	0.5896
4535/F	4/1	240.9	0.0337	0.8152	0.3987	0.8837	3.7619	0.5888
4536/F	4/1	238.8	0.0379	0.7840	0.3553	0.9069	3.3287	0.5928
4537/F	4/1	206.6	0.0419	0.9434	0.4210	1.0255	3.8013	0.7098
4538/F	4/1	271.3	0.0287	0.7420	0.4093	0.9086	4.0961	0.6047
4539/F	4/1	238.0	0.0294	0.8194	0.3666	0.9194	3.3074	0.5432
4540/F	4/1	210.9	0.0336	0.9577	0.3550	0.8465	3.3099	1.1666
4541/F	4/1	206.2	0.0453	0.9043	0.4007	0.9948	3.5722	0.6518
4542/F	4/1	225.1	0.0357	0.8449	0.4064	0.8616	3.7197	0.4992
M e a n:		231.3	0.0341	0.8360	0.3855	0.9058	3.5435	0.6291
Standard deviation:		18.5	0.0056	0.0713	0.0249	0.0624	0.2902	0.1805
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
1531/F	1/1	244.4	0.0360	0.0350	0.2056	0.1872	0.2954
1532/F	1/1	227.5	0.0335	0.0304	0.2153	0.1497	0.5498
1533/F	1/1	226.4	0.0253	0.0253	0.2082	0.1950	0.3288
1534/F	1/1	247.0	0.0281	0.0303	0.4432	0.1561	0.3480
1535/F	1/1	243.0	0.0273	0.0327	0.2240	0.2014	0.3513
1536/F	1/1	253.9	0.0260	0.0353	0.2184	0.1883	0.3163
1537/F	1/1	190.4	0.0331	0.0285	0.1487	0.0967	0.3303
1538/F	1/1	229.8	0.0328	0.0313	0.2425	0.2650	0.4186
1539/F	1/1	226.5	0.0275	0.0299	0.2229	0.1890	0.2804
1540/F	1/1	218.9	0.0290	0.0265	0.2324	0.1500	0.2874
1541/F	1/1	207.4	0.0448	0.0456	0.2038	0.2103	0.3635
1542/F	1/1	226.4	0.0281	0.0284	0.2663	0.2478	0.2240
M e a n:		228.5	0.0310	0.0316	0.2359	0.1864	0.3411
Standard deviation:		17.7	0.0055	0.0054	0.0709	0.0452	0.0817
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	0.0399	0.0339	0.2426	0.1717	0.3492
2532/F	2/1	245.6	0.0279	0.0288	0.2866	0.2009	0.3680
2533/F	2/1	232.2	0.0321	0.0270	0.2488	0.1845	0.5086
2534/F	2/1	219.0	0.0220	0.0261	0.2339	0.2265	0.5512
2535/F	2/1	242.7	0.0232	0.0304	0.2370	0.2190	0.3148
2536/F	2/1	247.5	0.0285	0.0306	0.2889	0.2748	0.4580
2537/F	2/1	213.5	0.0351	0.0386	0.2868	0.1682	0.5568
2538/F	2/1	236.2	0.0426	0.0386	0.2088	0.2202	0.3717
2539/F	2/1	212.8	0.0246	0.0351	0.2559	0.2359	0.3847
2540/F	2/1	250.3	0.0213	0.0245	0.2561	0.1758	0.2398
2541/F	2/1	230.2	0.0282	0.0353	0.2499	0.1533	0.3102
2542/F	2/1	233.4	0.0232	0.0261	0.2475	0.1569	0.2863
M e a n:		234.0	0.0290	0.0312	0.2536	0.1990	0.3916
Standard deviation:		13.1	0.0071	0.0050	0.0240	0.0370	0.1046
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	0.0343	0.0244	0.2508	0.1402	0.3780
3532/F	3/1	197.4	0.0391	0.0378	0.2439	0.2911	0.3275
3533/F	3/1	228.8	0.0324	0.0279	0.2249	0.1900	0.3439
3534/F	3/1	219.4	0.0276	0.0208	0.1744	0.1679	0.3778
3535/F	3/1	241.0	0.0270	0.0302	0.2309	0.1742	0.2266
3536/F	3/1	252.4	0.0275	0.0310	0.2310	0.1947	0.3697
3537/F	3/1	234.3	0.0267	0.0338	0.2292	0.2229	0.5948
3538/F	3/1	234.5	0.0275	0.0191	0.2195	0.1403	0.5929
3539/F	3/1	252.8	0.0321	0.0243	0.2160	0.1917	0.5427
3540/F	3/1	223.5	0.0290	0.0268	0.1908	0.1525	0.2964
3541/F	3/1	232.9	0.0286	0.0302	0.2429	0.2264	0.3801
3542/F	3/1	211.8	0.0287	0.0302	0.2160	0.1989	0.5282
M e a n:		229.9	0.0300	0.0280	0.2225	0.1909	0.4132

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		15.8	0.0037	0.0053	0.0219	0.0425	0.1211
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	0.0369	0.0443	0.2215	0.1883	0.4241
4532/F	4/1	228.5	0.0311	0.0277	0.2032	0.1873	0.3656
4533/F	4/1	245.1	0.0244	0.0284	0.2068	0.1895	0.4209
4534/F	4/1	237.5	0.0277	0.0224	0.2515	0.3175	0.5368
4535/F	4/1	240.9	0.0291	0.0312	0.2406	0.2230	0.2217
4536/F	4/1	238.8	0.0271	0.0340	0.1960	0.1889	0.3611
4537/F	4/1	206.6	0.0274	0.0249	0.2246	0.1920	0.3439
4538/F	4/1	271.3	0.0424	0.0395	0.2488	0.2061	0.3844
4539/F	4/1	238.0	0.0304	0.0252	0.2077	0.1348	0.5645
4540/F	4/1	210.9	0.0255	0.0218	0.2151	0.2106	0.3330
4541/F	4/1	206.2	0.0432	0.0382	0.2329	0.1564	0.3757
4542/F	4/1	225.1	0.0272	0.0329	0.1835	0.1374	0.3877
M e a n:		231.3	0.0310	0.0309	0.2194	0.1943	0.3933
Standard deviation:		18.5	0.0064	0.0071	0.0213	0.0474	0.0901
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
				M a l e	A n i m a l s			
1031/M	1/1	389.5	3.6004	100.0000	23.4724	23.4121	57.6022	157.2264
1032/M	1/1	381.6	3.3936	100.0000	26.4411	27.0228	56.4018	161.5940
1033/M	1/1	334.4	3.5217	100.0000	30.3625	30.5002	63.3466	164.3844
1034/M	1/1	447.6	4.4461	100.0000	32.9923	30.2809	77.9509	175.7186
1035/M	1/1	399.9	4.1497	100.0000	34.6981	31.1161	59.6058	172.4566
1036/M	1/1	362.1	2.7920	100.0000	33.3464	35.7452	58.7987	147.8962
1037/M	1/1	414.7	2.7837	100.0000	30.7879	32.1819	56.8114	155.7350
1038/M	1/1	364.1	2.2528	100.0000	24.9040	26.5491	58.7416	166.3544
1039/M	1/1	375.3	4.6343	100.0000	26.0223	25.8467	56.0181	160.1765
1040/M	1/1	381.2	3.7239	100.0000	28.2585	29.8834	66.8762	169.8071
1041/M	1/1	385.7	3.6421	100.0000	32.2480	33.6517	61.6836	145.3160
1042/M	1/1	325.3	3.7206	100.0000	29.1160	32.1108	60.4192	145.2579
	M e a n:	380.1	3.5551	100.0000	29.3875	29.8584	61.1880	160.1603
Standard deviation:		33.0	0.6927	0.0000	3.6233	3.5462	6.1400	10.2940
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	3.3637	100.0000	27.5537	27.4661	57.4151	186.8130
2032/M	2/1	418.2	4.9138	100.0000	35.6370	31.3919	71.8824	192.9033
2033/M	2/1	377.5	4.0180	100.0000	23.7912	25.0963	66.1404	163.2906
2034/M	2/1	394.8	2.8352	100.0000	32.2966	28.5321	66.2574	151.8822
2035/M	2/1	389.8	3.8306	100.0000	29.3304	31.4833	64.4019	174.2299
2036/M	2/1	363.4	3.2402	100.0000	26.4871	26.2259	60.0348	149.7679
2037/M	2/1	352.0	3.0306	100.0000	30.5607	29.2248	54.8787	136.8380
2038/M	2/1	384.1	3.3762	100.0000	29.4688	26.7121	57.0791	172.9661
2039/M	2/1	394.8	3.0327	100.0000	29.7389	31.8178	70.0482	169.4370
2040/M	2/1	393.5	2.6547	100.0000	27.9640	29.4288	65.5606	165.8450
2041/M	2/1	354.5	3.6109	100.0000	35.5686	37.0383	65.5214	160.4701
2042/M	2/1	417.7	3.2775	100.0000	38.5893	38.1294	71.2045	156.6857
	M e a n:	385.8	3.4320	100.0000	30.5822	30.2122	64.2020	165.0941
Standard deviation:		21.4	0.6090	0.0000	4.2630	4.0579	5.6801	15.7050
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	4.4257	100.0000	29.0606	31.8384	63.8297	154.3172
3032/M	3/1	373.9	3.9665	100.0000	23.6200	23.1186	56.4669	141.8857
3033/M	3/1	334.8	2.5375	100.0000	27.4235	35.0646	60.4020	141.0521
3034/M	3/1	358.7	3.5980	100.0000	30.9807	29.1317	64.0965	165.9312
3035/M	3/1	383.6	4.1299	100.0000	28.1729	29.5952	60.3567	183.1054
3036/M	3/1	402.9	2.5735	100.0000	29.0592	28.3181	65.9528	153.2033
3037/M	3/1	383.7	3.7177	100.0000	32.4190	28.4200	66.7521	163.4012
3038/M	3/1	382.2	2.6266	100.0000	27.7102	28.5286	60.7207	153.9249
3040/M	3/1	404.8	4.0566	100.0000	32.9831	31.4574	81.2983	195.5747
3041/M	3/1	359.4	3.6934	100.0000	28.8322	30.4507	66.7498	184.2194
3042/M	3/1	343.5	3.9142	100.0000	36.3475	35.1439	64.4584	172.8310
3043/M	3/1	394.0	3.4732	100.0000	29.6859	27.2010	68.5038	177.9731
	M e a n:	373.8	3.5594	100.0000	29.6912	29.8557	64.9656	165.6183

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymis Left	Epididymis Right	Heart	Kidneys
Standard deviation:		22.3	0.6433	0.0000	3.2194	3.3189	6.1883	17.4361
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	4.3808	100.0000	28.5255	29.4047	57.1967	165.6318
4032/M	4/1	363.3	2.9134	100.0000	29.3898	29.6801	60.9547	162.8248
4033/M	4/1	310.9	3.6274	100.0000	27.0436	29.0997	62.5088	140.3708
4034/M	4/1	412.8	3.9004	100.0000	30.9851	28.5039	64.4653	167.4010
4035/M	4/1	386.9	3.0528	100.0000	27.2557	29.6540	66.2179	154.7592
4036/M	4/1	384.2	3.5706	100.0000	28.8652	29.5865	60.6290	158.1022
4037/M	4/1	371.9	3.6015	100.0000	31.3674	31.5168	74.1121	196.5579
4038/M	4/1	409.1	3.7484	100.0000	28.8167	33.6295	76.8522	181.5817
4039/M	4/1	336.1	2.8589	100.0000	28.2456	29.8067	55.4991	142.6530
4040/M	4/1	376.2	2.9847	100.0000	25.8317	29.0215	69.3615	158.4290
4041/M	4/1	337.4	3.7814	100.0000	35.8994	35.5917	60.1471	154.3734
4042/M	4/1	381.6	3.0854	100.0000	26.2025	26.1372	58.7248	167.9670
M e a n:		371.4	3.4588	100.0000	29.0357	30.1360	63.8891	162.5543
Standard deviation:		30.2	0.4749	0.0000	2.7447	2.4538	6.6418	15.4723
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
				Male Animals				
1031/M	1/1	389.5	532.4131	91.1149	35.3501	72.1199	72.9690	33.2761
1032/M	1/1	381.6	529.6796	92.9995	29.1705	84.1858	83.8900	21.9470
1033/M	1/1	334.4	616.7922	86.7198	38.0011	85.1754	82.5292	14.3180
1034/M	1/1	447.6	661.2316	113.2639	42.3496	77.5184	78.1276	32.2668
1035/M	1/1	399.9	586.7938	84.2319	32.1224	86.0829	85.7921	18.4038
1036/M	1/1	362.1	625.8799	74.9558	29.7385	85.5584	86.7135	19.9862
1037/M	1/1	414.7	554.5395	82.3584	35.9979	73.7118	77.7484	25.8205
1038/M	1/1	364.1	484.8840	70.3848	29.9899	72.3268	68.6209	20.3025
1039/M	1/1	375.3	590.2417	85.3671	28.1199	59.3079	60.2412	19.9510
1040/M	1/1	381.2	573.9324	80.0116	27.3879	76.5488	76.9793	22.5226
1041/M	1/1	385.7	549.0208	92.0453	34.2354	76.6184	75.7501	23.2224
1042/M	1/1	325.3	501.8459	80.7191	26.2270	77.8493	76.8831	16.6755
Mean:		380.1	567.2712	86.1810	32.3909	77.2503	77.1870	22.3910
Standard deviation:		33.0	52.1017	10.8774	4.8648	7.6532	7.5076	5.7090
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2031/M	2/1	389.6	653.0109	96.8887	35.6668	77.7469	78.9368	28.6818
2032/M	2/1	418.2	697.2412	126.1948	52.3710	77.9481	75.2822	37.3647
2033/M	2/1	377.5	668.0574	90.3423	36.6239	70.3466	70.2225	28.1558
2034/M	2/1	394.8	607.0643	94.4766	41.0250	78.7455	82.1402	23.7389
2035/M	2/1	389.8	564.7980	86.4719	39.1724	73.3119	76.7650	27.4104
2036/M	2/1	363.4	638.6837	84.7326	28.9100	68.2126	65.3690	13.8505
2037/M	2/1	352.0	494.6609	78.8595	37.0109	75.2972	71.6873	18.0061
2038/M	2/1	384.1	599.6351	101.5272	29.7186	75.8333	72.9277	22.1400
2039/M	2/1	394.8	695.9626	93.8420	32.5030	73.6411	75.4005	22.9327
2040/M	2/1	393.5	562.9107	85.6554	37.0562	85.4563	82.4556	26.0156
2041/M	2/1	354.5	595.8782	91.3670	66.0811	83.6294	83.0259	24.6533
2042/M	2/1	417.7	622.5117	102.5610	40.8695	88.7684	85.3796	20.0378
Mean:		385.8	616.7012	94.4099	39.7507	77.4114	76.6327	24.4156
Standard deviation:		21.4	59.1922	12.1908	10.3031	6.0832	6.0033	5.9632
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3031/M	3/1	364.2	571.9558	101.8502	35.6523	86.4417	84.4681	19.8885
3032/M	3/1	373.9	479.5497	79.6884	37.8117	57.7562	55.6521	13.7888
3033/M	3/1	334.8	554.1533	75.3802	26.5444	72.1821	75.4419	16.3467
3034/M	3/1	358.7	580.5090	78.7219	33.3302	72.8555	72.9365	15.0400
3035/M	3/1	383.6	554.1230	85.0354	35.5957	83.4118	84.7290	22.6069
3036/M	3/1	402.9	596.9536	90.9881	34.0745	69.8859	72.0047	26.2902
3037/M	3/1	383.7	620.6984	111.9970	40.8289	78.7340	77.2017	39.6534
3038/M	3/1	382.2	600.7198	89.4121	36.8626	74.5094	75.9148	20.1860
3040/M	3/1	404.8	650.4117	89.6135	32.5688	72.9932	75.0695	28.5476
3041/M	3/1	359.4	547.7322	91.6957	42.3920	80.8930	78.9546	26.0892
3042/M	3/1	343.5	548.2523	95.9184	41.0256	96.1800	96.4678	24.7776
3043/M	3/1	394.0	621.1812	111.7024	36.8509	71.0695	71.5351	23.6423
Mean:		373.8	577.1867	91.8336	36.1281	76.4094	76.6980	23.0714

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Liver	Lungs	Spleen	Testis Left	Testis Right	Thymus
Standard deviation:		22.3	45.2004	11.9325	4.3305	9.6806	9.6844	7.0209
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4031/M	4/1	386.2	629.7765	94.9410	38.5632	83.3710	81.9593	21.7634
4032/M	4/1	363.3	558.6073	89.4931	36.9833	75.8612	75.3642	29.2667
4033/M	4/1	310.9	503.5466	77.2254	32.1916	72.2593	71.0266	17.0658
4034/M	4/1	412.8	611.4415	96.5495	37.6264	71.9136	69.4834	30.1781
4035/M	4/1	386.9	582.0197	93.7214	33.2398	70.2571	73.5671	18.1159
4036/M	4/1	384.2	594.5612	92.4466	33.2288	74.3515	73.7781	22.3512
4037/M	4/1	371.9	628.6028	88.9415	36.5579	79.6364	77.5093	23.1133
4038/M	4/1	409.1	728.5668	144.2778	34.9530	68.2447	70.2439	30.2837
4039/M	4/1	336.1	487.2432	79.1226	26.8303	79.3107	78.7746	22.2598
4040/M	4/1	376.2	592.3013	74.9841	35.6602	73.3135	74.2221	21.1958
4041/M	4/1	337.4	525.4786	82.4493	32.2380	81.2236	80.6290	26.6729
4042/M	4/1	381.6	572.8468	76.5753	27.2418	72.1943	72.7163	25.6432
M e a n:		371.4	584.5827	90.8940	33.7762	75.1614	74.9395	23.9925
Standard deviation:		30.2	64.6293	18.5110	3.7792	4.7253	4.0335	4.4450
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1531/F	1/1	244.4	4.9489	100.0000	43.5072	103.7679	458.6810	66.5644
1532/F	1/1	227.5	3.5526	100.0000	45.7065	99.7615	358.3689	76.9438
1533/F	1/1	226.4	3.8158	100.0000	57.1573	106.9282	471.0670	61.1384
1534/F	1/1	247.0	5.3491	100.0000	55.7363	526.3332	943.3166	141.1378
1535/F	1/1	243.0	3.3204	100.0000	45.1353	104.0913	374.5000	77.6641
1536/F	1/1	253.9	4.3340	100.0000	44.2959	91.3368	376.5604	79.3292
1537/F	1/1	190.4	3.9404	100.0000	41.5381	95.3564	341.7725	57.5635
1538/F	1/1	229.8	5.3055	100.0000	49.4143	116.0530	469.6644	73.5778
1539/F	1/1	226.5	3.1890	100.0000	41.9619	101.1747	414.0084	76.1868
1540/F	1/1	218.9	3.3476	100.0000	47.3176	94.7318	373.0365	78.9968
1541/F	1/1	207.4	4.6676	100.0000	46.1815	101.5746	423.5632	70.0821
1542/F	1/1	226.4	4.3054	100.0000	51.6528	99.7515	549.1795	74.9249
M e a n:		228.5	4.1730	100.0000	47.4671	136.7384	462.8098	77.8425
Standard deviation:		17.7	0.7686	0.0000	5.0901	122.8556	162.7199	21.1441
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	3.8450	100.0000	49.5051	111.9804	487.6831	79.4933
2532/F	2/1	245.6	5.4768	100.0000	49.5274	117.9689	477.3578	73.3197
2533/F	2/1	232.2	3.6430	100.0000	42.1626	94.0058	380.8757	62.0029
2534/F	2/1	219.0	4.0664	100.0000	39.1367	100.9155	396.3860	58.0637
2535/F	2/1	242.7	4.4208	100.0000	44.9569	115.0493	463.6885	78.3608
2536/F	2/1	247.5	3.4322	100.0000	45.6281	112.3819	524.1810	68.5327
2537/F	2/1	213.5	4.9498	100.0000	47.4150	125.1034	519.4396	65.4212
2538/F	2/1	236.2	4.9581	100.0000	49.0624	111.0488	448.6884	79.5534
2539/F	2/1	212.8	2.5502	100.0000	46.5989	93.0861	416.2459	65.1207
2540/F	2/1	250.3	2.8141	100.0000	48.9373	100.8167	421.7112	76.9212
2541/F	2/1	230.2	3.5405	100.0000	42.6387	98.1412	387.5492	72.7085
2542/F	2/1	233.4	3.9141	100.0000	47.6983	103.0286	428.5658	71.4243
M e a n:		234.0	3.9676	100.0000	46.1056	106.9606	446.0310	70.9102
Standard deviation:		13.1	0.8723	0.0000	3.3331	10.0677	49.0315	7.1541
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	3.2534	100.0000	47.3877	98.0490	381.9078	64.3285
3532/F	3/1	197.4	3.8202	100.0000	45.6332	97.0134	368.3063	57.2375
3533/F	3/1	228.8	5.0097	100.0000	44.0973	105.6511	501.9354	61.5151
3534/F	3/1	219.4	3.2980	100.0000	44.6023	109.7667	367.2694	80.9544
3535/F	3/1	241.0	3.2473	100.0000	51.7499	104.3297	418.9888	76.6919
3536/F	3/1	252.4	3.2745	100.0000	45.3879	110.4516	422.4087	61.2954
3537/F	3/1	234.3	4.9771	100.0000	54.9743	116.1962	425.1505	80.6662
3538/F	3/1	234.5	3.7327	100.0000	45.6039	106.1531	462.2747	74.1726
3539/F	3/1	252.8	4.1696	100.0000	42.6946	109.1691	437.5013	72.2244
3540/F	3/1	223.5	2.7896	100.0000	44.7419	96.3083	442.1484	68.0884
3541/F	3/1	232.9	3.9328	100.0000	47.9507	111.4307	404.6479	73.8847
3542/F	3/1	211.8	3.3571	100.0000	40.9006	98.3644	352.6781	65.6924
M e a n:		229.9	3.7385	100.0000	46.3104	105.2403	415.4348	69.7293

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		15.8	0.6949	0.0000	3.8486	6.5347	43.4347	7.8633
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	3.8881	100.0000	47.5085	101.2977	373.5084	63.5677
4532/F	4/1	228.5	4.3365	100.0000	46.3355	116.2343	471.6357	59.6438
4533/F	4/1	245.1	3.9874	100.0000	50.1294	106.8348	418.3401	77.9424
4534/F	4/1	237.5	3.1326	100.0000	44.1078	113.6310	432.8687	72.0231
4535/F	4/1	240.9	4.1295	100.0000	48.9027	108.3966	461.4492	72.2236
4536/F	4/1	238.8	4.8285	100.0000	45.3210	115.6768	424.5807	75.6169
4537/F	4/1	206.6	4.4433	100.0000	44.6229	108.7019	402.9451	75.2437
4538/F	4/1	271.3	3.8649	100.0000	55.1664	122.4590	552.0418	81.5003
4539/F	4/1	238.0	3.5896	100.0000	44.7362	112.2096	403.6563	66.2889
4540/F	4/1	210.9	3.5104	100.0000	37.0748	88.3894	345.6256	121.8151
4541/F	4/1	206.2	5.0088	100.0000	44.3128	110.0016	395.0180	72.0813
4542/F	4/1	225.1	4.2274	100.0000	48.1045	101.9770	440.2493	59.0883
M e a n:		231.3	4.0789	100.0000	46.3602	108.8175	426.8266	74.7529
Standard deviation:		18.5	0.5393	0.0000	4.3149	8.7853	52.8588	16.4121
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
1531/F	1/1	244.4	4.4939	4.3712	25.6902	23.3845	36.9070
1532/F	1/1	227.5	3.8622	3.5120	24.8579	17.2858	63.4846
1533/F	1/1	226.4	3.0537	3.0484	25.1172	23.5238	39.6664
1534/F	1/1	247.0	3.8725	4.1734	61.0018	21.4855	47.8910
1535/F	1/1	243.0	3.3406	4.0006	27.4198	24.6586	43.0141
1536/F	1/1	253.9	3.1446	4.2674	26.3844	22.7498	38.2065
1537/F	1/1	190.4	3.0811	2.6465	13.8232	8.9893	30.7031
1538/F	1/1	229.8	3.9555	3.7821	29.2693	31.9903	50.5279
1539/F	1/1	226.5	3.0240	3.2861	24.5025	20.7747	30.8223
1540/F	1/1	218.9	3.4067	3.1062	27.2908	17.6180	33.7500
1541/F	1/1	207.4	5.2300	5.3200	23.7656	24.5248	42.3968
1542/F	1/1	226.4	3.6755	3.7217	34.8359	32.4203	29.3054
Mean:		228.5	3.6783	3.7696	28.6632	22.4504	40.5562
Standard deviation:		17.7	0.6653	0.7232	11.2424	6.3006	9.8753
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2531/F	2/1	244.9	4.8347	4.1023	29.4042	20.8135	42.3199
2532/F	2/1	245.6	3.5917	3.7125	36.9670	25.9032	47.4533
2533/F	2/1	232.2	3.6043	3.0285	27.9536	20.7305	57.1360
2534/F	2/1	219.0	2.5601	3.0445	27.2674	26.4052	64.2538
2535/F	2/1	242.7	2.9076	3.8166	29.7113	27.4441	39.4515
2536/F	2/1	247.5	3.5477	3.8040	35.9347	34.1759	56.9648
2537/F	2/1	213.5	4.0210	4.4291	32.8716	19.2785	63.8160
2538/F	2/1	236.2	5.3748	4.8726	26.3557	27.7929	46.9092
2539/F	2/1	212.8	2.6619	3.7897	27.6657	25.5067	41.5900
2540/F	2/1	250.3	2.6223	3.0158	31.5360	21.6521	29.5287
2541/F	2/1	230.2	3.1914	3.9929	28.2897	17.3535	35.1101
2542/F	2/1	233.4	2.7268	3.0638	29.0587	18.4183	33.6167
Mean:		234.0	3.4704	3.7227	30.2513	23.7895	46.5125
Standard deviation:		13.1	0.9035	0.5980	3.4144	4.9075	11.7309
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3531/F	3/1	230.0	3.9624	2.8260	29.0089	16.2166	43.7220
3532/F	3/1	197.4	4.2564	4.1239	26.5761	31.7268	35.6906
3533/F	3/1	228.8	4.0973	3.5278	28.4545	24.0420	43.5057
3534/F	3/1	219.4	3.2078	2.4231	20.2916	19.5281	43.9502
3535/F	3/1	241.0	3.3555	3.7472	28.6789	21.6381	28.1532
3536/F	3/1	252.4	3.3321	3.7492	27.9509	23.5593	44.7358
3537/F	3/1	234.3	3.4580	4.3694	29.6581	28.8461	76.9762
3538/F	3/1	234.5	3.1300	2.1823	25.0207	15.9854	67.5723
3539/F	3/1	252.8	4.0354	3.0564	27.1345	24.0831	68.1791
3540/F	3/1	223.5	3.1818	2.9318	20.9050	16.7132	32.4803
3541/F	3/1	232.9	3.4510	3.6479	29.3072	27.3227	45.8728
3542/F	3/1	211.8	3.0643	3.2309	23.0956	21.2631	56.4794
Mean:		229.9	3.5443	3.3180	26.3402	22.5770	48.9431

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey

Summary Statistics for % Organ to Brain Weight
Study number: 034244

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Page: 4
Version 4.2.2

Terminal Sacrifice - Main Study

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		15.8	0.4234	0.6630	3.2829	5.0553	15.2180
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4531/F	4/1	226.7	4.2378	5.0945	25.4575	21.6353	48.7352
4532/F	4/1	228.5	3.9327	3.4958	25.6762	23.6683	46.2138
4533/F	4/1	245.1	3.2880	3.8332	27.9121	25.5769	56.8211
4534/F	4/1	237.5	3.3795	2.7365	30.7237	38.7840	65.5831
4535/F	4/1	240.9	3.5745	3.8240	29.5178	27.3486	27.1959
4536/F	4/1	238.8	3.4558	4.3318	24.9973	24.1000	46.0635
4537/F	4/1	206.6	2.9092	2.6424	23.8122	20.3489	36.4597
4538/F	4/1	271.3	5.7178	5.3204	33.5370	27.7745	51.8033
4539/F	4/1	238.0	3.7126	3.0768	25.3525	16.4556	68.8888
4540/F	4/1	210.9	2.6588	2.2726	22.4637	21.9884	34.7725
4541/F	4/1	206.2	4.7729	4.2259	25.7521	17.2896	41.5402
4542/F	4/1	225.1	3.2231	3.8961	21.7151	16.2574	45.8857
M e a n:		231.3	3.7386	3.7292	26.4098	23.4356	47.4969
Standard deviation:		18.5	0.8439	0.9449	3.4466	6.2353	12.1707
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

Data Requirement

EPA OPPTS 870.3650
OECD 422

STUDY NO. 03-4244

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

Final Report

VOLUME II of III

Author: [redacted]

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Attn: [redacted]

Date: 16 April 2010

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	Individual Animal Gross and Microscopic Observations Main Study Preface	Appendix L

Key to Abbreviations

LN	=	Lymph Node
Lymph/Retic	=	Lymphoreticular
M-	=	Malignant
N-	=	Metastatic
Oviducts/Fallop	=	Oviducts/Fallopian Tubes
SC	=	Spinal Cord
Sys	=	System

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Notes:

1. Unless otherwise specified in a histopathology note, the organ/tissue examined was the required (routine) section.

2. The testes and epididymides for Animal Nos. 2032, 3034 and 4032 were not properly labeled at necropsy; therefore, all tissues were examined microscopically and found to be WNL and reported as such.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1031
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1031
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Liver
Tibial Nerve	Prostate	Parathyroid	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Seminal vesicles	Testes	Thyroid	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1032
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Sternum	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1032
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Femur
Cecum	Colon	Duodenum	Epididymides	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Prostate	Parathyroid	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Seminal vesicles
Testes	Thyroid	Trachea	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1033
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Marked. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. - GERMINAL CENTERS ARE NOT EVIDENT.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1033
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		HEMORRHAGE(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Liver
Tibial Nerve	Prostate	Parathyroid	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Seminal vesicles	Testes	Thyroid	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Sternal Marrow	No gross observations on tissue.	Tissue is missing. - POOR SECTION QUALITY. RECUT: NO IMPROVEMENT.
Sternum	No gross observations on tissue.	Tissue is missing. - POOR SECTION QUALITY. RECUT: NO IMPROVEMENT.
Epididymides	No gross observations on tissue.	MONONUCLEAR CELL AGGREGATES, UNILATERAL, Focal, Minimal.
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Focal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. - FEW GERMINAL CENTER DEVELOPMENT EVIDENT.
Lungs	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight	Examined; no correlation found PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - SMALL TISSUE SPECIMEN. RECUT: NO IMPROVEMENT.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thoracic SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Testes	No gross observations on tissue.	GERM CELL DEGENERATION/MULTINUCLEATE CELLS, BILATERAL, Multifocal, Slight.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Focal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Femoral Marrow	Brain	Femur	Cecum
Colon	Duodenum	Heart	Ileum	Jejunum
Liver	Prostate	Rectum/Low Colon	Cervical SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Seminal vesicles	Thyroid
Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Epididymides	No gross observations on tissue.	MONONUCLEAR CELL AGGREGATES, UNILATERAL, Focal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Severe.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments			Microscopic Observations/Comments
Ileum	Jejunum	Kidneys	Tibial Nerve	Rectum/Low Colon
Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol	Spleen
Stomach	Seminal vesicles	Testes	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1036
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1036
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thoracic SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Thymus	Discolored, Bilateral, Red, Foci, 0.2 - 0.5 cm, Slight	Examined; 1 correlation found: HEMORRHAGE, Multifocal, Minimal. LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Prostate
Rectum/Low Colon	Cervical SC	Lumbar SC	Skin-protocol	Spleen

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1036
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Stomach	Seminal vesicles	Testes
Thyroid	Trachea	
Urinary bladder		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1037
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Sternal Marrow	No gross observations on tissue.	Tissue is unremarkable (with comment). - POOR SECTION QUALITY, BUT READABLE.
Sternum	No gross observations on tissue.	Tissue is unremarkable (with comment). - POOR SECTION QUALITY, BUT READABLE.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1037
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Femoral Marrow	Brain	Femur	Cecum
Colon	Duodenum	Epididymides	Heart	Ileum
Jejunum	Kidneys	Tibial Nerve	Prostate	Rectum/Low Colon
Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol	Spleen
Stomach	Seminal vesicles	Testes	Thyroid	Trachea
Urinary bladder				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Adrenal Glands	No gross observations on tissue.	EXTRACAPSULAR CORTICAL EPITHELIAL HYPERPLASIA, UNILATERAL, Focal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Slight.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. ULTIMOBRACHIAL REST(S), Focal, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Sternal Marrow	Femoral Marrow	Brain	Sternum	Femur
Cecum	Colon	Duodenum	Epididymides	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Parathyroid	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Seminal vesicles	Testes
Thyroid	Trachea	Urinary bladder		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1039
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1039
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Focal, Slight.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Liver
Tibial Nerve	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Seminal vesicles	Testes
Thyroid	Trachea	Urinary bladder		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1040
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1040
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, All lobes, Red, Foci, 0.2 - 0.5 cm, Slight	Examined; no correlation found PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1040
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments			Microscopic Observations/Comments
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Prostate	Parathyroid	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Seminal vesicles
Testes	Thyroid	Trachea	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	INTERSTITIAL MONONUCLEAR CELL AGGREGATES, UNILATERAL, Focal, Minimal.
Liver	No gross observations on tissue.	CENTRILOBULAR HEPATOCELLULAR NECROSIS (INDIVIDUAL CELL), Multifocal, Minimal. SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present. FOAMY HISTIOCYTES, Multifocal, Minimal.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Marked.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Minimal. PROMINENT PLASMA CELL POPULATION, Slight. - PLASMA CELLS MOST EVIDENT ON SLIDE #17 WITH THYMIC TISSUE.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal.
Parathyroid	No gross observations on tissue.	Tissue is missing.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thyroid	No gross observations on tissue.	ULTIMOBRANCHIAL REST(S), UNILATERAL, Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Seminal vesicles	Testes	Urinary bladder		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1042
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Multifocal, Minimal. CORTEX/CORTICO-MEDULLARY JUNCTION: TUBULE(S) DILATED, BILATERAL, Focal, Moderate. INTERSTITIAL MONONUCLEAR CELL AGGREGATES, BILATERAL, Focal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 1042
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 1042
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus		EPITHELIUM: HYPERPLASIA, Focal, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Parathyroid	Rectum/Low Colon
Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol	Spleen
Stomach	Seminal vesicles	Testes	Thyroid	Trachea
Urinary bladder				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2031
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2032
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus	Discolored, Bilateral, Red, Foci, 0.2 - 0.5 cm, Moderate	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Epididymides Testes

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2033
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2034
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2035
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2036
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2037
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 2038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, Right apical lobe, Red, Foci, </= 0.1 cm, Slight	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2039
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2040
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2041
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 2042
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3031
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3032
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3033
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3034
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Epididymides Testes

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3035
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3036
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3037
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3038
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3040
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3041
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3042
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 3043
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4031
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Adrenal Glands	No gross observations on tissue.	Tissue is unremarkable (with comment). - ONLY ONE MEDULLA PRESENT
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Focal, Minimal. CORTEX: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, BILATERAL, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4031
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Minimal. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lungs	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight	Examined; no correlation found PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Focal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	HEMORRHAGE, Multifocal, Minimal. LYMPHOID HYPERPLASIA, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4031
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Sternal Marrow	Femoral Marrow	Brain	Sternum	Femur
Cecum	Colon	Duodenum	Epididymides	Ileum
Jejunum	Liver	Tibial Nerve	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Seminal vesicles	Testes	Thyroid	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4032
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELLS, Multifocal, Slight.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4032
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Moderate. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Tibial Nerve

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4032
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments				Microscopic Observations/Comments
Prostate	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	
Skin-protocol	Spleen	Stomach	Seminal vesicles	Testes	
Thyroid	Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice | SEX: Male | ANIMAL: 4033
PHASE DAY OF DEATH: 30 | PHASE: Dosing phase | GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	INTERSTITIAL MONONUCLEAR CELL AGGREGATES, BILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4033
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal. HEMORRHAGE(S), Multifocal, Minimal. INTERSTITIUM: OSSEOUS METAPLASIA, Focal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	Tissue is missing.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Skin-protocol	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, UNILATERAL, Focal, Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4033
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Prostate	Rectum/Low Colon
Cervical SC	Thoracic SC	Lumbar SC	Spleen	Stomach
Seminal vesicles	Testes	Trachea	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Epididymides	No gross observations on tissue.	MONONUCLEAR CELL AGGREGATES, UNILATERAL, Focal, Minimal.
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Multifocal, Minimal. MEDULLA: MINERAL DEPOSIT(S), UNILATERAL, Focal, Minimal. INTERSTITIAL MONONUCLEAR CELL AGGREGATES, UNILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Minimal. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	Tissue is unremarkable (with comment).

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4034
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Prostate		- ARTIFACTUAL CHANGES ARE PRSENT; HOWEVER, TISSUE IS READABLE.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.
Trachea	No gross observations on tissue.	Tissue is unremarkable (with comment). - PARTIAL TISSUE PRESENT.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Tibial Nerve	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Seminal vesicles
Testes	Thyroid	Urinary bladder		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	MEDULLARY TUBULES: EOSINOPHILIC CASTS, UNILATERAL, Multifocal, Minimal. CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Multifocal, Minimal. CORTEX: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, UNILATERAL, Focal, Minimal.
Liver	No gross observations on tissue.	CENTRILOBULAR HEPATOCELLULAR NECROSIS (INDIVIDUAL CELL), Multifocal, Minimal. SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal. HEMORRHAGE(S), Focal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4035
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Prostate	Parathyroid
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Seminal vesicles	Testes	Thyroid
Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4036
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	INTERSTITIAL MONONUCLEAR CELL AGGREGATES, BILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4036
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal. HEMORRHAGE(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, UNILATERAL, Present. FOLLICULAR DILATATION, BILATERAL, Minimal.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Slight.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4036
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Prostate	Rectum/Low Colon
Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol	Spleen
Stomach	Seminal vesicles	Testes	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4037
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Multifocal, Minimal. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4037
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Slight.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Kidneys	Liver
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Seminal vesicles	Testes	Thyroid

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4037
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Trachea	Urinary bladder	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Epididymides	No gross observations on tissue.	SEMINIFEROUS TUBULES: TUBULAR DILATATION, UNILATERAL, Focal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Multifocal, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELLS, Multifocal, Slight.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal. HEMORRHAGE(S), Multifocal, Slight.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, UNILATERAL, Focal, Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4038
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Prostate	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Seminal vesicles	Testes
Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4039
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Femoral Marrow	No gross observations on tissue.	Tissue is missing.
Femur	No gross observations on tissue.	Tissue is missing.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Focal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4039
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		- TISSUE ALSO PRESENT ON SLIDE #17.
Lungs	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight	Examined; no correlation found PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Moderate. INTRALUMINAL CELLULAR/INFLAMMATORY DEBRIS, Multifocal, Moderate. GLANDULAR DILATATION, Focal, Marked.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4039
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Brain	Sternum	Cecum
Colon	Duodenum	Epididymides	Heart	Ileum
Jejunum	Kidneys	Tibial Nerve	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Seminal vesicles	Testes	Thyroid	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4040
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Focal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lungs	Discolored, All lobes, Red, Foci, 0.2 - 0.5 cm, Slight	Examined; no correlation found

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4040
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
		PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Heart	Ileum	Jejunum	Liver	Tibial Nerve
Prostate	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Seminal vesicles	Testes

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Male	ANIMAL: 4040
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thyroid	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. - TISSUE PRESENT ON SLIDE #17, WITH THYMUS.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal. HEMORRHAGE(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Focal, Slight.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4041
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Seminal vesicles	Testes	Thyroid
Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4042
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	CORTEX: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, UNILATERAL, Multifocal, Minimal. INTERSTITIAL MONONUCLEAR CELL AGGREGATES, BILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4042
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		- FINDINGS ALSO OBTAINED FROM SLIDE #17, WITH THYMIC TISSUE.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	MALE TYPE: (UNDIFFRENTIATED TYPE), Present.
Prostate	No gross observations on tissue.	INTERSTITAL MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Skin-protocol	No gross observations on tissue.	SUBCUTANEOUS MUSCLE: SUBACUTE/CHRONIC INFLAMMATORY FOCI WITH DEGENERATION/NECROSIS, Multifocal, Minimal.
Testes	No gross observations on tissue.	GERM CELL DEGENERATION/MULTINUCLEATE CELLS, UNILATERAL, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Male ANIMAL: 4042
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, UNILATERAL, Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Epididymides
Ileum	Jejunum	Tibial Nerve	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Spleen	Stomach	Seminal vesicles
Trachea	Urinary bladder			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1531
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	INTERSTITIAL MONONUCLEAR CELL AGGREGATES, BILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	CONGESTION, Slight. SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1531
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Focal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	Tissue is unremarkable (with comment). - ARTIFACTUAL CELLULAR AND VASCULAR CHANGES ARE PRESENT.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	LYMPHOID CELL AGGREGATE(S), UNILATERAL, Focal, Minimal. FOLLICULAR DILATATION, BILATERAL, Multifocal, Moderate.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1531
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Tibial Nerve	Oviducts/Fallop	Rectum/Low Colon	Cervical SC
Thoracic SC	Lumbar SC	Skin-protocol	Spleen	Stomach
Urinary bladder	Uterus	Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1532
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	INTERSTITIAL MONONUCLEAR CELL AGGREGATES, UNILATERAL, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1532
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	Tissue is missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Moderate.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1532
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Liver	Tibial Nerve	Oviducts/Fallop	Ovaries
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Trachea	Urinary bladder	Vagina

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1533
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1533
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Oviducts/Fallop	Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Thyroid
Trachea	Urinary bladder	Uterus	Vagina	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Adrenal Glands	No gross observations on tissue.	N-METASTATIC/INVASIVE NEOPLASM Metastatic from Lymph/Retic Sys.
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal. N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys.
Kidneys		
	Enlarged, Left, Severe	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys, Bilateral.
	Enlarged, Right, Slight	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys, Bilateral.
	Irregular Shape, Right, Slight	Examined; 2 correlations found: INFARCT, UNILATERAL, Multifocal, Moderate. N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys, Bilateral.
	Discolored, Bilateral, Pale, Moderate	Examined; 2 correlations found: INFARCT, UNILATERAL, Multifocal, Moderate. N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys, Bilateral.
Liver		
	Enlarged, All lobes , Moderate	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Liver		SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Lymph Node,other . . .	Enlarged, Retroperitoneal, Moderate	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys. CORTICAL LYMPHOID DEVELOPMENT, Moderate. PARACORTICAL LYMPHOID DEVELOPMENT, Slight. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. INCREASED HISTIOCYTES, Moderate. LYMPHOID CELL DEPLETION/ATROPHY, Moderate.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Minimal. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	Enlarged, Slight	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys. RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lymph/Retic Sys	No gross observations on tissue.	M-MALIGNANT LYMPHOMA, Incidental.
Lungs	No gross observations on tissue.	PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Slight. N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	N-METASTATIC/INVASIVE NEOPLASM Metastatic from Lymph/Retic Sys.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Spleen	Enlarged, Slight	Examined; 1 correlation found: N-MALIGNANT LYMPHOMA Metastatic from Lymph/Retic Sys.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thyroid	No gross observations on tissue.	Tissue is missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. N-METASTATIC/INVASIVE NEOPLASM Metastatic from Lymph/Retic Sys.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Sternal Marrow	Femoral Marrow	Brain	Sternum	Femur
Cecum	Colon	Duodenum	Ileum	Jejunum
Tibial Nerve	Oviducts/Fallop	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Stomach	Trachea	Urinary bladder
Vagina				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1535
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1535
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Moderate.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Tibial Nerve	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Trachea	Urinary bladder
Vagina				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1536
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Focal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. - TISSUE ALSO PRESENT ON SLIDE #17.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1536
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - SMALL FRAGMENTED TISSUE, BUT READABLE.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thyroid	No gross observations on tissue.	ECTOPIC THYMIC TISSUE, UNILATERAL, Focal, Present. ULTIMOBRANCHIAL REST(S), UNILATERAL, Focal, Present.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Urinary bladder	No gross observations on tissue.	Tissue is missing.
Uterus	No gross observations on tissue.	LUMEN: DILATED, UNILATERAL, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1536
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Oviducts/Fallop	Ovaries
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Trachea	Vagina	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1537
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Adrenal Glands	No gross observations on tissue.	Tissue is unremarkable (with comment). - ONLY ONE MEDULLA PRESENT/EVALUATED. RECUT: NO IMPROVEMENT.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Minimal. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1537
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	ATROPHY WITH EOSINOPHILIC GRANULOMATOUS INFLAMMATORY CELL INFILTRATE, Moderate. - ADJACENT MUSCLE: EOSINOPHILIC GRANULOMATOUS INFLAMMATORY CELL INFILTRATE.
Uterus	No gross observations on tissue.	LUMEN: DILATED, UNILATERAL, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Sternal Marrow	Femoral Marrow	Brain	Sternum	Femur
Cecum	Colon	Duodenum	Heart	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Thyroid	Trachea
Urinary bladder	Vagina			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1538
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	No gross observations on tissue.	MEDULLA: MINERAL DEPOSIT(S), UNILATERAL, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1538
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	SERTOLIFORM CELLS, BILATERAL, Present. MINERAL DEPOSIT(S), UNILATERAL, Focal, Minimal.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Uterus	No gross observations on tissue.	LUMEN: DILATED, UNILATERAL, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Liver	Tibial Nerve	Oviducts/Fallop

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1538
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments		
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Thyroid	Trachea	Urinary bladder
Vagina				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1539
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	No gross observations on tissue.	CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC, UNILATERAL, Focal, Minimal. INTERSTITIAL MONONUCLEAR CELL AGGREGATES, UNILATERAL, Multifocal, Minimal.
Liver	No gross observations on tissue.	CONGESTION, Slight. CENTRILOBULAR HEPATOCELLULAR NECROSIS (INDIVIDUAL CELL), Focal, Minimal. SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1539
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Mesentery/Perito . . .	No gross observations on tissue.	RENAL MESENTERY: MONONUCLEAR CELL AGGREGATES, UNILATERAL, Focal, Slight.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thyroid	No gross observations on tissue.	FOLLICULAR DILATATION, BILATERAL, Multifocal, Slight.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1539
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus		LYMPHOID HYPERPLASIA, Focal, Minimal. CYST(S), Focal, Slight.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Tibial Nerve	Oviducts/Fallop	Ovaries
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Urinary bladder	Uterus	Vagina

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1540
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELLS, Multifocal, Minimal.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1540
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		PROMINENT SINUS HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELL POPULATION, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1540
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Trachea	Urinary bladder
Uterus	Vagina			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1541
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Present.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - SMALL TISSUE SPECIMEN. RECUT: NO IMPROVEMENT.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Skin (other)	Scab, Upper dorsal, Red, 0.2 - 0.5 cm	Examined; 1 correlation found: ACANTHOSIS WITH SUPERIFICIAL ENCRUSTATION, Focal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 1541
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Mediastinal LN
Oviducts/Fallop	Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Thyroid
Trachea	Urinary bladder	Uterus	Vagina	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1542
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Extremity	Hair Thin/Absent, Both forelegs, Severe	Examined; no correlation found HAIR FOLLICLES/SKIN, FOREPAW, RIGHT AND LEFT: ABSENT HAIR SHAFT, Multifocal, Minimal.
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present. PROMINENT PLASMA CELLS, Multifocal, Slight.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1542
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	SERTOLIFORM CELLS, UNILATERAL, Multifocal, Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Focal, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
Adrenal Glands Sternal Marrow Femoral Marrow Brain Sternum

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 1542
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 1

Tissue	Gross Observations/Comments			Microscopic Observations/Comments
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Thyroid	Urinary bladder	Uterus
Vagina				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2531
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2532
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2533
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2534
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2535
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2536
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2537
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2538
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		No micropathology observations on tissue.
	Discolored, Left lobe(s)	
	Discolored, Accessory lobe, 0.2 - 0.5 cm	

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2539
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2540
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2541
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 2542
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 2

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3531
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3532
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3533
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3534
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3535
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3536
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3537
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3538
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3539
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	Discolored, Left lobe(s), Red, Foci, </= 0.1 cm, Slight	No micropathology observations on tissue.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3540
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3541
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 3542
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 3

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:
No tissues examined.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4531
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4531
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Tibial Nerve	No gross observations on tissue.	Tissue is unremarkable (with comment). - SMALL TISSUE SPECIMEN.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	Tissue is unremarkable (with comment); one-of-pair missing. - SMALL TISSUE SPECIMEN.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Slight.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4531
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Skin-protocol	Spleen	Stomach
Trachea	Urinary bladder	
Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4532
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4532
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thoracic SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Oviducts/Fallop	Ovaries	Rectum/Low Colon	Cervical SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Thyroid	Trachea
Urinary bladder	Uterus	Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4533
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4533
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	SERTOLIFORM CELLS, UNILATERAL, Focal, Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Trachea	No gross observations on tissue.	MUCOSA: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Focal, Slight.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Moderate.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4533
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments				Microscopic Observations/Comments
	Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
	Oviducts/Fallop	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
	Skin-protocol	Spleen	Stomach	Urinary bladder	Vagina

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	No gross observations on tissue.	MEDULLA: MINERAL DEPOSIT(S), UNILATERAL, Focal, Minimal.
Liver	No gross observations on tissue.	SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Focal, Slight.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Slight. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice | SEX: Female | ANIMAL: 4534
PHASE DAY OF DEATH: 30 | PHASE: Dosing phase | GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Cervical SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Thoracic SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Lumbar SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Uterus	Distended, Bilateral horns, Slight	Examined; 1 correlation found: LUMEN: DILATED, BILATERAL, Moderate.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4534
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Tibial Nerve	Oviducts/Fallop	Ovaries
Rectum/Low Colon	Skin-protocol	Spleen	Stomach	Thyroid
Trachea	Urinary bladder	Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4535
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Liver	No gross observations on tissue.	CONGESTION, Slight. SUBACUTE/CHRONIC INFLAMMATORY CELL FOCI, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Multifocal, Minimal. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4535
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable (with comment); one-of-pair missing. - ONE PRESENT
Skin-protocol	No gross observations on tissue.	SUBCUTANEOUS MUSCLE: SUBACUTE/CHRONIC INFLAMMATORY FOCI WITH DEGENERATION/NECROSIS, Focal, Slight.
Thyroid	No gross observations on tissue.	ULTIMOBRANCHIAL REST(S), UNILATERAL, Multifocal, Present. FOLLICULAR DILATATION, UNILATERAL, Slight.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4535
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus		HEMORRHAGE, Multifocal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Kidneys	Tibial Nerve	Oviducts/Fallop	Ovaries
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Spleen
Stomach	Trachea	Urinary bladder	Uterus	Vagina

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4536
PHASE DAY OF DEATH: 30	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Slight.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thyroid	No gross observations on tissue.	ULTIMOBRANCHIAL REST(S), UNILATERAL, Focal, Present.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4536
PHASE DAY OF DEATH: 30 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.
Urinary bladder	No gross observations on tissue.	Tissue is missing.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Moderate.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Oviducts/Fallop	Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Skin-protocol	Spleen	Stomach	Trachea
Vagina				

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4537
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Slight. - GERMINAL CENTER DEVELOPMENT NOT APPARENT.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4537
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is missing.
Thoracic SC	No gross observations on tissue.	Tissue is unremarkable (with comment). - POOR SECTION QUALITY. RECUT: NO IMPROVEMENT.
Thyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Kidneys	Liver	Tibial Nerve
Oviducts/Fallop	Ovaries	Rectum/Low Colon	Cervical SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Trachea	Urinary bladder

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4537
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Uterus	Vagina	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4538
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Adrenal Glands	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4538
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mammary-protocol	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Ovaries	No gross observations on tissue.	Tissue is unremarkable (with comment). - TISSUE FRAGMENTED, BUT READABLE.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOID HYPERPLASIA, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Sternal Marrow	Femoral Marrow	Brain	Sternum	Femur
Cecum	Colon	Duodenum	Heart	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC	Skin-protocol
Spleen	Stomach	Thyroid	Trachea	Urinary bladder
Uterus	Vagina			

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4539
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Kidneys	No gross observations on tissue.	MEDULLA: MINERAL DEPOSIT(S), UNILATERAL, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Multifocal, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. PERIALVEOLAR/PERIVASCULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE, Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4539
PHASE DAY OF DEATH: 31 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Skin-protocol	Hair Thin/Absent, Inguinal, Right, Moderate	Examined; 1 correlation found: HAIR FOLLICLES: EMPTY/WITHOUT HAIR SHAFT, Multifocal, Slight.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Multifocal, Minimal.
Uterus	No gross observations on tissue.	LUMEN: DILATED, BILATERAL, Moderate.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Heart
Ileum	Jejunum	Liver	Tibial Nerve	Oviducts/Fallop
Ovaries	Parathyroid	Rectum/Low Colon	Cervical SC	Thoracic SC
Lumbar SC	Spleen	Stomach	Thyroid	Trachea

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4539
PHASE DAY OF DEATH: 31	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Urinary bladder	Vagina	

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4540
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Moderate. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Marked. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Slight. ALVEOLAR ACUTE INFLAMMATORY CELL INFILTRATE, Focal, Slight.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4540
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Thyroid	Trachea
Urinary bladder	Uterus	Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4541
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Sternal Marrow	No gross observations on tissue.	Tissue is unremarkable (with comment). - POOR SECTION QUALITY. RECUT: NO IMPROVEMENT.
Sternum	No gross observations on tissue.	Tissue is unremarkable (with comment). - POOR SECTION QUALITY. RECUT: NO IMPROVEMENT.
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Kidneys	No gross observations on tissue.	MEDULLA: MINERAL DEPOSIT(S), BILATERAL, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Slight. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4541
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Mediastinal LN		RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Slight. RETICULOENDOTHELIAL CELLS: BROWN PIGMENT, Slight. PROMINENT SINUS HISTIOCYTES, Multifocal, Present.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Cervical SC	No gross observations on tissue.	Tissue is missing.
Thoracic SC	No gross observations on tissue.	Tissue is missing.
Lumbar SC	No gross observations on tissue.	Tissue is missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice	SEX: Female	ANIMAL: 4541
PHASE DAY OF DEATH: 32	PHASE: Dosing phase	GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Femoral Marrow	Brain	Femur	Cecum
Colon	Duodenum	Ileum	Jejunum	Liver
Tibial Nerve	Oviducts/Fallop	Ovaries	Parathyroid	Rectum/Low Colon
Skin-protocol	Spleen	Stomach	Thyroid	Trachea
Urinary bladder	Uterus	Vagina		

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4542
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Heart	No gross observations on tissue.	MYOCARDIUM: SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION, Multifocal, Minimal.
Mesenteric LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/T-LYMPHOCYTE AREA, Moderate. FOLLICULAR GERMINAL CENTER DEVELOPMENT, Present. PROMINENT SINUS/PARACORTICAL HISTIOCYTES, Multifocal, Present.
Mediastinal LN	No gross observations on tissue.	RELATIVE CORTICAL LYMPHOID CELLULARITY/B-LYMPHOCYTE AREA, Minimal. RELATIVE PARACORTICAL LYMPHOID CELLULARITY/ T-LYMPHOCYTE AREA, Moderate. FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS, Multifocal, Minimal.
Lungs	No gross observations on tissue.	PERIBRONCHIOLAR/PERIVASCULAR MONONUCLEAR CELL AGGREGATES, Multifocal, Minimal. ALVEOLAR/INTRAALVEOLAR MACROPHAGES, Multifocal, Minimal. VESSEL(S): MINERAL DEPOSIT(S), Multifocal, Minimal.

Isobutane: Combined Repeated-Exposure Toxicity, Reproduction
and Neurotoxicity Screening in Rats
via Whole-Body Inhalation Exposures
Individual Animal Gross and Microscopic Observations

STATUS: Final phase sacrifice SEX: Female ANIMAL: 4542
PHASE DAY OF DEATH: 32 PHASE: Dosing phase GROUP: 4

Tissue	Gross Observations/Comments	Microscopic Observations/Comments
Lungs		INTERSTITIUM: OSSEOUS METAPLASIA, Multifocal, Minimal.
Mammary-protocol . . .	No gross observations on tissue.	FEMALE TYPE (DIFFERENTIATED TYPE), Present.
Parathyroid	No gross observations on tissue.	Tissue is unremarkable; one-of-pair missing.
Thymus	No gross observations on tissue.	LYMPHOCYTOLYSIS/INVOLUTION, Minimal. HEMORRHAGE, Focal, Minimal.

Tissues without comment under Gross Observations were within normal limits at necropsy.
The following tissues were unremarkable microscopically:

Adrenal Glands	Sternal Marrow	Femoral Marrow	Brain	Sternum
Femur	Cecum	Colon	Duodenum	Ileum
Jejunum	Kidneys	Liver	Tibial Nerve	Oviducts/Fallop
Ovaries	Rectum/Low Colon	Cervical SC	Thoracic SC	Lumbar SC
Skin-protocol	Spleen	Stomach	Thyroid	Trachea
Urinary bladder	Uterus	Vagina		

APPENDIX M

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
1543	TERMINAL SACRIFICE	24-JAN-04	40	P
1544	TERMINAL SACRIFICE	27-JAN-04	43	P
1545	TERMINAL SACRIFICE	26-JAN-04	42	P
1546	TERMINAL SACRIFICE	27-JAN-04	43	P
1547	TERMINAL SACRIFICE	26-JAN-04	42	P
1548	TERMINAL SACRIFICE	29-JAN-04	45	P
1549	TERMINAL SACRIFICE	26-JAN-04	42	P
1550	TERMINAL SACRIFICE	29-JAN-04	45	P
1551	TERMINAL SACRIFICE	25-JAN-04	41	P
1552	TERMINAL SACRIFICE	26-JAN-04	42	P
1553	TERMINAL SACRIFICE	27-JAN-04	43	P
1554	TERMINAL SACRIFICE	29-JAN-04	45	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX M

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
2543	TERMINAL SACRIFICE	26-JAN-04	42	P
2544	TERMINAL SACRIFICE	25-JAN-04	41	P
2545	TERMINAL SACRIFICE	30-JAN-04	46	P
2546	TERMINAL SACRIFICE	29-JAN-04	45	P
2547	TERMINAL SACRIFICE	25-JAN-04	41	NP
2548	TERMINAL SACRIFICE	25-JAN-04	41	P
2549	TERMINAL SACRIFICE	29-JAN-04	45	P
2550	TERMINAL SACRIFICE	25-JAN-04	41	P
2551	TERMINAL SACRIFICE	25-JAN-04	41	P
2552	TERMINAL SACRIFICE	25-JAN-04	41	P
2553	TERMINAL SACRIFICE	27-JAN-04	43	P
2554	TERMINAL SACRIFICE	25-JAN-04	41	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX M

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 3000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
3543	TERMINAL SACRIFICE	27-JAN-04	43	P
3544	TERMINAL SACRIFICE	6-FEB-04	53	P
3545	TERMINAL SACRIFICE	24-JAN-04	40	P
3546	TERMINAL SACRIFICE	27-JAN-04	43	P
3547	TERMINAL SACRIFICE	27-JAN-04	43	P
3548	TERMINAL SACRIFICE	29-JAN-04	45	P
3549	TERMINAL SACRIFICE	25-JAN-04	41	P
3550	TERMINAL SACRIFICE	27-JAN-04	43	P
3551	TERMINAL SACRIFICE	29-JAN-04	45	NP
3552	TERMINAL SACRIFICE	29-JAN-04	45	P
3553	TERMINAL SACRIFICE	29-JAN-04	45	P
3554	TERMINAL SACRIFICE	29-JAN-04	45	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX M

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
4543	TERMINAL SACRIFICE	24-JAN-04	40	P
4544	TERMINAL SACRIFICE	27-JAN-04	43	P
4545	TERMINAL SACRIFICE	25-JAN-04	41	NP
4546	TERMINAL SACRIFICE	27-JAN-04	43	P
4547	TERMINAL SACRIFICE	29-JAN-04	45	P
4548	TERMINAL SACRIFICE	29-JAN-04	45	P
4549	TERMINAL SACRIFICE	25-JAN-04	41	P
4550	TERMINAL SACRIFICE	27-JAN-04	43	NP
4551	TERMINAL SACRIFICE	30-JAN-04	46	P
4552	TERMINAL SACRIFICE	27-JAN-04	43	P
4553	TERMINAL SACRIFICE	27-JAN-04	43	NP
4554	TERMINAL SACRIFICE	25-JAN-04	41	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX N

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	1 2
1543	WITHIN NORMAL LIMITS	P	P	P		
1544	WITHIN NORMAL LIMITS	P	P	P	P	
1545	WITHIN NORMAL LIMITS	P	P	P	P	
1546	WITHIN NORMAL LIMITS	P	P	P	P	
1547	WITHIN NORMAL LIMITS	P	P	P	P	
1548	WITHIN NORMAL LIMITS	P	P	P	P	
1549	WITHIN NORMAL LIMITS	P	P	P	P	
1550	WITHIN NORMAL LIMITS	P	P	P	P	
1551	WITHIN NORMAL LIMITS	P	P	P	P	
1552	WITHIN NORMAL LIMITS	P	P	P	P	
1553	WITHIN NORMAL LIMITS	P	P	P	P	
1554	WITHIN NORMAL LIMITS	P	P	P	P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX N

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	1 2
2543	WITHIN NORMAL LIMITS	P	P	P	P	
2544	WITHIN NORMAL LIMITS	P	P	P	P	
2545	WITHIN NORMAL LIMITS	P	P	P	P	
2546	WITHIN NORMAL LIMITS	P	P	P	P	
2547	WITHIN NORMAL LIMITS	P	P	P		
2548	WITHIN NORMAL LIMITS	P	P	P		
2549	WITHIN NORMAL LIMITS	P	P	P	P	
2550	WITHIN NORMAL LIMITS	P	P	P		
2551	WITHIN NORMAL LIMITS	P	P	P		
2552	WITHIN NORMAL LIMITS	P	P	P		
2553	WITHIN NORMAL LIMITS	P	P			
	ALOPECIA - EXTREMITIES/SNOUT					2 2
2554	WITHIN NORMAL LIMITS	P	P	P		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX N

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	5	1 2
3543	WITHIN NORMAL LIMITS	P	P	P	P	
3544	WITHIN NORMAL LIMITS	P	P	P	P	P
3545	WITHIN NORMAL LIMITS	P	P	P		
3546	WITHIN NORMAL LIMITS	P	P	P	P	
3547	WITHIN NORMAL LIMITS	P	P	P	P	
3548	WITHIN NORMAL LIMITS	P	P	P	P	
3549	WITHIN NORMAL LIMITS	P	P	P		
3550	WITHIN NORMAL LIMITS	P	P	P	P	
3551	WITHIN NORMAL LIMITS	P	P	P	P	
3552	WITHIN NORMAL LIMITS	P	P	P	P	
3553	WITHIN NORMAL LIMITS	P	P	P	P	
3554	WITHIN NORMAL LIMITS	P	P	P	P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX N

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	8	1 5	2
4543	WITHIN NORMAL LIMITS	P	P	P		
4544	WITHIN NORMAL LIMITS	P	P	P	P	
4545	WITHIN NORMAL LIMITS	P	P	P		
4546	WITHIN NORMAL LIMITS	P	P	P	P	
4547	WITHIN NORMAL LIMITS	P	P	P	P	
4548	WITHIN NORMAL LIMITS	P	P	P	P	
4549	WITHIN NORMAL LIMITS	P	P	P	P	
4550	WITHIN NORMAL LIMITS	P	P	P	P	
4551	WITHIN NORMAL LIMITS	P	P	P	P	
4552	WITHIN NORMAL LIMITS	P	P	P	P	
4553	WITHIN NORMAL LIMITS	P	P	P	P	
4554	WITHIN NORMAL LIMITS	P	P	P	P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX O

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1543	WITHIN NORMAL LIMITS		P							P						P						P	
1544	WITHIN NORMAL LIMITS		P							P						P						P	
1545	WITHIN NORMAL LIMITS		P							P						P						P	
1546	ALOPECIA - EXTREMITIES/SNOUT									3						3						3	
	WITHIN NORMAL LIMITS		P																				
1547	WITHIN NORMAL LIMITS		P							P						P						P	
1548	WITHIN NORMAL LIMITS		P							P						P						P	
1549	WITHIN NORMAL LIMITS		P							P						P						P	
1550	WITHIN NORMAL LIMITS		P							P						P						P	
1551	WITHIN NORMAL LIMITS		P							P						P						P	
1552	WITHIN NORMAL LIMITS		P							P						P						P	
1553	WITHIN NORMAL LIMITS		P							P						P						P	
1554	WITHIN NORMAL LIMITS		P							P						P						P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX O

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0 1 2 3 4 5 6 7 8 9	1 0 1 2 3 4 5 6 7 8 9	2 0
2543	WITHIN NORMAL LIMITS	P	P	P
2544	WITHIN NORMAL LIMITS	P	P	P
2545	WITHIN NORMAL LIMITS	P	P	P
2546	ALOPECIA - EXTREMITIES/SNOUT			3
	WITHIN NORMAL LIMITS	P	P	
2547	CHROMODACRYORRHEA - UNILATERAL			P
	INCISORS MALOCCLUDED			P
	WITHIN NORMAL LIMITS	P	P	
2548	WITHIN NORMAL LIMITS	P	P	P
2549	WITHIN NORMAL LIMITS	P	P	P
2550	WITHIN NORMAL LIMITS	P	P	P
2551	WITHIN NORMAL LIMITS	P	P	P
2552	WITHIN NORMAL LIMITS	P	P	P
2553	ALOPECIA - EXTREMITIES/SNOUT	2	2	2
2554	WITHIN NORMAL LIMITS	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX O

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0 1 2 3 4 5 6 7 8 9	1 0 1 2 3 4 5 6 7 8 9	2 0
3543	WITHIN NORMAL LIMITS	P	P P	P
3544	WITHIN NORMAL LIMITS	P	P P	P
3545	WITHIN NORMAL LIMITS	P	P P	P
3546	WITHIN NORMAL LIMITS	P	P P	P
3547	WITHIN NORMAL LIMITS	P	P P	P
3548	WITHIN NORMAL LIMITS	P	P P	P
3549	WITHIN NORMAL LIMITS	P	P P	P
3550	WITHIN NORMAL LIMITS	P	P P	P
3551	WITHIN NORMAL LIMITS	P	P P	P
3552	WITHIN NORMAL LIMITS	P	P P	P
3553	ALOPECIA - EXTREMITIES/SNOUT WITHIN NORMAL LIMITS	P	P P	2
3554	WITHIN NORMAL LIMITS	P	P P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX O

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0 1 2 3 4 5 6 7 8 9	1 0 1 2 3 4 5 6 7 8 9	2 0
4543	WITHIN NORMAL LIMITS	P	P	P
4544	WITHIN NORMAL LIMITS	P	P	P
4545	WITHIN NORMAL LIMITS	P	P	P
4546	WITHIN NORMAL LIMITS	P	P	P
4547	WITHIN NORMAL LIMITS	P	P	P
4548	WITHIN NORMAL LIMITS	P	P	P
4549	WITHIN NORMAL LIMITS	P	P	P
4550	WITHIN NORMAL LIMITS	P	P	P
4551	ALOPECIA - EXTREMITIES/SNOUT			2
	WITHIN NORMAL LIMITS	P	P	
4552	WITHIN NORMAL LIMITS	P	P	P
4553	WITHIN NORMAL LIMITS	P	P	P
4554	WITHIN NORMAL LIMITS	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
1543	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1544	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1545	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1546	TERMINAL SACRIFICE						P	
	ALOPECIA - EXTREMITIES/SNOUT		3	3			3	
1547	TERMINAL SACRIFICE						P	
	ALOPECIA - EXTREMITIES/SNOUT		3	2			3	
1548	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE							P
1549	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1550	WITHIN NORMAL LIMITS		P	P				
	TERMINAL SACRIFICE							P
	ALOPECIA - GENERAL						2	
1551	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1552	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
1553	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
1554	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE							P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5
2543	WITHIN NORMAL LIMITS		P			P	
	TERMINAL SACRIFICE					P	
2544	WITHIN NORMAL LIMITS		P			P	
	TERMINAL SACRIFICE					P	
2545	WITHIN NORMAL LIMITS	P	P			P	
	TERMINAL SACRIFICE					P	
2546	TERMINAL SACRIFICE						P
	ALOPECIA - EXTREMITIES/SNOUT	3	3			3	
2548	WITHIN NORMAL LIMITS	P	P			P	
	TERMINAL SACRIFICE					P	
2549	WITHIN NORMAL LIMITS	P	P			P	
	TERMINAL SACRIFICE						P
2550	WITHIN NORMAL LIMITS	P	P			P	
	TERMINAL SACRIFICE					P	
2551	WITHIN NORMAL LIMITS	P	P			P	
	TERMINAL SACRIFICE					P	
2552	WITHIN NORMAL LIMITS	P	P				
	TERMINAL SACRIFICE					P	
	ALOPECIA - GENERAL					2	
2553	TERMINAL SACRIFICE					P	
	ALOPECIA - EXTREMITIES/SNOUT			3		3	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
2554	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
3543	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3544	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3545	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3546	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3547	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3548	WITHIN NORMAL LIMITS			P			P	
	TERMINAL SACRIFICE						P	
3549	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3550	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
3552	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE							P
3553	TERMINAL SACRIFICE							P
	ALOPECIA - EXTREMITIES/SNOUT		2	2			3	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
3554	TERMINAL SACRIFICE							P
	ALOPECIA - EXTREMITIES/SNOUT		2	2			2	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX P

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5
4543	WITHIN NORMAL LIMITS			P			P	
	TERMINAL SACRIFICE						P	
4544	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
4546	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
4547	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE							P
4548	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE							P
4549	WITHIN NORMAL LIMITS			P			P	
	TERMINAL SACRIFICE						P	
4551	TERMINAL SACRIFICE						P	
	ALOPECIA - EXTREMITIES/SNOUT		2	2			3	
4552	WITHIN NORMAL LIMITS		P	P			P	
	TERMINAL SACRIFICE						P	
4554	WITHIN NORMAL LIMITS			P			P	
	TERMINAL SACRIFICE						P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX Q

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY								
ANIMAL#	-7	0	4	7	11	14	18	21	25
1543	162	192	206	215	225	241			
1544	162	187	199	206	215	219			
1545	176	189	196	212	221	231			
1546	178	206	214	223	232	241			
1547	165	194	201	210	221	229			
1548	170	194	205	215	219	222			
1549	165	182	196	207	219	227			
1550	169	189	202	213	223	219			
1551	173	192	201	215	223	227			
1552	157	171	173	171	185	198			
1553	178	194	196	205	214	222			
1554	171	204	211	224	230	230			
MEAN	169	191	200	210	219	225			
S.D.	6.7	9.4	10.3	13.4	11.8	11.4			
N	12	12	12	12	12	12			

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APPENDIX Q

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY								
ANIMAL#	-7	0	4	7	11	14	18	21	25
2543	157	186	195	193	214	225			
2544	164	194	197	202	202	219			
2545	168	182	196	209	224	235	237		
2546	165	197	198	204	213	217			
2547	172	197	204	202	209	205			
2548	171	195	205	205	217	229			
2549	160	179	188	197	208	209			
2550	165	186	191	200	199	210			
2551	178	203	215	225	233	239			
2552	178	208	212	216	221	240			
2553	171	199	207	213	221	217			
2554	174	198	209	213	218	234			
MEAN	168	194	202	207	215	223	237		
S.D.	6.6	8.7	8.4	9.0	9.6	12.1	0.0		
N	12	12	12	12	12	12	1		

Huntingdon Life Sciences 03-4244S
SATELLITE STUDY

APPENDIX Q

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY								
ANIMAL#	-7	0	4	7	11	14	18	21	25
3543	177	194	201	215	226	235			
3544	174	196	202	209	217	234	252	269	288
3545	172	191	203	202	209	221			
3546	160	194	204	210	214	218			
3547	166	198	206	213	219	228			
3548	171	197	200	217	233	229	235		
3549	178	203	211	216	229	245			
3550	164	197	209	221	224	233			
3551	168	196	204	216	226	227			
3552	170	197	200	217	230	228			
3553	152	173	181	186	191	189			
3554	164	193	204	215	222	223			
MEAN	168	194	202	212	220	226	244	269	288
S.D.	7.5	7.4	7.4	9.4	11.5	13.6	12.5	0.0	0.0
N	12	12	12	12	12	12	2	1	1

APPENDIX Q

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY								
ANIMAL#	-7	0	4	7	11	14	18	21	25
4543	176	216	227	239	251	261			
4544	165	185	192	205	211	215			
4545	167	191	203	211	221	226			
4546	170	194	202	211	221	221			
4547	173	193	216	235	245	245			
4548	171	204	211	216	229	228			
4549	157	178	178	188	195	204			
4550	161	182	190	196	205	208			
4551	163	186	193	209	221	226	234		
4552	177	210	220	229	238	257			
4553	182	214	227	235	249	252			
4554	168	196	212	218	220	233			
MEAN	169	196	206	216	225	231	234		
S.D.	7.4	12.7	15.6	16.1	17.6	18.8	0.0		
N	12	12	12	12	12	12	1		

APPENDIX R

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY								
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	0-14
1543	30	14	10	10	17				50
1544	25	12	8	9	3				32
1545	13	8	16	9	10				42
1546	29	8	9	9	9				34
1547	29	7	9	11	8				34
1548	24	11	9	5	3				28
1549	17	15	11	12	8				45
1550	20	12	12	10	-5				29
1551	19	8	15	7	5				35
1552	14	2	-2	14	12				27
1553	17	2	9	9	8				27
1554	33	7	12	6	0				25
MEAN	22	9	10	9	6				34
S.D.	6.8	4.2	4.4	2.5	5.6				7.8
N	12	12	12	12	12				12

APPENDIX R

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY								
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	0-14
2543	30	9	-3	22	11				39
2544	30	3	5	1	17				25
2545	14	14	13	15	11	3			52
2546	32	2	6	9	4				20
2547	25	7	-2	7	-4				8
2548	24	10	0	12	12				34
2549	19	9	9	10	2				30
2550	21	5	9	-1	11				24
2551	25	12	10	8	6				36
2552	30	4	4	5	19				32
2553	29	7	6	8	-4				17
2554	24	11	4	5	16				36
MEAN	25	8	5	8	8	3			29
S.D.	5.3	3.8	4.9	6.1	7.7	0.0			11.5
N	12	12	12	12	12	1			12

APPENDIX R

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY								
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	0-14
3543	18	7	14	12	9				41
3544	21	7	7	8	17	18	17	18	38
3545	20	12	-1	6	12				30
3546	34	10	6	4	4				24
3547	32	8	7	5	10				30
3548	26	3	17	15	-4	6			32
3549	25	9	5	12	16				42
3550	33	12	13	3	9				36
3551	28	8	13	10	1				31
3552	28	2	18	13	-2				31
3553	21	9	5	5	-2				16
3554	29	11	12	6	2				30
MEAN	26	8	9	8	6	12	17	18	32
S.D.	5.3	3.1	5.6	4.0	7.1	8.6	0.0	0.0	7.1
N	12	12	12	12	12	2	1	1	12

APPENDIX R

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY								
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	0-14
4543	40	11	12	13	9				45
4544	20	7	13	7	3				30
4545	24	12	9	10	5				35
4546	24	8	9	10	0				27
4547	20	23	19	9	1				52
4548	33	7	5	13	-1				24
4549	21	0	9	7	10				26
4550	22	8	6	9	4				26
4551	24	6	17	12	5	9			39
4552	33	9	9	9	19				47
4553	32	13	8	13	3				37
4554	28	15	6	3	13				37
MEAN	27	10	10	10	6	9			35
S.D.	6.4	5.7	4.3	3.1	6.0	0.0			9.2
N	12	12	12	12	12	1			12

APPENDIX S

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
1543	245	284	332	411
1544	220	257	291	349
1545	233	268	308	388
1546	248	289	331	399
1547	236	267	300	381
1548	231	269	310	368
1549	229	262	300	351
1550	239	275	308	382
1551	232	271	300	363
1552	201	248	284	338
1553	224	255	293	348
1554	243	277	317	387
MEAN	232	269	306	372
S.D.	12.9	11.9	14.8	22.8
N	12	12	12	12

APPENDIX S

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
2543	228	266	302	376
2544	217	243	270	329
2545	236	269	309	381
2546	229	260	293	345
2547x NP	200	238	247	238
2548	230	257	291	349
2549	223	249	277	353
2550	207	245	276	348
2551	237	270	312	374
2552	231	274	308	359
2553	219	256	291	362
2554	233	273	306	321
MEAN	226	260	294	354
S.D.	9.1	11.2	14.8	19.0
N	11	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX S

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

		DAY OF GESTATION			
ANIMAL#		0	7	14	20
3543		231	269	300	356
3544		275	303	342	415
3545		223	263	304	372
3546		218	250	276	352
3547		231	269	292	373
3548		241	283	311	366
3549		243	280	311	374
3550		241	284	319	401
3551x	NP	238	248	270	283
3552		241	280	312	372
3553		208	237	265	338
3554		234	268	301	362
MEAN		235	271	303	371
S.D.		17.2	17.7	20.6	21.6
N		11	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX S

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
4543	264	293	336	417
4544	214	252	289	360
4545x NP	224	245	250	243
4546	222	247	274	333
4547	263	319	360	428
4548	237	275	308	379
4549	208	236	272	343
4550x NP	207	240	241	246
4551	237	266	297	370
4552	245	287	316	386
4553x NP	250	272	287	296
4554	229	273	307	364
MEAN	236	272	306	376
S.D.	19.8	25.6	28.5	31.5
N	9	9	9	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX T

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
1543	38	48	79	166
1544	37	34	58	129
1545	35	40	80	155
1546	41	42	68	151
1547	31	33	81	145
1548	39	41	58	138
1549	33	38	51	122
1550	37	33	74	144
1551	40	29	63	131
1552	48	36	54	137
1553	31	38	55	125
1554	33	40	70	143
MEAN	37	38	66	140
S.D.	4.6	5.1	10.9	12.8
N	12	12	12	12

APPENDIX T

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 900 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
2543	37	36	74	147
2544	26	27	59	111
2545	33	40	73	146
2546	31	33	51	116
2547x NP	38	9	-9	38
2548	27	34	58	119
2549	26	28	76	130
2550	37	32	71	140
2551	33	42	62	137
2552	42	34	51	128
2553	37	35	71	143
2554	40	33	15	88
MEAN	34	34	60	128
S.D.	5.8	4.5	17.5	18.0
N	11	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX T

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 3000 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
3543	37	31	56	124
3544	28	39	73	140
3545	40	41	68	148
3546	32	26	76	134
3547	38	24	80	142
3548	42	28	55	125
3549	37	31	63	132
3550	43	35	82	160
3551x NP	10	22	13	45
3552	39	32	60	131
3553	30	28	73	130
3554	34	33	60	128
MEAN	36	32	68	136
S.D.	4.9	5.3	9.6	10.8
N	11	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX T

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 9000 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
4543	29	43	82	153
4544	37	37	71	146
4545x NP	21	5	-7	19
4546	25	27	59	111
4547	56	41	68	165
4548	38	34	71	142
4549	28	36	71	135
4550x NP	33	1	5	39
4551	29	31	73	133
4552	41	29	71	141
4553x NP	21	16	9	45
4554	43	35	57	135
MEAN	36	35	69	140
S.D.	9.8	5.3	7.4	14.9
N	9	9	9	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX U

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

	DAY OF LACTATION	
Animal No.	1	4
1543	301	311
1544	267	268
1545	279	292
1546	300	316
1547	269	288
1548	290	314
1549	277	288
1550	293	295
1551	270	277
1552	261	272
1553	272	286
1554	283	303
MEAN	280	292
S.D.	13.3	16.0
N	12	12

APPENDIX U

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

	DAY OF LACTATION	
Animal No.	1	4
2543	262	286
2544	237	252
2545	283	294
2546	266	272
2547x NP		
2548	258	274
2549	256	277
2550	257	265
2551	284	304
2552	278	301
2553	265	283
2554	287	300
MEAN	267	282
S.D.	15.1	16.5
N	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX U

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

	DAY OF LACTATION	
Animal No.	1	4
3543	251	294
3544	290	305
3545	266	281
3546	248	247
3547	266	260
3548	300	301
3549	298	313
3550	307	315
3551x NP		
3552	290	307
3553	246	264
3554	279	299
MEAN	276	290
S.D.	22.2	23.3
N	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX U

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM

	DAY OF LACTATION	
Animal No.	1	4
4543	313	330
4544	269	253
4545x NP		
4546	242	251
4547	345	353
4548	292	307
4549	235	249
4550x NP		
4551	270	284
4552	291	304
4553x NP		
4554	276	281
MEAN	281	290
S.D.	33.9	36.6
N	9	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX V

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

	DAY OF LACTATION
FEMALE#	1 - 4
1543	10
1544	1
1545	13
1546	16
1547	19
1548	24
1549	11
1550	2
1551	7
1552	11
1553	14
1554	20
MEAN	12
S.D.	6.9
N	12

APPENDIX V

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 900 PPM

FEMALE#	DAY OF LACTATION 1 - 4
2543	24
2544	15
2545	11
2546	6
2547x NP	
2548	16
2549	21
2550	8
2551	20
2552	24
2553	18
2554	13
MEAN	16
S.D.	5.9
N	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX V

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 3000 PPM

FEMALE#	DAY OF LACTATION 1 - 4
3543	42
3544	14
3545	15
3546	-1
3547	-6
3548	0
3549	16
3550	8
3551x NP	
3552	18
3553	18
3554	20
MEAN	13
S.D.	13.1
N	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX V

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 9000 PPM

FEMALE#	DAY OF LACTATION 1 - 4
4543	17
4544	-16
4545x	NP
4546	9
4547	8
4548	15
4549	14
4550x	NP
4551	13
4552	13
4553x	NP
4554	5
MEAN	9
S.D.	9.8
N	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX W

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
1543	98	90	84
1544	98	81	75
1545	98	91	86
1546	97	76	75
1547	98	84	83
1548	93	84	83
1549	97	87	85
1550	90	85	78
1551	97	89	78
1552	93	82	86
1553	100	81	86
1554	92	81	78
MEAN	96	84	81
S.D.	3.1	4.4	4.1
N	12	12	12

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APPENDIX W

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 2 900 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
2543	105	84	88
2544	104	81	75
2545	SF	90	81
2546	100	79	80
2547	97	86	80
2548	87	84	78
2549	SF	83	SF
2550	99	86	86
2551	100	90	81
2552	98	83	83
2553	95	89	76
2554	97	88	83
MEAN	98	85	81
S.D.	5.2	3.6	4.0
N	10	12	11

SF=Spilled Feeder

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SATELLITE STUDY

APPENDIX W

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
3543	96	81	82
3544	92	84	85
3545	95	86	87
3546	97	83	76
3547	105	88	79
3548	104	95	88
3549	96	86	88
3550	106	86	81
3551	95	89	84
3552	101	86	SF
3553	SF	83	86
3554	SF	92	85
MEAN	99	87	84
S.D.	5.1	3.8	3.9
N	10	12	11

SF=Spilled Feeder

APPENDIX W

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
4543	100	84	81
4544	93	83	81
4545	101	90	86
4546	106	86	82
4547	103	93	86
4548	99	84	82
4549	SF	89	84
4550	SF	87	81
4551	SF	90	84
4552	99	79	78
4553	105	90	86
4554	90	84	78
MEAN	100	87	82
S.D.	5.2	4.0	2.8
N	9	12	12

SF=Spilled Feeder

APPENDIX X

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 1 0 PPM

	DAY OF GESTATION		
ANIMAL#	0 - 7	7 - 14	14 - 20
1543	87	82	70
1544	81	81	66
1545	90	85	73
1546	83	77	65
1547	81	80	72
1548	88	83	71
1549	84	81	72
1550	81	74	70
1551	93	86	77
1552	95	86	74
1553	83	80	66
1554	85	78	67
MEAN	86	81	70
S.D.	4.7	3.8	3.7
N	12	12	12

APPENDIX X

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 2 900 PPM

ANIMAL#	DAY OF GESTATION 0 - 7	7 - 14	14 - 20
2543	86	85	68
2544	81	78	73
2545	81	78	68
2546	82	81	67
2547x NP	92	75	60
2548	81	75	66
2549	82	74	69
2550	90	83	78
2551	77	82	75
2552	90	80	72
2553	80	74	70
2554	89	79	63
MEAN	84	79	70
S.D.	4.5	3.6	4.2
N	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX X

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 3 3000 PPM

ANIMAL#	DAY OF GESTATION 0 - 7	7 - 14	14 - 20
3543	87	82	71
3544	75	75	64
3545	94	82	68
3546	83	74	64
3547	87	78	71
3548	91	91	77
3549	86	76	70
3550	90	79	76
3551x NP	72	73	69
3552	90	78	68
3553	93	79	75
3554	88	84	76
MEAN	88	80	71
S.D.	5.2	4.9	4.6
N	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

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APPENDIX X

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 4 9000 PPM

ANIMAL#	DAY OF GESTATION 0 - 7	7 - 14	14 - 20
4543	78	77	72
4544	85	82	75
4545x NP	76	71	62
4546	81	79	74
4547	90	79	74
4548	86	78	69
4549	88	84	75
4550x NP	91	78	71
4551	79	82	69
4552	79	73	67
4553x NP	76	70	71
4554	82	74	69
MEAN	83	79	71
S.D.	4.4	3.7	3.1
N	9	9	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX Y

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 1 0 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
1543	160
1544	135
1545	101
1546	125
1547	111
1548	128
1549	104
1550	115
1551	96
1552	113
1553	135
1554	112
MEAN	120
S.D.	18.0
N	12

APPENDIX Y

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 2 900 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
2543	115
2544	CF
2545	117
2546	110
2547x NP	
2548	135
2549	246
2550	136
2551	126
2552	122
2553	119
2554	133
MEAN	136
S.D.	39.6
N	10

NP=NOT PREGNANT x=EXCLUDED FROM MEAN
CF=Contaminated Feeder

APPENDIX Y

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 3 3000 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
3543	113
3544	100
3545	108
3546	146
3547	113
3548	75
3549	112
3550	98
3551x NP	
3552	115
3553	141
3554	115
MEAN	112
S.D.	19.4
N	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX Y

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 4 9000 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
4543	109
4544	105
4545x NP	
4546	117
4547	108
4548	146
4549	110
4550x NP	
4551	106
4552	99
4553x NP	
4554	CF
MEAN	112
S.D.	14.3
N	8

NP=NOT PREGNANT x=EXCLUDED FROM MEAN
CF=Contaminated Feeder

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APPENDIX Z

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 1 0 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1543	/C													
1544	D	D	/C											
1545	D	/C												
1546	D	D	/C											
1547	D	D	/C											
1548	D	D	D	/C										
1549	D	/C												
1550	D	D	D	/C										
1551	D	/C												
1552	D	/C												
1553	D	D	/C											
1554	/M	D	D	/C										

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

APPENDIX Z

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 2 900 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
2543	D	D	/C											
2544	D	/C												
2545	D	/E	M	D	D	/S								
2546	D	D	/P	C										
2547	/C													
2548	/C													
2549	D	D	/P	C										
2550	/S													
2551	/C													
2552	/C													
2553	D	D	D	/C										
2554	/C													

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

APPENDIX Z

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 3 3000 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
3543	/M	D	/S											
3544	/E	M	D	D	D	D	D	D	D	D	D	D	/S	
3545	/S													
3546	D	D	/S											
3547	D	D	/C											
3548	D	D	D	/P	C									
3549	/S													
3550	D	D	/S											
3551	D	D	D	/S										
3552	D	D	D	/C										
3553	D	D	/P	S										
3554	D	D	D	/S										

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

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APPENDIX Z

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 4 9000 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4543	/C													
4544	D	D	/C											
4545	/S													
4546	D	D	/C											
4547	/M	D	D	/C										
4548	D	D	/P	S										
4549	D	/C												
4550	D	/P	S											
4551	D	/E	M	M	D	/S								
4552	D	D	/C											
4553	D	D	/S											
4554	/E	S												

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

APPENDIX AA

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 1 0 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
1543	1031		+	P	29-DEC-03	30-DEC-03	20-JAN-04
1544	1032		+	P	29-DEC-03	1-JAN-04	23-JAN-04
1545	1033		+	P	29-DEC-03	31-DEC-03	22-JAN-04
1546	1034		+	P	29-DEC-03	1-JAN-04	23-JAN-04
1547	1035		+	P	29-DEC-03	1-JAN-04	22-JAN-04
1548	1036		+	P	29-DEC-03	2-JAN-04	24-JAN-04
1549	1037		+	P	29-DEC-03	31-DEC-03	22-JAN-04
1550	1038		+	P	29-DEC-03	2-JAN-04	24-JAN-04
1551	1039		+	P	29-DEC-03	31-DEC-03	21-JAN-04
1552	1040		+	P	29-DEC-03	31-DEC-03	22-JAN-04
1553	1041		+	P	29-DEC-03	1-JAN-04	23-JAN-04
1554	1042		+	P	29-DEC-03	2-JAN-04	24-JAN-04

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

P=PREGNANT

APPENDIX AA

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 2 900 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
2543	2031		+	P	29-DEC-03	1-JAN-04	22-JAN-04
2544	2032		+	P	29-DEC-03	31-DEC-03	21-JAN-04
2545	2033		+	P	29-DEC-03	4-JAN-04	26-JAN-04
2546	2034		+	P	29-DEC-03	2-JAN-04	24-JAN-04
2547	2035		+	NP	29-DEC-03	30-DEC-03	
2548	2036		+	P	29-DEC-03	30-DEC-03	21-JAN-04
2549	2037		+	P	29-DEC-03	2-JAN-04	24-JAN-04
2550	2038		+	P	29-DEC-03	30-DEC-03	21-JAN-04
2551	2039		+	P	29-DEC-03	30-DEC-03	21-JAN-04
2552	2040		+	P	29-DEC-03	30-DEC-03	21-JAN-04
2553	2041		+	P	29-DEC-03	2-JAN-04	23-JAN-04
2554	2042		+	P	29-DEC-03	30-DEC-03	21-JAN-04

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

NP=NOT PREGNANT P=PREGNANT

APPENDIX AA

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 3 3000 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
3543	3031		+	P	29-DEC-03	1-JAN-04	23-JAN-04
3544	3032		+	P	29-DEC-03	12-JAN-04	2-FEB-04
3545	3033		+	P	29-DEC-03	30-DEC-03	20-JAN-04
3546	3034		+	P	29-DEC-03	1-JAN-04	23-JAN-04
3547	3035		+	P	29-DEC-03	1-JAN-04	23-JAN-04
3548	3036		+	P	29-DEC-03	3-JAN-04	25-JAN-04
3549	3037		+	P	29-DEC-03	30-DEC-03	21-JAN-04
3550	3038		+	P	29-DEC-03	1-JAN-04	23-JAN-04
3551	3043		+	NP	29-DEC-03	2-JAN-04	
3552	3040		+	P	29-DEC-03	2-JAN-04	24-JAN-04
3553	3041		+	P	29-DEC-03	2-JAN-04	24-JAN-04
3554	3042		+	P	29-DEC-03	2-JAN-04	24-JAN-04

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

NP=NOT PREGNANT P=PREGNANT

APPENDIX AA

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 4 9000 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
4543	4031		+	P	29-DEC-03	30-DEC-03	20-JAN-04
4544	4032		+	P	29-DEC-03	1-JAN-04	23-JAN-04
4545	4033		+	NP	29-DEC-03	30-DEC-03	
4546	4034		+	P	29-DEC-03	1-JAN-04	23-JAN-04
4547	4035		+	P	29-DEC-03	2-JAN-04	24-JAN-04
4548	4036		+	P	29-DEC-03	2-JAN-04	24-JAN-04
4549	4037		+	P	29-DEC-03	31-DEC-03	21-JAN-04
4550	4038		+	NP	29-DEC-03	1-JAN-04	
4551	4039		+	P	29-DEC-03	4-JAN-04	26-JAN-04
4552	4040		+	P	29-DEC-03	1-JAN-04	23-JAN-04
4553	4041		+	NP	29-DEC-03	1-JAN-04	
4554	4042		+	P	29-DEC-03	31-DEC-03	21-JAN-04

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

NP=NOT PREGNANT P=PREGNANT

APPENDIX BB

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 1 0 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						DURATION OF GESTATION	TOTAL CORPORA	TOTAL IMPLAN-	PRE- IMPLAN-	POST- IMPLAN-
	LIVE	DEAD	TOTAL	0		1		4		(DAYS)	LUTEA	TATIONS	TATION LOSS	TATION LOSS
FEMALE#	N	N	N	M	F	M	F	M	F	N	N	N	N	N
1543	15	0	15	8	7	8	7	8	7	21	16	16	0	1
1544	13	0	13	4	9	4	9	4	9	22	18	13	5	0
1545	16	0	16	12	4	12	4	12	4	22	16	16	0	0
1546	16	0	16	6	10	6	10	6	10	22	18	16	2	0
1547	13	0	13	9	4	9	4	9	4	21	16	14	2	1
1548	12	0	12	9	3	9	3	9	3	22	18	15	3	3
1549	12	0	12	7	5	6	5	6	5	22	13	12	1	0
1550	13	0	13	11	2	11	2	11	2	22	16	15	1	2
1551	14	0	14	7	7	7	7	7	7	21	16	15	1	1
1552	12	0	12	6	6	6	6	4	6	22	13	13	0	1
1553	13	0	13	8	5	8	5	7	5	22	19	14	5	1
1554	16	0	16	9	7	9	6	9	6	22	17	16	1	0
MEAN	13.8	0.0	13.8	8.0	5.8	7.9	5.7	7.7	5.7	21.8	16.3	14.6	1.8	0.8
S.D.	1.6	0.0	1.6	2.2	2.4	2.3	2.3	2.5	2.3	0.5	1.9	1.4	1.8	0.9
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12

APPENDIX BB

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 2 900 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						DURATION OF GESTATION (DAYS)	TOTAL CORPORA LUTEA	TOTAL IMPLAN-TATIONS	PRE-IMPLAN-TATION LOSS	POST-IMPLAN-TATION LOSS
				0		1		4						
FEMALE#	LIVE N	DEAD N	TOTAL N	M	F	M	F	M	F	N	N	N	N	N
2543	16	0	16	12	4	12	4	11	4	21	20	16	4	0
2544	12	0	12	2	10	2	10	2	10	21	15	15	0	3
2545	14	0	14	4	10	3	10	3	10	22	17	17	0	3
2546	12	0	12	4	8	4	8	4	8	22	13	12	1	0
2547x NP														
2548	13	0	13	9	4	9	4	9	4	22	13	13	0	0
2549	15	0	15	7	8	7	8	7	8	22	16	15	1	0
2550	14	0	14	8	6	8	6	8	6	22	16	14	2	0
2551	14	0	14	8	6	8	6	8	6	22	15	14	1	0
2552	11	0	11	5	6	5	6	5	6	22	13	12	1	1
2553	14	0	14	7	7	7	7	7	7	21	14	14	0	0
2554	13	0	13	9	4	9	4	9	3	22	14	13	1	0
MEAN	13.5	0.0	13.5	6.8	6.6	6.7	6.6	6.6	6.5	21.7	15.1	14.1	1.0	0.6
S.D.	1.4	0.0	1.4	2.9	2.2	3.0	2.2	2.8	2.3	0.5	2.1	1.6	1.2	1.2
N	11	11	11	11	11	11	11	11	11	11	11	11	11	11

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX BB

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 3 3000 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						DURATION OF GESTATION	TOTAL CORPORA	TOTAL IMPLAN-	PRE-IMPLAN-	POST-IMPLAN-
				0		1		4						
FEMALE#	LIVE N	DEAD N	TOTAL N	M	F	M	F	M	F	(DAYS) N	LUTEA N	TATIONS N	TATION LOSS N	TATION LOSS N
3543	11	0	11	6	5	6	5	6	5	22	14	13	1	2
3544	17	0	17	11	6	11	6	11	6	21	17	17	0	0
3545	14	0	14	9	5	9	5	9	5	21	15	14	1	0
3546	17	0	17	6	11	6	10	6	10	22	18	18	0	1
3547	16	0	16	6	10	6	10	6	10	22	16	16	0	0
3548	8	0	8	2	5	2	5	2	5	22	11	9	2	1
3549	13	0	13	9	4	9	4	9	4	22	16	14	2	1
3550	12	2	14	6	6	6	6	6	6	22	15	14	1	2
3551 X NP														
3552	13	0	13	7	6	7	6	7	6	22	16	13	3	0
3553	13	0	13	8	5	8	5	8	5	22	14	14	0	1
3554	11	0	11	4	7	4	7	4	7	22	12	11	1	0
MEAN	13.2	0.2	13.4	6.7	6.4	6.7	6.3	6.7	6.3	21.8	14.9	13.9	1.0	0.7
S.D.	2.8	0.6	2.7	2.5	2.2	2.5	2.0	2.5	2.0	0.4	2.1	2.5	1.0	0.8
N	11	11	11	11	11	11	11	11	11	11	11	11	11	11

NP= NOT PREGANT X= EXCLUDED FROM MEAN

APPENDIX BB

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 4 9000 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						DURATION OF GESTATION	TOTAL CORPORA	TOTAL IMPLAN-	PRE- IMPLAN-	POST- IMPLAN-
	LIVE	DEAD	TOTAL	0		1		4		(DAYS)	LUTEA	TATIONS	TATION LOSS	TATION LOSS
FEMALE#	N	N	N	M	F	M	F	M	F	N	N	N	N	N
4543	15	0	15	10	5	10	5	10	5	21	20	18	2	3
4544	12	0	12	7	5	7	5	7	5	22	15	14	1	2
4545x NP														
4546	13	0	13	8	5	8	5	8	5	22	16	14	2	1
4547	12	0	12	7	5	7	5	7	5	22	17	15	2	3
4548	16	0	16	7	9	7	9	7	9	22	19	17	2	1
4549	14	0	14	5	9	5	9	5	9	21	15	15	0	1
4550 X NP														
4551	14	0	14	8	6	8	6	8	6	22	17	16	1	2
4552	14	0	14	6	8	6	8	6	8	22	16	14	2	1
4553 X NP														
4554	11	0	11	4	7	4	7	3	7	21	13	13	0	2
MEAN	13.4	0.0	13.4	6.9	6.6	6.9	6.6	6.8	6.6	21.7	16.4	15.1	1.3	1.8
S.D.	1.6	0.0	1.6	1.8	1.7	1.8	1.7	2.0	1.7	0.5	2.1	1.6	0.9	0.8
N	9	9	9	9	9	9	9	9	9	9	9	9	9	9

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX CC

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
1544	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
1545	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	MK 4	FK 4					
1546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
1547	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4									
1548	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5										
1549	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MD 1	FK 4	FK 4	FK 4	FK 4	FK 4										
1550	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5									
1551	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
1552	MK 4	MK 4	MD 3	MD 3	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4											
1553	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MD 2	FK 4	FK 4	FK 4	FK 4	FK 4										
1554	FD 0	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5							

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE D-DIED K-SCHEDULED SACRIFICE

APPENDIX CC

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
2543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MD 2	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4							
2544	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4										
2545	MM 1	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
2546	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5											
2548	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4										
2549	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5								
2550	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
2551	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
2552	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4											
2553	MK 4	MK 4	MK 4	MK 4	FK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
2554	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FD 4										

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE D-DIED M-MISSING K-SCHEDULED SACRIFICE

APPENDIX CC

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
3543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4												
3544	MK 4	MK 4	MK 4	MK 4	FK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4						
3545	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
3546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FD 1				
3547	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
3548	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	UM 1															
3549	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4									
3550	MS	FS	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
3552	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5										
3553	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5										
3554	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5												

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED M-MISSING K-SCHEDULED SACRIFICE

APPENDIX CC

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
4543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4544	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4										
4546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
4547	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5										
4548	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	MK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5	FK 5							
4549	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4551	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4552	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4554	MK 4	MD 2	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4												

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE D-DIED K-SCHEDULED SACRIFICE

	Raw Data Listing of Gross Observations Preface	Appendix DD

Key to Abbreviations

LN	=	Lymph Node
Oviducts/Fallop	=	Oviducts/Fallopian Tubes
SC	=	Spinal Cord

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1543	F	1/1		Thymus			
			24-Jan-04	Discolored, Left lobe, , Foci, , Moderate			
				Tissues marked 'Within normal limits':			
			24-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nose/Turbinates
				Ovaries	Oviducts/Fallop	Parathyroid	Rectum/Low Colon
				Skin-protocol	Spleen	Sternal Marrow	Sternum
				Stomach	Thoracic SC	Thyroid	Tibial Nerve
				Trachea	Urinary bladder	Uterus	Vagina
1544	F	1/1	27-Jan-04	Within normal limits			
1545	F	1/1	26-Jan-04	Within normal limits			
1546	F	1/1	27-Jan-04	Within normal limits			
1547	F	1/1	26-Jan-04	Within normal limits			
1548	F	1/1	29-Jan-04	Within normal limits			
1549	F	1/1		Lungs			
			26-Jan-04	Discolored, Right diaphragmatic lobe, Red, Focus, 0.2 - 0.5 cm, Slight			
				Tissues marked 'Within normal limits':			
			26-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nose/Turbinates	Ovaries
				Oviducts/Fallop	Parathyroid	Rectum/Low Colon	Skin-protocol
				Spleen	Sternal Marrow	Sternum	Stomach
				Thoracic SC	Thymus	Thyroid	Tibial Nerve
				Trachea	Urinary bladder	Uterus	Vagina
1550	F	1/1		Skin (other)			
			29-Jan-04	Hair Thin/Absent, Cervical, , , , Moderate			
				Tissues marked 'Within normal limits':			
			29-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1550	F	1/1	29-Jan-04	Tissues marked 'Within normal limits':			
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nose/Turbinates
				Ovaries	Oviducts/Fallop	Parathyroid	Rectum/Low Colon
				Skin-protocol	Spleen	Sternal Marrow	Sternum
				Stomach	Thoracic SC	Thymus	Thyroid
				Tibial Nerve	Trachea	Urinary bladder	Uterus
				Vagina			
1551	F	1/1		Lungs			
			25-Jan-04	Discolored, Left lobe(s), Red, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			25-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nose/Turbinates	Ovaries
				Oviducts/Fallop	Parathyroid	Rectum/Low Colon	Skin-protocol
				Spleen	Sternal Marrow	Sternum	Stomach
				Thoracic SC	Thymus	Thyroid	Tibial Nerve
				Trachea	Urinary bladder	Uterus	Vagina
1552	F	1/1	26-Jan-04	Within normal limits			
1553	F	1/1	27-Jan-04]	Within normal limits			
1554	F	1/1	29-Jan-04	Within normal limits			
2543	F	2/1	26-Jan-04	Within normal limits			
2544	F	2/1		Lungs			
			25-Jan-04	Discolored, Right diaphragmatic lobe, Red, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			25-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nose/Turbinates	Ovaries
				Oviducts/Fallop	Parathyroid	Rectum/Low Colon	Skin-protocol
				Spleen	Sternal Marrow	Sternum	Stomach
				Thoracic SC	Thymus	Thyroid	Tibial Nerve

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
2544	F	2/1	25-Jan-04	Tissues marked 'Within normal limits':			
				Trachea	Urinary bladder	Uterus	Vagina
2545	F	2/1	30-Jan-04	Within normal limits			
2546	F	2/1		Kidneys			
			29-Jan-04	Dilated Pelvis, Right, , , , Slight			
				Tissues marked 'Within normal limits':			
			29-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Larynx
				Liver	Lumbar SC	Lungs	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nose/Turbinates	Ovaries
				Oviducts/Fallop	Parathyroid	Rectum/Low Colon	Skin-protocol
				Spleen	Sternal Marrow	Sternum	Stomach
				Thoracic SC	Thymus	Thyroid	Tibial Nerve
				Trachea	Urinary bladder	Uterus	Vagina
2547	F	2/1	25-Jan-04	Within normal limits			
2548	F	2/1	25-Jan-04	Within normal limits			
2549	F	2/1	29-Jan-04	Within normal limits			
2550	F	2/1	25-Jan-04	Within normal limits			
2551	F	2/1	25-Jan-04	Within normal limits			
2552	F	2/1		Skin (other)			
			25-Jan-04	Hair Thin/Absent, General, , , ,			
				Tissues marked 'Within normal limits':			
			25-Jan-04	Adrenal Glands	Brain	Cecum	Cervical SC
				Colon	Duodenum	Femoral Marrow	Femur
				Heart	Ileum	Jejunum	Kidneys
				Larynx	Liver	Lumbar SC	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nose/Turbinates
				Ovaries	Oviducts/Fallop	Parathyroid	Rectum/Low Colon
				Skin-protocol	Spleen	Sternal Marrow	Sternum
				Stomach	Thoracic SC	Thymus	Thyroid
				Tibial Nerve	Trachea	Urinary bladder	Uterus
				Vagina			
2553	F	2/1	27-Jan-04	Within normal limits			

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
2554	F	2/1	25-Jan-04	Within normal limits
3543	F	3/1	27-Jan-04	Within normal limits
3544	F	3/1	06-Feb-04	Within normal limits
3545	F	3/1	24-Jan-04	Within normal limits
3546	F	3/1	27-Jan-04	Within normal limits
3547	F	3/1	27-Jan-04	Within normal limits
3548	F	3/1	29-Jan-04	Within normal limits
3549	F	3/1	25-Jan-04	Within normal limits
3550	F	3/1	27-Jan-04	Within normal limits
3551	F	3/1	29-Jan-04	Within normal limits
3552	F	3/1	29-Jan-04	Within normal limits
3553	F	3/1	29-Jan-04	Within normal limits
3554	F	3/1	29-Jan-04	Within normal limits
4543	F	4/1	24-Jan-04	Within normal limits
4544	F	4/1	27-Jan-04	Within normal limits
4545	F	4/1	25-Jan-04	Within normal limits
4546	F	4/1	27-Jan-04	Within normal limits
4547	F	4/1	29-Jan-04	Within normal limits
4548	F	4/1	29-Jan-04	Within normal limits
4549	F	4/1	25-Jan-04	Within normal limits
4550	F	4/1	27-Jan-04	Within normal limits
4551	F	4/1	30-Jan-04	Within normal limits

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Satellite

Raw Data Listing of Gross Observations with Modifiers
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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
4552	F	4/1	27-Jan-04	Within normal limits
4553	F	4/1	27-Jan-04	Within normal limits
4554	F	4/1	25-Jan-04	Within normal limits

	Individual Parental Organ Weights Satellite Study Preface	Appendix EE

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Parental Terminal Sacrifice
Absolute Organ Weights 548
% Organ to Body Weight Ratios..... 552
% Organ to Brain Weight Ratios 556

Terminal Sacrifice – Non-pregnant
Absolute Organ Weights 560

Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observations

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey

Summary statistics for absolute organ weights (g)
Study number: 034244

Printed: 06-Apr-04
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Terminal Sacrifice - Satellite

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				F e m a l e	A n i m a l s			
1543/F	1/1	310.5	0.0998	1.9871	1.0668	2.7702	14.9502	1.7813
1544/F	1/1	267.8	0.0656	2.0157	0.9291	2.0179	10.7148	1.3508
1545/F	1/1	291.9	0.1070	1.9481	0.9856	2.3113	12.5087	1.4991
1546/F	1/1	316.0	0.1142	2.1077	1.1905	2.5248	14.0872	1.4438
1547/F	1/1	288.2	0.0959	2.1799	0.9304	2.6661	12.2852	1.5928
1548/F	1/1	312.0	0.0846	1.9903	0.8921	2.2181	14.9112	1.6332
1549/F	1/1	287.5	0.0949	2.0532	1.0529	2.2126	11.9894	1.5542
1550/F	1/1	305.3	0.1020	2.0302	1.0659	2.6376	14.9843	1.3828
1551/F	1/1	276.8	0.0875	2.1399	0.8820	2.5194	13.7371	1.4919
1552/F	1/1	271.5	0.0814	2.0311	0.9902	2.1460	11.2635	1.3973
1553/F	1/1	286.0	0.0838	1.9427	1.0045	2.2494	14.6614	1.5187
1554/F	1/1	322.3	0.0887	2.1415	0.9721	2.5463	12.1881	1.6896
M e a n:		294.7	0.0921	2.0473	0.9968	2.4016	13.1901	1.5280
Standard deviation:		18.2	0.0130	0.0786	0.0875	0.2383	1.5408	0.1297
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	0.0856	1.9455	0.9352	2.2100	12.1921	1.2932
2544/F	2/1	252.0	0.1120	1.9833	0.9225	2.7683	13.1986	1.4574
2545/F	2/1	293.8	0.1102	1.9947	1.0510	2.5518	13.8650	1.4976
2546/F	2/1	283.5	0.0658	1.8830	0.9699	2.0150	11.3345	1.5957
2548/F	2/1	273.7	0.0876	1.9188	0.8573	2.5445	13.7127	1.5195
2549/F	2/1	276.9	0.0844	2.0284	0.9739	2.2645	12.9682	1.2669
2550/F	2/1	264.5	0.0993	2.1116	0.9847	2.6984	14.7233	1.6570
2551/F	2/1	304.0	0.1134	2.1086	1.1610	2.6099	16.0311	1.7059
2552/F	2/1	301.2	0.0989	2.1135	1.1229	2.6588	16.8603	1.8267
2553/F	2/1	282.7	0.0900	2.0024	1.2133	2.5317	13.7215	1.4253
2554/F	2/1	299.5	0.1298	2.0577	1.1365	2.9741	13.9031	1.8393
M e a n:		283.4	0.0979	2.0134	1.0298	2.5297	13.8646	1.5531
Standard deviation:		16.1	0.0177	0.0793	0.1142	0.2728	1.5778	0.1928
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	0.0746	1.9652	1.0346	2.4563	12.4789	1.3817
3544/F	3/1	290.2	0.0659	1.9754	0.9841	2.5444	13.3738	1.4711
3545/F	3/1	281.3	0.0968	1.9501	0.8540	2.4571	16.2719	1.5884
3546/F	3/1	246.6	0.1090	1.9792	0.9991	2.4192	10.7350	1.3776
3547/F	3/1	260.2	0.0973	1.8905	0.9943	2.2677	11.1818	1.4835
3548/F	3/1	300.5	0.1158	2.0076	1.0648	2.4100	13.1545	1.7160
3549/F	3/1	313.4	0.1155	2.1033	1.1891	2.6891	15.0678	1.9205
3550/F	3/1	314.7	0.0743	1.9645	1.1296	2.3419	11.6573	1.4015
3552/F	3/1	307.0	0.0686	2.0134	1.0073	2.0750	12.5693	1.6085
3553/F	3/1	262.8	0.0704	1.8036	0.9732	2.0420	11.6993	1.2345
3554/F	3/1	313.8	0.0966	2.0294	1.0266	2.5403	13.5416	1.4981
M e a n:		289.5	0.0895	1.9711	1.0233	2.3857	12.8847	1.5165
Standard deviation:		23.9	0.0193	0.0769	0.0866	0.1958	1.6637	0.1872
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4543/F	4/1	329.7	0.1232	2.0160	1.1930	3.0473	18.2508	1.8635
4544/F	4/1	253.2	0.0966	1.9745	1.1223	2.1342	10.5077	1.2714
4546/F	4/1	251.1	0.1075	1.8050	0.9573	2.2027	12.0871	1.4494
4547/F	4/1	353.2	0.0942	2.1635	1.0924	2.9064	15.2203	1.8295
4548/F	4/1	321.3	0.0831	2.0288	1.1144	2.5981	14.2528	1.4649
4549/F	4/1	248.6	0.1097	1.9788	1.0972	2.4910	11.7625	1.7985
4551/F	4/1	283.5	0.1015	1.9013	1.0151	2.4779	13.0770	1.5425
4552/F	4/1	303.9	0.1094	1.8840	1.0077	2.2060	11.5697	1.7994
4554/F	4/1	280.9	0.1008	2.0528	1.0106	2.5223	12.9282	1.8090
M e a n:		291.7	0.1029	1.9783	1.0678	2.5095	13.2951	1.6476
Standard deviation:		37.8	0.0114	0.1053	0.0743	0.3129	2.3431	0.2170
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
1543/F	1/1	310.5	0.1091	0.0777	0.8977	0.3176	1.4540
1544/F	1/1	267.8	0.0491	0.0659	0.5517	0.4352	1.0842
1545/F	1/1	291.9	0.0904	0.0852	0.5370	0.2817	1.2604
1546/F	1/1	316.0	0.0818	0.0785	0.5935	0.3741	0.9464
1547/F	1/1	288.2	0.0699	0.0714	0.7918	0.4357	1.3570
1548/F	1/1	312.0	0.0544	0.0973	0.5855	0.2804	0.9355
1549/F	1/1	287.5	0.0697	0.0741	0.6003	0.3320	1.1635
1550/F	1/1	305.3	0.0744	0.0702	0.7637	0.2881	0.8830
1551/F	1/1	276.8	0.0834	0.0822	0.6156	0.2919	1.1576
1552/F	1/1	271.5	0.0724	0.0634	0.6920	0.3169	0.9137
1553/F	1/1	286.0	0.0837	0.0780	0.5961	0.3249	1.0592
1554/F	1/1	322.3	0.0747	0.0810	0.5882	0.1597	0.9080
	Mean:	294.7	0.0761	0.0771	0.6511	0.3199	1.0935
Standard deviation:		18.2	0.0158	0.0091	0.1113	0.0740	0.1895
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	0.0908	0.0815	0.7665	0.3354	1.1235
2544/F	2/1	252.0	0.0623	0.0667	0.4369	0.1956	1.2288
2545/F	2/1	293.8	0.0953	0.0779	0.6525	0.2691	0.8882
2546/F	2/1	283.5	0.0597	0.0548	0.5874	0.2483	0.7769
2548/F	2/1	273.7	0.0746	0.0681	0.4883	0.2445	0.9288
2549/F	2/1	276.9	0.0643	0.0929	0.5570	0.1805	0.8943
2550/F	2/1	264.5	0.0806	0.1091	0.6851	0.2874	1.2076
2551/F	2/1	304.0	0.0900	0.0814	0.6068	0.3001	1.3187
2552/F	2/1	301.2	0.0771	0.0940	0.6167	0.3020	1.0160
2553/F	2/1	282.7	0.0765	0.0810	0.6740	0.3440	1.0889
2554/F	2/1	299.5	0.0737	0.0805	0.6510	0.2891	1.0803
	Mean:	283.4	0.0768	0.0807	0.6111	0.2724	1.0502
Standard deviation:		16.1	0.0118	0.0147	0.0927	0.0519	0.1666
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	0.0543	0.0792	0.5591	0.3268	1.0058
3544/F	3/1	290.2	0.0765	0.1023	0.5995	0.1803	1.1400
3545/F	3/1	281.3	0.0687	0.0883	0.6037	0.2745	1.0650
3546/F	3/1	246.6	0.0746	0.0784	0.4521	0.2264	1.1352
3547/F	3/1	260.2	0.0679	0.0925	0.5650	0.1762	1.1075
3548/F	3/1	300.5	0.0768	0.0901	0.6786	0.3516	1.0447
3549/F	3/1	313.4	0.0800	0.0954	0.7534	0.3562	1.1025
3550/F	3/1	314.7	0.0674	0.0659	0.6801	0.2458	1.1256
3552/F	3/1	307.0	0.0620	0.0748	0.7294	0.3063	0.7854
3553/F	3/1	262.8	0.0783	0.0698	0.4867	0.1713	0.8218
3554/F	3/1	313.8	0.0518	0.0706	0.7093	0.3111	0.8616
	Mean:	289.5	0.0689	0.0825	0.6197	0.2660	1.0177
Standard deviation:		23.9	0.0096	0.0119	0.0991	0.0702	0.1325
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
4543/F	4/1	329.7	0.1059	0.1059	0.6936	0.4092	1.1035
4544/F	4/1	253.2	0.0589	0.0643	0.5555	0.2996	0.8881
4546/F	4/1	251.1	0.0683	0.0908	0.5293	0.1831	1.0536
4547/F	4/1	353.2	0.1051	0.0683	0.9355	0.5570	1.0526
4548/F	4/1	321.3	0.0692	0.0769	0.6807	0.2601	0.9685
4549/F	4/1	248.6	0.0718	0.0941	0.5961	0.3121	1.0830
4551/F	4/1	283.5	0.0833	0.0797	0.5367	0.2701	0.9114
4552/F	4/1	303.9	0.0960	0.0645	0.6402	0.2300	1.0518
4554/F	4/1	280.9	0.0834	0.0787	0.6349	0.3127	1.0121
M e a n:		291.7	0.0824	0.0804	0.6447	0.3149	1.0138
Standard deviation:		37.8	0.0169	0.0142	0.1243	0.1103	0.0756
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1543/F	1/1	310.5	0.0321	0.6400	0.3436	0.8922	4.8149	0.5737
1544/F	1/1	267.8	0.0245	0.7527	0.3469	0.7535	4.0010	0.5044
1545/F	1/1	291.9	0.0367	0.6674	0.3376	0.7918	4.2853	0.5136
1546/F	1/1	316.0	0.0361	0.6670	0.3767	0.7990	4.4580	0.4569
1547/F	1/1	288.2	0.0333	0.7564	0.3228	0.9251	4.2627	0.5527
1548/F	1/1	312.0	0.0271	0.6379	0.2859	0.7109	4.7792	0.5235
1549/F	1/1	287.5	0.0330	0.7142	0.3662	0.7696	4.1702	0.5406
1550/F	1/1	305.3	0.0334	0.6650	0.3491	0.8639	4.9081	0.4529
1551/F	1/1	276.8	0.0316	0.7731	0.3186	0.9102	4.9628	0.5390
1552/F	1/1	271.5	0.0300	0.7481	0.3647	0.7904	4.1486	0.5147
1553/F	1/1	286.0	0.0293	0.6793	0.3512	0.7865	5.1264	0.5310
1554/F	1/1	322.3	0.0275	0.6644	0.3016	0.7900	3.7816	0.5242
	Mean:	294.7	0.0312	0.6971	0.3388	0.8153	4.4749	0.5189
Standard deviation:		18.2	0.0037	0.0488	0.0271	0.0668	0.4311	0.0352
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	0.0299	0.6802	0.3270	0.7727	4.2630	0.4522
2544/F	2/1	252.0	0.0444	0.7870	0.3661	1.0985	5.2375	0.5783
2545/F	2/1	293.8	0.0375	0.6789	0.3577	0.8686	4.7192	0.5097
2546/F	2/1	283.5	0.0232	0.6642	0.3421	0.7108	3.9981	0.5629
2548/F	2/1	273.7	0.0320	0.7011	0.3132	0.9297	5.0101	0.5552
2549/F	2/1	276.9	0.0305	0.7325	0.3517	0.8178	4.6834	0.4575
2550/F	2/1	264.5	0.0375	0.7983	0.3723	1.0202	5.5665	0.6265
2551/F	2/1	304.0	0.0373	0.6936	0.3819	0.8585	5.2734	0.5612
2552/F	2/1	301.2	0.0328	0.7017	0.3728	0.8827	5.5977	0.6065
2553/F	2/1	282.7	0.0318	0.7083	0.4292	0.8955	4.8537	0.5042
2554/F	2/1	299.5	0.0433	0.6870	0.3795	0.9930	4.6421	0.6141
	Mean:	283.4	0.0346	0.7121	0.3630	0.8953	4.8950	0.5480
Standard deviation:		16.1	0.0062	0.0437	0.0309	0.1118	0.5063	0.0601
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	0.0254	0.6696	0.3525	0.8369	4.2518	0.4708
3544/F	3/1	290.2	0.0227	0.6807	0.3391	0.8768	4.6085	0.5069
3545/F	3/1	281.3	0.0344	0.6932	0.3036	0.8735	5.7845	0.5647
3546/F	3/1	246.6	0.0442	0.8026	0.4052	0.9810	4.3532	0.5586
3547/F	3/1	260.2	0.0374	0.7266	0.3821	0.8715	4.2974	0.5701
3548/F	3/1	300.5	0.0385	0.6681	0.3543	0.8020	4.3775	0.5710
3549/F	3/1	313.4	0.0369	0.6711	0.3794	0.8580	4.8078	0.6128
3550/F	3/1	314.7	0.0236	0.6242	0.3589	0.7442	3.7043	0.4453
3552/F	3/1	307.0	0.0223	0.6558	0.3281	0.6759	4.0942	0.5239
3553/F	3/1	262.8	0.0268	0.6863	0.3703	0.7770	4.4518	0.4697
3554/F	3/1	313.8	0.0308	0.6467	0.3272	0.8095	4.3154	0.4774
	Mean:	289.5	0.0312	0.6841	0.3546	0.8278	4.4588	0.5247
Standard deviation:		23.9	0.0075	0.0473	0.0291	0.0803	0.5207	0.0543
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4543/F	4/1	329.7	0.0374	0.6115	0.3618	0.9243	5.5356	0.5652
4544/F	4/1	253.2	0.0382	0.7798	0.4432	0.8429	4.1500	0.5021
4546/F	4/1	251.1	0.0428	0.7188	0.3812	0.8772	4.8137	0.5772
4547/F	4/1	353.2	0.0267	0.6125	0.3093	0.8229	4.3093	0.5180
4548/F	4/1	321.3	0.0259	0.6314	0.3468	0.8086	4.4360	0.4559
4549/F	4/1	248.6	0.0441	0.7960	0.4414	1.0020	4.7315	0.7235
4551/F	4/1	283.5	0.0358	0.6707	0.3581	0.8740	4.6127	0.5441
4552/F	4/1	303.9	0.0360	0.6199	0.3316	0.7259	3.8071	0.5921
4554/F	4/1	280.9	0.0359	0.7308	0.3598	0.8979	4.6024	0.6440
	M e a n:	291.7	0.0359	0.6857	0.3704	0.8640	4.5553	0.5691
Standard deviation:		37.8	0.0062	0.0729	0.0455	0.0778	0.4826	0.0795
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				F e m a l e	A n i m a l s		
1543/F	1/1	310.5	0.0351	0.0250	0.2891	0.1023	0.4683
1544/F	1/1	267.8	0.0183	0.0246	0.2060	0.1625	0.4049
1545/F	1/1	291.9	0.0310	0.0292	0.1840	0.0965	0.4318
1546/F	1/1	316.0	0.0259	0.0248	0.1878	0.1184	0.2995
1547/F	1/1	288.2	0.0243	0.0248	0.2747	0.1512	0.4709
1548/F	1/1	312.0	0.0174	0.0312	0.1877	0.0899	0.2998
1549/F	1/1	287.5	0.0242	0.0258	0.2088	0.1155	0.4047
1550/F	1/1	305.3	0.0244	0.0230	0.2501	0.0944	0.2892
1551/F	1/1	276.8	0.0301	0.0297	0.2224	0.1055	0.4182
1552/F	1/1	271.5	0.0267	0.0234	0.2549	0.1167	0.3365
1553/F	1/1	286.0	0.0293	0.0273	0.2084	0.1136	0.3703
1554/F	1/1	322.3	0.0232	0.0251	0.1825	0.0496	0.2817
M e a n:		294.7	0.0258	0.0262	0.2214	0.1097	0.3730
Standard deviation:		18.2	0.0051	0.0026	0.0371	0.0289	0.0698
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	0.0317	0.0285	0.2680	0.1173	0.3928
2544/F	2/1	252.0	0.0247	0.0265	0.1734	0.0776	0.4876
2545/F	2/1	293.8	0.0324	0.0265	0.2221	0.0916	0.3023
2546/F	2/1	283.5	0.0211	0.0193	0.2072	0.0876	0.2740
2548/F	2/1	273.7	0.0273	0.0249	0.1784	0.0893	0.3393
2549/F	2/1	276.9	0.0232	0.0336	0.2012	0.0652	0.3230
2550/F	2/1	264.5	0.0305	0.0412	0.2590	0.1087	0.4566
2551/F	2/1	304.0	0.0296	0.0268	0.1996	0.0987	0.4338
2552/F	2/1	301.2	0.0256	0.0312	0.2047	0.1003	0.3373
2553/F	2/1	282.7	0.0271	0.0287	0.2384	0.1217	0.3852
2554/F	2/1	299.5	0.0246	0.0269	0.2174	0.0965	0.3607
M e a n:		283.4	0.0271	0.0285	0.2154	0.0959	0.3721
Standard deviation:		16.1	0.0037	0.0055	0.0300	0.0165	0.0665
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	0.0185	0.0270	0.1905	0.1113	0.3427
3544/F	3/1	290.2	0.0264	0.0353	0.2066	0.0621	0.3928
3545/F	3/1	281.3	0.0244	0.0314	0.2146	0.0976	0.3786
3546/F	3/1	246.6	0.0303	0.0318	0.1833	0.0918	0.4603
3547/F	3/1	260.2	0.0261	0.0355	0.2171	0.0677	0.4256
3548/F	3/1	300.5	0.0256	0.0300	0.2258	0.1170	0.3477
3549/F	3/1	313.4	0.0255	0.0304	0.2404	0.1137	0.3518
3550/F	3/1	314.7	0.0214	0.0209	0.2161	0.0781	0.3577
3552/F	3/1	307.0	0.0202	0.0244	0.2376	0.0998	0.2558
3553/F	3/1	262.8	0.0298	0.0266	0.1852	0.0652	0.3127
3554/F	3/1	313.8	0.0165	0.0225	0.2260	0.0991	0.2746
M e a n:		289.5	0.0241	0.0287	0.2130	0.0912	0.3546
Standard deviation:		23.9	0.0044	0.0049	0.0198	0.0200	0.0603
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
4543/F	4/1	329.7	0.0321	0.0321	0.2104	0.1241	0.3347
4544/F	4/1	253.2	0.0233	0.0254	0.2194	0.1183	0.3508
4546/F	4/1	251.1	0.0272	0.0362	0.2108	0.0729	0.4196
4547/F	4/1	353.2	0.0298	0.0193	0.2649	0.1577	0.2980
4548/F	4/1	321.3	0.0215	0.0239	0.2119	0.0810	0.3014
4549/F	4/1	248.6	0.0289	0.0379	0.2398	0.1255	0.4356
4551/F	4/1	283.5	0.0294	0.0281	0.1893	0.0953	0.3215
4552/F	4/1	303.9	0.0316	0.0212	0.2107	0.0757	0.3461
4554/F	4/1	280.9	0.0297	0.0280	0.2260	0.1113	0.3603
	M e a n:	291.7	0.0282	0.0280	0.2203	0.1069	0.3520
Standard deviation:		37.8	0.0036	0.0064	0.0215	0.0281	0.0479
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1543/F	1/1	310.5	5.0224	100.0000	53.6863	139.4092	752.3628	89.6432
1544/F	1/1	267.8	3.2545	100.0000	46.0932	100.1091	531.5672	67.0139
1545/F	1/1	291.9	5.4925	100.0000	50.5929	118.6438	642.0975	76.9519
1546/F	1/1	316.0	5.4182	100.0000	56.4834	119.7893	668.3683	68.5012
1547/F	1/1	288.2	4.3993	100.0000	42.6809	122.3038	563.5672	73.0676
1548/F	1/1	312.0	4.2506	100.0000	44.8224	111.4455	749.1936	82.0580
1549/F	1/1	287.5	4.6221	100.0000	51.2809	107.7635	583.9373	75.6965
1550/F	1/1	305.3	5.0241	100.0000	52.5022	129.9182	738.0701	68.1115
1551/F	1/1	276.8	4.0890	100.0000	41.2169	117.7345	641.9506	69.7182
1552/F	1/1	271.5	4.0077	100.0000	48.7519	105.6570	554.5518	68.7952
1553/F	1/1	286.0	4.3136	100.0000	51.7064	115.7873	754.6920	78.1747
1554/F	1/1	322.3	4.1420	100.0000	45.3934	118.9026	569.1385	78.8980
Mean:		294.7	4.5030	100.0000	48.7676	117.2887	645.7914	74.7192
Standard deviation:		18.2	0.6459	0.0000	4.7109	10.6277	85.7038	6.8520
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	4.3999	100.0000	48.0699	113.5955	626.6821	66.4714
2544/F	2/1	252.0	5.6472	100.0000	46.5134	139.5805	665.4869	73.4836
2545/F	2/1	293.8	5.5246	100.0000	52.6896	127.9290	695.0920	75.0790
2546/F	2/1	283.5	3.4944	100.0000	51.5082	107.0101	601.9385	84.7424
2548/F	2/1	273.7	4.5654	100.0000	44.6790	132.6089	714.6498	79.1901
2549/F	2/1	276.9	4.1609	100.0000	48.0132	111.6397	639.3315	62.4581
2550/F	2/1	264.5	4.7026	100.0000	46.6329	127.7894	697.2581	78.4713
2551/F	2/1	304.0	5.3780	100.0000	55.0602	123.7741	760.2723	80.9020
2552/F	2/1	301.2	4.6794	100.0000	53.1299	125.8008	797.7431	86.4301
2553/F	2/1	282.7	4.4946	100.0000	60.5923	126.4333	685.2527	71.1796
2554/F	2/1	299.5	6.3080	100.0000	55.2316	144.5352	675.6622	89.3862
Mean:		283.4	4.8505	100.0000	51.1018	125.5179	687.2154	77.0722
Standard deviation:		16.1	0.7917	0.0000	4.8021	11.4101	56.8401	8.3467
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	3.7961	100.0000	52.6460	124.9898	634.9940	70.3084
3544/F	3/1	290.2	3.3360	100.0000	49.8178	128.8043	677.0174	74.4710
3545/F	3/1	281.3	4.9638	100.0000	43.7926	125.9987	834.4138	81.4522
3546/F	3/1	246.6	5.5073	100.0000	50.4800	122.2312	542.3909	69.6039
3547/F	3/1	260.2	5.1468	100.0000	52.5946	119.9524	591.4733	78.4713
3548/F	3/1	300.5	5.7681	100.0000	53.0385	120.0438	655.2351	85.4752
3549/F	3/1	313.4	5.4914	100.0000	56.5350	127.8515	716.3885	91.3089
3550/F	3/1	314.7	3.7821	100.0000	57.5006	119.2110	593.3979	71.3413
3552/F	3/1	307.0	3.4072	100.0000	50.0298	103.0595	624.2823	79.8897
3553/F	3/1	262.8	3.9033	100.0000	53.9588	113.2180	648.6639	68.4465
3554/F	3/1	313.8	4.7600	100.0000	50.5864	125.1749	667.2711	73.8199
Mean:		289.5	4.5329	100.0000	51.9073	120.9577	653.2299	76.7808
Standard deviation:		23.9	0.9061	0.0000	3.6977	7.4519	76.4552	7.2633
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4543/F	4/1	329.7	6.1111	100.0000	59.1766	151.1558	905.2976	92.4355
4544/F	4/1	253.2	4.8924	100.0000	56.8397	108.0881	532.1703	64.3910
4546/F	4/1	251.1	5.9557	100.0000	53.0360	122.0332	669.6455	80.2992
4547/F	4/1	353.2	4.3541	100.0000	50.4923	134.3379	703.5036	84.5620
4548/F	4/1	321.3	4.0960	100.0000	54.9290	128.0609	702.5237	72.2053
4549/F	4/1	248.6	5.5438	100.0000	55.4478	125.8844	594.4260	90.8884
4551/F	4/1	283.5	5.3385	100.0000	53.3898	130.3266	687.7926	81.1287
4552/F	4/1	303.9	5.8068	100.0000	53.4873	117.0913	614.1031	95.5096
4554/F	4/1	280.9	4.9104	100.0000	49.2303	122.8712	629.7838	88.1235
M e a n:		291.7	5.2232	100.0000	54.0032	126.6499	671.0273	83.2826
Standard deviation:		37.8	0.7084	0.0000	3.0504	11.9752	104.4646	10.0582
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
1543/F	1/1	310.5	5.4904	3.9102	45.1764	15.9831	73.1720
1544/F	1/1	267.8	2.4359	3.2693	27.3701	21.5905	53.7878
1545/F	1/1	291.9	4.6404	4.3735	27.5653	14.4602	64.6990
1546/F	1/1	316.0	3.8810	3.7244	28.1587	17.7492	44.9020
1547/F	1/1	288.2	3.2066	3.2754	36.3228	19.9872	62.2506
1548/F	1/1	312.0	2.7333	4.8887	29.4177	14.0883	47.0030
1549/F	1/1	287.5	3.3947	3.6090	29.2373	16.1699	56.6676
1550/F	1/1	305.3	3.6647	3.4578	37.6170	14.1907	43.4933
1551/F	1/1	276.8	3.8974	3.8413	28.7677	13.6408	54.0960
1552/F	1/1	271.5	3.5646	3.1215	34.0702	15.6024	44.9855
1553/F	1/1	286.0	4.3084	4.0150	30.6841	16.7241	54.5221
1554/F	1/1	322.3	3.4882	3.7824	27.4667	7.4574	42.4002
Mean:		294.7	3.7255	3.7724	31.8212	15.6370	53.4982
Standard deviation:		18.2	0.8234	0.4993	5.4826	3.5314	9.5939
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2543/F	2/1	286.0	4.6672	4.1892	39.3986	17.2398	57.7487
2544/F	2/1	252.0	3.1412	3.3631	22.0289	9.8624	61.9574
2545/F	2/1	293.8	4.7777	3.9053	32.7117	13.4908	44.5280
2546/F	2/1	283.5	3.1705	2.9102	31.1949	13.1864	41.2586
2548/F	2/1	273.7	3.8878	3.5491	25.4482	12.7423	48.4053
2549/F	2/1	276.9	3.1700	4.5800	27.4601	8.8986	44.0889
2550/F	2/1	264.5	3.8170	5.1667	32.4446	13.6105	57.1889
2551/F	2/1	304.0	4.2682	3.8604	28.7774	14.2322	62.5391
2552/F	2/1	301.2	3.6480	4.4476	29.1791	14.2891	48.0719
2553/F	2/1	282.7	3.8204	4.0451	33.6596	17.1794	54.3797
2554/F	2/1	299.5	3.5817	3.9121	31.6373	14.0497	52.5004
Mean:		283.4	3.8136	3.9935	30.3582	13.5256	52.0606
Standard deviation:		16.1	0.5685	0.6138	4.5894	2.5312	7.3363
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)
3543/F	3/1	293.5	2.7631	4.0301	28.4500	16.6294	51.1805
3544/F	3/1	290.2	3.8726	5.1787	30.3483	9.1273	57.7098
3545/F	3/1	281.3	3.5229	4.5280	30.9574	14.0762	54.6126
3546/F	3/1	246.6	3.7692	3.9612	22.8426	11.4390	57.3565
3547/F	3/1	260.2	3.5916	4.8929	29.8863	9.3203	58.5824
3548/F	3/1	300.5	3.8255	4.4879	33.8016	17.5134	52.0373
3549/F	3/1	313.4	3.8035	4.5357	35.8199	16.9353	52.4176
3550/F	3/1	314.7	3.4309	3.3545	34.6195	12.5121	57.2970
3552/F	3/1	307.0	3.0794	3.7151	36.2273	15.2131	39.0086
3553/F	3/1	262.8	4.3413	3.8700	26.9849	9.4977	45.5644
3554/F	3/1	313.8	2.5525	3.4789	34.9512	15.3297	42.4559
Mean:		289.5	3.5048	4.1848	31.3535	13.4176	51.6566
Standard deviation:		23.9	0.5243	0.5834	4.2021	3.1949	6.6358
Number of observ. :		(11)	(11)	(11)	(11)	(11)	(11)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
4543/F	4/1	329.7	5.2530	5.2530	34.4048	20.2976	54.7371
4544/F	4/1	253.2	2.9830	3.2565	28.1337	15.1735	44.9785
4546/F	4/1	251.1	3.7839	5.0305	29.3241	10.1440	58.3712
4547/F	4/1	353.2	4.8579	3.1569	43.2401	25.7453	48.6526
4548/F	4/1	321.3	3.4109	3.7904	33.5519	12.8204	47.7376
4549/F	4/1	248.6	3.6285	4.7554	30.1243	15.7722	54.7301
4551/F	4/1	283.5	4.3812	4.1919	28.2281	14.2061	47.9356
4552/F	4/1	303.9	5.0955	3.4236	33.9809	12.2081	55.8280
4554/F	4/1	280.9	4.0627	3.8338	30.9285	15.2329	49.3034
M e a n:		291.7	4.1619	4.0769	32.4351	15.7333	51.3638
Standard deviation:		37.8	0.7894	0.7789	4.7137	4.6921	4.5964
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)

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Terminal Sacrifice - Non-pregnant

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female Animals			
2547/F	2/1	247.6	0.0742	0.0914	0.4749	0.2940	0.7765
Mean:		247.6	0.0742	0.0914	0.4749	0.2940	0.7765
Standard deviation:		0.0	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :		(1)	(1)	(1)	(1)	(1)	(1)
3551/F	3/1	254.6	0.0675	0.0668	0.5945	0.2600	0.9016
Mean:		254.6	0.0675	0.0668	0.5945	0.2600	0.9016
Standard deviation:		0.0	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :		(1)	(1)	(1)	(1)	(1)	(1)
4545/F	4/1	241.3	0.0929	0.0852	0.5988	0.3106	0.9420
4550/F	4/1	243.5	0.0912	0.0819	0.5098	0.4069	0.8732
4553/F	4/1	284.3	0.0863	0.0845	0.6333	0.4365	0.9591
Mean:		256.4	0.0901	0.0839	0.5806	0.3847	0.9248
Standard deviation:		24.2	0.0034	0.0017	0.0637	0.0658	0.0455
Number of observ. :		(3)	(3)	(3)	(3)	(3)	(3)

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Terminal Sacrifice - Non-pregnant

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				F e m a l e	A n i m a l s			
2547/F	2/1	247.6	0.0915	1.9169	1.0163	2.3842	12.4708	1.5540
M e a n:		247.6	0.0915	1.9169	1.0163	2.3842	12.4708	1.5540
Standard deviation:		0.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :		(1)	(1)	(1)	(1)	(1)	(1)	(1)
3551/F	3/1	254.6	0.0650	1.9557	0.9282	2.1161	10.4723	1.6344
M e a n:		254.6	0.0650	1.9557	0.9282	2.1161	10.4723	1.6344
Standard deviation:		0.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Number of observ. :		(1)	(1)	(1)	(1)	(1)	(1)	(1)
4545/F	4/1	241.3	0.1135	1.8839	0.9659	2.3157	10.1306	1.5722
4550/F	4/1	243.5	0.0810	1.7311	0.8430	2.0161	9.0329	1.5010
4553/F	4/1	284.3	0.0810	1.9188	1.0186	2.3930	11.0017	1.5932
M e a n:		256.4	0.0918	1.8446	0.9425	2.2416	10.0551	1.5555
Standard deviation:		24.2	0.0188	0.0998	0.0901	0.1991	0.9866	0.0483
Number of observ. :		(3)	(3)	(3)	(3)	(3)	(3)	(3)

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
1543	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
	PUP# 15 WITHIN NORMAL LIMITS	P				P
1544	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
1545	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
	PUP# 15	WITHIN NORMAL LIMITS	P				P
	PUP# 16	WITHIN NORMAL LIMITS	P				P
1546	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
	PUP# 15	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	4
1546	PUP# 16 WITHIN NORMAL LIMITS	P	P
1547	PUP# 1 WITHIN NORMAL LIMITS	P	P
	PUP# 2 WITHIN NORMAL LIMITS	P	P
	PUP# 3 WITHIN NORMAL LIMITS	P	P
	PUP# 4 WITHIN NORMAL LIMITS	P	P
	PUP# 5 WITHIN NORMAL LIMITS	P	P
	PUP# 6 WITHIN NORMAL LIMITS	P	P
	PUP# 7 WITHIN NORMAL LIMITS	P	P
	PUP# 8 WITHIN NORMAL LIMITS	P	P
	PUP# 9 WITHIN NORMAL LIMITS	P	P
	PUP# 10 WITHIN NORMAL LIMITS	P	P
	PUP# 11 WITHIN NORMAL LIMITS	P	P
	PUP# 12 WITHIN NORMAL LIMITS	P	P
	PUP# 13 WITHIN NORMAL LIMITS	P	P
1548	PUP# 1 WITHIN NORMAL LIMITS	P	P
	PUP# 2 WITHIN NORMAL LIMITS	P	P
	PUP# 3 WITHIN NORMAL LIMITS	P	P
	PUP# 4 WITHIN NORMAL LIMITS	P	P
	PUP# 5 WITHIN NORMAL LIMITS	P	P
	PUP# 6 WITHIN NORMAL LIMITS	P	P
	PUP# 7 WITHIN NORMAL LIMITS	P	P
	PUP# 8 WITHIN NORMAL LIMITS	P	P
	PUP# 9 WITHIN NORMAL LIMITS	P	P
	PUP# 10 WITHIN NORMAL LIMITS	P	P
	PUP# 11 WITHIN NORMAL LIMITS	P	P
	PUP# 12 WITHIN NORMAL LIMITS	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
1549	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
1550	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
1551	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
1551	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
1552	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				
	PUP# 4	WITHIN NORMAL LIMITS	P				
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
1553	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				
	PUP# 9	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
1553	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
	PUP# 12 WITHIN NORMAL LIMITS		P				P
	PUP# 13 WITHIN NORMAL LIMITS		P				P
1554	PUP# 2 WITHIN NORMAL LIMITS		P				P
	PUP# 3 WITHIN NORMAL LIMITS		P				P
	PUP# 4 WITHIN NORMAL LIMITS		P				P
	PUP# 5 WITHIN NORMAL LIMITS		P				P
	PUP# 6 WITHIN NORMAL LIMITS		P				P
	PUP# 7 WITHIN NORMAL LIMITS		P				P
	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
	PUP# 12 WITHIN NORMAL LIMITS		P				P
	PUP# 13 WITHIN NORMAL LIMITS		P				P
	PUP# 14 WITHIN NORMAL LIMITS		P				P
	PUP# 15 WITHIN NORMAL LIMITS		P				P
	PUP# 16 WITHIN NORMAL LIMITS		P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
2543	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
	PUP# 15	WITHIN NORMAL LIMITS	P				P
	PUP# 16	WITHIN NORMAL LIMITS	P				P
2544	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
2545	PUP# 1	WITHIN NORMAL LIMITS	P				
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
2546	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
2548	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
2548	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
2549	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
	PUP# 15 WITHIN NORMAL LIMITS	P				P
2550	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
2550	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
2551	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
2552	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
2552	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
2553	PUP# 1 WITHIN NORMAL LIMITS		P				P
	PUP# 2 WITHIN NORMAL LIMITS		P				P
	PUP# 3 WITHIN NORMAL LIMITS		P				P
	PUP# 4 WITHIN NORMAL LIMITS		P				P
	PUP# 5 WITHIN NORMAL LIMITS		P				P
	PUP# 6 WITHIN NORMAL LIMITS		P				P
	PUP# 7 WITHIN NORMAL LIMITS		P				P
	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
	PUP# 12 WITHIN NORMAL LIMITS		P				P
	PUP# 13 WITHIN NORMAL LIMITS		P				P
	PUP# 14 WITHIN NORMAL LIMITS		P				P
2554	PUP# 1 WITHIN NORMAL LIMITS		P				P
	PUP# 2 WITHIN NORMAL LIMITS		P				P
	PUP# 3 WITHIN NORMAL LIMITS		P				P
	PUP# 4 WITHIN NORMAL LIMITS		P				P
	PUP# 5 WITHIN NORMAL LIMITS		P				P
	PUP# 6 WITHIN NORMAL LIMITS		P				P
	PUP# 7 WITHIN NORMAL LIMITS		P				P
	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
	PUP# 12 WITHIN NORMAL LIMITS		P				P
	PUP# 13 WITHIN NORMAL LIMITS		P				

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	4
3543	PUP# 1 WITHIN NORMAL LIMITS	P	P
	PUP# 2 WITHIN NORMAL LIMITS	P	P
	PUP# 3 WITHIN NORMAL LIMITS	P	P
	PUP# 4 WITHIN NORMAL LIMITS	P	P
	PUP# 5 WITHIN NORMAL LIMITS	P	P
	PUP# 6 WITHIN NORMAL LIMITS	P	P
	PUP# 7 WITHIN NORMAL LIMITS	P	P
	PUP# 8 WITHIN NORMAL LIMITS	P	P
	PUP# 9 WITHIN NORMAL LIMITS	P	P
	PUP# 10 WITHIN NORMAL LIMITS	P	P
	PUP# 11 WITHIN NORMAL LIMITS	P	P
3544	PUP# 1 WITHIN NORMAL LIMITS	P	P
	PUP# 2 WITHIN NORMAL LIMITS	P	P
	PUP# 3 WITHIN NORMAL LIMITS	P	P
	PUP# 4 WITHIN NORMAL LIMITS	P	P
	PUP# 5 WITHIN NORMAL LIMITS	P	P
	PUP# 6 WITHIN NORMAL LIMITS	P	P
	PUP# 7 WITHIN NORMAL LIMITS	P	P
	PUP# 8 WITHIN NORMAL LIMITS	P	P
	PUP# 9 WITHIN NORMAL LIMITS	P	P
	PUP# 10 WITHIN NORMAL LIMITS	P	P
	PUP# 11 WITHIN NORMAL LIMITS	P	P
	PUP# 12 WITHIN NORMAL LIMITS	P	P
	PUP# 13 WITHIN NORMAL LIMITS	P	P
	PUP# 14 WITHIN NORMAL LIMITS	P	P
	PUP# 15 WITHIN NORMAL LIMITS	P	P
	PUP# 16 WITHIN NORMAL LIMITS	P	P
	PUP# 17 WITHIN NORMAL LIMITS	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
3545	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
3546	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
	PUP# 15 WITHIN NORMAL LIMITS	P				P
	PUP# 16 WITHIN NORMAL LIMITS	P				P
	PUP# 17 WITHIN NORMAL LIMITS	P				

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

Huntingdon Life Sciences 03-4244S
SATELLITE STUDY

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
3547	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
	PUP# 15	WITHIN NORMAL LIMITS	P				P
	PUP# 16	WITHIN NORMAL LIMITS	P				P
3548	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
3549	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
3549	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
3550	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
3552	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
3552	PUP# 13 WITHIN NORMAL LIMITS		P				P
3553	PUP# 1 WITHIN NORMAL LIMITS		P				P
	PUP# 2 WITHIN NORMAL LIMITS		P				P
	PUP# 3 WITHIN NORMAL LIMITS		P				P
	PUP# 4 WITHIN NORMAL LIMITS		P				P
	PUP# 5 WITHIN NORMAL LIMITS		P				P
	PUP# 6 WITHIN NORMAL LIMITS		P				P
	PUP# 7 WITHIN NORMAL LIMITS		P				P
	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P
	PUP# 12 WITHIN NORMAL LIMITS		P				P
	PUP# 13 WITHIN NORMAL LIMITS		P				P
3554	PUP# 1 WITHIN NORMAL LIMITS		P				P
	PUP# 2 WITHIN NORMAL LIMITS		P				P
	PUP# 3 WITHIN NORMAL LIMITS		P				P
	PUP# 4 WITHIN NORMAL LIMITS		P				P
	PUP# 5 WITHIN NORMAL LIMITS		P				P
	PUP# 6 WITHIN NORMAL LIMITS		P				P
	PUP# 7 WITHIN NORMAL LIMITS		P				P
	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
4543	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P
	PUP# 13	WITHIN NORMAL LIMITS	P				P
	PUP# 14	WITHIN NORMAL LIMITS	P				P
	PUP# 15	WITHIN NORMAL LIMITS	P				P
4544	PUP# 1	WITHIN NORMAL LIMITS	P				P
	PUP# 2	WITHIN NORMAL LIMITS	P				P
	PUP# 3	WITHIN NORMAL LIMITS	P				P
	PUP# 4	WITHIN NORMAL LIMITS	P				P
	PUP# 5	WITHIN NORMAL LIMITS	P				P
	PUP# 6	WITHIN NORMAL LIMITS	P				P
	PUP# 7	WITHIN NORMAL LIMITS	P				P
	PUP# 8	WITHIN NORMAL LIMITS	P				P
	PUP# 9	WITHIN NORMAL LIMITS	P				P
	PUP# 10	WITHIN NORMAL LIMITS	P				P
	PUP# 11	WITHIN NORMAL LIMITS	P				P
	PUP# 12	WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
4546	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
4547	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
4548	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
4548	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
	PUP# 15 WITHIN NORMAL LIMITS	P				P
	PUP# 16 WITHIN NORMAL LIMITS	P				P
4549	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
4551	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
4551	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
4552	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				P
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P
	PUP# 8 WITHIN NORMAL LIMITS	P				P
	PUP# 9 WITHIN NORMAL LIMITS	P				P
	PUP# 10 WITHIN NORMAL LIMITS	P				P
	PUP# 11 WITHIN NORMAL LIMITS	P				P
	PUP# 12 WITHIN NORMAL LIMITS	P				P
	PUP# 13 WITHIN NORMAL LIMITS	P				P
	PUP# 14 WITHIN NORMAL LIMITS	P				P
4554	PUP# 1 WITHIN NORMAL LIMITS	P				P
	PUP# 2 WITHIN NORMAL LIMITS	P				
	PUP# 3 WITHIN NORMAL LIMITS	P				P
	PUP# 4 WITHIN NORMAL LIMITS	P				P
	PUP# 5 WITHIN NORMAL LIMITS	P				P
	PUP# 6 WITHIN NORMAL LIMITS	P				P
	PUP# 7 WITHIN NORMAL LIMITS	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX FF

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4
4554	PUP# 8 WITHIN NORMAL LIMITS		P				P
	PUP# 9 WITHIN NORMAL LIMITS		P				P
	PUP# 10 WITHIN NORMAL LIMITS		P				P
	PUP# 11 WITHIN NORMAL LIMITS		P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

Data Requirement

EPA OPPTS 870.3650
OECD 422

STUDY NO. 03-4244

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

Final Report

VOLUME III of III

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Date: 16 April 2010

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APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1543	6.3	6.7	6.2	6.6	6.6	6.5	6.1	6.4	6.4	6.3	6.1	5.9	6.5	5.9	5.4	6.6				
1544	6.9	7.7	7.2	6.9	7.2	6.6	7.1	7.1	7.0	6.6	7.1	6.4	6.9	6.5						
1545	7.1	6.8	7.5	7.7	7.0	7.1	7.3	7.2	7.9	7.3	7.2	6.7	6.6	6.8	6.2	7.8	7.2			
1546	6.6	7.3	7.5	6.9	4.8	6.9	7.0	6.6	6.5	6.8	6.5	6.2	6.4	7.0	6.7	6.6	6.1			
1547	6.3	6.3	6.3	6.0	6.5	6.4	6.3	6.6	6.1	6.5	6.0	6.5	6.0	6.4						
1548	7.3	7.8	7.2	7.3	7.3	7.5	7.3	7.1	7.2	7.8	6.5	7.0	7.4							
1549	7.4	8.4	7.4	7.7	7.5	7.5	7.6	D	7.3	6.7	7.5	7.3	6.8							
1550	7.8	8.6	8.4	7.7	8.1	7.6	7.8	7.0	8.4	7.8	7.9	6.9	7.6	7.3						
1551	6.4	6.4	6.4	6.0	6.8	6.7	6.8	7.0	6.3	6.0	6.7	6.3	6.0	5.9	5.8					
1552	7.5	7.4	7.5	7.5	7.8	7.6	7.4	7.1	7.6	7.2	7.5	7.6	7.6							
1553	7.5	7.2	7.6	7.8	7.6	8.0	7.6	8.2	7.1	7.3	7.5	6.9	7.4	7.3						
1554	7.0	D	6.9	6.6	7.0	7.5	6.9	7.6	6.6	7.1	7.1	6.6	6.5	7.2	7.3	6.6	7.0			
MEAN	7.0																			
S.D.	0.52																			
N	12																			

PUP STATUS CODES: D-DIED

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2543	6.1	6.5	6.1	6.1	6.7	6.0	5.9	6.4	6.1	6.4	6.0	6.3	6.7	5.9	5.6	5.4	5.9			
2544	6.3	6.7	7.0	6.3	6.0	6.0	6.3	6.3	6.5	6.1	6.3	6.6	6.0							
2545	6.8	M	7.0	7.1	7.1	6.1	6.7	6.6	7.1	6.9	6.5	6.7	6.9	6.7	7.1					
2546	7.5	7.5	8.3	7.8	8.0	7.8	7.2	7.9	7.1	7.0	8.6	4.6	7.8							
2547	NOT PREGNANT																			
2548	6.9	6.9	7.4	6.9	7.3	7.2	6.9	6.9	7.0	7.8	5.9	7.2	5.2	7.1						
2549	6.5	6.5	6.7	7.1	7.1	7.2	7.2	7.3	5.7	6.1	6.7	6.1	6.4	6.1	5.5	6.3				
2550	6.9	7.0	7.1	7.6	6.7	7.0	6.8	7.2	7.1	6.8	6.8	6.9	6.8	6.4	6.9					
2551	7.5	7.7	7.4	7.9	7.7	7.1	7.4	7.9	7.5	7.6	7.4	7.2	6.8	7.3	8.0					
2552	8.2	8.2	8.1	8.5	8.9	8.0	7.8	7.9	8.0	8.0	8.5	8.8								
2553	6.5	6.3	6.7	6.5	6.9	7.0	6.6	6.1	6.6	6.7	6.5	5.4	6.1	6.6	6.5					
2554	6.8	7.1	6.5	7.1	6.6	7.5	6.8	7.2	6.9	6.9	6.7	6.3	6.2	6.5						
MEAN	6.9																			
S.D.	0.61																			
N	11																			

PUP STATUS CODES: M-MISSING

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
3543	7.8	8.2	7.4	8.3	7.8	8.7	7.4	7.8	7.9	7.6	7.4	7.6								
3544	6.1	6.1	6.8	5.1	6.1	5.8	6.0	6.5	6.6	6.2	5.9	6.7	6.0	5.9	5.9	5.2	5.8	6.3		
3545	6.1	6.7	6.4	6.3	5.9	6.1	5.8	6.3	6.2	5.9	5.8	6.0	6.0	5.5	5.8					
3546	6.5	6.0	7.2	6.3	6.2	6.6	6.8	6.9	6.5	5.9	6.2	6.0	6.9	6.4	6.6	5.8	6.9	D		
3547	7.0	7.8	6.3	7.6	6.9	6.8	8.1	6.4	6.6	7.3	7.0	6.1	7.2	7.3	6.5	6.8	7.3			
3548	7.9	8.2	8.6	7.9	8.0	7.4	7.5	8.0	M											
3549	7.5	7.1	7.3	7.5	7.9	7.8	8.1	8.1	7.3	7.3	7.4	7.1	7.3	7.0						
3550	7.8	S	S	7.6	7.5	7.9	8.0	8.4	8.5	7.7	7.9	7.7	7.0	7.7	7.8					
3551	NOT PREGNANT																			
3552	6.8	6.8	6.6	6.8	7.3	7.1	7.0	6.9	7.0	6.3	6.4	6.9	7.0	6.3						
3553	7.2	7.5	6.9	7.1	6.7	8.1	7.3	7.1	6.8	7.2	6.9	7.2	7.3	7.4						
3554	7.7	7.7	7.8	8.2	7.9	7.4	6.7	7.7	7.8	7.8	7.7	7.8								
MEAN	7.1																			
S.D.	0.70																			
N	11																			

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4543	6.7	7.1	6.9	7.1	6.7	6.0	6.7	6.9	6.8	7.0	7.2	6.4	6.1	6.2	6.5	6.5				
4544	6.9	7.1	7.4	7.1	7.0	6.9	5.9	7.6	7.2	6.5	7.0	6.5	7.1							
4545	NOT PREGNANT																			
4546	6.8	7.0	7.3	7.0	5.8	7.3	6.7	6.0	7.4	6.5	6.8	6.5	6.6	6.9						
4547	7.9	8.9	8.7	8.5	7.6	8.3	8.1	8.1	8.0	8.2	7.3	7.4	5.8							
4548	6.9	7.5	6.9	7.2	7.2	7.3	7.3	7.8	6.4	6.7	6.7	6.9	6.3	6.5	5.7	6.9	7.0			
4549	6.1	6.3	6.7	5.6	6.1	6.5	5.8	5.9	6.3	5.8	6.1	6.2	6.0	6.1	5.6					
4550	NOT PREGNANT																			
4551	6.6	6.3	6.8	7.0	7.0	6.5	6.5	6.8	6.6	6.5	6.3	6.2	6.5	6.3	6.5					
4552	7.2	7.3	7.8	7.6	8.1	7.7	7.1	6.6	6.9	7.0	7.2	6.8	6.7	7.1	7.1					
4553	NOT PREGNANT																			
4554	6.4	5.9	6.4	6.9	6.9	6.2	6.0	6.1	6.6	6.9	6.3	6.1								
MEAN	6.8																			
S.D.	0.52																			
N	9																			

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1543	9.1	9.7	8.7	9.6	9.7	9.2	8.9	9.9	9.3	9.5	8.4	8.4	9.3	9.0	7.6	9.4				
1544	9.8	11.0	10.6	10.1	9.8	8.7	10.1	9.7	9.3	9.5	10.2	9.3	9.8	9.3						
1545	9.4	9.2	9.4	9.9	9.2	9.4	9.6	9.5	10.1	9.6	9.8	8.9	9.2	9.5	8.2	9.4	9.7			
1546	9.5	10.6	10.3	9.6	6.4	9.4	10.2	9.0	10.1	9.6	10.2	9.4	9.0	9.3	10.1	10.0	9.1			
1547	9.4	9.3	9.4	9.2	9.7	9.6	9.6	9.6	9.1	9.2	9.1	9.6	8.9	9.4						
1548	10.9	11.0	10.6	10.5	11.0	11.4	10.7	10.8	10.9	11.5	10.3	10.7	11.2							
1549	11.5	12.5	11.8	12.1	11.4	11.9	11.8	D	11.4	10.5	11.5	10.9	10.6							
1550	11.3	12.5	11.6	11.1	11.5	11.2	11.5	10.3	12.1	11.5	11.5	10.2	11.1	10.9						
1551	8.7	8.7	8.6	8.4	9.4	8.5	9.5	9.2	8.4	8.6	9.2	9.0	8.2	8.2	8.5					
1552	11.4	10.9	11.5	D	D	11.7	11.6	10.9	11.5	11.2	11.7	12.0	11.4							
1553	11.2	11.0	11.3	11.6	11.2	11.8	11.3	11.7	D	10.8	11.6	10.6	11.1	10.7						
1554	9.1	D	8.6	7.8	9.3	9.2	9.6	10.2	9.0	9.4	9.7	8.5	8.7	9.4	9.2	8.6	9.4			
MEAN	10.1																			
S.D.	1.06																			
N	12																			

PUP STATUS CODES: D-DIED

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2543	8.8	9.7	9.1	8.0	9.4	8.7	8.3	D	8.6	9.1	8.6	8.8	10.2	7.7	8.1	7.9	9.1			
2544	8.3	9.0	8.8	8.5	8.1	8.1	8.6	8.0	8.0	7.9	8.3	8.5	8.1							
2545	10.1	M	10.3	10.4	10.5	9.1	9.9	10.0	10.1	10.0	10.1	10.4	9.8	10.1	10.5					
2546	10.1	10.1	10.9	10.2	10.8	10.0	9.6	10.7	9.7	9.9	11.3	6.6	10.9							
2547	NOT PREGNANT																			
2548	10.3	10.5	10.9	10.4	10.6	11.0	10.4	10.1	9.6	11.5	9.0	10.8	8.0	10.6						
2549	9.5	9.6	9.3	10.2	9.8	10.1	9.8	11.0	8.5	9.6	9.9	8.9	8.6	9.7	8.0	8.8				
2550	9.8	10.1	9.6	10.7	9.7	10.1	10.0	9.7	9.6	9.9	9.2	10.2	9.4	9.1	9.6					
2551	10.3	10.2	10.1	11.4	10.6	10.2	10.3	10.1	10.3	10.2	9.9	10.2	9.7	10.3	10.5					
2552	11.9	12.3	11.6	12.2	12.8	11.7	11.6	11.5	11.7	11.7	12.3	11.9								
2553	9.2	8.5	9.6	9.1	9.3	9.9	9.6	9.3	9.6	9.4	8.8	8.0	9.0	9.5	8.8					
2554	10.5	11.6	10.1	10.8	10.5	11.0	10.7	11.2	10.6	10.9	9.9	9.6	9.3	D						
MEAN	9.9																			
S.D.	0.97																			
N	11																			

PUP STATUS CODES: D-DIED M-MISSING

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
3543	10.8	11.0	10.3	11.3	10.6	12.0	10.3	10.8	10.9	10.3	10.5	10.4								
3544	8.6	8.7	9.8	7.1	8.6	7.5	8.2	9.3	9.8	8.5	8.6	9.3	8.3	8.8	8.4	8.4	8.6	9.0		
3545	9.2	9.6	9.2	9.1	9.4	9.4	9.1	9.3	9.5	8.9	8.9	9.8	8.8	8.7	9.1					
3546	8.3	8.3	8.8	8.3	7.5	8.7	8.5	8.7	8.5	7.5	8.0	7.9	8.5	8.8	8.9	7.3	8.8	D		
3547	9.6	9.9	8.6	10.6	9.4	9.4	10.8	9.3	8.8	10.0	9.4	8.2	10.1	10.2	9.4	9.9	9.9			
3548	11.8	12.4	12.5	11.8	11.6	11.0	11.4	11.9	M											
3549	11.1	10.7	11.2	10.8	11.3	11.5	11.8	11.4	11.0	10.9	10.9	10.6	10.9	10.8						
3550	11.5	S	S	11.7	10.7	11.7	12.1	12.2	12.1	11.4	11.5	11.2	10.4	11.4	11.5					
3551	NOT PREGNANT																			
3552	10.0	10.0	10.2	10.3	10.6	10.2	10.5	10.4	9.8	9.3	10.0	9.8	10.1	9.1						
3553	10.6	11.2	10.6	10.3	9.9	11.5	10.0	10.8	10.0	10.5	10.2	10.8	10.4	11.0						
3554	11.2	11.5	10.9	11.9	11.5	10.6	9.9	11.1	11.7	11.2	11.3	11.4								
MEAN	10.2																			
S.D.	1.17																			
N	11																			

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

APPENDIX GG

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4543	9.7	10.0	10.2	10.5	9.6	9.3	9.9	9.7	9.7	10.0	10.3	9.4	8.9	9.1	9.3	9.3				
4544	9.8	10.1	10.5	10.5	9.8	10.0	8.5	10.2	9.9	9.3	9.6	9.3	9.8							
4545	NOT PREGNANT																			
4546	8.8	8.9	8.9	9.2	8.0	9.2	8.3	7.9	9.5	8.5	9.1	8.7	8.5	9.2						
4547	12.2	13.7	13.1	12.9	11.5	13.2	12.3	12.9	12.7	12.7	11.4	11.7	8.4							
4548	9.9	11.0	10.5	10.6	10.7	10.5	10.6	11.5	9.6	9.7	9.0	9.4	8.8	9.5	7.7	9.9	9.8			
4549	8.0	8.2	9.0	7.3	8.1	8.5	7.7	7.7	8.4	7.4	7.8	8.1	7.9	8.2	7.1					
4550	NOT PREGNANT																			
4551	9.5	9.2	10.1	9.9	10.5	9.5	9.5	10.0	9.6	9.3	8.7	9.0	9.3	9.2	9.3					
4552	9.5	9.9	10.3	10.1	10.2	10.3	9.0	8.9	9.5	9.1	9.6	8.9	8.9	9.5	9.4					
4553	NOT PREGNANT																			
4554	10.1	9.5	D	11.0	10.7	9.8	9.5	9.6	10.0	10.9	10.0	9.5								
MEAN	9.7																			
S.D.	1.14																			
N	9																			

PUP STATUS CODES: D-DIED

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
1544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
1545	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1545 (CONTINUED)					
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11M	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15M	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
1546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
1548	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8M	K	5		NO REMARKABLE OBSERVATIONS
	9M	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
1549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1549 (CONTINUED)					
	7M	D	1	LUNGS	LUNG FLOATAION TEST - LUNGS FLOAT
				STOMACH	MILK IN STOMACH
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
1550	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8M	K	5		NO REMARKABLE OBSERVATIONS
	9M	K	5		NO REMARKABLE OBSERVATIONS
	10M	K	5		NO REMARKABLE OBSERVATIONS
	11M	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS
1551	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1551 (CONTINUED)					
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
1552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	D	3	GROSS EXAM	AUTOLYSIS
	4M	D	3	GROSS EXAM	AUTOLYSIS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
1553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	D	2		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1554	1F	D	0	LUNGS	LUNG FLOATAION TEST - LUNGS FLOAT
				STOMACH	NO MILK IN STOMACH
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8M	K	5		NO REMARKABLE OBSERVATIONS
	9M	K	5		NO REMARKABLE OBSERVATIONS
	10M	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS
	14F	K	5		NO REMARKABLE OBSERVATIONS
	15F	K	5		NO REMARKABLE OBSERVATIONS
	16F	K	5		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	D	2		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11M	K	4		NO REMARKABLE OBSERVATIONS
	12M	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
2544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3F	K	4		NO REMARKABLE OBSERVATIONS
	4F	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
2545	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2545	(CONTINUED)				
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
2546	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5F	K	5		NO REMARKABLE OBSERVATIONS
	6F	K	5		NO REMARKABLE OBSERVATIONS
	7F	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
2548	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2548	(CONTINUED)				
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
2549	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS
	14F	K	5		NO REMARKABLE OBSERVATIONS
	15F	K	5		NO REMARKABLE OBSERVATIONS
2550	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2550 (CONTINUED)					
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
2551	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
2552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
2553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2553 (CONTINUED)					
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
2554	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	D	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
3544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11M	K	4		NO REMARKABLE OBSERVATIONS
	12M	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS
3545	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3545 (CONTINUED)					
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
3546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	D	1	GROSS EXAM	AUTOLYSIS
3547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3547	(CONTINUED)				
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
3548	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3F	K	4		NO REMARKABLE OBSERVATIONS
	4F	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
3549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3549	(CONTINUED)				
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
3550	1M	S		LUNGS	LUNG FLOATATION TEST - LUNGS DO NOT FLOAT
				STOMACH	NO MILK IN STOMACH
	2F	S		LUNGS	LUNG FLOATATION TEST - LUNGS DO NOT FLOAT
				STOMACH	NO MILK IN STOMACH
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
3552	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3553	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8M	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS
3554	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5F	K	5		NO REMARKABLE OBSERVATIONS
	6F	K	5		NO REMARKABLE OBSERVATIONS
	7F	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
4544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
4546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4546	(CONTINUED)				
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
4547	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
4548	1M	K	5		NO REMARKABLE OBSERVATIONS
	2M	K	5		NO REMARKABLE OBSERVATIONS
	3M	K	5		NO REMARKABLE OBSERVATIONS
	4M	K	5		NO REMARKABLE OBSERVATIONS
	5M	K	5		NO REMARKABLE OBSERVATIONS
	6M	K	5		NO REMARKABLE OBSERVATIONS
	7M	K	5		NO REMARKABLE OBSERVATIONS
	8F	K	5		NO REMARKABLE OBSERVATIONS
	9F	K	5		NO REMARKABLE OBSERVATIONS
	10F	K	5		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4548 (CONTINUED)					
	11F	K	5		NO REMARKABLE OBSERVATIONS
	12F	K	5		NO REMARKABLE OBSERVATIONS
	13F	K	5		NO REMARKABLE OBSERVATIONS
	14F	K	5		NO REMARKABLE OBSERVATIONS
	15F	K	5		NO REMARKABLE OBSERVATIONS
	16F	K	5		NO REMARKABLE OBSERVATIONS
4549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4551	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

ISOBUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4551	(CONTINUED)				
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4554	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	D	2	GROSS EXAM	AUTOLYSIS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

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1. INTRODUCTION

This appendix presents the methodology for exposure atmosphere generation monitoring and results.

2. MATERIALS AND METHODS

2.1. HUSBANDRY DURING EXPOSURE PERIODS

2.1.1. HOUSING

Animals were individually housed in a 1000 liter glass and stainless steel whole-body exposure chamber. The placement of the animals in the whole-body exposure chamber was rotated daily to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.1.2. FEED

None was provided during exposure.

2.1.3. WATER

None was provided during exposure.

2.1.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were recorded every half-hour during exposure and maintained, to the maximum extent possible, within the ranges presented below. Excursions outside the specified range did not affect the integrity of the study.

Temperature

Desired:	20 to 24°C
Actual:	21 to 25°C

Relative Humidity

Desired:	40 to 60%
Actual:	52 to 59%

2.2. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATIONS

2.2.1. ROUTE OF ADMINISTRATION

Inhalation as a gas, via whole-body exposures

2.2.2. TEST SUBSTANCE ADMINISTRATION

The test substance was administered as a gas in the breathing air of the animals. The test atmosphere was generated by an appropriate procedure determined during the pre-study trials. The trials were performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the target exposure levels and maintain uniform conditions throughout the exposure chambers.

2.2.3. TARGET EXPOSURE LEVELS

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

2.2.4. DURATION AND FREQUENCY OF ADMINISTRATION

Main Study male rats were exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats (12/group) continued during the mating and post-mating periods for a minimum exposure of 28 days. Main Study female rats (12/group) were exposed once daily, seven days/week for 4-weeks for a minimum exposure of 28 days. Satellite female rats (12/group) for the reproduction study were exposed once daily, seven days/week for at least two weeks prior to mating initiation. Satellite female rats continued to be treated once daily during mating. Once mated, Satellite female rats were treated once daily during gestation (Days 0-19).

2.2.5. CHAMBER OPERATIONS

The whole-body exposure chambers each had a volume of approximately 1000 liters. The chambers operated at a minimum flow rate of 200 liters per minute. 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 T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes. The initial setting for the airflow rate for each group was 204 Lpm.

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 30 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static pressure were made every half-hour during the exposure.

The chamber atmospheres were exhausted through the in-house filtering system, which consisted of a coarse filter, a HEPA filter, and an activated charcoal bed.

See Figures 1 and 2, and Table III (Inhalation Report) for equipment list.

2.2.6. EXPOSURE PROCEDURE

Group 1

Room air was directed into the inlet of 1000 liter glass and stainless steel exposure chamber.

Groups 2 - 4

The test substance was delivered from a single cylinder, through a regulator and two backpressure gauges, via a stainless steel cross and ¼" tubing to the three exposure chambers. For each chamber, ¼" tubing directed the test substance to a flowmeter, regulated by a

metering valve, and into the inlet of a 1000 liter stainless steel and glass whole-body exposure chamber.

See Figures 1 and 2, and Table III for equipment list.

2.3. EXPOSURE CONCENTRATION DETERMINATION

2.3.1. NOMINAL CONCENTRATION

A nominal exposure concentration (ppm) was calculated by dividing the average test substance flow (ccm) during each exposure by the average chamber airflow (Lpm).

$$\text{Nominal (ppm)} = \frac{\text{Test Substance Flow (ccm)} \times 1000\mu\text{L/cc}}{\text{Chamber Airflow (Lpm)}}$$

An overall nominal exposure concentration (ppm) was also calculated by weighing the cylinder before and after each day of exposure and dividing the weight differential (grams) by the total chamber airflow (L).

$$\text{Nominal (ppm)} = \frac{\Delta\text{Wt (g)} \times 10^6\ \mu\text{g/g} \times 22.4\ \mu\text{L/}\mu\text{mole} \times 295^\circ\text{K}/273^\circ\text{K}}{\text{Chamber Airflow (Lpm)} \times \text{Exposure Duration (min)} \times 58.12\ \mu\text{g/}\mu\text{mole}}$$

See Table III for equipment list.

2.3.2. CHAMBER SAMPLING

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

See Table III for equipment list.

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2.3.3. PARTICLE SIZE DISTRIBUTION

Particle size samples were drawn once during each week of exposure for 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.

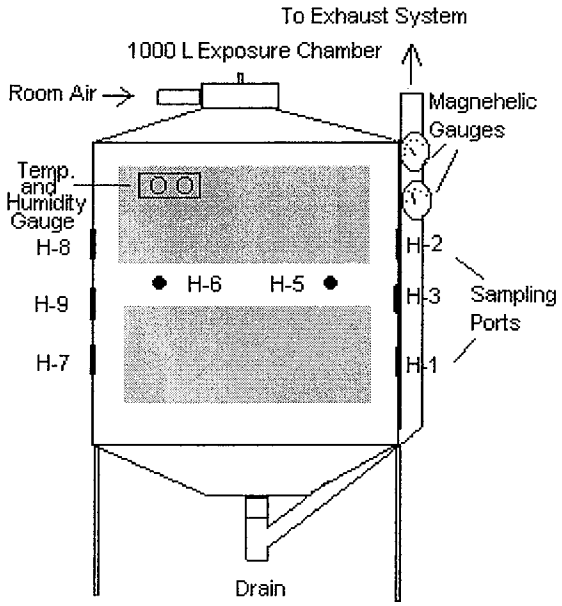
See Table III for equipment list.

2.3.4. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber oxygen levels (maintained at least 19%) were measured pretest and at the beginning, middle and end of the study. Air samples were taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room were measured pretest and at the beginning, middle and end of the study.

See Table III for equipment list.

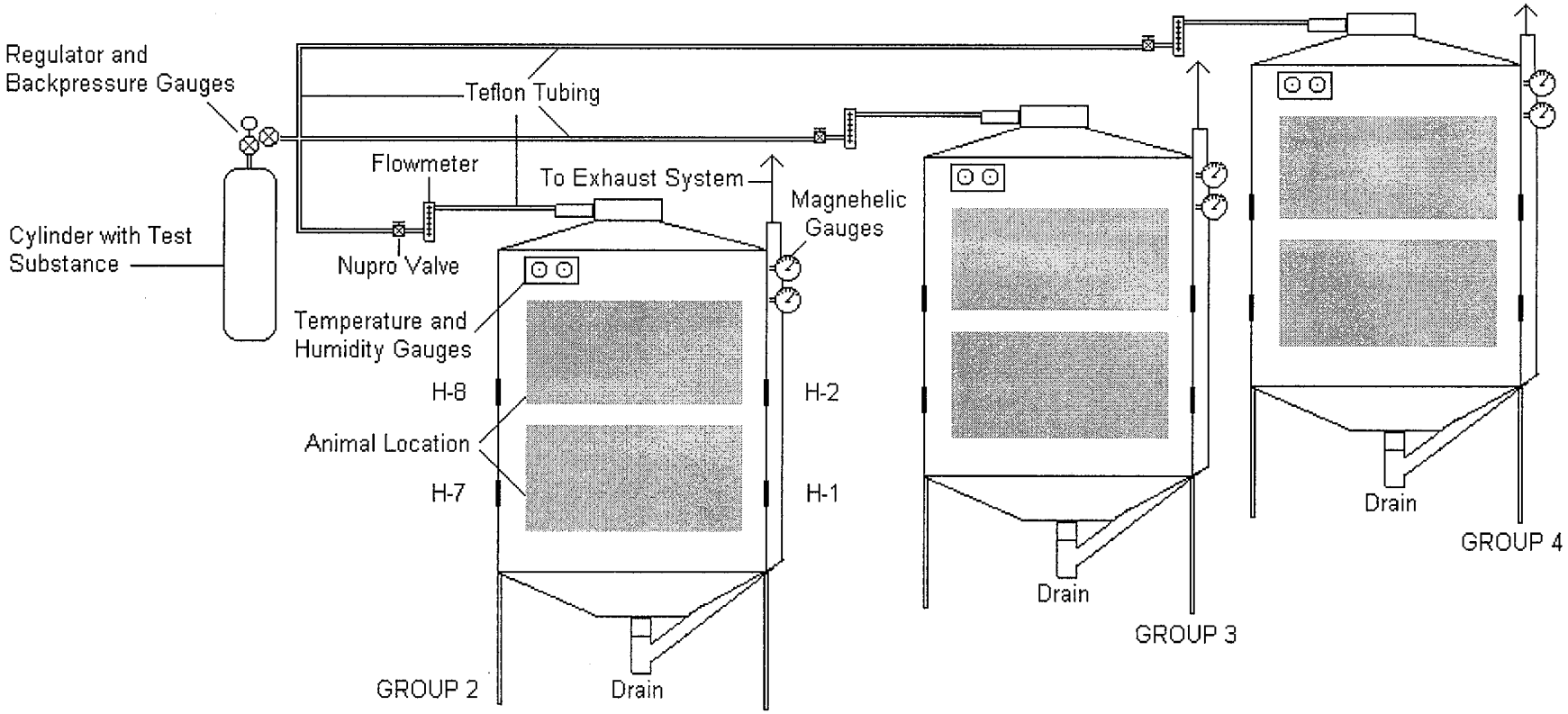
Figure 1
Chamber Generation System
and Whole-Body Exposure Chamber



Note: Animals were individually housed on three levels within the exposure chamber.

Groups 2 - 4	Inhalation Report	Appendix II

Figure 2
Chamber Generation System
and Whole-Body Exposure Chamber



Notes: 1) Sampling Ports H-11 (left-bottom), H-12 (left-top), H-13 (right-bottom) and H-14 (right-top) used for pretest distribution sampling, were located on the back wall of the chambers.
2) Animals were individually housed on three levels within the exposure chamber.

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Table I
Summary of In-Chamber Observations

Exposure Day	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Group 1 – 0 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 900 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 3000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

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Table I
Summary of In-Chamber Observations

Exposure Day	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**
Group 1 – 0 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 900 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 3000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

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Table I
Summary of In-Chamber Observations

Exposure Day	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**
Group 1 – 0 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	a	All	All	All
Group 2 – 900 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	a	All	All	All
Group 3 – 3000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	a	All	All	All
Group 4 – 9000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	a	All	All	All

All = 100% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.
[a]Due to an oversight, observations were not performed on this day.

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Table I
Summary of In-Chamber Observations

Exposure Day	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**	**46**	**47**
Group 1 – 0 ppm												
Within Normal Limits	All	All										
Group 2 – 900 ppm												
Within Normal Limits	All	All	All	All								
Group 3 – 3000 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm												
Within Normal Limits	All	All	All	All								

All = 100% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

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Table II
Chamber Monitoring Results
Preface

Key to Abbreviations

MMAD	=	Mass Median Aerodynamic Diameter
GSD	=	Geometric Standard Deviation
TMC	=	Total Mass Concentration
N (gf)	=	Nominal (by gas flow)
N (wt)	=	Nominal (by weight)

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 ppm (Air Control)

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
0	15-Dec-03	1	0	0.00	0.00	0.00	0.00	0.00				25	56
1	16-Dec-03	2	0	0.00	0.00	0.00	0.00	0.00				25	57
2	17-Dec-03	3	0	0.00	0.00	0.00	0.00	0.00	2.197	2.292	3.98E-03	25	59
3	18-Dec-03	4	0	0.00	0.00	0.00	0.00	0.00				25	57
4	19-Dec-03	5	0	0.00	0.00	0.00	0.00	0.00				25	55
5	20-Dec-03	6	0	0.00	0.00	0.00	0.00	0.00				25	57
6	21-Dec-03	7	0	0.00	0.00	0.00	0.00	0.00				25	56
7	22-Dec-03	8	0	0.00	0.00	0.00	0.00	0.00				25	57
8	23-Dec-03	9	0	0.00	0.00	0.00	0.00	0.00				25	56
9	24-Dec-03	10	0	0.00	0.00	0.00	0.00	0.00	1.958	2.122	1.79E-03	25	59
10	25-Dec-03	11	0	0.00	0.00	0.00	0.00	0.00				25	57
11	26-Dec-03	12	0	0.00	0.00	0.00	0.00	0.00				25	55
12	27-Dec-03	13	0	0.00	0.00	0.00	0.00	0.00				25	56
13	28-Dec-03	14	0	0.00	0.00	0.00	0.00	0.00				25	55
14	29-Dec-03	15	0	0.00	0.00	0.00	0.00	0.00				25	55
15	30-Dec-03	16	0	0.00	0.00	0.00	0.00	0.00				25	54
16	31-Dec-03	17	0	0.00	0.00	0.00	0.00	0.00	0.8689	1.967	2.11E-03	25	55
17	1-Jan-04	18	0	0.00	0.00	0.00	0.00	0.00				25	55
18	2-Jan-04	19	0	0.00	0.00	0.00	0.00	0.00				25	55
19	3-Jan-04	20	0	0.00	0.00	0.00	0.00	0.00				25	55
20	4-Jan-04	21	0	0.00	0.00	0.00	0.00	0.00				25	57
21	5-Jan-04	22	0	0.00	0.00	0.00	0.00	0.00				24	56
22	6-Jan-04	23	0	0.00	0.00	0.00	0.00	0.00				25	54
23	7-Jan-04	24	0	0.00	0.00	0.00	0.00	0.00	1.374	1.761	8.31E-04	25	56
24	8-Jan-04	25	0	0.00	0.00	0.00	0.00	0.00				24	57
25	9-Jan-04	26	0	0.00	0.00	0.00	0.00	0.00				24	56

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 ppm (Air Control)

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
26	10-Jan-04	27	0	0.00	0.00	0.00	0.00	0.00				25	57
27	11-Jan-04	28	0	0.00	0.00	0.00	0.00	0.00				25	57
28	12-Jan-04	29	0	0.00	0.00	0.00	0.00	0.00				25	54
29	13-Jan-04	30	0	0.00	0.00	0.00	0.00	0.00				25	56
30	14-Jan-04	31	0	0.00	0.00	0.00	0.00	0.00	6.332	2.362	4.32E-03	24	55
31	15-Jan-04	32	0	0.00	0.00	0.00	0.00	0.00				23	55
32	16-Jan-04	33	0	0.00	0.00	0.00	0.00	0.00				23	56
33	17-Jan-04	34	0	0.00	0.00	0.00	0.00	0.00				23	56
34	18-Jan-04	35	0	0.00	0.00	0.00	0.00	0.00				23	56
35	19-Jan-04	36	0	0.00	0.00	0.00	0.00	0.00				22	56
36	20-Jan-04	37	0	0.00	0.00	0.00	0.00	0.00				22	56
37	21-Jan-04	38	0	0.00	0.00	0.00	0.00	0.00	2.461	2.259	1.48E-03	21	57
		Mean	**0**		**0.00**				**2.532**	**2.127**	**2.42E-03**	**24.4**	**56.0**
		S.D.	**0**		**0.00**				**1.949**	**0.228**	**1.41E-03**	**1.1**	**1.2**

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 900 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
0	15-Dec-03	1	822	958.5	963	957	957	957				24	55
1	16-Dec-03	2	822	951.5	979	979	959	889				24	57
2	17-Dec-03	3	879	912.3	871	920	938	920	0.9046	2.000	1.99E-03	24	56
3	18-Dec-03	4	885	927.3	927	927	929	926				24	55
4	19-Dec-03	5	885	932.8	932	942	938	919				24	55
5	20-Dec-03	6	885	911.0	942	931	876	895				24	57
6	21-Dec-03	7	885	904.0	903	895	903	915				24	54
7	22-Dec-03	8	885	913.5	910	918	924	902				24	54
8	23-Dec-03	9	885	942.5	959	927	937	947				24	54
9	24-Dec-03	10	885	905.3	916	892	897	916	2.393	2.079	1.62E-03	24	57
10	25-Dec-03	11	885	922.0	958	924	929	877				24	56
11	26-Dec-03	12	885	919.3	938	908	910	921				24	53
12	27-Dec-03	13	885	935.3	918	940	957	926				24	55
13	28-Dec-03	14	885	917.0	903	930	904	931				24	54
14	29-Dec-03	15	885	915.8	888	922	922	931				24	53
15	30-Dec-03	16	885	916.5	910	930	897	929				24	53
16	31-Dec-03	17	885	927.5	921	924	927	938	0.8323	1.951	1.82E-03	24	54
17	1-Jan-04	18	885	929.0	941	897	910	968				24	53
18	2-Jan-04	19	885	928.5	929	900	938	947				24	55
19	3-Jan-04	20	885	953.8	953	953	957	952				24	54
20	4-Jan-04	21	885	940.0	974	925	945	916				24	55
21	5-Jan-04	22	885	923.3	926	906	920	941				24	55
22	6-Jan-04	23	885	930.8	951	904	938	930				24	54
23	7-Jan-04	24	885	928.3	938	926	951	898	4.803	2.147	2.59E-03	24	54
24	8-Jan-04	25	885	988.0	985	982	985	1000				24	56
25	9-Jan-04	26	885	938.8	969	908	940	938				24	55

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 900 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Mean Humidity (%)
26	10-Jan-04	27	885	913.8	921	899	903	932				24	55
27	11-Jan-04	28	885	945.3	938	932	945	966				24	55
28	12-Jan-04	29	885	953.8	978	929	950	958				24	54
29	13-Jan-04	30	885	935.3	967	926	926	922				24	53
30	14-Jan-04	31	885	942.8	938	953	954	926	3.482	2.008	3.94E-03	23	55
31	15-Jan-04	32	885	917.0	932	921	909	906				22	55
32	16-Jan-04	33	885	920.3	940	913	918	910				22	56
33	17-Jan-04	34	885	962.8	951	977	945	978				22	55
34	18-Jan-04	35	885	959.5	982	925	956	975				22	56
35	19-Jan-04	36	885	892.8	900	888	883	900				21	56
36	20-Jan-04	37	885	963.0	935	966	963	988				22	55
37	21-Jan-04	38	885	926.5	930	910	942	924	2.503	1.948	1.39E-03	21	56
38	22-Jan-04	39	885	902.3	894	977	867	871				21	55
39	23-Jan-04	40	885	894.3	852	882	957	886				21	56
		Mean	**882**		**930.0**				**2.486**	**2.022**	**2.23E-03**	**23.4**	**54.9**
		S.D.	**14**		**27.8**				**1.523**	**0.078**	**9.33E-04**	**1.1**	**1.1**

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 3000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
0	15-Dec-03	1	2950	3053	3050	3130	3030	3000				24	57
1	16-Dec-03	2	2950	2995	3040	3020	2950	2970				24	58
2	17-Dec-03	3	2950	3105	3090	3130	3070	3130	1.862	2.944	3.20E-03	24	58
3	18-Dec-03	4	2950	3140	3210	3120	3100	3130				24	58
4	19-Dec-03	5	2950	3130	3120	3130	3180	3090				24	56
5	20-Dec-03	6	2950	3075	3150	3000	3060	3090				24	59
6	21-Dec-03	7	2950	2953	2890	3020	2930	2970				24	58
7	22-Dec-03	8	2950	3130	3300	3050	2990	3180				24	55
8	23-Dec-03	9	2950	3225	3190	3260	3210	3240				24	56
9	24-Dec-03	10	2950	3080	3050	3070	3100	3100	1.386	1.786	1.07E-03	24	59
10	25-Dec-03	11	2950	3175	3240	3140	3180	3140				24	58
11	26-Dec-03	12	2950	3095	3170	3070	3110	3030				24	57
12	27-Dec-03	13	2950	3130	3110	3100	3150	3160				24	57
13	28-Dec-03	14	2950	3075	3010	3030	3100	3160				24	57
14	29-Dec-03	15	2950	3070	3020	3060	3030	3170				24	55
15	30-Dec-03	16	2950	3098	3090	2970	3180	3150				24	55
16	31-Dec-03	17	2950	3065	3080	2960	3150	3070	0.8167	1.814	2.11E-03	24	56
17	1-Jan-04	18	2950	3080	2970	3050	3130	3170				24	57
18	2-Jan-04	19	2950	3078	2940	3060	3180	3130				24	56
19	3-Jan-04	20	2950	3203	3220	3160	3240	3190				24	57
20	4-Jan-04	21	2950	3205	3270	3190	3180	3180				24	57
21	5-Jan-04	22	2950	3110	3120	3080	3040	3200				24	57
22	6-Jan-04	23	2950	3053	2970	2950	3140	3150				24	56
23	7-Jan-04	24	2950	3050	2890	3100	3120	3090	5.097	2.023	4.77E-03	24	58
24	8-Jan-04	25	2950	3220	3130	3230	3240	3280				24	57
25	9-Jan-04	26	2950	3185	3270	3180	3090	3200				24	59
26	10-Jan-04	27	2950	3033	3010	3010	3070	3040				24	57

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 3000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)					MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
27	11-Jan-04	28	2950	3110	3050	3050	3150	3190					25	56
28	12-Jan-04	29	2950	3113	3010	3110	3150	3180					24	56
29	13-Jan-04	30	2950	3198	3240	3150	3120	3280					24	56
30	14-Jan-04	31	2950	3133	3050	3100	3190	3190		1.217	1.672	1.33E-03	23	57
31	15-Jan-04	32	2950	3108	3130	3170	3090	3040					22	55
32	16-Jan-04	33	2950	3140	3160	3010	3180	3210					22	56
33	17-Jan-04	34	2950	3240	3250	3210	3260	3240					22	56
34	18-Jan-04	35	2950	3188	3010	3210	3270	3260					22	56
35	19-Jan-04	36	2950	3148	3250	3130	3130	3080					22	55
36	20-Jan-04	37	2950	3195	3130	3200	3210	3240					22	56
37	21-Jan-04	38	2950	3135	3080	3080	3220	3160		2.266	2.025	1.12E-03	22	56
38	22-Jan-04	39	2950	3110	3140	3120	3120	3060					21	56
39	23-Jan-04	40	2950	3118	3030	3060	3230	3150					21	57
40	24-Jan-04	41	2950	3120	3140	3050	3130	3160					21	56
41	25-Jan-04	42	2950	3095	3080	3080	3100	3120					21	56
42	26-Jan-04	43	2950	3175	3180	3130	3210	3180					21	55
43	27-Jan-04	44	2950	3088	3160	3080	3080	3030					21	56
44	28-Jan-04	45	2950	3173	3210	3160	3130	3190		1.348	1.924	1.24E-03	21	55
45	29-Jan-04	46	2950	3180	3220	3200	3150	3150					21	56
46	30-Jan-04	47	2950	3108	3080	3100	3120	3130					21	55
47	31-Jan-04	48	2950	3170	3220	3070	3210	3180					21	56
		Mean	**2950**		**3122**					**1.999**	**2.027**	**2.12E-03**	**23.1**	**56.5**
		S.D.	**0**		**83**					**1.443**	**0.424**	**1.40E-03**	**1.3**	**1.1**

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 9000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
0	15-Dec-03	1	8730	9173	9220	9350	9190	8930				24	55
1	16-Dec-03	2	8730	9280	9380	9060	9210	9470				24	55
2	17-Dec-03	3	8730	9090	9010	9010	9190	9150	0.8498	2.086	1.89E-03	24	56
3	18-Dec-03	4	8730	9415	9900	9180	9190	9390				24	56
4	19-Dec-03	5	8730	8980	8920	8950	8980	9070				24	55
5	20-Dec-03	6	8730	9153	8860	9010	9500	9240				24	56
6	21-Dec-03	7	8730	9030	8840	9100	9090	9090				24	56
7	22-Dec-03	8	8730	9040	9010	9120	9190	8840				24	55
8	23-Dec-03	9	8730	9180	9190	9070	9130	9330				24	54
9	24-Dec-03	10	8730	9185	9060	9090	9120	9470	2.007	2.133	1.40E-03	24	56
10	25-Dec-03	11	8730	8995	9210	8970	8830	8970				24	56
11	26-Dec-03	12	8730	9270	9350	9040	9300	9390				24	55
12	27-Dec-03	13	8730	9263	9210	9210	9450	9180				24	56
13	28-Dec-03	14	8730	9213	9090	9190	9190	9380				24	55
14	29-Dec-03	15	8730	9280	9090	9100	9480	9450				24	54
15	30-Dec-03	16	8730	9223	9250	9040	9210	9390				24	55
16	31-Dec-03	17	8730	9338	9210	9450	9300	9390	0.8539	2.002	2.08E-03	24	52
17	1-Jan-04	18	8730	9415	9210	9220	9440	9790				24	53
18	2-Jan-04	19	8730	8945	9100	8810	9060	8810				24	53
19	3-Jan-04	20	8730	9040	9000	8980	9090	9090				24	54
20	4-Jan-04	21	8730	9003	9250	9040	8890	8830				25	54
21	5-Jan-04	22	8730	8905	8770	8770	8900	9180				24	53
22	6-Jan-04	23	8730	8963	8830	9000	8920	9100				24	54
23	7-Jan-04	24	8730	8975	8930	8780	9090	9100	1.917	1.914	9.97E-04	24	54
24	8-Jan-04	25	8730	9573	9520	9470	9650	9650				24	55
25	9-Jan-04	26	8730	9233	9580	9150	9040	9160				24	55

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 9000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
26	10-Jan-04	27	8730	9165	9060	9250	9250	9100				24	55
27	11-Jan-04	28	8730	9260	9070	9220	9390	9360				24	56
28	12-Jan-04	29	8730	9183	8970	9150	9250	9361				24	54
29	13-Jan-04	30	8730	9093	8980	9120	9150	9120				24	54
30	14-Jan-04	31	8730	9123	9010	9160	9160	9160	2.127	2.331	1.89E-03	23	53
31	15-Jan-04	32	8730	8985	8770	8970	9040	9160				22	54
32	16-Jan-04	33	8730	8913	8800	8950	8870	9030				22	54
33	17-Jan-04	34	8730	9055	8980	9100	9100	9040				22	55
34	18-Jan-04	35	8730	8993	8970	8930	9090	8980				22	54
35	19-Jan-04	36	8730	9155	9130	9210	9150	9130				22	53
36	20-Jan-04	37	8730	9133	8930	9190	9220	9190				22	54
37	21-Jan-04	38	8730	9348	9240	9560	9180	9410	1.490	1.717	8.83E-04	21	54
38	22-Jan-04	39	8730	9160	9190	9090	9120	9240				21	54
39	23-Jan-04	40	8730	9183	9190	9180	9180	9180				21	55
		Mean	**8730**		**9148**				**1.541**	**2.031**	**1.52E-03**	**23.5**	**54.5**
		S.D.	**0**		**201**				**0.575**	**0.208**	**5.06E-04**	**1.0**	**1.0**

Exposures Summary						
	Nominal by gas flow (ppm)					
Date	Group 2	Group 3	Group 4	Total Nominal by gas flow (ppm)	Total Nominal by weight (ppm)	N(gf):N(wt)
15-Dec-03	822	2950	8730	12502	11300	1.11
16-Dec-03	822	2950	8730	12502	11300	1.11
17-Dec-03	879	2950	8730	12559	12400	1.01
18-Dec-03	885	2950	8730	12565	11200	1.12
19-Dec-03	885	2950	8730	12565	12400	1.01
20-Dec-03	885	2950	8730	12565	13500	0.93
21-Dec-03	885	2950	8730	12565	13500	0.93
22-Dec-03	885	2950	8730	12565	13500	0.93
23-Dec-03	885	2950	8730	12565	12400	1.01
24-Dec-03	885	2950	8730	12565	12400	1.01
25-Dec-03	885	2950	8730	12565	13500	0.93
26-Dec-03	885	2950	8730	12565	13500	0.93
27-Dec-03	885	2950	8730	12565	12400	1.01
28-Dec-03	885	2950	8730	12565	13500	0.93
29-Dec-03	885	2950	8730	12565	12400	1.01
30-Dec-03	885	2950	8730	12565	12400	1.01
31-Dec-03	885	2950	8730	12565	12400	1.01
1-Jan-04	885	2950	8730	12565	13500	0.93
2-Jan-04	885	2950	8730	12565	13500	0.93
3-Jan-04	885	2950	8730	12565	11200	1.12
4-Jan-04	885	2950	8730	12565	13500	0.93
5-Jan-04	885	2950	8730	12565	12400	1.01
6-Jan-04	885	2950	8730	12565	13500	0.93
7-Jan-04	885	2950	8730	12565	13500	0.93
8-Jan-04	885	2950	8730	12565	11200	1.12
9-Jan-04	885	2950	8730	12565	12400	1.01
10-Jan-04	885	2950	8730	12565	12400	1.01
11-Jan-04	885	2950	8730	12565	12400	1.01

Exposures Summary						
	Nominal by gas flow (ppm)					
Date	Group 2	Group 3	Group 4	Total Nominal by gas flow (ppm)	Total Nominal by weight (ppm)	N(gf):N(wt)
12-Jan-04	885	2950	8730	12565	12400	1.01
13-Jan-04	885	2950	8730	12565	13500	0.93
14-Jan-04	885	2950	8730	12565	13500	0.93
15-Jan-04	885	2950	8730	12565	12400	1.01
16-Jan-04	885	2950	8730	12565	12400	1.01
17-Jan-04	885	2950	8730	12565	12400	1.01
18-Jan-04	885	2950	8730	12565	12400	1.01
19-Jan-04	885	2950	8730	12565	13500	0.93
20-Jan-04	885	2950	8730	12565	12400	1.01
21-Jan-04	885	2950	8730	12565	13500	0.93
22-Jan-04	885	2950	8730	12565	11200	1.12
23-Jan-04	885	2950	8730	12565	13500	0.93
24-Jan-04	-	2950	-	2950	3400	0.87
25-Jan-04	-	2950	-	2950	3400	0.87
26-Jan-04	-	2950	-	2950	3400	0.87
27-Jan-04	-	2950	-	2950	3400	0.87
28-Jan-04	-	2950	-	2950	2270	1.30
29-Jan-04	-	2950	-	2950	2270	1.30
30-Jan-04	-	2950	-	2950	2270	1.30
31-Jan-04	-	2950	-	2950	3400	0.87
					Mean:	1.00

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Table III
Equipment List

Exposure Chamber
1000 Liter glass and stainless steel chamber (Wahmann)

Compound Reservoir
Isobutane Cylinder (MG Industries)

Flowmeter
Dwyer®, size 0-20 Lpm (Dwyer® Instruments)
Top Trak™ Mass Flow Meter, sizes 0 – 1, Model 821-1 and 0 -10 Lpm, Model 822-13-001-PVI-VI (Sierra Instruments)

Pressure/Vacuum Gauges
Backpressure gauge (MG Industries), P/N 10206 and 10201
GAST® vacuum gauge

Chamber Air Flow
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with a Side Trak™ III, equipped with a Digital Meter, Model 831-N2 (Sierra Instruments, Inc.)

Chamber Static Pressure
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with Dwyer® Mark II Manometer, Model 25 (Dwyer® Instruments, Inc.)

Regulators
MG Industries Series 300

Metering Valve
Metering Valve, Model 316 Series (Whitey)

Vacuum Pumps
Thomas Industries Inc., Model 707CM50
Closed-loop pump

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Table III
Equipment List

Tubing
Clear plastic, sizes ¼", ½" (Norton, Baxter)
Plastic, size 1/8" (Tygon)
½" stainless steel
Teflon®, size ¼ "
Plastic "T"
Stainless steel cross

Air Analyzer
MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter, Model No. 22-195
Gas-tight syringe, size 0-25 mL, plastic, No. 1025 (Hamilton)
Balston® Microfibre™ Disposable Filter Unit was attached in-line
Syringe, size 0 - 10 mL, plastic (Precision)
Syringe, size 0 - 100 mL, plastic, No. 1100 (Hamilton)

Particle Sizer
TSI Aerodynamic Particle Sizer, Model 331001, and a DELL computer, Model 486P/25, equipped with an Epson LQ-5707 printer, Model P630B

Environmental Monitoring
VWR Temperature and Humidity Gauge, tested prestudy with a Big Digit Traceable Hygrometer/Thermometer
Digital Sound Meter 840029 (SPER Scientific & Quantum Instruments Photo Meter 1)

Balance
Pelouze, No. 4040

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Table IV
Chamber Distribution Records

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
2 (900 ppm)	4 December 2003	H-1	945	1.00
		H-2	945	1.00
		H-7	951	1.01
		H-1	899	1.00
		H-8	904	1.01
	5 December 2003	H-1	911	1.00
		H-14	926	1.02
		H-13	908	1.00
		H-1	902	1.00
		H-12	884	0.98
		H-11	899	1.00
3 (3000 ppm)	4 December 2003	H-1	2970	1.00
		H-2	3020	1.02
		H-7	2890	0.97
		H-1	3050	1.00
		H-8	2860	0.94
	5 December 2003	H-1	2980	1.00
		H-14	3060	1.03
		H-13	2970	1.00
		H-1	3010	1.00
		H-12	3100	1.03
		H-11	2970	0.99
4 (9000 ppm)	4 December 2003	H-1	9030	1.00
		H-2	8870	0.98
		H-7	9070	1.00
		H-1	8780	1.00
		H-8	9130	1.04
	5 December 2003	H-1	8740	1.00
		H-14	9030	1.03
		H-13	9190	1.05
		H-1	8830	1.00
		H-12	9320	1.06
		H-11	9130	1.03

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Table V
Miran Calibration

Methodology for Isobutane

Settings: The instrument settings for the Miran 07 unit are summarized below:

wavelength, microns	10.9
pathlength, dial setting	9.65
slit width, mm	1
range, absorbance	1
response, seconds	40
gain	High
chart speed, cm/min	1
chart volts	1

Calibrations: The Miran® was turned on and allowed to warm up for approximately 10 minutes. The cell was flushed with room air for approximately one minute. The loop was closed, the unit was zeroed and the calibration series was performed as shown below. The resultant data were plotted to obtain a calibration curve. Each observer used a separate syringe for calibration.

Injection Volume (µL)	Calculated Concentration[1] (ppm)	Absorbance		
		Operator 1 (volts)	Operator 2 (volts)	Average (volts)
4000	709	0.0592	0.0618	0.0605
5000	887	0.0737	0.0739	0.0738
17000	3014	0.2444	0.2367	0.2406
51000	9043	0.688	0.676	0.682
61000	10816	0.800	0.784	0.792

[1]Calculated Conc. (ppm) = $\frac{\text{Injection volume (µL)}}{\text{5.64 L (Volume of Miran cell)}}$

	Inhalation Report	Appendix II

Table V
Miran Calibration

Calibration Checks: A three-point calibration check of the Miran® was performed for each exposure prior to sampling the chambers. The parameters are shown below:

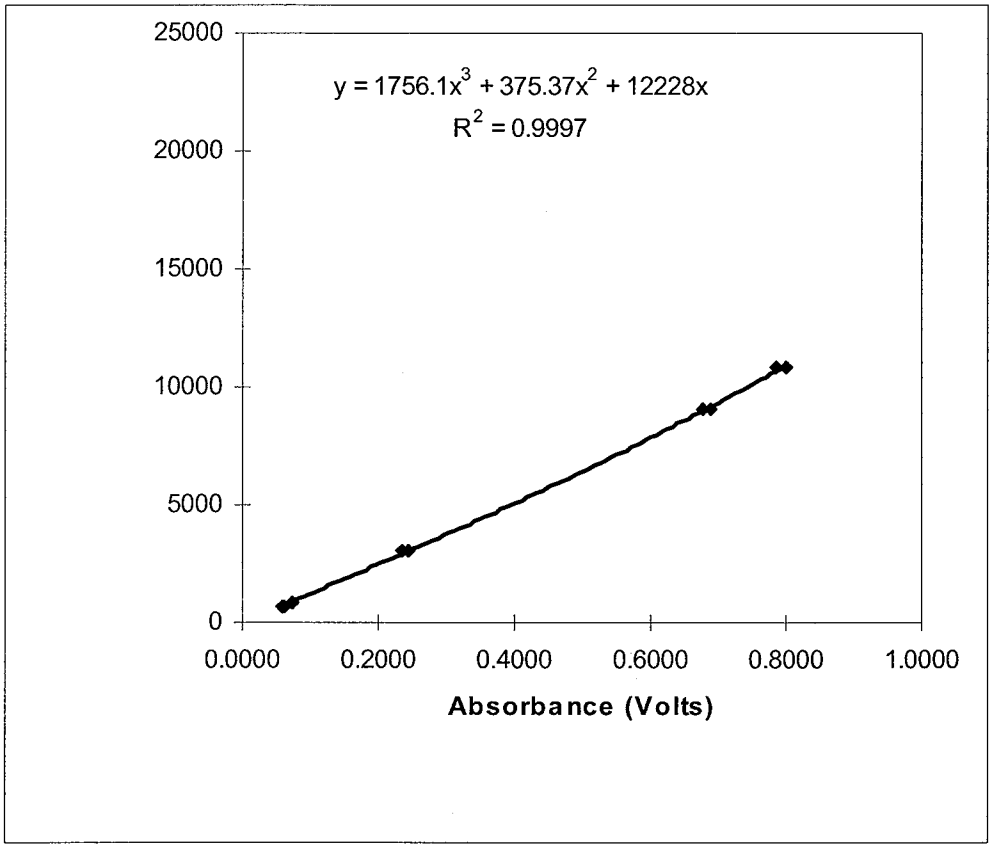
Injection Volume (µL)	Calculated Concentration (ppm)	Expected Absorbance Reading (volts)	Acceptable Absorbance Range (volts)
5000	887	0.0738	0.0627 – 0.0849
17000	3014	0.2406	0.2045 – 0.2767
51000	9043	0.682	0.580 – 0.784

The absorbance was recorded after each injection. The absorbance was considered satisfactory if it was within 15% of the original calibration series. If any of the absorbance values fell outside the 15% range, the injection was rechecked as follows. The volume for the value that was out of range was reinjected twice. The closer pair of the three injections were averaged and the results were compared to the original curve. If the average of the pair was within the 15% range, the original was accepted. If the value of the average was outside the 15% range, the Study Director decided if a new graph was to be prepared.

	Inhalation Report	Appendix II

Table V
Miran Calibration

Calibration Curve for Isobutane



		Appendix II

Table VI
Testing Room and Chambers Environmental Monitoring

Interval	Location	Test Substance (mg/m^3)[a]	Light (Ft Candles)	Noise (dB)	Oxygen (%)	Particle Sizing (mg/m^3)[b]
Pretest	Room 813 Front	0	38.6	67.5	NM	NM
	Group 1	0	NM	NM	21	8.85×10^{-4}
	Group 2	905	NM	NM	21	9.20×10^{-4}
	Group 3	2990	NM	NM	21	9.73×10^{-4}
	Group 4	8750	NM	NM	21	1.14×10^{-3}
Week 1	Room 813	0	36.1	64.0	NM	
	Group 1	0	NM	NM	21	
	Group 2	952	NM	NM	21	
	Group 3	2300	NM	NM	21	
	Group 4	9280	NM	NM	21	
Week 3	Room 813	0	37.0	62.5	NM	
	Group 1	0	NM	NM	21	
	Group 2	917	NM	NM	21	
	Group 3	3100	NM	NM	21	
	Group 4	9220	NM	NM	21	
Week 6	Room 813	0	36.6	65.1	NM	
	Group 1	0	NM	NM	21	
	Group 2	893	NM	NM	21	
	Group 3	3150	NM	NM	21	
	Group 4	9160	NM	NM	21	

NM = Not Measured

[a]Values presented are the daily average for the chamber samples and a single time point for the room air samples.
[b]Pretest results presented. For on-test results, see CMR (Table II).

	Analytical Report	Appendix JJ

STUDY TITLE

Analytical Report For:

Isobutane:
Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

AUTHOR

[redacted]

REPORT DATE

9 April 2010

STUDY NUMBER

03-4244

	Analytical Report	Appendix JJ

SIGNATURES

Written by: [redacted]
Formulation Chemistry Services
07 Apr 10
Date

Reviewed by: [redacted]
Formulation Chemistry Services
9 Apr 10
Date

Approved by: [redacted]
Analytical Services
07 Apr 10
Date

	Analytical Report	Appendix JJ

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	Analytical Report	Appendix JJ

1. Summary

The test substance and the analytical standard (Isobutane) were analyzed ("pre-study" and "post-study") to determine the purity and stability of the test substance by comparison to the analytical standard. The analytical method was validated at Huntingdon Life Sciences (HLS). The analytical method involved gas bag sampling of the test substance and the analytical standard and quantification using Gas Chromatography with Flame Ionization Detection (FID).

2. Experimental Procedures

The analytical method (HLS-013-03R1) was validated by Formulation Chemistry at HLS. Details of the analytical method and the validation are maintained in this study file.

Gas bag sampling of the test substance and the analytical standard was performed in the Inhalation Department at HLS. The test substance and the analytical standard were analyzed using a Gas Chromatograph equipped with a HP Plot Q (30 m x 0.32 mm, 20 µm) column and Flame Ionization Detector (FID) to determine the purity of Isobutane test substance. HP 3396A integrator was used for data collection and Excel was used for processing the data.

Date of sample analysis is listed as follows:

Interval	Date Analyzed
"Pre-Study" Characterization	28 May 03
"Post-Study" Characterization	06 Feb 04

3. Results and Discussion

The test substance and analytical standard (Isobutane) were analyzed prior to the initiation of the study and after completion of the study to determine the purity and stability of the test substance. The results of the characterization are presented in Table I. A typical chromatogram of Isobutane standard is presented in Figure I. A typical chromatogram of Isobutane test substance is presented in Figure II.

	Analytical Report	Appendix JJ

Table I: Isobutane Characterization ("Pre-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % of other Impurities	Area % of Isobutane Standard	Mean Area % of Isobutane Standard
Isobutane Standard	0.00	0.53	0.00	0.02	99.45	99.51
Isobutane Standard	0.00	0.43	0.01	0.01	99.55	
Isobutane Standard	0.00	0.47	0.00	0.01	99.53	

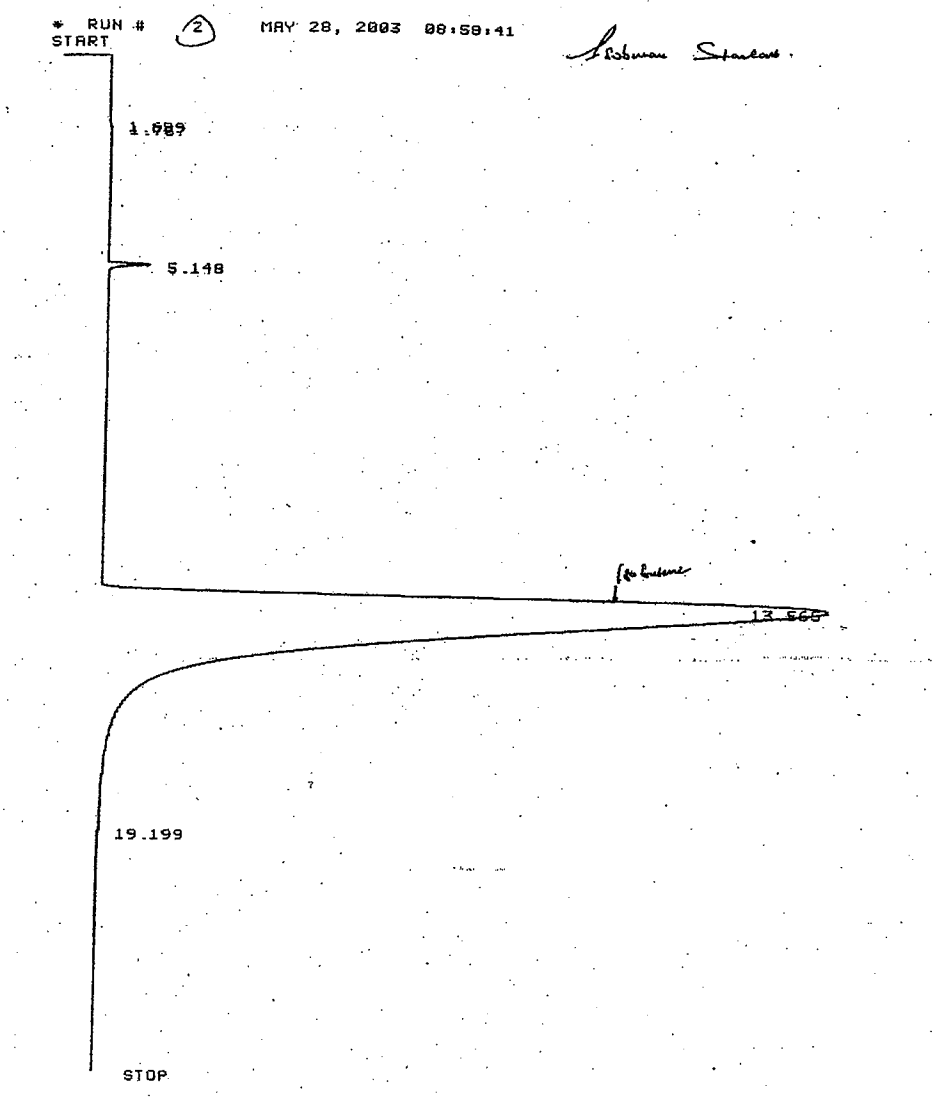
Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % Other Impurities	Area % of Isobutane Substance	Mean Area % of Isobutane Test Substance
Isobutane Test Substance	0.00	0.06	0.10	0.01	99.83	99.84
Isobutane Test Substance	0.01	0.07	0.11	0.01	99.81	
Isobutane Test Substance	0.00	0.06	0.06	0.01	99.87	

Table II: Isobutane Characterization ("Post-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % of other Impurities	Area % of Isobutane Standard	Mean Area % of Isobutane Standard
Isobutane Standard	0.00	0.46	0.03	0.01	99.51	99.50
Isobutane Standard	0.00	0.51	0.00	0.01	99.48	
Isobutane Standard	0.00	0.48	0.00	0.01	99.51	

Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % Other Impurities	Area % of Isobutane Substance	Mean Area % of Isobutane Test Substance
Isobutane Test Substance	0.00	0.41	0.17	0.01	99.41	99.53
Isobutane Test Substance	0.00	0.26	0.13	0.00	99.61	
Isobutane Test Substance	0.00	0.29	0.14	0.00	99.56	

Figure I. A Typical Gas Chromatogram of Isobutane Analytical Standard



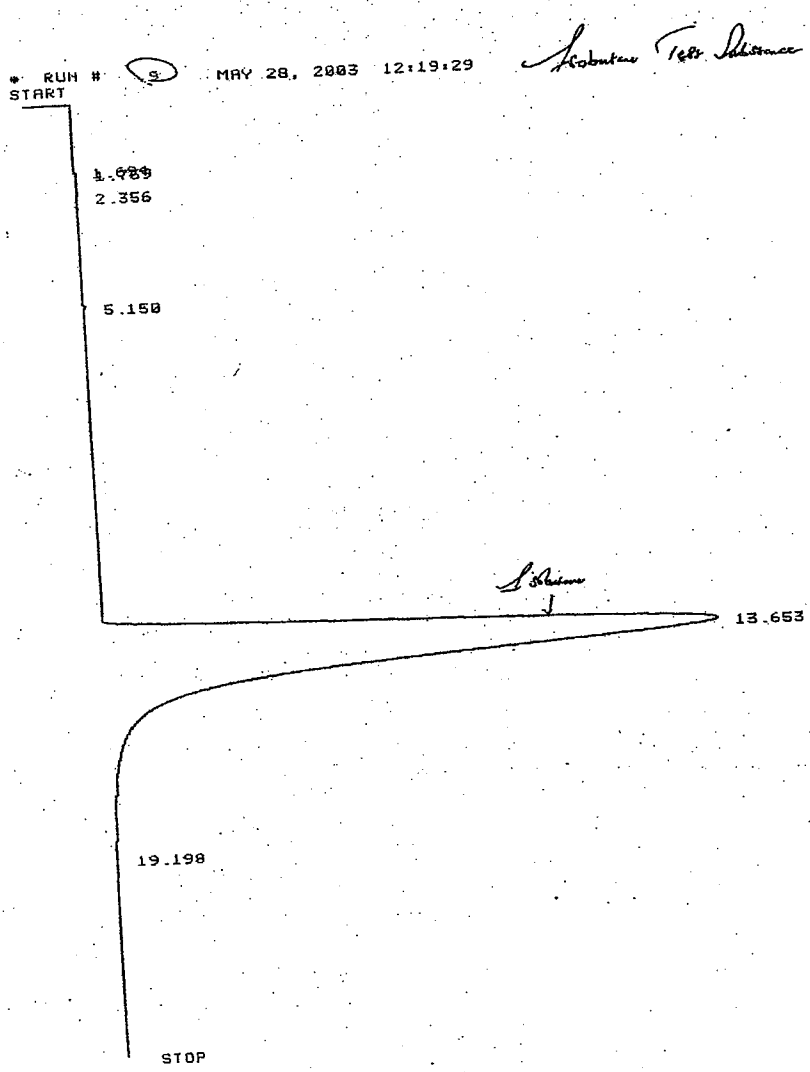
RUN# 2 MAY 28, 2003 08:58:41

AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.689	212	PB	.025	.00244
1.757	287	PB	.017	.00330
5.148	37515	PB	.083	.43199
13.565	8645011	PB	1.131	99.54944
19.199	1113	BP	.096	.01282

Response (mV) vs Time (minutes)

Figure II. A Typical Gas Chromatogram of Isobutane Test Substance



RUN# 9 MAY 28, 2003 12:19:29

AREA% RT	AREA	TYPE	WIDTH	AREA%
1.694	199	PU	.827	.00281
1.759	463	UB	.017	.00653
2.356	297	PB	.019	.00419
5.150	4196	PB	.082	.05919
13.653	7079331	PB	1.092	99.86563
19.198	4370	BP	.269	.06165

TOTAL AREA=7088858
AREA FACTOR=1.0000E+00

Response (mV) vs Time (minutes)

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This is an abridged version of text and tables from Study No. H-34, 00-14500 as amended on 24 November 2008.

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	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

1. INTRODUCTION

This study was designed to train technicians to perform the functional observational battery evaluations for rats and to provide evidence, by use of test materials with known neurological effects, that the observational methods used at Huntingdon Life Sciences, Princeton Research Center, are capable of detecting major neurotoxic endpoints. In addition, these studies were used to demonstrate interobserver reliability for neurobehavioral assessments by evaluating consistency of observations performed by different technicians.

2. MATERIALS AND METHODS

2.1. REGULATORY REFERENCES

2.1.1. TEST GUIDELINES

This study was designed to provide positive control data for neurotoxicity screening studies in accord with the US EPA Health Effects Test Guidelines, OPPTS 870.6200 Neurotoxicity Screening Battery, August 1998.

2.1.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Part 160 of 40 CFR (EPA/FIFRA Good Laboratory Practice Standards) with the exception that assays to verify concentration, stability and homogeneity of the test articles in carriers were not performed.

2.1.3. ANIMAL WELFARE ACT COMPLIANCE

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.

2.1.4. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.2. STUDY MANAGEMENT

2.2.1. SPONSOR

Huntingdon Life Sciences
P.O. Box 2360
Mettlers Road
East Millstone, New Jersey 08875-2360

2.2.2. TESTING FACILITY

Huntingdon Life Sciences
P.O. Box 2360
Mettlers Road
East Millstone, New Jersey 08875-2360

2.2.3. STUDY DIRECTOR

[redacted]

2.3. EXPERIMENTAL DESIGN

2.3.1. TRAINING SESSIONS

Training consisted of two parts. In the first part, the technicians were required to view a training video for a functional observational battery (United States Environmental Protection Agency/American Industrial Health Council Training Video and Reference Manual for an FOB, 1996). The second part consisted of observations of animals treated with chemicals known to produce neurological effects as indicated below:

Group	Route of Admin.	Test Article	Daily Doses[a]			Number of Animals			
						Initial		Functional Observational Battery	
			Dose (mg/kg)	Volume (mL/kg)	Conc. (mg/mL)	M	F	M	F
1[b]	i.p.	Control	-	5	-	3	-	3	-
2	i.p.	Chlorpromazine	4	5	0.8	3	-	3	-
3	i.p.	Amphetamine	2	5	0.4	3	-	3	-
4	i.p.	Amphetamine	8	5	1.6	-	3	-	3
5	i.p.	Physostigmine	1	5	0.2	-	3	-	3
6	Oral	Ethanol	3000	10	300	-	3	-	3

[a]Represent doses of test article as supplied; i.e., no correction for percent active ingredient was made.
[b]Control animals received 0.9% saline.
M = Male; F = Female; i.p. = intraperitoneal; Oral, via gastric intubation;
mg/kg = milligrams of test article per kilogram of body weight

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.3.2. FOB PERFORMANCE EVALUATIONS

After completion of the training session, each technician was required to perform a functional observational battery evaluation in which the technician was blinded as to the treatment group. Each technician evaluated 20 males or 20 females (5 animals/group).

Group	Route of Admin.	Test Article	Daily Doses[a]			Number of Animals			
						Initial		Functional Observational Battery	
			Dose (mg/kg)	Volume (mL/kg)	Conc. (mg/mL)	M	F	M	F
1[b]	i.p.	Control	-	5	-	5	5	5	5
2	i.p.	Chlorpromazine	4	5	0.8	5	5	5	5
3	i.p.	Amphetamine	2	5	0.4	5	5	5	5
4	s.c.[c]	Physostigmine	1	5	0.2	5	5	5	5

[a]Represent doses of test article as supplied; i.e., no correction for percent active ingredient was made.
[b]Control animals received 0.9% saline.
[c]Intraperitoneal injections were administered for the Training Sessions and for the Performance Evaluations conducted by Observer 8; subcutaneous injections were administered for the Performance Evaluations conducted by all other observers.

M = Male; F = Female; i.p. = intraperitoneal; s.c. = subcutaneous injection
mg/kg = milligrams of test article per kilogram of body weight

2.4. STUDY DATES

2.4.1. STUDY INITIATION

15 February 2000 (Date Study Director signed the Protocol)

2.4.2. DATE OF ANIMAL RECEIPT

3 March 2000

2.4.3. DOSING INITIATION

Training Session: 23 March 2000 (Experimental Start Date)
Performance Evaluations: 26 April 2000

2.4.4. DOSING TERMINATION

6 July 2000

2.4.5. EXPERIMENTAL TERMINATION

1 August 2001

2.4.6. STUDY COMPLETION

1 August 2003 (Date Study Director signed the Final Report)

2.5. TEST ARTICLES

2.5.1. CHLORPROMAZINE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

Lot Number

48H1403

Purity

98%

Description

White/white with a yellow cast powder

Date Received

1 December 1999

Expiration Date

April 2001

Storage

Room temperature, protected from light

2.5.2. D-AMPHETAMINE SULFATE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

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Lot Number

69H1239

Purity

Assume 100%

Description

Powder

Date Received

7 January 2000

Expiration Date

June 2001

Storage

Room temperature

2.5.3. PHYSOSTIGMINE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

Lot Number

48H1126

Purity

Assume 100%

Description

Powder

Date Received

1 December 1999

Expiration Date

1 December 2004

Storage

Room temperature, protected from light

2.5.4. ETHANOL

Manufacturer

Spectrum Chemical Manufacturing Corporation
Gardena, California 90248

Lot Number

MI0504

Purity

100%

Description

Clear liquid

Date Received

16 March 1998

Expiration Date

March 2003

Storage

Room temperature

2.5.5. ANALYSIS

Documentation of the identity, strength, purity, composition and stability; and synthesis, fabrication, and/or derivation of the test articles was the responsibility of the Manufacturers.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.5.6. ARCHIVAL SAMPLE

Samples from the lots of Chlorpromazine, D-Amphetamine Sulfate, Physostigmine and Ethanol are stored in the Archives of the Testing Facility under conditions specified for test article storage.

2.5.7. DISPOSITION

The unused portions of Chlorpromazine, D-Amphetamine Sulfate and Physostigmine were submitted to the Archives of the Testing Facility as archival samples. The remaining portions of Ethanol were retained by the Testing Facility for possible future use.

2.6. CONTROL ARTICLE

0.9% Saline

2.6.1. MANUFACTURER

Baxter Healthcare Corporation
Deerfield, Illinois 60015

2.6.2. LOT NUMBER

G949941

2.6.3. PURITY

100%

2.6.4. DESCRIPTION

Clear, colorless liquid

2.6.5. DATE RECEIVED

5 November 1999

2.6.6. EXPIRATION DATE

October 2000

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.6.7. STORAGE

Room Temperature

2.6.8. ANALYSIS

Documentation of the identity, strength, purity, composition and stability; and synthesis, fabrication, and/or derivation of the control article was the responsibility of the Manufacturer.

2.6.9. ARCHIVAL SAMPLE

A sample from each lot of control article is stored in the Archives of the Testing Facility under conditions specified for control article storage.

2.6.10. DISPOSITION

The unused portion of the control article will be retained for use in future studies. Any empty control article containers will be discarded by the Testing Facility following completion of the study.

2.7. TEST ANIMALS

2.7.1. SPECIES

Albino Rats (Outbred) VAF/Plus®
CD® (Sprague-Dawley derived) [Crl:CD® (SD)IGS BR]

2.7.2. SUPPLIER

Charles River Laboratories
Kingston, New York 12484

2.7.3. JUSTIFICATION FOR ANIMAL SELECTION

The rat is the animal model recommended by the testing guidelines for use in neurotoxicity screening studies. In addition, a historical database is available for comparative evaluation.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.7.4. NUMBER OF ANIMALS

Transferred from the In-house Colony:
60 total (30 males, 30 females)

Placed on test:
40 total (20 males, 20 females)

Females were nulliparous and non-pregnant.

2.7.5. JUSTIFICATION FOR NUMBER OF ANIMALS

The neurotoxicants used in this study were chosen because they produce transient neurological effects and do not cause permanent damage to the nervous system at the doses used in this study. Therefore, the animals were used more than once during the training program. During the training portion of the study, a total of 18 animals (3 males or 3 females/chemical) were used. This was considered the minimum number necessary to demonstrate the range of effects of the chemical based on individual animal variability. During the performance part of the study, a total of 20 males and 20 females were used (including animals used in the training portion of the study). This allowed each technician undergoing training to perform the FOB evaluation for 20 animals (5 males or 5 females/group) and allowed two separate evaluations per week. Five animals per group were considered the minimum number necessary to produce scientific and statistically valid data.

2.7.6. AGE AT RECEIPT

23 days

2.7.7. AGE AT INITIATION OF TRAINING SESSION

43 days

2.7.8. AGE AT INITIATION OF PERFORMANCE EVALUATIONS

77 days

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.7.9. WEIGHT AT INITIATION OF TRAINING SESSION (GRAMS)

	Mean	Range
Male:	205	178 to 225
Female:	172	161 to 180

2.7.10. WEIGHT AT INITIATION OF PERFORMANCE EVALUATIONS (GRAMS)

	Mean	Range
Male:	440	379 to 498
Female:	270	235 to 339

2.7.11. ACCLIMATION PERIOD

Animals were acclimated for approximately 3 weeks. All animals were examined during the acclimation period to confirm suitability for study.

2.8. SELECTION AND GROUP ASSIGNMENT

More animals than required for the study were transferred from the in-house colony. Twenty males and twenty females were randomly selected for use on study and randomly assigned to control or treatment groups. Individual weights of animals used on study at initiation of the training session were within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study is maintained in the study file.

2.9. ANIMAL IDENTIFICATION

Each rat was identified with a metal ear tag 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 dose level identification and contained study number and animal number information.

2.10. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.11. HUSBANDRY

2.11.1. HOUSING

Animals were doubly housed in elevated, stainless steel, wire mesh cages during the first week of the acclimation period and individually housed thereafter.

2.11.2. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly.

2.11.3. FEED ANALYSIS

Analysis of each feed lot used during this study was performed by the manufacturer. Results are maintained on file.

2.11.4. WATER

Water was available without restriction via an automated watering system (Elizabethtown Water Company, Westfield, New Jersey).

2.11.5. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East 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.

2.11.6. CONTAMINANTS

There were no known contaminants in the feed or water which were expected to interfere with the results of this study.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.11.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve hour light/dark cycle was provided and controlled via an automatic timer.

Temperature

Temperature was monitored and recorded twice daily and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired: 18 to 26°C
Actual: 15 to 24°C

Relative Humidity

Relative humidity was monitored and recorded once daily and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired: 30 to 70%
Actual: 28 to 68%

2.12. TEST ARTICLE PREPARATION

Appropriate amounts of the test articles were mixed with 0.9% saline to achieve the desired concentrations. Dosing solutions were prepared either the day prior to or the day of dose administration and were stored refrigerated when not in use.

2.13. ANALYSIS OF DOSE SOLUTIONS

Analysis of the dosing solutions was not performed for this study.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.14. TEST ARTICLE ADMINISTRATION

2.14.1. ROUTE OF ADMINISTRATION

Chlorpromazine, D-Amphetamine Sulfate and saline were administered by intraperitoneal injection into the abdominal cavity near the inguinal region using a sterile needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

Physostigmine was administered by intraperitoneal injection into the abdominal cavity near the inguinal region or by subcutaneous injection into an area on the back, using a sterile needle and syringe of appropriate size. Intraperitoneal injections were administered for the Training Sessions and for the Performance Evaluations conducted by Observer 8; subcutaneous injections were administered for the Performance Evaluations conducted by all other observers. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

Ethanol was administered by oral intubation using a stainless steel dosing needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 10 mL/kg of body weight was administered.

2.14.2. ROUTE JUSTIFICATION

The intraperitoneal, subcutaneous and oral routes provide rapid test article absorption and have been used in previous studies with the test articles.

2.14.3. DOSE LEVELS

Training Sessions

4 mg Chlorpromazine/kg body weight (males)
2 mg D-Amphetamine Sulfate/kg body weight (males)
8 mg D-Amphetamine Sulfate/kg body weight (females)
1 mg Physostigmine/kg body weight (females)
3000 mg Ethanol/kg body weight (females)

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

Performance Evaluations

4 mg Chlorpromazine/kg body weight
2 mg D-Amphetamine Sulfate/kg body weight
1 mg Physostigmine/kg body weight

2.14.4. DOSE VOLUME

0.9% Saline, Chlorpromazine, D-Amphetamine Sulfate, and Physostigmine were administered at a volume of 5 mL/kg of body weight. Ethanol was administered at a volume of 10 mL/kg of body weight.

2.14.5. FREQUENCY OF DOSING

Each animal was dosed no more than once per week. There was a washout period of approximately one to five weeks between doses.

2.15. EXPERIMENTAL EVALUATIONS

2.15.1. VIABILITY CHECKS

Animals were observed in their cages once daily for mortality and signs of severe toxic or pharmacologic effects.

2.15.2. PHYSICAL/NEUROBEHAVIORAL EXAMINATIONS

Animals were removed from their cages and examined once pretest to determine suitability for study. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern), changes in gait or posture, response to handling, presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) and bizarre behavior (e.g., self-mutilation, walking backward).

2.15.3. BODY WEIGHT

Animals were removed from their cages and weighed once pretest and once prior to each dose to determine dose volumes. Body

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

weights were also recorded during the study as part of the functional observational battery.

2.15.4. FUNCTIONAL OBSERVATIONAL BATTERY EVALUATIONS

Training Session

Training consisted of two parts. In the first part, all technicians were required to view a training video for a functional observational battery (United States Environmental Protection Agency/American Industrial Health Council Training Video and Reference Manual for an FOB, 1996). The second part consisted of observations of animals treated with chemicals known to produce neurological effects. Two experienced technicians performed the FOB evaluations and instructed the novice technicians, under the direction of the Study Director or other senior staff member. These evaluations were not performed "blind".

FOB Performance Evaluation

After training, the experienced and novice technicians were each required to evaluate 20 animals (5 males or females/group) using the Functional Observational Battery. Observations by each technician were performed blind, i.e., the observer was unaware of the treatment of each animal. Animals were randomized and blinded according to the standard operating procedures of the Testing Facility.

The results of each FOB evaluation were tabulated and the Study Director determined whether the observations performed by each technician comprised a treatment profile consistent with known neurological effects of each test article. Interobserver reliability was considered established for technicians that accurately identified the treatment profile for each test article. The expected neurological effects were based on published reports in the literature, a previous validation study conducted at the Testing

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Facility (Study No. 96-4516), and observations by the experienced technicians.

Technicians not accurately identifying the treatment profile for each test article were given additional training and/or conducted additional performance evaluations before being allowed to conduct FOB evaluations on a study.

In addition to being able to identify the treatment profile for each test article, each technician was required to demonstrate consistency in performing the quantitative measures of hindlimb and forelimb grip strength and landing foot splay. This was done by determining the mean and standard deviation for the control animals during the performance evaluation for each technician and calculating the coefficient of variance [(standard deviation/mean) x 100%]. The coefficient of variance was required to be approximately 25% or lower to be considered consistent. If a technician did not achieve this level of consistency, further training and evaluations were performed.

Parameters Evaluated

Temperature, humidity, noise level and illumination were measured and recorded to ensure that variations in environmental conditions were minimal during all evaluations.

Evaluations were performed according to the Testing Facility's standard operating procedures that include defined scales for each function listed below:

1. Assessment of signs of autonomic function:
   Ranking of the degree of lacrimation and salivation
   Presence or absence of piloerection and exophthalmus
   Count of urination and defecation
   Pupillary function (constriction of pupil in response to light)
   Degree of palpebral closure

2. Description, incidence, and severity of any convulsions, tremors, or abnormal motor movements

3. Ranking of general level of activity in the open field

4. Description and incidence of posture and gait abnormalities and ranking of gait abnormalities

5. Quantitative measures of forelimb and hindlimb grip strength

6. Quantitative measure of landing foot splay

7. Ranking of reactivity to general stimuli; sensorimotor responses to visual and auditory stimuli; and the response to a tail pinch.

2.16. POSTMORTEM

At the conclusion of all evaluations, all animals were sacrificed and discarded. No necropsy was performed and no tissues were collected. Animals were euthanized by carbon dioxide inhalation.

2.17. STATISTICAL ANALYSIS

The following parameters were analyzed statistically:

body weight (from the functional observational battery)
forelimb and hindlimb grip strength measurements
landing foot splay measurements

2.17.1. METHOD OF ANALYSIS

Mean values of all dose groups were compared to the mean value for the control group at each time interval.

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) was performed to determine if groups had equal variances. If the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. 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, Dunnett's test (Dunnett, 1955, 1964) or

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Williams test (Williams, 1971, 1972) were used to determine which means were significantly different from the control. The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Shirley's test (Shirley, 1977) or Dunn's test (Dunn, 1964) 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.

2.18. DATA STORAGE

All raw data and retained samples, as well as the original study protocol and the original final report will be maintained in the Archives of the Testing Facility upon completion of the study.

2.19. PROTOCOL DEVIATIONS

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

1. Viability checks were performed once per day instead of twice per day as specified in the Protocol.

2. Animals were approximately 3 weeks old at receipt instead of approximately 4 weeks old as specified in the protocol. In addition, the animals were approximately 11 weeks old at initiation of performance evaluations rather than 8 weeks or less as specified by the protocol.

3. Animals were not randomly assigned to study groups to try to equalize mean body weights as specified in the Protocol. Animals were arbitrarily assigned animal numbers and placed into groups by animal number (i.e. Nos. 5001 to 5005 were assigned to Group 1; Nos. 5006 to 5010 were assigned to Group 2; etc.).

4. Body weights of some animals exceeded the Protocol specified range of 150 to 250 grams at first dose.

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5. Initial FOB performance evaluations by Observers 1 and 6 conducted on 26 April 2000 were performed on 10 animals/sex/observer instead of 20 males or 20 females/observer as specified in the Protocol. Evaluations were re-conducted by these observers using the correct number of animals. The initial evaluations are not presented in this report, but are maintained with the study data.

6. The washout period between doses was approximately one to five weeks instead of approximately one week as specified in the Protocol.

7. Body weights for the calculation of dose volumes were not recorded weekly as specified in the Protocol, but were recorded prior to each dose.

8. Fresh dosing solutions were prepared on the day prior to or on day of dose rather than once weekly as required by protocol.

9. The acceptable variability established in the report of 25-30% differed from the range specified in the protocol of 25% or less.

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3. RESULTS AND DISCUSSION

3.1. FUNCTIONAL OBSERVATIONAL BATTERY (FOB) EVALUATIONS

Nine technicians were trained or retrained in the performance of the FOB evaluations and subsequently tested for their ability to identify the behavioral pattern produced by three test articles that are known to produce neurological effects. Three of the technicians (Observers 1, 5, and 6) had been previously trained and helped to set the standard for the expected pattern of observations for each compound. Results of a previous training study conducted at the Testing Facility (Study No. 96-4516), as well as published data, were also used to set the performance standards. Results of the FOB evaluations for each test article are presented in Table 2 for all nine observers. The standard pattern of effects for each of the test articles and the comparative evaluations for each observer are presented in the following sections for all observers, with the exception of Observer 3 who is no longer employed at the Testing Facility.

3.2. FOB EVALUATIONS FOR RATS TREATED WITH CHLORPROMAZINE

The pattern of effects observed after administration of chlorpromazine (Text Table 1) are consistent with the actions of the drug which is a central nervous system depressant. The pattern of effects is also similar to that observed in previous training studies. All observers noted postural effects in the home cage, with the animal lying on its side or flattened; effects on gait and posture in the open field, mainly body drags or limbs splayed or dragging; decreased or no locomotion; low or very low arousal level; and no response to the approach of a blunt object. Seven of the eight observers that were compared also noted effects on palpebral closure in the home cage, with eyelids slightly drooping or half-closed and moderate or extreme lacrimation. Six of the eight observers also noted no response to an auditory stimulus and some in coordination in the air righting reflex. In the functional evaluations, there was an increase in landing foot splay of

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17% to 46% for the Chlorpromazine-treated animals, as compared to the saline controls, for 7/7 observers.

Text Table 1 - FOB Evaluations for Rats Treated with Chlorpromazine

	No. of Observations							
	Males (n = 5))				Females (n = 5)			
Evaluations	Obs. 1	Obs. 2	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9
Home Cage								
• Posture								
lying on Side	2	0	2	0	1	0	0	0
flattened	1	1	0	1	2	2	1	4
• Palpebral Closure								
sl. drooping	4	1	0	1	1	2	4	4
half-closed	1	0	0	1	0	0	0	0
Handling								
• Lacrimation								
moderate	4	1	2	0	1	1	2	2
extreme	0	0	0	0	3	2	1	2
Open Field								
• Gait and Posture								
body drags	1	0	2	2	1	2	3	2
limbs splayed	5	5	1	1	3	2	2	3
• Locomotion								
decreased	0	0	0	1	0	1	4	1
none	5	5	3	4	4	4	1	4
• Arousal								
low	0	0	0	0	0	2	1	1
very low	5	5	3	5	4	3	4	4
Reflex								
• Approach								
no response	3	3	2	4	3	5	2	5
• Audition								
no response	0	2	2	0	2	2	2	4
• Air Righting								
sl. uncoordinated	3	2	0	3	2	0	0	1
lands on side	1	0	1	0	0	0	0	1
Landing Foot Splay								
• % increase	35%	34%	17%	21%	46%	17%	[a]	25%

[a]Some measurements were performed incorrectly and not considered valid. The number of valid measurements was considered to be too small to provide a valid comparison.

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3.3. FOB EVALUATIONS FOR RATS TREATED WITH AMPHETAMINE

D-amphetamine, a catecholamine analog, is a central nervous system stimulant that induces increased locomotor activity, mainly through noradrenergic receptors, and/or produces stereotypic behavior via dopaminergic mechanisms. The predominant effects that are produced are dependent on both the dose of amphetamine and individual variability. The effects observed in the FOB after administration of D-amphetamine to rats are consistent with both actions of the drug. Stereotypic behavior, consisting of excessive repetitive actions such as sniffing, was noted by all eight observers and was seen in most of the animals. Increased locomotor activity and high or very high arousal state was noted by seven of eight observers, although the incidence was lower than that for stereotypic behavior. Decreased locomotor activity and low or very low arousal was also noted by some observers. This paradoxical effect was attributed to the predominance of the stereotypic effects compared to the stimulation of motor activity, which resulted in less movement and arousal in the animals.

Text Table 2 – FOB Evaluations for Rats Treated with Amphetamine

	No. of Observations							
	Males (n = 5))				Females (n = 5)			
Evaluations	**Obs. 1**	**Obs. 2**	**Obs. 4**	**Obs. 5**	**Obs. 6**	**Obs. 7**	**Obs. 8**	**Obs. 9**
Open Field								
• Locomotion								
increased	1	2	2	0	3	5	4	4
decreased	3	1	0	0	2	0	0	0
• Arousal								
high, sl. excitement	1	0	2	4	4	5	4	5
very high, hyperalert	1	1	0	0	0	0	0	0
low	1	1	0	1	1	0	0	0
very low	1	1	0	0	0	0	0	0
Stereotypic Behavior								
present	4	5	2	4	5	5	4	5
Reflex								
• Approach								
no response	1	0	3	1	4	1	0	0

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3.4. FOB EVALUATIONS FOR RATS TREATED WITH PHYSOSTIGMINE

Physostigmine is a cholinesterase inhibitor whose administration results in an excess of the neurotransmitter acetylcholine at cholinergic nerve endings. This results in stimulation of cholinergic nerves in both the peripheral and central nervous system. The effects observed in the FOB are consistent with the wide range of effects produced by cholinergic stimulation (Text Table 3). Findings associated with stimulation of the parasympathetic nervous system, including increased salivation and miosis, were noted by all observers in most of the animals. Effects on muscles, as indicated by abnormal posture in the home cage, abnormal posture and gait in the open field, decreased or absent locomotion, muscle fasciculations, and incoordination in the air righting reflex, were also noted by all observers in most animals. In addition, 5/7 observers noted increases of 19% to 30% in mean landing foot splay measurements. Findings indicative of depression of the central nervous system included a low or very low arousal state, as noted by all observers, and no reaction to the approach of a blunt object (6/8 observers) and no reaction to a pain stimulus (7/8 observers). The incidence scores for Observer No. 8 were lower than those recorded by the other observers. Since the scores were low for all measures of cholinergic activity, this suggests that the animals were not evaluated at the time of peak effect or that the animals did not receive a full dose of physostigmine and this was not considered an indication of inability to recognize these effects.

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Text Table 3 – FOB Evaluations for Rats Treated with Physostigmine

Evaluations	No. of Observations							
	Males (n = 5))				Females (n = 5)			
	Obs. 1	Obs. 2	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9
Home Cage								
• Posture								
lying on side	0	3	0	0	0	0	0	0
flattened	5	2	4	5	5	1	1	5
Handling								
• Salivation								
slight	3	2	2	2	2	3	1	2
moderate	2	1	3	3	1	1	0	0
extreme	0	2	0	0	0	0	0	0
Open Field								
• Gait and Posture								
ataxia	0	0	0	0	0	2	0	2
body drags	3	5	5	5	3	1	1	3
limbs splayed	5	3	0	3	3	1	0	1
hunched posture	0	0	0	0	0	1	0	0
• Locomotion								
decreased	0	0	3	0	2	5	1	3
none	5	5	2	5	3	0	0	2
• Arousal								
low	2	0	1	0	1	3	1	0
very low	3	5	4	5	4	2	0	5
Motor Movements								
• Fasciculations								
slight	4	4	5	4	1	5	1	3
severe	1	1	0	1	4	0	0	2
Reflex								
• Approach								
no response	2	0	3	4	2	2	0	2
• Pain								
no reaction	4	4	5	5	1	1	0	4
• Pupil Response								
miosis	5	5	5	5	5	5	2	5
• Air Righting								
sl. uncoordinated	3	5	1	2	2	2	0	2
lands on side	2	0	3	0	3	2	1	1
lands on back	0	0	1	1	0	0	0	0
Landing Foot Splay								
• % increase	29%	22%	[a]	23%	30%	[a]	[b]	19%

[a]No change in landing foot splay, as compared to saline-treated animals.

[b]Some measurements were performed incorrectly and not considered valid. The number of valid measurements was considered to be too small to provide a valid comparison.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

3.5. CONSISTENCY OF GRIP STRENGTH AND LANDING FOOT SPLAY MEASUREMENTS

Acceptable variability (25-30%) in the measurement of forelimb and hindlimb grip strength and landing foot splay was achieved by all observers.

Text Table 4 - Consistency of Grip Strength and Landing Foot Splay Measurements

Evaluations	Coefficient of Variability (%)							
	Obs. 1	Obs. 2	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9
Forelimb grip strength	11.1	21.1	21.3	22.0	16.0[b]	8.7	8.8	21.1[b]
Hindlimb grip strength	15.3	25.3	32.8[a] 27.2[a]	13.6	18.4	20.5	16.0	20.6
Landing foot splay	23.5	19.1	25.4	22.4	15.4	23.4	9.8[c]	29.1

[a]Original value was unacceptable. Evaluations were repeated using untreated animals (5 males and 5 females).

[b]Original value was unacceptable. Evaluations were repeated using untreated animals (10 females).

[c]Measurements of landing foot splay were performed incorrectly and were repeated with ten untreated animals.

4. CONCLUSION

Treatment of Sprague-Dawley rats with Chlorpromazine, D-Amphetamine Sulfate, or Physostigmine produced patterns of behavior consistent with their expected neurological effects. These data provide evidence that the procedures used for the Functional Observational Battery evaluations in the Testing Facility are capable of detecting major neurotoxic endpoints. In addition, the neurobehavioral profiles for each compound were correctly identified by Observers 1-2 and 4-9, who were blinded with respect to treatment. This demonstrates that there is interobserver reliability among the trained technicians at the Testing Facility in the conduct of the Functional Observational Battery evaluations. Acceptable variability in the performance of forelimb and hindlimb grip strength measurements and landing foot splay measurements were achieved by all observers. In conclusion, Observers 1, 2, 4, 5, 6, 7, 8, and 9 were considered to be fully qualified to perform Functional Observational Battery evaluations.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 1 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	567.0	569.7	604.1	544.0
	S.D.	27.9	25.0	39.8	45.7
	N	5	5	5	5
Forelimb Grip Strength	Mean	926.0	680.5 *	1070.0	851.5
	S.D.	102.5	142.5	137.5	167.6
	N	5	5	5	5
	%CV	11.1			
Hindlimb Grip Strength	Mean	781.5	635.5	831.0	622.5 *
	S.D.	119.8	85.6	69.9	80.4
	N	5	5	5	5
	%CV	15.3			
Landing Foot Splay	Mean	4.8	6.5	5.4	6.2
	S.D.	1.1	1.6	1.7	1.6
	N	5	5	5	5
	%CV	23.5			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 2 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	572.4	572.0	608.2	547.6
	S.D.	20.9	26.6	36.4	45.9
	N	5	5	5	5
Forelimb Grip Strength	Mean	858.0	1210.0	797.0	941.5
	S.D.	181.2	369.8	266.0	244.6
	N	5	5	5	5
	%CV	21.1			
Hindlimb Grip Strength	Mean	908.5	876.5	773.0	807.5
	S.D.	230.1	216.4	103.4	127.5
	N	5	5	5	5
	%CV	25.3			
			*		
Landing Foot Splay	Mean	6.7	9.0	5.7	8.2
	S.D.	1.3	1.8	0.9	1.0
	N	5	5	5	5
	%CV	19.1			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 3 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	475.4	490.0	506.3	462.3
	S.D.	24.2	30.2	28.9	37.5
	N	5	5	5	5
Forelimb Grip Strength	Mean	1499.5	1323.5	1909.0	1278.0
	S.D.	470.4	715.3	344.9	351.5
	N	5	5	5	5
	%CV	31.4			
Hindlimb Grip Strength	Mean	955.5	837.5	1102.0	906.5
	S.D.	270.5	255.7	230.2	251.5
	N	5	5	5	5
	%CV	28.3			
Landing Foot Splay	Mean	6.8	8.3	6.1	6.3
	S.D.	0.9	2.5	0.8	1.4
	N	5	5	5	5
	%CV	13.4			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 4 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	456.9	468.7	494.6	448.3
	S.D.	21.3	30.1	26.5	37.0
	N	5	5	5	5
					*
Forelimb Grip Strength	Mean	1224.0	1161.0	1311.0	901.5
	S.D.	261.3	149.0	179.6	276.0
	N	5	5	5	5
	%CV	21.3			
Hindlimb Grip Strength	Mean	622.5	577.5	601.0	572.0
	S.D.	238.7	202.9	122.3	206.0
	N	5	5	5	5
	%CV	38.3			
Landing Foot Splay	Mean	7.2	8.4	7.1	6.9
	S.D.	1.8	1.8	1.1	1.5
	N	5	5	5	5
	%CV	25.4			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 5 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	558.9	564.5	591.7	530.9
	S.D.	27.4	30.3	37.8	41.4
	N	5	5	5	5
Forelimb Grip Strength	Mean	1352.5	1179.0	1458.5	980.5 *
	S.D.	296.9	327.7	170.8	186.7
	N	5	5	5	5
	%CV	22.0			
Hindlimb Grip Strength	Mean	1428.0	1105.0	1266.0	941.0 **
	S.D.	193.8	312.4	162.7	300.3
	N	5	5	5	5
	%CV	13.6			
Landing Foot Splay	Mean	8.7	10.5	8.9	10.7
	S.D.	1.9	1.7	1.3	1.5
	N	5	5	5	5
	%CV	22.4			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 6 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	313.0	314.5	311.5	311.0
	S.D.	18.4	26.3	46.9	10.5
	N	5	5	5	5
Forelimb Grip Strength	Mean	667.0	847.5	1005.5	708.0
	S.D.	294.4	143.6	159.5	203.3
	N	5	5	5	5
	%CV	44.1			
Hindlimb Grip Strength	Mean	827.5	835.5	947.0	820.0
	S.D.	152.2	161.6	50.1	136.6
	N	5	5	5	5
	%CV	18.4			
			*		
Landing Foot Splay	Mean	5.0	7.3	4.0	6.5
	S.D.	0.8	0.6	0.8	1.8
	N	5	5	5	5
	%CV	15.4			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 7 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	313.0	312.3	305.5	310.1
	S.D.	17.5	26.1	33.0	13.2
	N	5	5	5	5
Forelimb Grip Strength	Mean	815.0	869.5	975.5	766.5
	S.D.	71.2	124.3	147.4	161.4
	N	5	5	5	5
	%CV	8.7			
Hindlimb Grip Strength	Mean	620.0	560.5	673.0	642.5
	S.D.	127.2	116.7	105.2	174.5
	N	5	5	5	5
	%CV	20.5			
Landing Foot Splay	Mean	6.6	7.7	5.7	6.4
	S.D.	1.5	0.8	0.8	1.8
	N	5	5	5	5
	%CV	23.4			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 8 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	268.7	298.0	276.1	280.3
	S.D.	19.5	55.7	27.3	12.4
	N	5	5	5	5
Forelimb Grip Strength	Mean	1006.5	799.5	912.5	829.5
	S.D.	88.6	148.1	108.9	180.2
	N	5	5	5	5
	%CV	8.8			
Hindlimb Grip Strength	Mean	735.0	605.5	571.0	695.5
	S.D.	117.9	158.6	101.9	238.0
	N	5	5	5	5
	%CV	16.0			
Landing Foot Splay	Mean	6.4	6.2	6.0	5.1
	S.D.	1.6	0.3	-	0.6
	N	3	3	1	2
	%CV	25.0			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 9 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	315.9	313.5	310.8	311.1
	S.D.	18.3	25.5	48.3	11.1
	N	5	5	5	5
Forelimb Grip Strength	Mean	539.5	963.0	823.0	606.5
	S.D.	292.8	456.9	330.6	327.3
	N	5	5	5	5
	%CV	54.3			
Hindlimb Grip Strength	Mean	632.0	588.0	637.0	647.5
	S.D.	130.3	67.2	128.0	161.7
	N	5	5	5	5
	%CV	20.6			
Landing Foot Splay	Mean	6.3	7.9	4.4	7.5
	S.D.	1.8	1.4	1.3	1.8
	N	5	5	5	5
	%CV	29.1			

*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.

%CV = (Control Group S.D./Control Group Mean) x 100.

Repeats	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 4 Repeat Test Article:		**Untreated Males**	**Untreated Females**
Forelimb Grip Strength	Mean	1373.0	1167.0
	S.D.	168.3	293.8
	N	5	5
	%CV	12.3	25.2
Hindlimb Grip Strength	Mean	864.5	645.5
	S.D.	235.0	211.9
	N	5	5
	%CV	27.2	32.8

Observer 6 Repeat Test Article:		**Untreated Females**
Forelimb Grip Strength	Mean	970.5
	S.D.	154.9
	N	10
	%CV	16.0
Hindlimb Grip Strength	Mean	743.3
	S.D.	147.0
	N	10
	%CV	19.8

Observer 8 Repeat Test Article:		**Saline Males**
Landing Foot Splay	Mean	9.5
	S.D.	0.9
	N	10
	%CV	9.8

%CV = (Control Group S.D./Control Group Mean) x 100.

Repeats	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 9 Repeat

Test Article:		**Untreated Females**
Forelimb Grip Strength	Mean	882.0
	S.D.	186.0
	N	10
	%CV	21.1
Hindlimb Grip Strength	Mean	555.8
	S.D.	178.3
	N	10
	%CV	32.1

%CV = (Control Group S.D./Control Group Mean) x 100.

	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations Preface	Appendix KK

Corresponding test articles for each group were as follows:

Group 1	-	Saline
Group 2	-	Chlorpromazine
Group 3	-	D-Amphetamine Sulfate
Group 4	-	Physostigmine

For summarization purposes, comments describing location [i.e., forelimb, hindlimb, right, unilateral, etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

When an animal received two scores during Open Field Evaluations of Gait and Posture (i.e. the animal was noted to be dragging it's body and it's limbs were splayed or dragging), the two scores were summarized individually. Therefore, the total incidence of scores may be greater than the number of animals examined.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		1	2	1	0
	Alert, Oriented Toward Observer		4	0	4	0
	Asleep		0	0	0	0
	Lying on Side		0	2	0	0
	Flattened		0	1	0	5
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	0	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	4	0	0
	Eyelids Half Closed		0	1	0	0
Handling Evaluations						
Ease of Removal	Very Easy		3	4	2	5
	Easy		1	1	2	0
	Moderately Difficult		1	0	1	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		4	5	4	5
	Moderately Difficult		1	0	1	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	5	5	5
	Present		0	0	0	0
Lacrimation	Not Present		5	1	5	5
	Moderate		0	4	0	0
	Extreme		0	0	0	0
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	4	0
	Slight		0	0	1	3
	Moderate		0	0	0	2
	Extreme		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	0	4	0
	Ataxia		0	0	1	0
	Body Drags		0	1	0	3
	Limbs Splayed or Dragging		0	5	0	5
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	0	1	0
	Increased Movement		0	0	1	0
	Decreased Movement		0	0	3	0
	None		0	5	0	5
Arousal	Normal		4	0	1	0
	Low, Slight Stupor		1	0	1	2
	Very Low, Stupor		0	5	1	3
	High, Slight Excitement, Tense		0	0	1	0
	Very High, Hyper-Alert		0	0	1	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		6	11	0	3
	Unformed Stool		0	0	0	0
Urine	Number of Pools		4	3	0	5
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	1	5
	Present		0	0	4	0
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	4
	Severe		0	0	0	1
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	2	4	3
	No Reaction		0	3	1	2
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	5	5	5
	No Reaction		0	0	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away		5	4	3	1
	No Reaction		0	1	2	4
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	4	5	0
	No Constriction		0	0	0	0
	Miosis		0	1	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	0	0	0
	Animal Shakes Head		5	5	5	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	5
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		5	1	5	0
	Slightly Uncoordinated		0	3	0	3
	Lands on Side		0	1	0	2
	Lands on Back		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		4	3	1	0
	Alert, Oriented Toward Observer		1	1	4	0
	Asleep		0	0	0	0
	Lying on Side		0	0	0	3
	Flattened		0	1	0	2
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	4	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	1	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		0	1	4	4
	Easy		5	4	1	1
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	5	5	5
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	4	5	5
	Present		0	1	0	0
Lacrimation	Not Present		5	4	5	5
	Moderate		0	1	0	0
	Extreme		0	0	0	0
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	4	0
	Slight		0	0	1	2
	Moderate		0	0	0	1
	Extreme		0	0	0	2

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	0	4	0
	Ataxia		0	0	1	0
	Body Drags		0	0	0	5
	Limbs Splayed or Dragging		0	5	0	3
	Hunched Posture		0	0	0	0
Locomotion	Normal		4	0	2	0
	Increased Movement		0	0	2	0
	Decreased Movement		1	0	1	0
	None		0	5	0	5
Arousal	Normal		4	0	2	0
	Low, Slight Stupor		1	0	1	0
	Very Low, Stupor		0	5	1	5
	High, Slight Excitement, Tense		0	0	0	0
	Very High, Hyper-Alert		0	0	1	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		6	1	1	1
	Unformed Stool		0	0	0	0
Urine	Number of Pools		12	7	6	12
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	0	4
	Present		0	0	5	1
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	4
	Severe		0	0	0	1
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	2	5	5
	No Reaction		0	3	0	0
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		4	3	5	3
	No Reaction		1	2	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	2
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	5	1
	No Reaction		0	0	0	4
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	3	4	0
	No Constriction		0	0	0	0
	Miosis		0	2	1	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	0	1	0
	Animal Shakes Head		5	5	4	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	5
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		5	3	5	0
	Slightly Uncoordinated		0	2	0	5
	Lands on Side		0	0	0	0
	Lands on Back		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		2	3	0	1
	Alert, Oriented Toward Observer		3	0	5	0
	Asleep		0	0	0	0
	Lying on Side		0	0	0	1
	Flattened		0	2	0	3
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	3	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	2	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		3	3	5	5
	Easy		1	2	0	0
	Moderately Difficult		1	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		3	4	5	5
	Moderately Difficult		2	1	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	5	5	4
	Present		0	0	0	1
Lacrimation	Not Present		5	3	5	5
	Moderate		0	2	0	0
	Extreme		0	0	0	0
Coat	Normal		5	5	5	4
	Slightly Soiled		0	0	0	1
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	5	2
	Slight		0	0	0	1
	Moderate		0	0	0	2
	Extreme		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	0	5	0
	Ataxia		0	1	0	1
	Body Drags		0	3	0	4
	Limbs Splayed or Dragging		0	3	0	3
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	0	4	0
	Increased Movement		0	0	1	1
	Decreased Movement		0	2	0	1
	None		0	3	0	3
Arousal	Normal		5	0	1	0
	Low, Slight Stupor		0	2	0	2
	Very Low, Stupor		0	3	0	3
	High, Slight Excitement, Tense		0	0	4	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		1	1	0	2
	Unformed Stool		0	0	0	0
Urine	Number of Pools		3	5	0	3
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	2	5
	Present		0	0	3	0
Motor Movements						
Fasciculations	Not Present		5	5	5	2
	Slight		0	0	0	2
	Severe		0	0	0	1
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	4
	Slight		0	0	0	0
	Severe		0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	1	2	3
	No Reaction		0	4	3	2
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	4	5	4
	No Reaction		0	1	0	1
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	5	3
	No Reaction		0	0	0	2
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	5	5	2
	No Constriction		0	0	0	1
	Miosis		0	0	0	2
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	0	1	0
	Animal Shakes Head		5	5	4	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	4
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	1
Air Righting Reflex	Normal: Lands on All Four Feet		5	5	5	1
	Slightly Uncoordinated		0	0	0	2
	Lands on Side		0	0	0	2
	Lands on Back		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		5	3	3	1
	Alert, Oriented Toward Observer		0	0	2	0
	Asleep		0	0	0	0
	Lying on Side		0	0	0	0
	Flattened		0	2	0	4
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	5	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	0	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		4	4	4	5
	Easy		1	1	0	0
	Moderately Difficult		0	0	1	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	5	5	5
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	5	5	5
	Present		0	0	0	0
Lacrimation	Not Present		5	3	5	3
	Moderate		0	2	0	0
	Extreme		0	0	0	2
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	5	0
	Slight		0	0	0	2
	Moderate		0	0	0	3
	Extreme		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	2	5	0
	Ataxia		0	0	0	0
	Body Drags		0	2	0	5
	Limbs Splayed or Dragging		0	1	0	0
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	2	3	0
	Increased Movement		0	0	2	0
	Decreased Movement		0	0	0	3
	None		0	3	0	2
Arousal	Normal		4	2	3	0
	Low, Slight Stupor		0	0	0	1
	Very Low, Stupor		0	3	0	4
	High, Slight Excitement, Tense		1	0	2	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	4	5
	Present		0	0	1	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		5	8	0	1
	Unformed Stool		0	0	0	0
Urine	Number of Pools		4	5	2	6
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	3	4
	Present		0	0	2	1
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	5
	Severe		0	0	0	0
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	3
	Slight		0	0	0	1
	Severe		0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	3	2	2
	No Reaction		0	2	3	3
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	3	5	4
	No Reaction		0	2	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	1
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	4	0
	No Reaction		0	0	1	5
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	5	5	0
	No Constriction		0	0	0	0
	Miosis		0	0	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	1	1	0
	Animal Shakes Head		5	4	4	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	5
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		5	4	5	0
	Slightly Uncoordinated		0	0	0	1
	Lands on Side		0	1	0	3
	Lands on Back		0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		3	3	0	0
	Alert, Oriented Toward Observer		2	1	5	0
	Asleep		0	0	0	0
	Lying on Side		0	0	0	0
	Flattened		0	1	0	5
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	3	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	1	0	0
	Eyelids Half Closed		0	1	0	0
Handling Evaluations						
Ease of Removal	Very Easy		5	4	5	5
	Easy		0	1	0	0
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	4	5	5
	Moderately Difficult		0	1	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	5	5	5
	Present		0	0	0	0
Lacrimation	Not Present		5	5	5	5
	Moderate		0	0	0	0
	Extreme		0	0	0	0
Coat	Normal		5	5	5	4
	Slightly Soiled		0	0	0	1
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	4	0
	Slight		0	0	1	2
	Moderate		0	0	0	3
	Extreme		0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture[a]	Normal		5	1	5	0
	Ataxia		0	0	0	0
	Body Drags		0	2	0	5
	Limbs Splayed or Dragging		0	1	0	3
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	0	5	0
	Increased Movement		0	0	0	0
	Decreased Movement		0	1	0	0
	None		0	4	0	5
Arousal	Normal		4	0	0	0
	Low, Slight Stupor		1	0	1	0
	Very Low, Stupor		0	5	0	5
	High, Slight Excitement, Tense		0	0	4	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		6	4	0	1
	Unformed Stool		0	0	0	0
Urine	Number of Pools		2	6	0	6
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	1	5
	Present		0	0	4	0
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	4
	Severe		0	0	0	1
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

[a]Gait for two Group 2 animals could not be determined because the animals did not move during the observation period.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	1	4	1
	No Reaction		0	4	1	4
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	5	4	4
	No Reaction		0	0	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	1	1
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	4	0
	No Reaction		0	0	0	5
	Apparent Increased Pain		0	0	1	0
Pupil Response	Pupil Constricts		5	5	5	0
	No Constriction		0	0	0	0
	Miosis		0	0	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		2	1	1	0
	Animal Shakes Head		3	4	4	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	4	5	1
	Returns Leg Only Partially to Original Position		0	0	0	1
	No Response		0	1	0	3
Air Righting Reflex	Normal: Lands on All Four Feet		5	2	5	2
	Slightly Uncoordinated		0	3	0	2
	Lands on Side		0	0	0	0
	Lands on Back		0	0	0	1

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		4	1	0	0
	Alert, Oriented Toward Observer		1	1	5	0
	Asleep		0	0	0	0
	Lying on Side		0	1	0	0
	Flattened		0	2	0	5
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	4	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	1	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		3	5	4	5
	Easy		1	0	1	0
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	5	5	5
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	5	5	5
	Present		0	0	0	0
Lacrimation	Not Present		5	1	5	3
	Moderate		0	1	0	1
	Extreme		0	3	0	1
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	5	2
	Slight		0	0	0	2
	Moderate		0	0	0	1
	Extreme		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	1	5	0
	Ataxia		0	0	0	0
	Body Drags		0	1	0	3
	Limbs Splayed or Dragging		0	3	0	3
	Hunched Posture		0	1	0	0
Locomotion	Normal		5	1	0	0
	Increased Movement		0	0	3	0
	Decreased Movement		0	0	2	2
	None		0	4	0	3
Arousal	Normal		5	1	0	0
	Low, Slight Stupor		0	0	1	1
	Very Low, Stupor		0	4	0	4
	High, Slight Excitement, Tense		0	0	4	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		0	3	0	0
	Unformed Stool		0	0	0	0
Urine	Number of Pools		0	5	0	4
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	0	3
	Present		0	0	5	2
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	1
	Severe		0	0	0	4
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	2	1	3
	No Reaction		0	3	4	2
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	3	5	5
	No Reaction		0	2	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	5	4
	No Reaction		0	0	0	1
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	5	5	0
	No Constriction		0	0	0	0
	Miosis		0	0	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	0	2	0
	Animal Shakes Head		5	5	3	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	3	5	3
	Returns Leg Only Partially to Original Position		0	1	0	1
	No Response		0	1	0	1
Air Righting Reflex	Normal: Lands on All Four Feet		5	3	5	0
	Slightly Uncoordinated		0	2	0	2
	Lands on Side		0	0	0	3
	Lands on Back		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		2	3	1	3
	Alert, Oriented Toward Observer		3	0	4	1
	Asleep		0	0	0	0
	Lying on Side		0	0	0	0
	Flattened		0	2	0	1
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	3	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	2	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		5	5	4	5
	Easy		0	0	1	0
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	5	4	5
	Moderately Difficult		0	0	1	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	4	5	5
	Present		0	1	0	0
Lacrimation	Not Present		5	2	5	5
	Moderate		0	1	0	0
	Extreme		0	2	0	0
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		4	5	5	1
	Slight		1	0	0	3
	Moderate		0	0	0	1
	Extreme		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	1	5	0
	Ataxia		0	0	0	2
	Body Drags		0	2	0	1
	Limbs Splayed or Dragging		0	2	0	1
	Hunched Posture		0	0	0	1
Locomotion	Normal		2	0	0	0
	Increased Movement		1	0	5	0
	Decreased Movement		2	1	0	5
	None		0	4	0	0
Arousal	Normal		3	0	0	0
	Low, Slight Stupor		2	2	0	3
	Very Low, Stupor		0	3	0	2
	High, Slight Excitement, Tense		0	0	5	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		0	8	0	0
	Unformed Stool		0	0	0	0
Urine	Number of Pools		0	4	1	4
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	0	1
	Present		0	0	5	4
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	5
	Severe		0	0	0	0
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		3	0	4	3
	No Reaction		2	5	1	2
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	3	5	5
	No Reaction		0	2	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away		5	5	5	4
	No Reaction		0	0	0	1
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	4	5	0
	No Constriction		0	1	0	0
	Miosis		0	0	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		3	0	4	0
	Animal Shakes Head		2	5	1	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	4	5	5
	Returns Leg Only Partially to Original Position		0	1	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		4	5	4	1
	Slightly Uncoordinated		1	0	1	2
	Lands on Side		0	0	0	2
	Lands on Back		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		0	4	0	3
	Alert, Oriented Toward Observer		4	0	4	1
	Asleep		1	0	0	0
	Lying on Side		0	0	0	0
	Flattened		0	1	0	1
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		4	1	5	5
	Eyelids Completely Closed		1	0	0	0
	Eyelids Slightly Drooping		0	4	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		3	4	4	3
	Easy		2	1	1	2
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		4	5	5	5
	Moderately Difficult		1	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	4	5	5
	Present		0	1	0	0
Lacrimation	Not Present		5	2	5	5
	Moderate		0	2	0	0
	Extreme		0	1	0	0
Coat	Normal		5	5	5	5
	Slightly Soiled		0	0	0	0
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	5	4
	Slight		0	0	0	1
	Moderate		0	0	0	0
	Extreme		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	1	5	4
	Ataxia		0	0	0	0
	Body Drags		0	3	0	1
	Limbs Splayed or Dragging		0	2	0	0
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	0	1	4
	Increased Movement		0	0	4	0
	Decreased Movement		0	4	0	1
	None		0	1	0	0
Arousal	Normal		5	0	1	4
	Low, Slight Stupor		0	1	0	1
	Very Low, Stupor		0	4	0	0
	High, Slight Excitement, Tense		0	0	4	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		0	4	0	0
	Unformed Stool		0	0	0	0
Urine	Number of Pools		0	0	0	1
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	1	4
	Present		0	0	4	1
Motor Movements						
Fasciculations	Not Present		5	5	5	4
	Slight		0	0	0	1
	Severe		0	0	0	0
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		5	3	5	5
	No Reaction		0	2	0	0
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	3	5	5
	No Reaction		0	2	0	0
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away		5	4	5	5
	No Reaction		0	1	0	0
	Apparent Increased Pain		0	0	0	0
Pupil Response	Pupil Constricts		5	3	4	2
	No Constriction		0	2	0	1
	Miosis		0	0	0	2
	Mydriasis		0	0	1	0
Pinna	Ear Flattens Against Head		0	1	1	0
	Animal Shakes Head		5	4	4	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	5
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		5	5	5	4
	Slightly Uncoordinated		0	0	0	0
	Lands on Side		0	0	0	1
	Lands on Back		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Home Cage Evaluations						
Posture	Sitting or Standing Normally		4	1	4	0
	Alert, Oriented Toward Observer		1	0	1	0
	Asleep		0	0	0	0
	Lying on Side		0	0	0	0
	Flattened		0	4	0	5
	Crouched		0	0	0	0
Vocalizations	Not Present		5	5	5	5
	Present		0	0	0	0
Palpebral Closure	Eyelids Open		5	1	5	5
	Eyelids Completely Closed		0	0	0	0
	Eyelids Slightly Drooping		0	4	0	0
	Eyelids Half Closed		0	0	0	0
Handling Evaluations						
Ease of Removal	Very Easy		3	4	4	4
	Easy		2	1	1	1
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
Ease of Handling	Normal (easy, alert)		5	5	5	5
	Moderately Difficult		0	0	0	0
	Freezes		0	0	0	0
	Difficult		0	0	0	0
	Totally limp		0	0	0	0
Chromodacryorrhea	Not Present		5	4	5	5
	Present		0	1	0	0
Lacrimation	Not Present		5	1	5	3
	Moderate		0	2	0	2
	Extreme		0	2	0	0
Coat	Normal		5	5	4	2
	Slightly Soiled		0	0	1	3
	Moderately Soiled		0	0	0	0
	Extremely Soiled		0	0	0	0
Salivation	Not Present		5	5	5	3
	Slight		0	0	0	2
	Moderate		0	0	0	0
	Extreme		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9		Group:	1	2	3	4
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture	Normal		5	1	5	0
	Ataxia		0	0	0	2
	Body Drags		0	2	0	3
	Limbs Splayed or Dragging		0	3	0	1
	Hunched Posture		0	0	0	0
Locomotion	Normal		3	0	1	0
	Increased Movement		0	0	4	0
	Decreased Movement		2	1	0	3
	None		0	4	0	2
Arousal	Normal		3	0	0	0
	Low, Slight Stupor		2	1	0	0
	Very Low, Stupor		0	4	0	5
	High, Slight Excitement, Tense		0	0	5	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		0	3	0	0
	Unformed Stool		0	0	0	0
Urine	Number of Pools		0	2	0	0
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	0	0
	Present		0	0	5	5
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	3
	Severe		0	0	0	2
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Reflex Assessments						
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away		3	0	5	3
	No Reaction		2	5	0	2
	Freezes or Pulls Away Slightly		0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or		0	0	0	0
Audition	Normal: Flinches or Flicks Ears		5	1	5	3
	No Reaction		0	4	0	2
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pain	Normal: Flinches or Flicks Ears		5	5	5	1
	No Reaction		0	0	0	4
	Exaggerated; Jumps, Flips, Bites		0	0	0	0
Pupil Response	Pupil Constricts		4	3	5	0
	No Constriction		1	1	0	0
	Miosis		0	1	0	5
	Mydriasis		0	0	0	0
Pinna	Ear Flattens Against Head		0	0	0	0
	Animal Shakes Head		5	5	5	5
	No Response		0	0	0	0
Proprioception	Normal: Returns Leg to Original Position		5	5	5	5
	Returns Leg Only Partially to Original Position		0	0	0	0
	No Response		0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet		5	3	5	2
	Slightly Uncoordinated		0	1	0	2
	Lands on Side		0	1	0	1
	Lands on Back		0	0	0	0

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This is a reformat of text and tables from Study No. H-34, 00-14501

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1. INTRODUCTION

This study was designed to assess the effect of Amphetamine and Chlorpromazine on the locomotor activity in young rats 13, 17, 21, and 62 days of age. This work was performed in order to provide Positive Control data and was conducted according to test guidelines of the U.S. Environmental Protection Agency (Office of Prevention, Pesticides and Toxic Substances, Health Effects Guidelines, OPPTS 870.6300, Developmental Neurotoxicity, August 1998).

2. MATERIALS AND METHODS

2.1. REGULATORY REFERENCES

2.1.1. TEST GUIDELINES

This study was designed to provide positive control data for neurotoxicity screening studies in accord with the US EPA Health Effects Test Guidelines, OPPTS 870.6200 Neurotoxicity Screening Battery, August 1998.

2.1.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Part 160 of 40 CFR (EPA/FIFRA Good Laboratory Practice Regulations) with the exception that assays to verify concentration, stability and homogeneity of the test articles in carriers were not performed.

2.1.3. ANIMAL WELFARE ACT COMPLIANCE

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.

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2.2. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.3. STUDY MANAGEMENT

2.3.1. SPONSOR AND TESTING FACILITY

Huntingdon Life Sciences
Mettlers Road
PO Box 2360
East Millstone, NJ 08875-2360

2.3.2. STUDY DIRECTOR[1]

[redacted]

2.4. EXPERIMENTAL DESIGN

Group	Treatment	Dosage (mg/kg)	Dose Volume (mL/kg)	Treatment Schedule	Locomotor Activity Assessment	Number of Animals
I[a]	Control	0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after injection	10/sex
II	Amphetamine	2.0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after	10/sex

[redacted] served as Study Director during the testing portion of Study No. 00-14501. Effective 19 May 2000, [redacted] assumed the responsibilities of Study Director. [redacted] assumed all Study Director responsibilities following [redacted] departure from Huntingdon Life Sciences, effective 22 December 2000. Effective 10 Nov 2008, [redacted] assumed Study Director responsibilities for Study No. 00-14501 for the purpose of amending the Final Report only.

					injection	
III	Chlorpromazine	10.0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after injection	10/sex

[a]Control animals were administered 0.9% saline at the same dose volume as the test articles.

2.5. STUDY DATES

2.5.1. STUDY INITIATION

10 February 2000

2.5.2. DATE OF ANIMAL RECEIPT

11 February 2000

2.5.3. DOSE INITIATION DATES FOR LOCOMOTOR ACTIVITY ASSESSMENTS

Postnatal Day 13: 14 February 2000
Postnatal Day 17: 18 February 2000
Postnatal Day 21: 22 February 2000
Postnatal Day 62: 03 April 2000

2.5.4. TRANSFER OF ANIMALS TO EXTRA RAT COLONY

04 April 2000

2.5.5. STUDY COMPLETION

13 March 2001 (Date Study Director signed the Final Report)

2.6. TEST ARTICLES

2.6.1. AMPHETAMINE

Supplier

Sigma
3050 Spruce Street
St. Louis, MO 63103

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

Lot Number

69H1239

Purity

Assume 100%

Date Received

07 January 2000

Expiration Date

June 2001

Description

Powder

Storage

Room temperature

Archival Sample

A sample of amphetamine is stored in the Archives of the Testing Facility under conditions specified for test article storage.

Disposition of Unused Test Article

Unused test article was used as the archival sample for this test article.

2.6.2. CHLORPROMAZINE

Supplier

Sigma
3050 Spruce Street
St. Louis, MO 63103

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

Lot Number

48H1403

Purity

98%

Date Received

01 December 1999

Expiration Date

April 2001

Description

White/White with a yellow cast, powder

Characteristics

Light sensitive

Storage

Room temperature, protected from light

Archival Sample

A sample of chlorpromazine is stored in the Archives of the Testing Facility under conditions specified for test article storage.

Disposition of Unused Test Article

Unused test article was used as the archival sample for this test article.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.7. CONTROL ARTICLE

0.9 % Saline

2.7.1. SUPPLIER

VWR Scientific Products
200 Center Square Rd.
Bridgeport, NJ 08014

2.7.2. LOT/BATCH NUMBER

G-949941 / 173-191

2.7.3. DATE RECEIVED

04 June 1999

2.7.4. EXPIRATION DATE

October 2000

2.7.5. DESCRIPTION

Clear liquid

2.7.6. STORAGE

Room temperature

2.7.7. ARCHIVAL SAMPLE

A sample of the control article is stored in the Archives of the Testing Facility under conditions specified for test article storage.

2.8. TEST ARTICLE AND CONTROL ARTICLE PREPARATION

2.8.1. CONTROL ARTICLE PREPARATION

Control article was used neat; as received.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.8.2. TEST ARTICLE PREPARATION

Appropriate amounts of test article were mixed with 0.9% saline to achieve the desired concentrations in a graduated cylinder, capped, inverted and shaken well prior to use. Fresh dosing solutions were prepared either 1 or 3 days prior to or the day of dose administration and were refrigerated (2-8°C) when not in use.

2.9. ANALYSIS OF DOSING SUSPENSIONS

Analyses were not performed in this study.

2.10. TEST ANIMALS

2.10.1. SPECIES

Albino Rats
[Crl: CD® (SD) IGS BR]

2.10.2. SUPPLIER

Charles River Laboratories
Kingston, NY facility

2.10.3. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model commonly utilized in reproduction studies as recommended in the referenced guidelines.

2.10.4. ANIMAL RECEIPT INFORMATION

Purchased	8 litters (dam and 5 pups/sex/litter)
Placed on study	6 litters (dam and 5/sex/litter)

2.10.5. AGE OF PUPS AT RECEIPT

Pups were received on Postnatal Day 10.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.10.6. ACCLIMATION PERIOD

All female rats and their litters were acclimated from the time they were received until locomotor activity assessment began on the pups.

2.11. SELECTION/GROUP ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered suitable for the study on the basis of pretest physical examinations were randomized into groups at receipt using a method which ranked the Postnatal Day 10 body weights and randomly assigned each within the block of three into groups. Animals were replaced as required based on physical examinations and/or body weight change up to Postnatal Day 13 to achieve the desired number of animals (10/sex/group). Disposition of all animals not utilized in this study is maintained in the study file.

2.12. ANIMAL IDENTIFICATION

Each female was ear tagged (metal ear tag) with a unique identification number by the supplier. Each Postnatal Day 10 pup was uniquely identified by tattoo upon receipt. At weaning (Postnatal Day 21), each pup was ear-tagged with a number assigned by the Testing Facility upon receipt. These numbers plus the study number served as each animal's unique and permanent identification for the duration of the study. Each cage was also provided with a cage card which contained the study number and animal number.

2.13. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.14. ANIMAL HUSBANDRY

2.14.1. HOUSING

Each female rat and litter, from the time of receipt through Postnatal Day 20 were individually housed in a covered, clear plastic "shoebox" with bedding. From Postnatal Day 21 until Postnatal Day 28, the weanling pups (two or three of the same sex) were housed in stainless steel suspended cages with wire mesh floors and fronts. After Postnatal Day 28, and for the remainder of the study, animals were individually housed in stainless steel suspended cages with wire mesh floors. A glass food jar with a stainless steel lid, and food saver, was secured in each cage. Clean food jars and fresh feed were provided at least weekly.

2.14.2. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, MO) was provided *ad libitum*.

Analytical certification of batches of feed, provided by the manufacturer, were maintained on file at the Testing Facility. Feed was analyzed for nutritional content (protein, fat, fiber), inorganic constituents (arsenic, cadmium, calcium, lead, mercury, phosphorus, selenium), organophosphates (diazinon, ethion, methyl parathion, thimet, trithion, disulfoton, malathion, parathion, thiodan), and pesticides (aldrin, beta-BHC, DDE, delta-BHC, endrin, heptachlor, lindane, mirex, alpha-BHC, chlordane, total DDT, dieldrin, HCB, heptachlor epoxide, methoxychlor), plus PCB, and aflatoxin.

There were no known contaminants in the feed which were considered capable of interfering with the results of this study.

2.14.3. WATER

Facility water was supplied by Elizabethtown Water Company, (Westfield, NJ); and was provided *ad libitum* to individual animal cages via an automated watering system.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

Monthly water analyses were conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water analyses, provided by the supplier, were maintained on file at the Testing Facility. In addition, water samples were collected biannually from representative rooms in the Testing Facility; chemical and microbiological water analyses were conducted on these samples by a subcontract laboratory. Results were maintained on file at the Testing Facility. There are no known contaminants in the water which are expected to interfere with this study.

2.14.4. BEDDING ARTICLE

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) was provided for each female rat and litter from time of receipt through Postnatal Day 20. Fresh bedding was provided weekly and as needed.

Bedding was analyzed for inorganic constituents (arsenic, bismuth, cadmium, lead, magnesium, manganese, mercury, nickel, zinc), organophosphates (diazinon, ethion, methyl parathion, trithion, malthion, ethyl parathion), and pestcides (aldrin, beta-BHC, DDE, delta-BHC, endrin, heptchlor, lindane, mirex, alpha-BHC, chlordane, total DDT, dieldrin, HCB, heptachlor epoxide, methoxychlor), plus PCB, and aflatoxin. There were no known contaminants in the bedding which were expected to interfere with the results of this study. Contaminant analyses were performed periodically. Results of the bedding analysis were maintained on file at the Testing Facility.

2.14.5. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve-hour light/dark cycle provided via automatic timer.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

Temperature

Temperature was monitored and recorded twice daily and maintained within the desired ranges to the maximum extent possible.

Desired: 18 - 26°C
Actual: 21 - 24°C

Relative Humidity

Relative humidity was monitored and recorded once daily and maintained within the desired ranges to the maximum extent possible.

Desired: 30 - 70%
Actual: 20 – 68%

Relative humidity was not within the specified range on eight occasions during this study (20-28%). This was not considered to have affected the integrity of the study.

2.15. TEST ARTICLE ADMINISTRATION

2.15.1. ROUTE OF ADMINISTRATION

Intraperitoneal injection

2.15.2. JUSTIFICATION FOR ROUTE OF ADMINISTRATION

The intraperitoneal route provides rapid test article absorption and has been used in previous studies with the test articles.

2.15.3. FREQUENCY AND DURATION OF ADMINISTRATION

The test articles (Amphetamine, Chlorpromazine) and control article were administered to pups on Postnatal Days 13, 17, 21, and 62. Each animal was dosed more than once per week with a washout period of 4 to 41 days between doses.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.15.4. ADMINISTRATION OF TEST AND/OR CONTROL ARTICLE

The test articles (Amphetamine, Chlorpromazine) and the control article (saline) were administered by intraperitoneal injection into the abdominal cavity near the inguinal region using a sterile needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

2.16. EXPERIMENTAL EVALUATION

2.16.1. VIABILITY OBSERVATIONS (CAGESIDE)

Observations for mortality, morbidity and signs of severe toxic or pharmacological effects were made at least twice daily (morning and afternoon) for the female rats and pups.

2.16.2. CLINICAL OBSERVATIONS

A detailed physical examination was given to all female rats and pups upon receipt. The rat pups had a detailed physical examination on the day of locomotor activity behavioral assessment and weekly during the postweaning period until they were placed in a colony.

2.16.3. BODY WEIGHTS

Body weights were recorded for pups on Postnatal Days 10, 13, 17, 21, 62, and weekly during the postweaning period.

2.17. LITTER EVALUATIONS

2.17.1. OBSERVATIONS

Litters were observed and each pup was sexed at the time of receipt. Pups in the litter were counted on Postnatal Days 10,13,17, and 21.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.17.2. WEANING

Pups were weaned on Postnatal Day 21 and housed two or three of the same sex per cage.

2.17.3. LOCOMOTOR ACTIVITY BEHAVIORAL ASSESSMENT

The locomotor activity assessment was measured in 10 pups/sex/group on Postnatal Days 13, 17, 21 and 62. On each day of testing, 10 rat pups/sex/group were adminstered either vehicle, amphetamine, or chlorpromazine. Approximately thirty minutes after the injection they were placed in a clear plastic shoebox cage equipped with a 5-beam automated Photobeam Activity System (PAS; San Diego Instruments, Inc.). Activity was monitored during a 60-minute session composed of 12, five-minute intervals. A record was made of the total number of photobeam breaks which occurred during each of the 12, five-minute intervals. The locomotor activity was assessed using a repeated measures analysis of variance to determine if there was a test article effect. Rat pups were randomized so that there was an equal representation of the treatment groups during each locomotor activity session.

Temperature

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 18 to 26°C
Actual: 22 to 24°C

Relative Humidity

Relative humidity was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 30 to 70%
Actual: 29 to 56%

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

Noise Level

Noise level was monitored using a Digital Sound Level Meter, Model 840029 (Sper Scientific, Ltd., Scottsdale, Arizona) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 55 to 65 dB
Actual: 60.1 to 61.4 dB

Illumination

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, New York) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: <80 footcandles
Actual: 36.5 to 55.3 footcandles

2.18. POSTMORTEM

No postmortem examinations were performed as all animals were transferred to the in-house rat colony.

2.19. DISPOSITION OF ANIMALS

After the pups were weaned, the female rats were euthanized via an overdose of carbon dioxide and discarded. After the locomotor activity behavioral assessment on 62, the rats were transferred to the in-house rat colony.

2.20. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations were recorded and maintained as raw data.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

At the completion of the study, all reports, raw data, protocol and amendments, and retained samples will be maintained in the Testing Facility's Archives.

2.21. PROTOCOL DEVIATIONS

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

1. Litter counts were not recorded on Postnatal Days 10, 13, 17, and 21 due to technician error. However, individual body weights recorded for those days (Postnatal Days 10, 13, 17, and 21) are considered documentation for the count.

2. Documentation of pups not selected for this study was omitted from the data due to technician error.

3. As there is no documentation in the study data indicating the age of the dams at time of receipt at the Testing Facility, it can not be determined that the protocol requirement that the dams be 75-90 days old was met.

4. Protocol specified that the washout period between doses would be approximately 2 days even though it also specified dosing would occur on Postnatal Days 13, 17, 21 and 60 (±2) days. The washout periods in this study ranged from 4 to 41 days.

5. Fresh dosing solutions were prepared either 1 or 3 days prior to or the day of dose administration rather than once weekly as specified in the protocol.

2.22. COMPUTER SYSTEM

The Toxicology Analysis System Customized - Reproduction Module (TASC-R), version 1.1.13, from Pathologist Associates International (PAI), Frederick, Maryland, was the computer software system utilized during the conduct of this study for randomizations, data collection, reporting, and statistical analysis.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

2.23. STATISTICAL EVALUATIONS

The locomotor activity behavioral assessments were analyzed for each period using split-plot repeated measures analysis of variance with model terms for group, animal within group, interval and group by interval interaction. If the group by treatment interaction was statistically significant, 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 for each animal) was used to test for the overall treatment effect with respect to 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. No investigation of model fit was requested or performed. Analyses were performed for sexes separately and combined. Treatment group effects were deemed significant at the α=0.05 level. Plots, tables, listings, and analyses were generated using SAS® version 6.12 for WINDOWS. Analyses were conducted by CATO Research, 200 Westpark Corporate Center, 4364 South Alston Avenue, Durham, NC 27713-2280.

3. RESULTS

Results from pups treated with 2 mg/kg Amphetamine (Group II) indicate a statistically significant increase in locomotor activity for male and female rats combined, on Postnatal Days 13, 17, 21, and 62, when compared to the control group. Statistically significant increases in locomotor activity were observed for Group II male and female rats individually, on Postnatal Day 21 and 62 only.

Results from pups treated with 10 mg/kg Chlorpromazine (Group III) indicated a statistically significant decrease in locomotor activity for male and female rats combined, on Postnatal Days 17, 21, and 62, when compared to the control group. Statistically significant decreases in locomotor activity were observed for Group III male and female rats individually, on Postnatal Days 17, 21, and 62 only.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

4. DISCUSSION

This study evaluated the behavioral effects of Amphetamine and Chlorpromazine on locomotor activity of young male and female rats, in order to generate positive control data for future developmental neurotoxicity studies.

Rats dosed and tested on Postnatal Day 17, 21, and 62 responded to test article treatment, with increased activity for Group II (2 mg/kg amphetamine) and decreased activity for Group III (10 mg/kg chlorpromazine). Amphetamine or Chlorpromazine behavioral effects were observed equally in both male and female rats in the treatment groups.

Rats treated with Amphetamine exhibited locomotor activity similar to control levels at the beginning of the testing period. Unlike the control animals, the Amphetamine treated animals did not habituate, and remained in a more active state for the duration of the 60-minute testing period.

Rats treated with Chlorpromazine exhibited decreased locomotor activity compared to control levels at the beginning of the testing period. Unlike the control animals, the Chlorpromazine treated animals did not habituate, and remained in a less active state for the duration of the 60-minute testing period.

The pups dosed and tested on Postnatal Day 13 did not respond to treatment as dramatically as in latter dosing/testing days. The lack of statistically significant locomotor activity differences in the Postnatal Day 13 treatment groups may stem from the low basal level of activity in pups of such a young age. The presence of age-related differences in locomotor activity in this study suggests the importance of evaluating behavioral endpoints at several different time-points, when testing for developmental neurotoxicity.

5. CONCLUSION

Under the conditions of this study, 2 mg/kg of Amphetamine or 10 mg/kg of Chlorpromazine, administered to young male and female rats on Postnatal Days 13, 17, 21, and 62, via intraperitoneal injection produced statistically significant behavioral effects on locomotor activity. Based on these results, it was shown that both amphetamine and chlorpromazine are excellent model compounds for the generation of locomotor activity alterations in young Sprague Dawley rats.

	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Preface	Appendix KK

Summary of Statistical Results for Motor Activity Data

Post Natal Day	Sex	Parallel Hypothesis (p-value)	Level Hypothesis (p-value)	Significant Pairwise Results*
13	Male	0.1824	0.3593	NA
	Female	0.1097	0.0723	NA
	Combined	0.0074	NA	**1**:NS; **2**:NS;**10**:II>I; **11**:II>I; **12**:II>I
17	Male	0.0203	NA	**1**:I>III; **2**:I>III; **4**:I>III
	Female	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:NS; **5**:I>III
	Combined	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:I>III; **8**:NS; **10**:NS; **11**:NS; **12**:II>I
21	Male	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
	Female	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
	Combined	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I, I>III; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
62	Male	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:I>III; **6**:II>I, I>III; **7**:II>I, I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I; **12**:II>I
	Female	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:II>I, I>III; **6**:II>I, I>III; **7**:I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I; **12**:II>I, I>III
	Combined	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:II>I, I>III; **6**:II>I, I>III; **7**:II>I, I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I, I>III; **12**:II>I, I>III

*Only intervals with significant differences between treatments are reported.

NA = Not applicable; NS = No significant differences from control

x: a>b indicates mean for group a significantly greater than mean for group b in interval x.

I = control, II = amphetamine, III = chlorpromazine

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 13	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	27.70	12.30	18.40	23.60	10.60	14.10	12.90	7.40	7.10	9.40	8.80	9.90
S.D.	21.88	15.32	30.96	40.81	12.43	20.80	12.81	10.24	11.32	10.15	7.18	11.90
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	37.70	21.10	18.40	17.20	10.20	9.20	6.10	8.10	19.60	36.70	28.80	41.60
S.D.	39.38	25.14	29.86	25.17	14.29	11.15	8.48	9.05	20.01	43.02	39.89	58.17
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	14.80	8.10	8.80	12.30	7.40	5.70	8.20	25.70	12.80	12.00	8.60	17.70
S.D.	26.95	15.17	13.21	21.67	11.84	13.05	11.38	55.13	22.52	27.05	27.20	54.93
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 13	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	25.00	14.70	17.10	20.90	16.60	14.30	9.70	6.20	12.50	10.00	7.60	5.70
S.D.	32.00	17.81	24.47	19.77	19.29	14.19	11.61	8.98	13.82	10.72	11.35	4.27
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	36.30	19.40	29.10	24.00	30.40	26.40	41.30	33.20	38.90	52.00	49.90	31.90
S.D.	45.41	26.53	40.16	34.50	51.56	49.40	65.11	55.36	74.84	87.22	55.36	38.23
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	4.00	1.50	11.40	24.30	0.80	2.50	3.50	4.90	3.10	5.10	6.20	1.90
S.D.	8.07	3.75	19.41	50.71	1.62	4.06	5.76	9.34	5.51	10.79	10.25	2.88
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 17	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**0**	**11**	**12**
Group I – Control												
Mean	75.00	55.80	49.40	50.90	36.30	36.00	39.10	35.20	32.00	31.00	33.20	14.50
S.D.	42.95	49.40	33.92	40.33	35.24	38.39	43.53	32.15	39.34	39.73	39.81	18.33
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	52.00	30.80	42.70	41.20	29.90	26.50	32.40	52.40	64.10	62.00	51.60	28.80
S.D.	45.11	34.37	45.49	30.49	26.91	30.95	34.10	46.85	69.09	59.57	55.35	29.13
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	13.10	10.80	12.30	8.20	13.40	9.20	10.30	18.30	10.70	17.30	10.60	11.60
S.D.	29.41	24.51	22.45	18.00	25.18	16.30	15.91	18.29	19.24	27.38	13.85	14.45
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 17	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	99.10	39.90	34.00	22.70	30.20	16.30	24.60	32.10	30.70	25.60	27.70	14.50
S.D.	37.91	43.36	30.81	43.34	36.66	25.23	29.95	42.49	36.06	39.64	39.21	22.14
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	85.20	47.40	30.20	47.40	34.00	15.80	17.50	18.40	26.50	33.60	19.10	34.40
S.D.	35.75	31.80	26.19	26.08	24.68	13.77	19.73	23.20	21.84	31.32	22.29	26.34
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	2.20	4.80	1.00	0.90	2.70	17.70	14.20	3.70	23.60	4.80	6.10	12.60
S.D.	3.16	6.09	2.31	2.51	6.96	52.49	37.67	5.85	46.08	9.17	18.94	28.88
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 21	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	73.60	50.10	25.30	17.10	16.50	28.50	25.70	14.60	27.00	16.10	7.90	8.80
S.D.	46.33	35.63	29.06	26.53	20.99	28.32	23.84	21.48	25.73	18.54	10.16	10.77
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	157.30	154.00	144.00	152.60	141.50	141.20	127.50	136.70	133.80	127.10	125.00	113.20
S.D.	30.36	22.58	9.13	36.00	25.08	28.27	27.20	26.42	28.39	23.50	31.85	25.57
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	14.20	6.90	0.70	2.60	5.10	4.50	4.20	11.50	8.60	10.50	5.20	5.20
S.D.	18.40	12.31	1.49	8.22	7.69	7.68	7.28	17.28	10.48	14.39	10.81	7.13
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 21	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	93.30	29.80	27.50	17.50	17.80	27.10	15.10	14.50	8.70	7.80	8.80	10.40
S.D.	51.26	23.93	20.88	25.10	29.56	30.45	23.90	20.60	14.43	12.41	17.87	21.70
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	149.10	133.50	114.30	118.80	118.40	116.60	108.60	104.90	113.20	111.30	108.00	95.00
S.D.	27.65	29.30	18.88	27.45	32.05	33.02	36.06	30.71	20.07	22.88	27.81	22.40
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	8.00	3.40	3.20	4.70	4.40	5.60	5.00	10.80	4.60	5.20	5.90	8.00
S.D.	11.19	6.92	4.78	5.72	7.79	7.73	12.27	12.46	7.44	12.89	12.75	9.43
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 62	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	233.1	211.1	182.2	156.5	157.3	120.3	82.4	80.1	65.4	51.3	44.2	18.3
S.D.	49.84	31.37	18.05	28.60	35.20	50.12	53.69	57.66	63.58	56.90	52.93	23.21
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	242.5	228.8	190.8	190.5	185.6	163.8	165	169.4	160.5	155.7	142.5	133.2
S.D.	61.10	44.69	47.22	55.66	32.24	41.13	48.15	53.80	49.25	35.92	38.54	42.49
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	28.8	31.3	26.4	20.3	16.8	19.7	10.6	9.1	5.9	7.4	6.3	4.2
S.D.	69.09	63.0	54.62	60.03	34.86	29.18	31.09	8.57	11.08	18.65	12.41	9.07
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 62	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	171.10	153.40	143.90	124.00	103.60	95.50	91.00	55.80	57.60	37.90	32.30	32.20
S.D.	24.85	23.08	37.22	35.57	29.28	37.63	28.77	30.97	42.84	39.45	42.60	30.80
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	150.10	144.90	133.60	132.00	137.80	150.50	120.30	130.40	124.00	134.10	143.30	105.30
S.D.	45.19	29.05	31.40	33.97	31.90	46.83	39.06	43.90	39.58	35.23	31.92	40.12
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	33.30	18.20	12.40	10.20	8.70	0.90	4.10	2.30	6.90	5.50	2.50	0.00
S.D.	43.27	30.08	33.27	13.49	23.79	2.51	8.57	2.63	9.69	8.45	5.04	0.00
N	10	10	10	10	10	10	10	10	10	10	10	10

PROTOCOL

ISOBUTANE

COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

CONFIDENTIAL

HLS Study No.:	**03-4244**
Protocol No.:	**Final**
Date:	**20 November 2003**

PROTOCOL PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

HLS Study No.: 03-4244

This is the Final Protocol. It has been reviewed and approved by:

[redacted]

26 NOV 03
Date

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1. INTRODUCTION

HLS Study No.	03-4244
Title	Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures
Testing Facility	Huntingdon Life Sciences 100 Mettlers Road East Millstone, NJ 08875-2360
Purpose	This study is designed to assess the potential toxicity, including neurotoxicity, and reproductive performance in male and female rats when the test substance is administered by whole-body inhalation exposure. For male and female rats, it should permit detection of effects on gonadal function which may not be detected by histological examination of the reproductive organs and on mating behavior. In addition, for female rats this study should detect effects on conception, development of the conceptus and parturition and pup survival to Lactation Day 4.

2. STUDY PERSONNEL

Study Director	[redacted]
Alternate Contact	[redacted]
Director of Reproductive Toxicology	[redacted]

Additional personnel will be documented in the project file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation Date	Date Study Director Signs Protocol
Receipt of Test Animals	2 December 2003 (Experimental Start)
Initiation of Exposures	15 December 2003
Initiation of Mating	29 December 2003
Termination of Mating	12 January 2004
Termination of Exposures	Main Study Rats: 14 January 2004 Satellite Female Rats: 31 January 2004
Necropsy:	Main Study Rats: 14-15 January 2004 Satellite Female Rats: 24 January-7 February 2004
Submission of Draft Final Report:	25 June 2004
Experimental Termination:	Date of last data collection
Study Completion Date:	Date final report is signed by Study Director

4. EXPERIMENTAL DESIGN

Group	Group Designation	Exposure Levels (ppm)	Treatment Schedule Pre-mating Period		Number of Animals	
			Main Study Male Rats[b]	Main Study and Satellite Female Rats[b,c]	Main Study Male Rats	Main Study and Satellite Female Rats*
1	Air Control[a]	0	2 weeks	2 weeks	12	24
2	Low	900	2 weeks	2 weeks	12	24
3	Mid	3000	2 weeks	2 weeks	12	24
4	High	9000	2 weeks	2 weeks	12	24

*12/group = main study animals for subchronic evaluations only

*12/group = satellite animals for reproductive evaluations only

[a] Control animals will be treated with air only with the same treatment regimen as the treated groups.

[b] Main Study male rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats will continue during the mating and post-mating periods for a minimum exposure of 28 days. Main Study female rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 4 weeks for a minimum exposure of 28 days.

[c] Satellite female rats (12/group) for the reproduction study will be exposed once daily (6 hours/day), seven days/week for at least two weeks prior to mating initiation. Satellite female rats will continue to be treated once daily (6 hours/day) during mating. Once mated, Satellite female rats will be treated once daily (6 hours/day) during gestation (days 0-19). Satellite female rats without evidence of mating will continue to be treated for 19 days (6 hours/day) following completion of the mating period and then held for an additional 7 days. In the event that Satellite female rats without evidence of mating appear pregnant, exposure will be terminated on the estimated Gestation Day 19.

The first day of exposures will be defined as Day 0 of the study.

4.1. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

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

4.2. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model acceptable under OECD and EPA testing guidelines for reproductive toxicity and neurotoxicity studies. In addition, a historical database is available in the Testing Facility for comparative evaluation with this strain of rat.

4.3. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in this study is considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD and EPA guidelines. Ten pregnancies per group are considered an adequate number for screening for developmental toxicities. The reference guideline indicates 8-10 litters per group provide the necessary degree of consistency between studies. With the group size of 12 used in this study, and with recent pregnancy rates of 80-90%, this should provide between 8-10 litters/group for evaluation. On this basis, group sizes of 12 paired Main Study male and Satellite female rats are considered appropriate for this study and will provide a sufficient number of litters in each group to meet guideline requirements. Group sizes of 12 Main Study female rats are considered appropriate for providing comparable data to the Main Study male rats.

4.4. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels are based on results of a 2-week range-finding Study 03-6145 which showed no toxicity at exposure levels of 90, 900 and 9000 ppm. Therefore, the high exposure level was established (for safety reasons) at 9000 ppm since it is 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE ISOBUTANE

Test Substance Category: industrial gas

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data. The Testing Facility will purchase the test substance from a Sponsor approved vendor (MG Industries, Malvern PA). The test substance will be stored (ambient conditions) in an outside solvent shed except when in use in the inhalation laboratory. The test substance will be handled as a flammable gas.

5.1.1. Purity	To be determined by the Testing Facility by assaying by GC before the study.
5.1.2. Stability	To be determined by the Testing Facility by assaying by GC before and after the study.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability, and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Supplier. This documentation will be maintained by the Supplier. The Testing Facility will ensure that the location of the documentation of fabrication is provided in the report.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and stored in the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA 20166). If multiple studies are conducted with the same test substance, a common archival sample may be taken and appropriately labeled.

5.4. UNUSED TEST SUBSTANCE

The unused portion of the test substance as well as any empty test substance containers will be returned to the Supplier following submission of the final report of the final study with this test substance.

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus®
Sprague-Dawley - derived (CD®)
Crl: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories
Raleigh, North Carolina
Note: males and females will be supplied from separate colony rooms

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. Number

Male Rats	Female Rats	Total
48	96	144

6.3.2. Age and Weight

Animals will be ordered with body weight stipulations to allow all rats of the same sex to be within ± 20% of the mean weight at the time of randomization.

Male rats will be approximately six weeks at receipt and approximately 8 weeks (200-300 grams) at initiation of treatment. Animals outside this weight range will be used at the discretion of the Study Director.

Female rats will be approximately six weeks at receipt and approximately 8 weeks (150-250 grams) at initiation of treatment. Female rats will be nulliparous and non-pregnant. Animals outside this weight range will be used at the discretion of the Study Director.

6.4. ANIMAL HUSBANDRY

6.4.1. Facilities Management/Animal Husbandry

Currently acceptable practices of good animal husbandry will be followed, e.g., Guide for the Care and Use of Laboratory Animals; National Academy Press 1996. Huntingdon Life Sciences is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.4.2. Veterinary Care

Animals are monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.4.3. Housing

All animals will be housed individually in stainless steel suspended cages with wire mesh floors and fronts except for the mating period when one Main Study male and one Satellite female rat will

be housed together. During cohabitation (when Satellite female rats will be brought to the Main Study male rat's cages), male and female rats will then be housed in stainless steel cages of appropriate size for group housing animals. Each cage will be fitted to secure a glass feeder jar with a stainless steel lid. Clean feeder jars and fresh feed will be provided at least weekly. From Day 18 of gestation and during lactation, the dam will be housed with her litter in plastic "shoebox" cages with bedding. Clean feed jars and fresh feed will be provided at least weekly for periods when feed consumption is not being recorded and at each interval when feed consumption will be recorded.

6.4.4. Feed and Feed Analysis

Certified Rodent Diet, No. 5002; (Meal) supplied by PMI Nutrition International (St. Louis, MO) and provided *ad libitum.*

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.4.5. Water and Water Analysis

Facility water is supplied by Elizabethtown Water Company (Westfield, NJ) and will be provided *ad libitum* to individual animal cages via an automated watering system.

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file at the Testing Facility. There are no known contaminants which are expected to interfere with the objectives of this study.

6.4.6. Bedding and Bedding Analysis

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) will be provided for each mated female rat on Gestation Day 18. Fresh bedding will be provided weekly or as needed throughout lactation.

Analyses for each batch of bedding used on study provided by the supplier, will be maintained on file at the Testing Facility. There are no known contaminants in the bedding that are expected to interfere with the results of this study.

6.4.7. Environmental Conditions

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain suitability for study.

6.6. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Female animals will be randomly assigned to Main Study or Satellite groups. Individual weights of animals placed on test shall be within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

6.7. ANIMAL IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. If the tag is lost, it will be replaced or the animal will be tattooed for identification. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study

number and animal number.

6.8. MATING PROCEDURE

Within each treatment group, the Main Study male and Satellite female rats will be co-housed (1:1) until evidence of mating is seen or for 2 consecutive weeks. During mating, cohabitation of male and female littermates will be prohibited. Satellite female rats will be observed at approximately the same time each morning for the presence of a vaginal plug or sperm in the vaginal smear. If not mated, the stage of estrous will instead be recorded. The day on which evidence of mating is observed will be defined as day 0 of gestation. Once mated, the Satellite female rat will be removed from the mating unit and housed individually for the remainder of the study. After the mating period is over, Satellite female rats without evidence of copulation will be removed from the mating unit and housed individually for the remainder of the study (26 days) and monitored for visible signs of pregnancy with corresponding body weight gain.

6.9. ANIMAL HUSBANDRY DURING EXPOSURE

Housing - individually in suspended stainless steel cages
Feed – none
Water - none

7. TEST SUBSTANCE ADMINISTRATION

7.1. ROUTE OF ADMINISTRATION

Inhalation via whole-body exposure.

7.2. JUSTIFICATION FOR ROUTE OF ADMINISTRATION

The inhalation route is one of the potential routes of human exposure to this test substance.

7.3. DURATION AND FREQUENCY OF ADMINISTRATION

Main Study male rats will be exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats (12/group) will continue during the mating and post-mating periods for a minimum exposure of 28 days. Main Study female rats (12/group) will be exposed once daily, seven days/week for 4 weeks for a minimum exposure of 28 days. Satellite female rats (12/group) for the reproduction study will be exposed once daily, seven days/week for at least two weeks prior to mating initiation. Satellite female rats will continue to be treated once

daily during mating. Once mated, Satellite female rats will be treated once daily during gestation (days 0-19). Satellite female rats without evidence of mating will continue to be treated for 19 days following completion of the mating period and then held for an additional 7 days. In the event that Satellite female rats without evidence of mating appear pregnant, exposure will be terminated on the estimated Gestation Day 19.

7.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered as a gas in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure level(s). The method will be described in the raw data of the study and in the report.

The whole-body exposure chambers will each have a volume of approximately 1000 liters. The chambers will be operated at a minimum flow rate of 200 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time of at most 23 minutes. This chamber size and air flowrate is considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the 6-hour exposure, all animals will remain in the chambers for a minimum of 30 minutes. During this time, the chambers will be operated at approximately the same flow rate using clean air only.

7.5. EXPOSURE CONCENTRATION ADMINISTRATION

A nominal exposure concentration will be calculated daily, if possible. The flow of test substance into the chamber and the flow of air through the chamber will be monitored using appropriate calibrated equipment. The average test substance flow during each exposure will be divided by the average chamber airflow to give the nominal concentration. Also, the additive nominal concentration for all 3 test substance chambers for each exposure day will be measured by weighing the test substance cylinder before and after the exposure and dividing the difference by the average chamber airflow.

During each exposure, measurements of airborne concentrations of test substance in the animal's breathing zone will be performed at least four times using an appropriate sampling procedure and infrared spectrophotometric analytical procedure. If more than the normal amount of trials is required because of test substance generation or monitoring problems (50 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

7.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each week of exposure, particle size determinations will be performed using a TSI Aerodynamic Particle Sizer to characterize the aerodynamic particle size distribution of any aerosol present.

7.7. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber temperature, humidity, airflow rate and static pressure will be monitored continuously and recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the maximum extent possible, between 20 to 24°C and 40 to 60%, respectively. Chamber oxygen levels (maintained at least 19%) will be measured pretest and at the beginning, middle and end of the study.

Air samples will be taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room will be measured pretest and at the beginning, middle and end of the study.

7.8. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/week
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate	13X/day
Nominal Test Substance Concentration (excluding the air control chamber)	1X/day
Rotation Pattern of Exposure Cages	1X/day
Loading/Unloading Verification	1X/day

8. EXPERIMENTAL EVALUATION

8.1. OBSERVATIONS

8.1.1. Viability Checks (Cageside)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

8.1.2. Detailed Physical Observations

All animals will be observed as a group at least once during each exposure. This will routinely be performed near the middle of each exposure and may be performed more frequently if significant signs of toxicity are noted.

Each animal will be removed from its cage and a detailed physical observation performed prior to randomization. Main Study male rats will have a detailed physical observation performed once weekly beginning during the premating period and continuing through euthanasia. Main Study female rats will have a detailed physical observation performed once weekly beginning after randomization and continuing through euthanasia. Satellite female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 and Lactation Days 0, 1 and 4. Satellite female rats without evidence of mating will continue to be observed weekly during the mating and post-mating period until euthanized.

Examinations during non-exposure periods will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded.

8.2. BODY WEIGHTS

Body weights of the Main Study male rats and the Main Study female rats will be recorded at the time of randomization into test groups, on the day treatment is initiated and weekly thereafter throughout the study until euthanized. Satellite female rats for the reproduction study will be weighed at the time of randomization into test groups, on the day treatment is initiated and twice weekly until evidence of copulation is observed. Mated Satellite female rats will be weighed on Gestation Days 0, 7, 14 and 20 and Satellite female rats that deliver litters will be weighed on Lactation Days 1 and 4. Satellite female rats without evidence of mating will continue to be weighed twice weekly during the mating and post-mating period until euthanized. A terminal body weight will also be recorded for each animal.

8.3. FEED CONSUMPTION

Feed consumption for the Main Study male rats will be recorded pretest and weekly during the pre-mating treatment period. Feed consumption for the Main Study female rats will be recorded pretest and weekly during the treatment period. Feed consumption for Satellite female rats will be recorded pretest and weekly during the pre-mating treatment period and, if not mated, during the post-mating period. Feed consumption will not be recorded during the mating period when Main Study male rats are being co-housed with Satellite female rats. For pregnant or confirmed mated Satellite female rats, feed consumption will be recorded on Gestation Days 0-7, 7-14, and 14-20 and on Lactation Days 1-4.

8.4. PARTURITION AND LACTATION

On Day 18 of Gestation, several days prior to expected parturition, Satellite female rats will be transferred to solid, plastic cages with bedding article provided. Thereafter, examination for signs of parturition will be made twice daily (morning and afternoon). The duration of gestation will be documented. Evidence of difficult or prolonged parturition or bizarre behavior (including but not limited to self-mutilation, walking backwards), if observed, will be recorded. The day on which parturition initiates will be defined as Lactation Day 0. Litters will be observed as soon as possible after parturition completion for the number of live and dead pups, pup abnormalities and each pup will be sexed. Thereafter, litters will be observed twice daily (morning and afternoon). All pups in the litter will be uniquely identified by toe tattoo after parturition completion. The presence of dead pups will be recorded, and these will be removed from the litter as found. Unusual observations and the absence of milk in the stomach will be noted.

8.5. F_1 PUP EVALUATIONS

8.5.1. Pup Physical Examinations

Each pup will be given a gross physical examination on Lactation Days 0 and 4. Pups will also be observed for any abnormal behavior.

8.5.2. Body Weights and Sexing Data

Individual pup body weights data will be recorded on Lactation Days 1 and 4. Pups will be sexed on Lactation Day 0 and sex verified on Lactation Day 4.

8.6. NEUROBEHAVIORAL EXAMINATIONS

Observations, as outlined below, on all Main Study male rats and all Main Study female rats from all exposure groups will be recorded. Observations will be assessed during the last week of exposure to the test substance. The functional observational battery and motor activity assessments will be performed for all animals on a non-exposure day. Testing will be staggered over several sessions. Each session will consist of approximately equal numbers of animals per sex per exposure level. Noise level will be maintained within a level of 55 to 65 decibels by a white noise generator. Temperature, humidity, and illumination will be measured and recorded to ensure that variations in environmental conditions are minimal during all evaluations. The functional observational battery will be performed for all animals before evaluation of motor activity.

FUNCTIONAL OBSERVATIONAL BATTERY

The time of testing will be balanced across treatment groups. All observations during the treatment period will be performed blind, i.e., the observer will be unaware of the animals' treatment.

Sensory Observations
- startle response to auditory stimuli
- tail pinch response

Neuromuscular Observations
- grip strength – hindlimb and forelimb

Physiological Observations
- rectal temperature

MOTOR ACTIVITY

Activity will be monitored using an automated Photobeam Activity System (San Diego Instruments, Inc.) Sessions will be 60 minutes in length; each session will be divided into 12 five-minute intervals. The time of testing will be balanced across treatment groups. Positive historical control data demonstrating the sensitivity of the procedure will be documented in the final report.

8.7. CLINICAL PATHOLOGY

Clinical pathology procedures and parameters are based on those recommended in guidelines published by the Joint Scientific Committee for International Harmonization of Clinical Pathology Testing in "Harmonization of Animal Clinical Pathology Testing in Toxicity and Safety Studies", *Fund. Appl. Tox.*: 29, 198-201 (1996).

Blood samples for hematology, coagulation and clinical chemistry studies will be obtained from lightly anesthetized (CO_2/O_2) Main Study animals via puncture of the orbital sinus (retrobulbar). Animals will be fasted overnight prior to clinical chemistry blood collection. Blood will be collected and studies performed as follows:

8.7.1. HEMATOLOGY

Blood for hematology studies (~ 0.25 mL) will be collected into tubes containing EDTA anticoagulant.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

erythrocyte count
hematocrit
hemoglobin
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin concentration
leukocyte count (total and differential)
platelet count
reticulocyte count
erythrocyte morphology (from peripheral blood smear)
platelet morphology (from peripheral blood smear)

To be evaluated only if deemed necessary by the Study Director, based on results of other hematology and/or pathology results (additional cost):

bone marrow differential count

8.7.2. COAGULATION

Blood for coagulation studies (~ 0.75 mL) will be collected into tubes containing sodium citrate anticoagulant.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

prothrombin time
activated partial thromboplastin time

8.7.3. CLINICAL CHEMISTRY

Blood for clinical chemistry studies (~ 1.0 mL) will be collected into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum. If an adequate volume of serum is not available for all assays, they will be performed in the order listed.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

alanine aminotransferase
aspartate aminotransferase
alkaline phosphatase
gamma glutamyl transpeptidase
urea nitrogen
creatinine
glucose
total cholesterol
triglycerides
total protein
albumin
globulin (calculated as total protein - albumin = globulin)
albumin/globulin ratio (calculated)
bilirubin (total)
sodium
potassium
chloride
calcium
phosphorus

8.7.4. RETENTION/STORAGE OF SPECIMENS

Any remaining (frozen) serum, which may have limited storage stability, will be stored for up to 6 months after completion of assays and will then be discarded. Peripheral blood smears will be retained and archived with the study.

9. POSTMORTEM

9.1. METHOD OF EUTHANASIA

All animals (except Lactation day 4 pups) will be euthanized by

exsanguination following an overexposure of inhaled carbon dioxide. Lactation day 4 pups will be euthanized using an intraperitoneal injection of sodium pentobarbital.

9.2. POSTMORTEM EXAMINATION - ANIMALS DYING DURING THE STUDY

Animals that die during the study will be given a macroscopic postmortem examination and gross lesions will be saved and preserved in 10% neutral buffered formalin. Reproductive tissues as indicated below will also be saved but no organ weights recorded. Satellite female rats dying during the study will have the number of implantation sites and corpora lutea recorded.

9.3. EUTHANASIA SCHEDULE

9.3.1. Main Study Male and Female Rats

Main Study male rats and female rats will be euthanized after at least 28 days of exposure.

9.3.2. Satellite Female Rats in the Reproduction Study

Mated Satellite female rats will be euthanized on post-partum day 4. Satellite female rats in which evidence of mating was detected but failed to deliver will be sacrificed 26 days after evidence of mating. Satellite female rats where no evidence of mating was detected and who failed to deliver will be euthanized 26 days after the completion of the mating period. Satellite female rats with total litter loss will be euthanized on post-partum day 4.

9.4. MACROSCOPIC EXAMINATION – MAIN STUDY MALE RATS

Macroscopic postmortem examinations will be performed on all Main Study male rats, including those dying spontaneously or euthanized in a moribund condition. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. Gross lesions or tissues with significant findings will be preserved in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.5. MACROSCOPIC EXAMINATIONS – FEMALE RATS

Macroscopic postmortem examinations will be performed on all Main Study and Satellite female rats, including those dying spontaneously or euthanized in a moribund condition and on Satellite female rats sacrificed after aborting or premature delivery of a litter. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. The number of implantation sites and corpora lutea will be recorded for each Satellite female rat. Gross lesions or tissues with significant findings will be saved in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.6. ORGAN WEIGHTS

Organs indicated below will be taken at the scheduled necropsy, weighed wet, recorded and organ/body and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition and for those Satellite female rats not delivering pups. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissue in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired reproductive organs will be weighed separately. All other paired organs will be weighed together.

Main Study Male Rats	Main Study and Satellite Female Rats	All Rats	
Testes	Ovaries with Oviducts	Adrenal Glands	
Epididymides	Uterus with Vagina	Brain with Brainstem	
		Heart	Lungs
		Kidneys	Spleen
		Liver	Thymus

9.7. TISSUES PRESERVED

Tissues listed in Appendix A will be obtained at necropsy for all Main Study male and all Main Study and Satellite female rats from each exposure group and preserved in 10% neutral buffered formalin with the exception of testes and epididymides which will be preserved in a modified Davidson's fixative for at least 24 hours and then stored in 10% neutral buffered formalin. Lungs and urinary bladder will be infused with 10% neutral buffered formalin for optimal preservation.

9.8. MICROSCOPIC PATHOLOGY EVALUATIONS

Microscopic examinations for control and high exposure group Main Study male and Main Study female animals will be performed on tissues and organs as designated in Appendix A. During the microscopic examination of the testes, special emphasis will be placed on the stages of spermatogenesis and the histopathology of interstitial testicular cell structure. Note: Any abnormalities not noted during macroscopic postmortem examinations which are seen during histological processing will be recorded. If treatment-related changes are observed in the high exposure group, microscopic examinations will be performed on the animals of the low and mid exposure groups upon Sponsor approval (additional cost).

Stains: Standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

9.9. MACROSCOPIC POSTMORTEM EXAMINATION - F_1 PUPS

Macroscopic postmortem examinations (internal and external) will be performed on all F_1 pups found dead during lactation. Unusual observations, including gross abnormalities and the absence of milk in the stomach, will be noted and then the carcasses will be discarded. F_1 pups found dead at birth will be identified (lung floatation test) as stillborn or alive but found dead. Macroscopic postmortem examinations (external only) will be performed on all F_1 pups on Lactation Day 4 for pups surviving to that interval. Unusual observations, including gross abnormalities, will be noted and then the carcasses will be discarded.

10. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report. Biological samples collected for clinical pathology will be discarded as described elsewhere in this protocol.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond 1 year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

11. STATISTICAL EVALUATIONS

11.1. CONTINUOUS DATA - to include but not be limited to:

- Body weights
- Body weight changes
- Feed consumption values
- Rectal temperature
- Grip strength measurements
- Hematology and Coagulation values
- Clinical Chemistry values
- Gestation length
- Corpora lutea
- F_1 pup weights (each weighing interval during lactation)
- Number of pups (F_1 litters) per pregnant female rats
- Number of male and female pups
- Pup weight distinguished by sex and as a composite for both sexes (litter as experimental unit)
- Organ weights and organ weight to body weight and brain weight ratios

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all FOB and clinical pathology parameters, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. All other data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977) or Steel's test (Steel, 1959) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

11.2. INCIDENCE DATA - to include but not be limited to:

- Mortality rate
- Mating indices, pregnancy rates, male rat fertility indices
- Litter survival indices
- Gestation indices
- Incidence of dams with no viable pups
- Mean pup survival indices (Days 0 and 4)

A Fisher Exact Test with Bonferonni correction (Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.) will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

11.3. MOTOR ACTIVITY DATA

The data will be 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 is statistically significant (p=0.05), indicating non-parallelism in the behavioral profile between groups, a separate one-way ANOVA for group effects will be performed at each interval. If the response data passes on the parallel hypothesis, an ANOVA (using summed responses over intervals) will be used to test for the overall treatment effect which constitutes the level hypothesis. If any significant overall treatment group effect is found by any of the above ANOVAs, Dunnett's t-test will be used to find groups that differed from control. Analyses will be performed for sexes separately and combined. Treatment group effects will be deemed significant at the p=0.05 level. Plots, tables, listings, and analyses will be generated using SAS® version 8.2 for WINDOWS. Analyses will be conducted by CATO Research, 200 Westpark Corporate Center, 4364 South Alston Avenue, Durham, NC 27713-2280. The Testing Facility will be responsible for the GLP compliance of this subcontractor.

12. REPORTING

12.1. STATUS REPORTS

Periodic verbal and written updates on study progress will be provided by the Study Director. In general, written status reports will be submitted weekly and at termination of the study.

12.2. FINAL REPORT

One unbound hard copy and one electronic copy of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

12.2.1. Body of Report

- Compliance Statement (including Sponsor signature line)
- Quality Assurance Statement
- Summary
- Introduction
- Experimental Design
- Materials and Methods
- Results and Discussion

- Conclusion concerning a No-Observed-Adverse Effect Level (NOAEL)
- Statistical Procedures
- Protocol deviations and study impact statements

12.2.2. Summary Tables

- Exposures
- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Mean body weight data
- Mean animal weight gain data
- Mean feed consumption data
- Mean Hematology and Coagulation
- Mean Clinical Chemistry
- Mean Functional Observation Battery
- Mean gestation length
- Mean number of corpora lutea
- Mean female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Litter survival indices
- Mean litter pup survival indices (Lactation Days 0 and 4)
- Mean pup weights (Lactation Days 1 and 4)
- Mean pup sex ratio (Days 0 and 4)
- Macroscopic postmortem examination (Male Rats, Female Rats, F_1 pups)
- Mean organ weights and organ weight to body weight and brain weight ratios
- Microscopic Pathology

12.2.3. Miscellaneous

- Mating performance data
- Recent historical control data for the Testing Facility

12.2.4. Appendix Tables (Individual data)

- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Individual body weight data
- Individual animal weight gain data
- Individual feed consumption data

- Individual Hematology and Coagulation
- Individual Clinical Chemistry
- Individual Functional Observation Battery
- Individual gestation length
- Individual number of corpora lutea
- Individual female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Individual litter survival indices
- Individual litter pup survival indices (Days 0 and 4)
- Individual pup weights (Days 1 and 4)
- Individual macroscopic postmortem examination (Male Rats, Female Rats, F_1 pups)
- Individual organ weights and organ weight to body weight and brain weight ratios
- Individual Microscopic Pathology

12.2.5. Appendices

- Motor activity evaluation by CATO
- Personnel involved in the study
- Protocol and Amendments

A Robust Summary in IUCLID electronic format will also be separately provided by the Testing Facility's UK office.

13. REGULATORY REFERENCES

13.1. TEST GUIDELINE

This study complies with the Organization for Economic Cooperation and Development (March 22, 1996). OECD Guidelines for Testing of Chemicals; OECD Guideline 422: Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, pp. 1-14 and US EPA OPPTS Health Effects Test Guidelines 870.3650, Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, July 2000.

13.2. GOOD LABORATORY PRACTICES

This study will be 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).

13.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply 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. The Sponsor should make particular note of the following:

1. The Sponsor's signature on this protocol documents for the study described, that there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments.

2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or in written laboratory standard operating procedures.

3. Any procedures outlined in this study protocol which are expected to cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing, by the Sponsor and the Study Director and approved by the IACUC; in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review form.

4. Animals experiencing more than momentary or slight pain or distress due to test substance or emergency situations such as injury or illness will be treated by the Testing Facility's veterinarian staff with approved analgesics or agents to relieve pain. If possible, the Study Director will be consulted prior to treatment; however, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

5. Methods of euthanasia used during this study are in conformance with the above referenced regulations.

13.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with appropriate animal welfare regulations.

14. QUALITY ASSURANCE MONITORING

The Quality Assurance Unit of Huntingdon Life Sciences (East Millstone, NJ) will monitor the facilities, equipment, personnel, methods, practices, records, raw data, draft and final reports and controls used in this study to assure that they are in conformance with this protocol, company Standard Operating Procedures and the referenced Good Laboratory Practice regulations.

15. ALTERATION OF DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by two members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A
TISSUES PRESERVED/EXAMINED

Tissue	Tissues Preserved	Microscopic[a] Examination
Adrenal Glands	X	X
Bone (sternum/femur)[b]	X	X
Bone Marrow (rib)[c]	X	
Brain (medulla/pons, cerebrum and cerebellum)	X	X
Epididymides	X	X
Heart	X	X
Kidneys	X	X
Large Intestine (cecum, colon, and rectum)	X	X
Larynx	X	
Liver	X	X
Lungs (with mainstem bronchi)	X	X
Lymph Node (mesenteric)	X	X
Lymph Node (mediastinal)	X	X
Mammary Gland (with adjacent skin)	X	X
Nasopharynx	X	
Ovary with oviducts	X	X
Prostate	X	X
Seminal Vesicles	X	X
Small Intestine (duodenum, ileum and jejunum)	X	X
Spinal Cord (cervical, thoracic, lumbar)	X	X
Spleen	X	X
Stomach	X	X
Testes	X	X
Thymus	X	X
Thyroid with Parathyroids	X	X
Tibial Nerve	X	X
Trachea	X	X
Urinary Bladder	X	X
Uterus with Vagina	X	X
All Macroscopic Lesions and Tissue Masses	X	X

[a] Control and high exposure Main Study male and female animals. If a treatment-related change is observed in the high exposure group, microscopic examinations will be performed on the low and mid exposure groups upon Sponsor approval (additional cost).

[b] Qualitative examination (no differential count).

[c] Bone marrow smears will be prepared. They will only be evaluated (Sponsor approval, additional cost) if needed.

Protocol Amendment No. 1

Study Title: Isobutane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

1. Proposed Study Dates, page 2:
Revise and Add:

Receipt of Test Animals	2 December 2003 (Experimental Start)*
Initiation of Exposures	15 December 2003 **(Experimental Start)****

***as per OECD GLP's**
****as per EPA GLP's**

2. Detailed Physical Observations, page 12:

Revise: .....Satellite female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 and Lactation Days 0 **(except if parturition doesn't complete on the same day as it initiates)**, 1 and 4.....

3. Statistical Evaluations, page 20:

Add for Continuous Data: .....Corpora lutea **and Implantation sites, Pre-implantation loss and Post-implantation loss**.....

Replace existing description for Continuous Data:

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all FOB and clinical pathology parameters, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. All other data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977) or Steel's test (Steel, 1959) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

Replace existing references for Continuous Data:

Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-

Protocol Amendment No. 1

Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

Add reference for Incidence Data:

A Fisher Exact Test with Bonferonni correction **(Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.)** will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

Revise: .....The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Shirley's test (Shirley, 1977), Steel's test (Steel, 1959) were used to determine which means differed from control.....

Add: **Exception: When 75% of the values for a clinical pathology parameter were the same, Fisher's Exact Test (Fisher, R.A. 1973. *Statistical Methods for Research Workers*. 14th edition. New York: Hafner Publishing Company) was performed followed by Mantel's test (Mantel, N. 1963. Chi-square test with one degree of freedom: extensions of the Mantel-Haenszel procedure. *Journal of the American Statistical Association* 58: 690-700).**

4. Final Report, page 22:

Add for Summary Tables:.....Mean number of corpora lutea **and Implantation sites, Pre-implantation loss and Post-implantation loss**.....

Add for Appendix Tables:.....Individual number of corpora lutea **and Implantation sites, Pre-implantation loss and Post-implantation loss**.....

Protocol Amendment No. 1

Reasons for Changes

1.Clarification of the Experimental Start dates as per the relevant GLPs.
2.Clarification of the observation intervals during lactation if a dam doesn't complete its delivery of pups until the morning after delivery is initiated.
3.Clarification of the appropriate statistical routines and/or their references for the data capture systems that were actually used.
4.This was an oversight in the original protocol since these parameters are required as per the relevant test guidelines.

Additional Cost Required: NO

Amendment approved by:

[redacted]

28 Jun 04
Date

[redacted]

June 28, 2004
Date

Protocol Amendment No. 2

Study Title: Isobutane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

Revise Study Title from:

Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

to

Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Reasons for Changes

Clarification of the study title to accurately reflect the relevant OECD and EPA test guidelines as per protocol.

Note that in the final report that the study title will only be revised on the Cover Page and the Summary Page since all other pages were computer generated based on the original study title.

Amendment approved by:

[redacted]

16 Nov 09
Date

[redacted]

11/3/2009
Date

	Testing Facility Personnel	Appendix MM

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	[redacted]
SENIOR DIRECTOR, SAFETY ASSESSMENT	[redacted]
DIRECTOR, ANALYTICAL SERVICES	[redacted]
DIRECTOR, TOXICOLOGY OPERATIONS	[redacted]
DIRECTOR, QUALITY ASSURANCE	[redacted]
STUDY DIRECTOR	[redacted]
DIRECTOR, REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY	[redacted]
PATHOLOGIST	[redacted]
STUDY MONITOR	[redacted]
VETERINARIAN	[redacted]
MANAGER/SUPERVISOR	
Reproductive Toxicology Inhalation Pharmacy Analytical Services Necropsy and Fetal Pathology Histology	[redacted]

	2-Week Range-Finding Study Report	Appendix NN

STUDY NO. 03-6145

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

Final Report

Submitted to: American Petroleum Institute (API)
1220 L Street, Northwest
Washington, DC 20005-4070

Attn: [redacted]

Date: 16 April 2010

STATEMENT OF COMPLIANCE

This study was conducted in compliance with the United States Environmental Protection Agency's (EPA) Good Laboratory Practice Standards 40 CFR Part 792 (TSCA) and the Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM/(98)17, with the following exceptions:

1. A lot number for the test substance was not available.

2. The actual location for the synthesis documentation of the test substance was not provided by the supplier.

[redacted]

16 April 10
Date

[redacted]

3/30/10
Date

SIGNATURE PAGE

SCIENTIST

The following scientist was responsible for the overall conduct of this study. Departmental supervisory personnel are listed on the personnel page of this report (Appendix O).

[redacted]

16 April 10
Date

SCIENTIFIC REVIEW

The following scientist has reviewed and approved this report:

[redacted]

14 APRIL 2010
Date

[redacted] was the original scientific reviewer of this report and is no longer employed at the Testing Facility. [redacted] is assuming responsibility for final review of this report.

QUALITY ASSURANCE STATEMENT

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management.

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
GLP Protocol Review	14 Jul 03	14 Jul 03
Exposure, Monitoring & Equipment Records	12 Aug 03	12 Aug 03
Body Weights & Training Records	19 Aug 03	19 Aug 03
Terminal Necropsy	26 Aug 03	03 Sep 03
Purity Analysis Report & Study Data	21 Oct 03	21 Oct 03
Final Report, Study Data & Protocol Amendment No. 1	31 Oct 03, 03 – 07 Nov 03	07 Nov 03
Final Report Review	5, 6 & 20 Nov 08	20 Nov 08

[redacted]

16 Apr 10
Date

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

SUMMARY

This study was designed to provide a preliminary assessment of the toxicity of isobutane, an industrial gas, when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study.

Male and female Sprague-Dawley CD® rats (10/sex/group) were exposed for six hours per day to 0 (air only), 90, 900 or 9000 ppm isobutane for up to 15 consecutive days. At the end of the treatment period, all animals were euthanized and necropsied. The following parameters were evaluated: viability, clinical observations, body weights, feed consumption, organ weights and macroscopic observations.

Exposure levels were determined using an infrared spectrophotometer 4 times per chamber per day. Particle size distribution measurements were also made once per chamber per day using a TSI Aerodynamic Particle Sizer.

The mean (± standard deviation) analytical exposure concentrations of isobutane were determined to be 90.80 ± 4.30, 911.6 ± 30.6 and 9251 ± 136 ppm for the exposure groups, respectively. Particle sizing results indicated that the atmospheres were essentially gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

All animals survived to termination except a 900 ppm exposed male animal, which was humanely sacrificed because of an injury. The test animals were unremarkable during the daily exposure periods and the non-exposure periods. There were no statistically significant or exposure-related differences in body weights or in feed consumption in the test substance exposed animals compared to the air control animals.

No gross abnormalities related to test substance exposure were evident at necropsy examination and there were no exposure-related differences in organ weights (absolute and relative to body weight or brain weight) in the test substance exposed animals compared to the air control animals.

In conclusion, two weeks of exposure of rats to isobutane gas at exposure levels of 90, 900 and 9000 ppm resulted in no effects of exposure. Therefore, the 9000 ppm exposure level was a no observable effect level (NOEL) and was considered an acceptable high exposure level (limited by safety considerations for a flammable gas) for a subsequent OECD 422 study.

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1. INTRODUCTION

This study was designed to provide a preliminary assessment of the toxicity of isobutane, an industrial gas, when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

American Petroleum Institute (API)
1220 L Street, Northwest
Washington, D.C. 20005-4070

2.1.2. SPONSOR REPRESENTATIVE

[redacted]

2.1.3. TESTING FACILITY

Huntingdon Life Sciences (HLS)
P.O. Box 2360
100 Mettlers Road
East Millstone, New Jersey 08875-2360

2.1.4. STUDY DIRECTOR

[redacted]

2.2. STUDY DATES

2.2.1. STUDY INITIATION

30 July 2003 (Date Study Director signed the Protocol)

2.2.2. DATE OF ANIMAL RECEIPT

29 July 2003 (Experimental Start Date)

2.2.3. EXPOSURE INITIATION

12 August 2003

2.2.4. EXPOSURE TERMINATION

26 August 2003

2.2.5. TERMINAL SACRIFICES

26 and 27 August 2003

2.2.6. EXPERIMENTAL TERMINATION DATE

27 August 2003 (Date of last data collection)

2.2.7. STUDY COMPLETION

16 April 2010 (Date Final Report is signed by the Study Director)

2.3. EXPERIMENTAL OUTLINE

Group	Test Substance	Exposure Level[a]	Number of Animals[b]	
		ppm	Males	Females
1	air control	0	10	10
2	isobutane	90	10	10
3	isobutane	900	10	10
4	isobutane	9000	10	10

[a]Exposures were 6 hours per day for 7 consecutive days per week for 2 weeks. Exposure levels are expressed as ppm of test substance. The exposures were conducted via whole-body exposure.

[b]Complete postmortem evaluations were performed on animals at termination of the study and one animal that was sacrificed for humane reasons on Test Day 10.

The first day of exposures was defined as Day 0 of the study.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures were considered to be the minimum necessary for determining exposure levels for a subsequent OECD 422 study.

2.4.2. TEST ANIMAL SELECTION

The rat is a rodent animal model commonly utilized in toxicity testing, as recommended in OECD and EPA guidelines, and will be the species used in the subsequent OECD 422 study. In addition, a historical database is available for comparative evaluation.

2.4.3. NUMBER OF ANIMALS

The number of animals in the study was considered to have been the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

2.4.4. EXPOSURE LEVEL SELECTION

The exposure levels were selected based on prior results of no toxicity up to 0.1% (1000 ppm). Therefore, the high exposure level was established (for safety reasons) as 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

2.5. TEST SUBSTANCE

Isobutane

2.5.1. TEST SUBSTANCE CATEGORY

Industrial gas

2.5.2. CAS NUMBER

75-28-5

2.5.3. SUPPLIER

MG Industries
3 Great Valley Parkway
Malvern, Pennsylvania 19355

2.5.4. LOT NUMBER

Not available

2.5.5. PURITY

99.0% per Supplier. The testing facility also determined the purity by gas chromatography (GC) before the study (see Appendix N).

2.5.6. DESCRIPTION

Colorless gas

2.5.7. DATE RECEIVED

6 May 2003

2.5.8. EXPIRATION DATE

Not available, stable per MSDS. The stability was determined by GC at the completion of the subsequent OECD 422 study.

2.5.9. ANALYSIS

Documentation of the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the batch of the test substance and the maintenance of these records was the responsibility of the supplier. Documentation of the identity, strength, composition and stability were also confirmed by the testing facility.

Note that the actual location for the synthesis of the test substance has not been provided by the supplier.

2.5.10. STORAGE

Ambient (in an outside solvent shed) when not in use in the inhalation laboratory.

2.5.11. ARCHIVAL SAMPLE

An archival sample of test substance was taken and stored in the archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, Virginia 20166). A common archival sample was taken for this range-finding study and the subsequent OECD 422 study.

2.5.12. DISPOSITION

The unused portion of the test substance as well as any empty test substance containers will be returned to the supplier following submission of the final report of the final study with this test substance.

2.6. TEST ANIMALS

2.6.1. SPECIES

Albino Rats (Outbred) VAF/Plus®
Sprague-Dawley – Derived (CD®)
Crl:CD® (SD) IGS BR

2.6.2. SUPPLIER

Charles River Laboratories
Raleigh, North Carolina 27610

2.6.3. NUMBER OF ANIMALS

Received:
87 total (44 males, 43 females)

Placed on test:
80 total (40 males, 40 females)

Females were nulliparous and non-pregnant.

2.6.4. AGE AT RECEIPT

Approximately 6 weeks

2.6.5. AGE AT INITIATION OF EXPOSURES

Approximately 8 weeks

2.6.6. WEIGHT AT INITIATION OF EXPOSURES (GRAMS)

	Mean	Range
Male:	275	254 - 303
Female:	206	176 - 225

Individual weights of animals placed on test were within ±20% of the mean weight for each sex.

2.6.7. ACCLIMATION PERIOD

Animals were acclimated for 2 weeks. All animals were checked for viability twice daily. Prior to assignment to study, all animals were examined to ascertain suitability for study.

2.7. ANIMAL ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered unsuitable for the study on the basis of pretest physical examinations and body weight data were eliminated prior to random selection for group assignment. Animals considered suitable for study were distributed into 4 groups of 10 animals per sex by a computerized random sort program so that body weight means for each group were comparable. Disposition of all animals not utilized in the study is maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon receipt. After selection for study, each animal was ear-tagged with a number assigned by the testing facility. The assigned animal number plus the study number comprised the unique animal number for each animal. If the tag was lost, it was replaced. 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.

2.9. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

2.10. HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.10.2. HOUSING

Animals were individually housed in suspended, stainless steel wire mesh cages during the study.

2.10.3. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction, except when animals were fasted for terminal sacrifice. Fresh feed was presented weekly.

2.10.4. FEED ANALYSIS

Analysis of the feed lot used during this study was performed by the manufacturer. Results are maintained on file at the Testing Facility. There were no known contaminants in the feed that were expected to interfere with the objectives of this study.

2.10.5. WATER

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction via an automated watering system.

2.10.6. WATER ANALYSIS

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.

2.10.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve-hour light/dark cycle, controlled via an automatic timer, was provided.

Temperature

Temperature was monitored in accordance with the testing facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:	18 to 26°C
Actual Range:	20.3 to 23.1°C
Daily Average Range:	20.8 to 22.0°C

Relative Humidity

Relative humidity was monitored in accordance with the testing facility SOPs and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired Range:	30 to 70%
Actual Range:	44.02 to 70.50%
Daily Average Range:	49.03 to 53.99%

2.11. HUSBANDRY DURING EXPOSURE

2.11.1. HOUSING

Animals were individually housed in stainless steel, wire mesh cages within 1000 liter stainless steel and glass whole-body exposure chambers. The placement of each animal in the chamber was rotated at each exposure to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.11.2. FEED

None was provided during exposure.

2.11.3. WATER

None was provided during exposure.

2.11.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were recorded at the initiation of exposures and every half-hour during exposure, and maintained to the maximum extent possible, within the ranges presented below.

Temperature

Desired Range:	20 to 24°C
Actual Range:	21 to 24°C

Relative Humidity

Desired Range:	40 to 60%
Actual Range:	52 to 60%

2.12. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

2.12.1. ROUTE OF ADMINISTRATION

Inhalation, as a gas, via whole-body exposure.

2.12.2. FREQUENCY AND DURATION OF ADMINISTRATION

The test substance was administered for 6 hours per day for 7 consecutive days per week for 14 or 15 days. Test substance administration continued through the day prior to necropsy.

2.12.3. PRE-STUDY TRIALS

Trials were performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the targeted exposure levels. During this time, samples were taken to determine the distribution of the test substance in the exposure chamber.

2.12.4. CHAMBER OPERATION

The whole-body exposure chambers each had a volume of 1000 liters. Each chamber was operated dynamically under slight negative pressure at a minimum calibrated flow rate of 200 liters per minute. 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 T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes. The chamber airflow rate, total flow rate, time for air change and 99% equilibrium time (T_{99}) for each group are summarized below.

Group	Airflow Rate (Lpm)	Air Change (min)	T_{99} (min)
1	221	4.5	20.7
2	212	4.7	21.6
3	210	4.8	22.1
4	212	4.7	21.6

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 30 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static

pressure were made at the initiation of the exposures and every half-hour during the exposures.

The chamber atmospheres were exhausted through the in-house filtering system, which consisted of a coarse filter, a HEPA filter, and an activated charcoal bed.

Refer to Figures 1 and 2, and Appendix I for equipment details.

2.12.5. EXPOSURE PROCEDURE

Group 1

Animals were exposed to room air only.

Groups 2, 3 and 4

The test substance was delivered from a single cylinder, through a regulator and two backpressure gauges, and branched, via ¼" tubing, to the three exposure chambers. For each chamber, ¼" tubing directed the test substance to a flowmeter, regulated by a metering valve, and into the inlet of a 1000 liter stainless steel and glass whole-body exposure chamber.

Refer to Figures 1 and 2, and Appendix I for equipment details.

2.13. EXPOSURE CHAMBER SAMPLING

2.13.1. CHAMBER SAMPLING

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

Refer to Appendix I for equipment details and Appendix J for MIRAN® calibration.

2.13.2. PARTICLE SIZE DISTRIBUTION ANALYSIS

Particle size samples were drawn once during each exposure for 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.

Refer to Appendix I for equipment details.

2.13.3. NOMINAL CONCENTRATION

The nominal exposure concentration (ppm) was calculated by dividing the average test substance flow (ccm) during the exposure by the average chamber airflow (Lpm).

$$\text{Nominal (ppm)} = \frac{\text{Test Substance Flow (ccm)} \times 1000\ \mu\text{L/cc}}{\text{Total Chamber Airflow (Lpm)}}$$

2.13.4. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber oxygen levels (maintained at least 19%) were measured pretest and at the beginning, middle and end of the study. Air samples were taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30 – 40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room were measured pretest and at the beginning, middle and end of the study.

Refer to Appendix I for equipment details.

2.14. EXPERIMENTAL EVALUATIONS

2.14.1. VIABILITY CHECKS (CAGE-SIDE)

Animals were observed in their cages for mortality and general condition twice daily (once in the morning and once in the afternoon). Animals in extremely poor health or in a possible

moribund condition were identified for further monitoring and possible euthanasia.

2.14.2. PHYSICAL EXAMINATIONS

In-Chamber: All animals were observed as a group at least once during each exposure.

Out-of-Chamber: Each animal was removed from its cage and examined twice pretest (including on the first day of exposure) and once per week during the study period. Examinations included general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling, as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) were recorded.

2.14.3. BODY WEIGHT

Animals were removed from their cages and weighed twice pretest (including on the first day of exposure) and weekly during treatment. Terminal, fasted body weights were obtained just prior to necropsy.

2.14.4. FEED CONSUMPTION

Feed consumption was measured during the week prior to treatment initiation and weekly during the study. Feed was available without restriction 7 days/week, except during exposures and terminal fasting. Animals were presented with full feeders of known weight. After 6 or 7 days, the feeders were reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal over the 6 or 7-day period.

Calculation

$$\text{Feed Consumption (g/kg/day)} = \frac{\text{grams of feed consumed}}{\text{body weight (kg)}^{a}} \div \text{6 or 7 days}$$

[a]The average of the current and previous weight was used.

2.15. POSTMORTEM

2.15.1. NECROPSY INFORMATION

Necropsy was performed on all surviving animals, after animals were treated for 14 or 15 days. Animals were fasted overnight prior to necropsy. A necropsy schedule was established in order to assure that approximately equal numbers of males and females were examined on each day of necropsy and that examination of animals of both sexes were performed at similar times of the day throughout the necropsy period.

Method of Euthanasia

Exsanguination following carbon dioxide inhalation.

2.15.2. MACROSCOPIC EXAMINATIONS

Complete macroscopic postmortem examinations were performed on all animals, including one animal euthanized in a moribund condition. The macroscopic examination included examination of the external surface of the body, all orifices and the cranial, thoracic, abdominal cavities and their content. Special attention was paid to the organs of the reproductive system.

2.15.3. ORGAN WEIGHTS

Organs indicated in Table I (page 23) were weighed for all animals at the scheduled necropsies. 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 in order to avoid drying. Paired organs were weighed together.

2.15.4. TISSUES PRESERVED

The tissues listed in Table I (page 23) were obtained at the scheduled sacrifice interval and preserved for all animals. No microscopic examination was performed.

TABLE I

ORGAN NAME	WEIGHED	PRESERVED
adrenal glands	X	X
aorta (thoracic)		X
bone (sternum, femur)		X
bone marrow (rib)		X
brain (medulla, pons, cerebrum and cerebellum)	X	X
epididymides	X	X
esophagus		X
eyes with optic nerve		X
heart	X	X
kidneys	X	X
lacrimal glands		X
large intestine (cecum, colon, rectum)		X
larynx		X
liver	X	X
lungs (with mainstem bronchi)	X	X
lymph nodes (mesenteric, mediastinal)		X
mammary gland		X
muscle (*biceps femoris*)		X
nasopharyngeal tissue		X
nerve (sciatic)		X
ovaries	X	X
pancreas		X
pituitary gland	X	X
prostate gland		X
salivary glands with submandibular lymph node		X
seminal vesicles	X	X
skin		X
small intestine (duodenum, ileum, jejunum)		X
spinal cord (cervical, thoracic, lumbar)		X
spleen	X	X
stomach		X
testes	X	X
thymus	X	X
thyroid/parathyroid glands		X
trachea		X
urinary bladder		X
uterus (body/horns with cervix)	X	X
zymbal's gland		X
tissues with macroscopic findings		X

Preservatives

All tissues - 10% neutral buffered formalin.
Eyes were placed in glutaraldehyde/paraformaldehyde initially and then retained in 10% formalin. Testes and epididymides were placed in Modified Davidson's solution initially and then retained in 10% formalin. Lungs and urinary bladder were infused with formalin 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.

2.16. STATISTICAL ANALYSIS

The following parameters were analyzed statistically:

mean body weight values
mean feed consumption values
mean organ weights, organ/body and organ/brain weight ratios

2.16.1. METHOD OF ANALYSIS

Mean values of all exposure groups were compared to the mean value for the control group at each time interval.

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Sokal and Rohlf, 1995) was performed to determine if groups had equal variances. For all parameters except organ weights, if the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. Organ 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 (Dunlap and Duffy, 1975). If significant differences among the means were indicated, additional tests were used to determine which means were significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964) 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, Pairwise

Comparison with Bonferroni Correction (Games and Howell, 1976) 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.

2.17. DATA STORAGE

All raw data, and preserved specimens, as well as the original study protocol and the original final report, are to be maintained in the Archives of the testing facility upon completion of the study. The sponsor will determine the final disposition of these materials.

2.18. REGULATORY REFERENCES

2.18.1. TEST GUIDELINES

This study was not designed to meet regulatory requirements. It was designed to provide preliminary toxicity data for the test substance in order to determine appropriate exposure levels for a subsequent OECD 422 inhalation study.

2.18.2. GOOD LABORATORY PRACTICES

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

2.18.3. ANIMAL WELFARE ACT COMPLIANCE

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.

2.19. PROTOCOL DEVIATIONS

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

Due to technician oversight, particle size determinations were not performed for any group during the first exposure.

3. RESULTS AND DISCUSSION

3.1. TEST SUBSTANCE ANALYSIS

(Appendix N)

Prestudy GC analysis of the test substance showed a purity of 99.84% for isobutane. This value compared closely to the purity of 99.51% for the analytical standard of isobutane and the 99.0% purity as guaranteed by the supplier of the test substance.

3.2. CHAMBER MONITORING

(Appendices A, K and L)

Chamber distribution analyses (see Appendix K) showed that the test substance was evenly distributed within each chamber. Chamber monitoring (see Appendix L) showed that the chamber oxygen levels were 21%. Chamber room monitoring (see Appendix L) showed that no test substance was present in the room and that the sound and light levels were acceptable.

The target and mean (± standard deviation) analytical (IR) and nominal concentrations (see Appendix A) are summarized as follows:

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0.00 ± 0.00	0 ± 0
2	Isobutane	90	90.80 ± 4.30	84.9 ± 0.0
3	Isobutane	900	911.6 ± 30.6	945 ± 18
4	Isobutane	9000	9251 ± 136	8490 ± 0

The analytically measured (IR) exposure levels of the airborne test substance were reasonably close, in the opinion of the study director, to the targeted exposure levels. The differences between measured and nominal concentrations varied somewhat from the expected 1:1 ratio for this type of gas exposure. The exact cause of the differences was not determined but was probably a result of a combination of slight variances in the calibration of the chamber airflows and the calibration of the IR

monitor. Chamber environmental conditions averaged 23°C temperature and 56% relative humidity.

Mean particle size distribution measurements for the exposures (see Appendix A) are summarized as follows:

Group	Test Substance	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m^3)
1	Air Control	1.228	2.021	4.85E-03
2	Isobutane	1.069	1.813	5.23E-03
3	Isobutane	1.921	1.989	5.51E-03
4	Isobutane	1.722	1.973	5.69E-03

These results indicated that the atmospheres were essentially gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

3.3. MORTALITY

(Appendix B)

All animals survived to termination except the 900 ppm exposed male animal #3010 which was humanely sacrificed on test day 10 after it injured it's snout on the exposure caging during removal from the chamber.

3.4. CLINICAL OBSERVATIONS

3.4.1. EXPOSURE PERIODS

(Table 1)

The test animals were unremarkable during the exposure periods.

3.4.2. NON-EXPOSURE PERIODS

(Table 2 & Appendix C)

The test animals were generally unremarkable during the non-exposure periods. Scattered observations such as red nasal discharge and chromodacryorrhea were noted but were not attributed to treatment.

3.5. BODY WEIGHTS

(Figures 2 and 3, Tables 3 and 4 & Appendices D and E)

There were no statistically significant or exposure-related differences in absolute body weights or in body weight changes in the test substance exposed animals compared to the air control animals.

3.6. FEED CONSUMPTION

(Figures 4 and 5, Table 5 & Appendix F)

There were no statistically significant or exposure-related differences in feed consumption in the test substance exposed animals compared to the air control animals.

3.7. ORGAN WEIGHTS

(Table 6 & Appendix G)

There were no exposure-related differences in organ weights (absolute and relative to body weight or brain weight) in the test substance exposed animals compared to the air control animals. A statistically significant increase was noted in adrenal weights (relative to brain weight) for the 900 ppm exposed female animals. However, in the absence of an exposure level related pattern (the percent difference from control values was actually the same for all 3 treated groups) and any corresponding macroscopic postmortem findings, this difference was considered incidental.

3.8. MACROSCOPIC PATHOLOGY

(Table 7 & Appendix H)

No gross abnormalities related to test substance exposure were evident at necropsy examination. The macroscopic lesions noted were similar to those routinely encountered in animals of this age and species or were represented by individual animals and considered incidental findings.

4. CONCLUSION

Two weeks of exposure of rats to isobutane gas at exposure levels of 90, 900 and 9000 ppm resulted in no effects of exposure. Therefore, the 9000 ppm exposure level was a no observable effect level (NOEL) and was considered an acceptable high exposure level (limited by safety considerations for a flammable gas) for a subsequent OECD 422 study.

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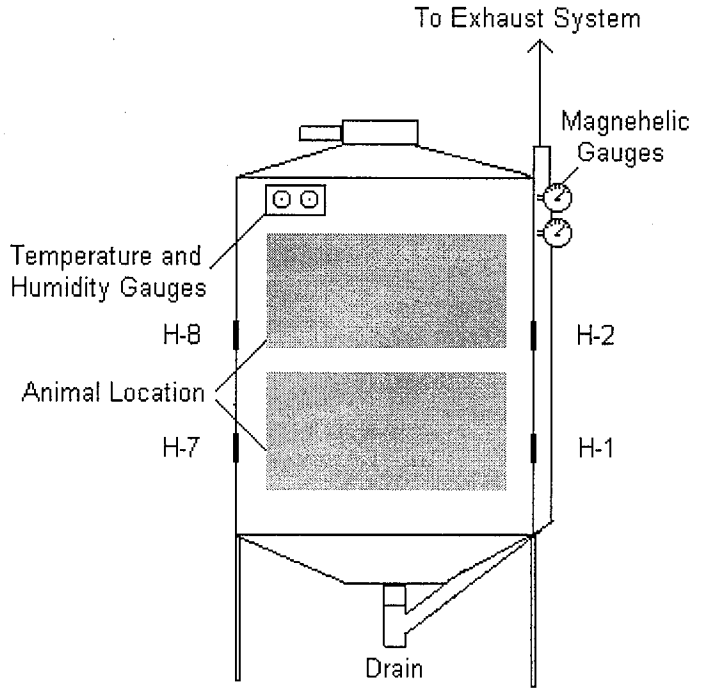
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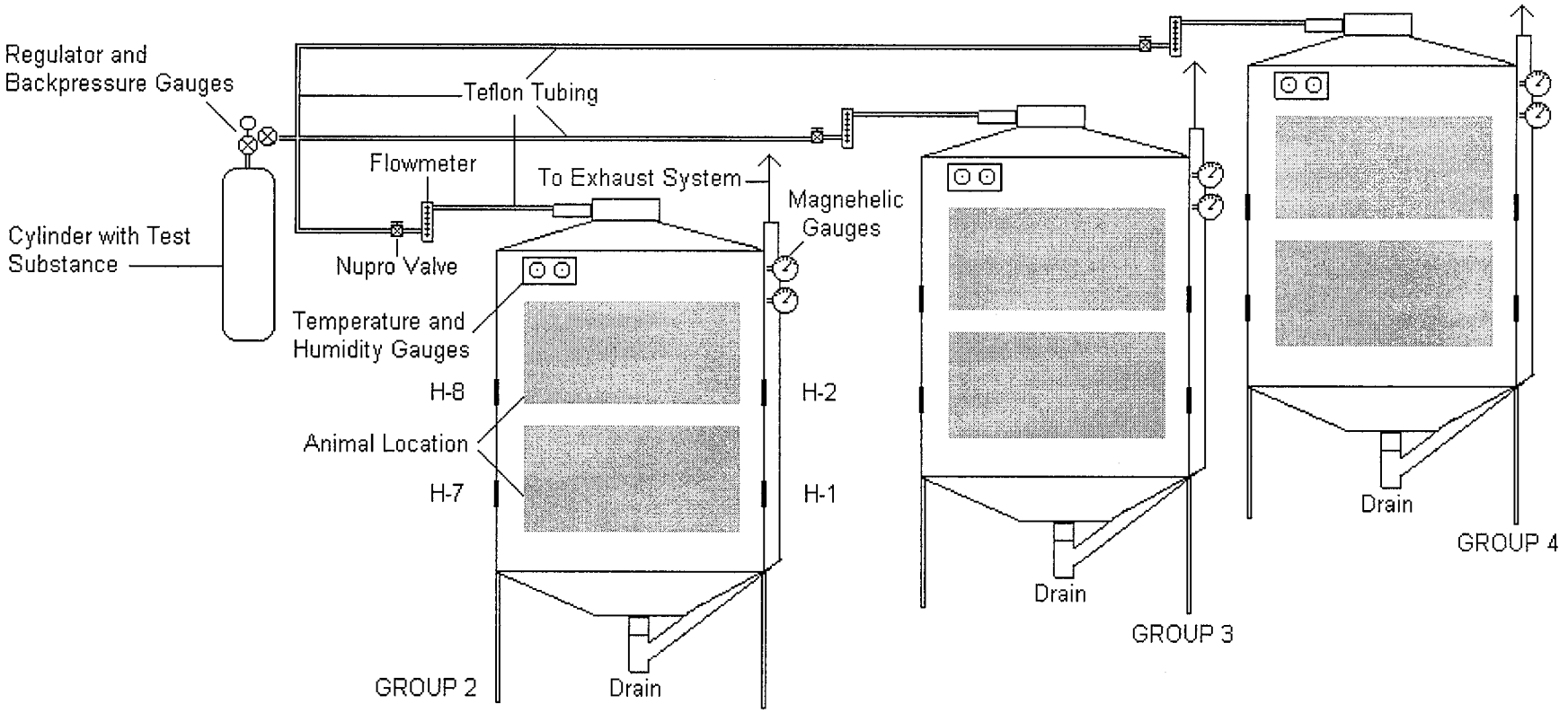
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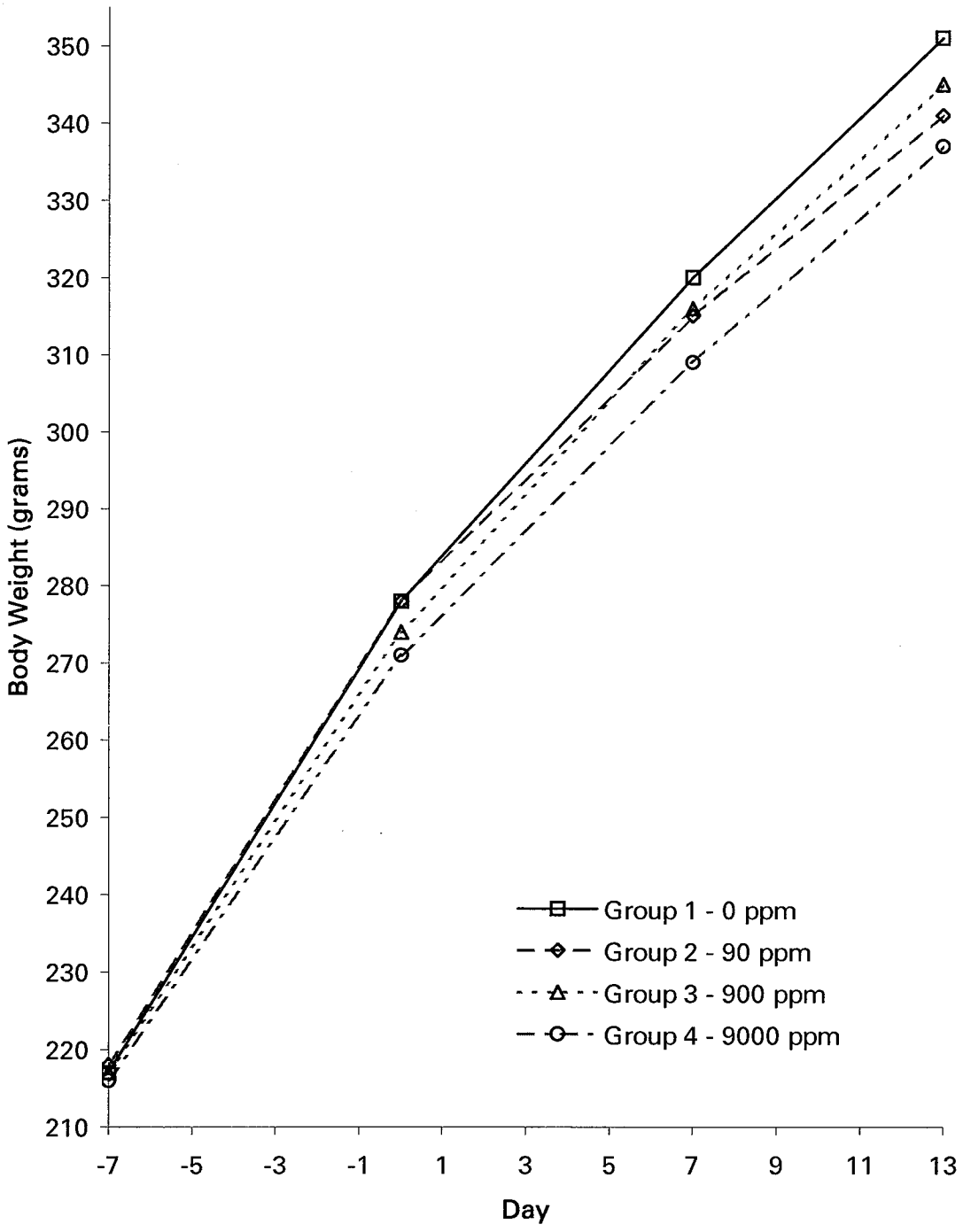
Group 1	Diagram of 1000-Liter Whole-Body Exposure Chamber and Generation System	Figure 1



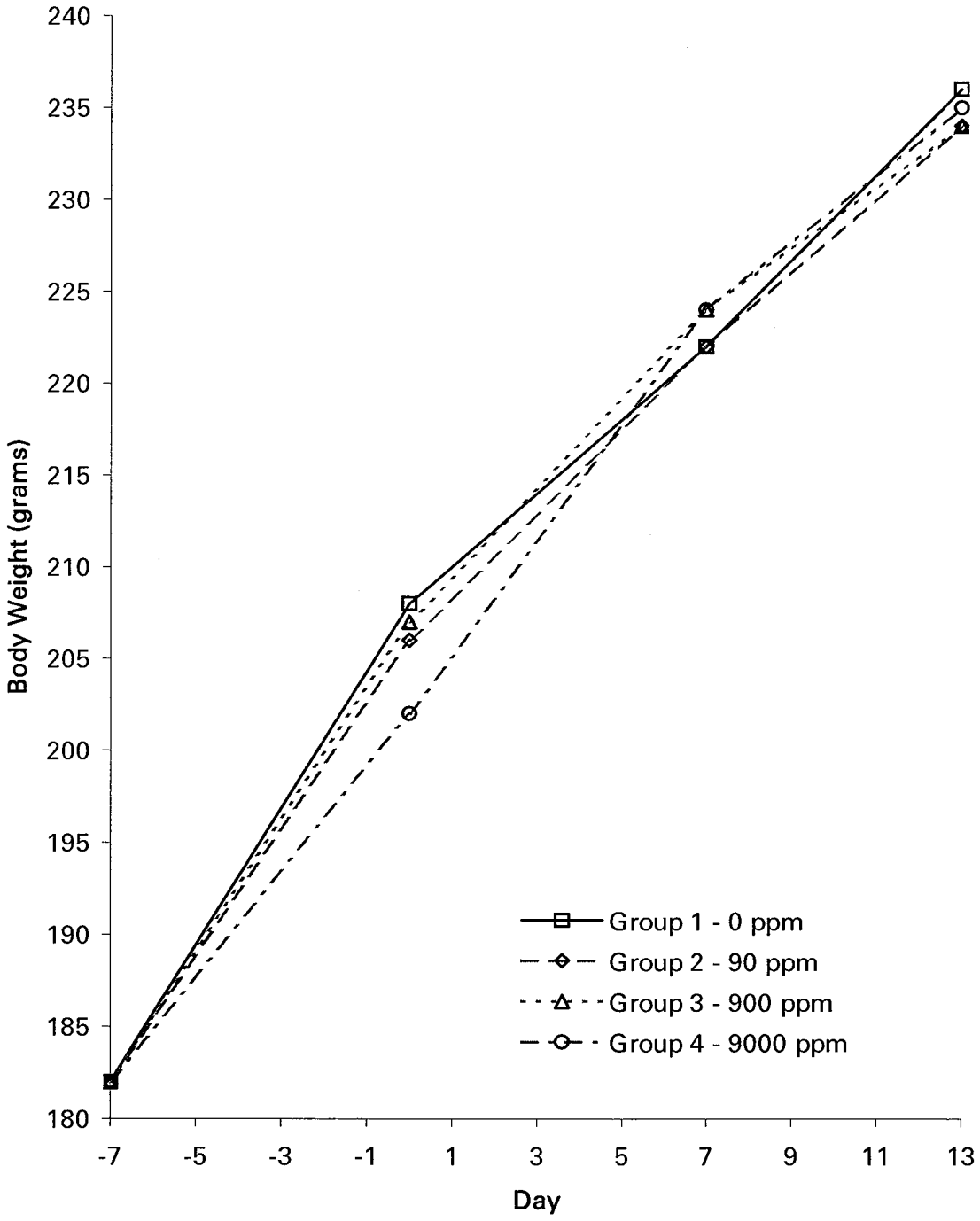
Groups 2, 3 & 4	Diagram of 1000-Liter Whole-Body Exposure Chamber and Generation System	Figure 2



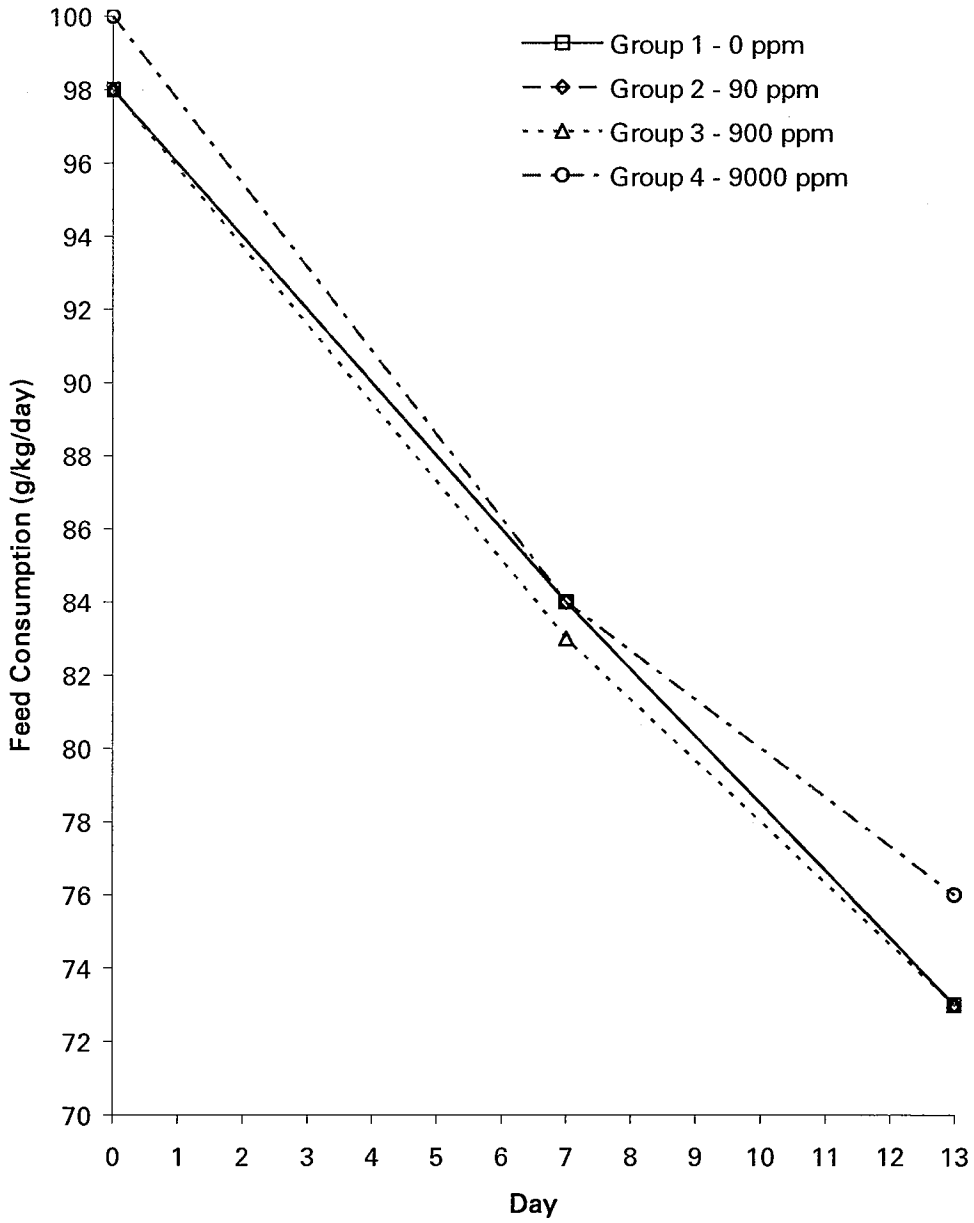
Males	Mean Body Weights	Figure 3



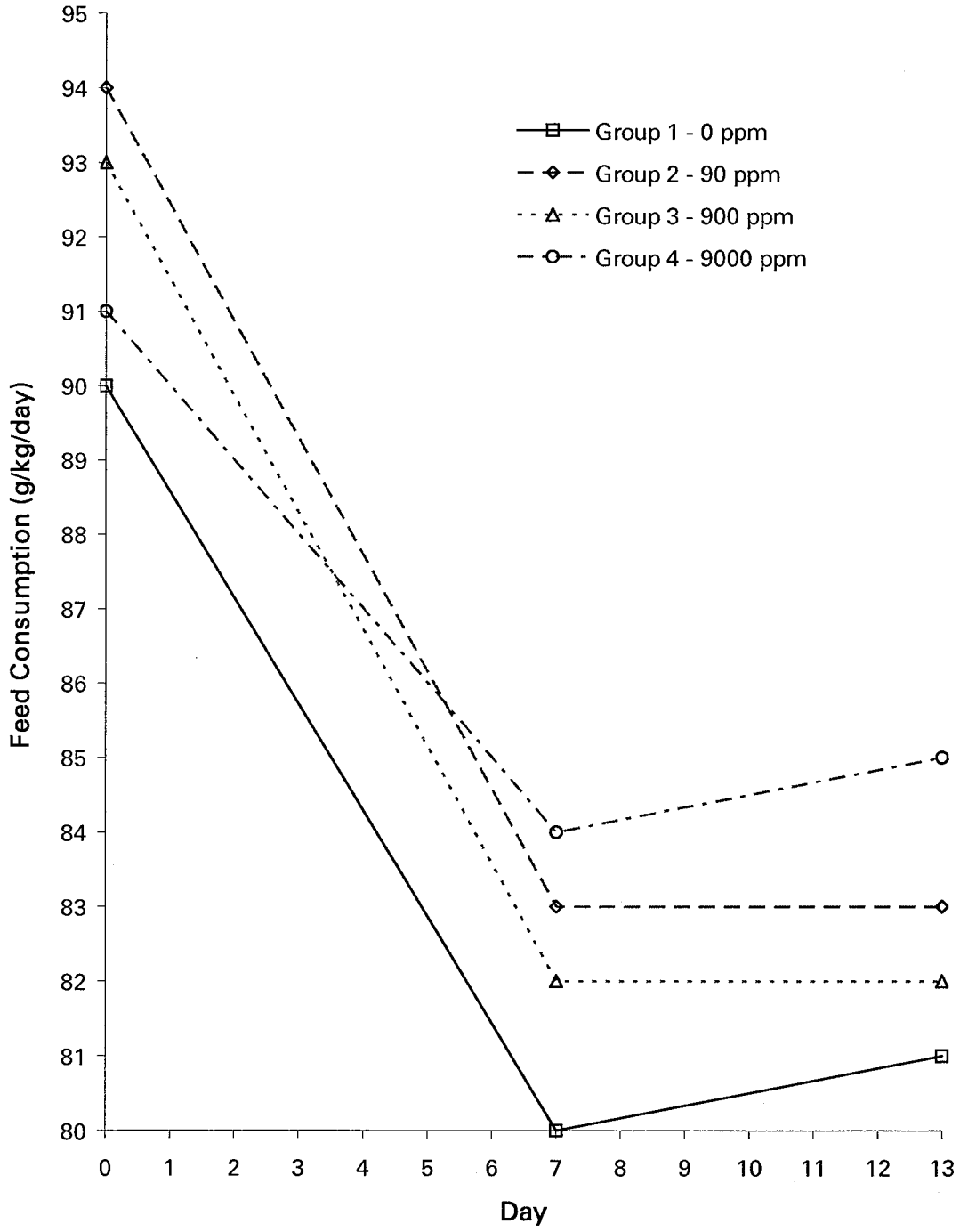
Females	Mean Body Weights	Figure 4



Males	Mean Feed Consumption	Figure 5



Females	Mean Feed Consumption	Figure 6



	General Preface	

General Notes

Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

	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 – 90 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 900 ppm															
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 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.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

	Summary of Clinical Observations Preface	Table 2

Number of animals examined represents the total number of animals observed and animals which were sacrificed for humane reasons or killed at a scheduled sacrifice for a given interval.

For summarization purposes, descriptive comments [i.e., location of scab(s) and/or sore(s), etc.] are not presented in this table. These data are contained in the study raw data if needed.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

TABLE 2

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY						
	GROUP#	-7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	8	2	
	2	10	10	10	10	8	2	
	3	10	10	10	10	8	1	
	4	10	10	10	10	8	2	
NORMAL								
WITHIN NORMAL LIMITS	1	10	10	8	8	0	0	10
	2	10	10	10	9	0	0	10
	3	10	10	8	9	0	0	10
	4	10	10	10	8	0	0	10
DEAD								
Humane Sacrifice	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	0	1	0	0	1
	4	0	0	0	0	0	0	0
Terminal Sacrifice	1	0	0	0	0	8	2	10
	2	0	0	0	0	8	2	10
	3	0	0	0	0	8	1	9
	4	0	0	0	0	8	2	10
DERMAL GENERAL								
Alopecia - General	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
Scab(s)	1	0	0	1	0	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0

TABLE 2

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY						
	GROUP#	-7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	8	2	
	2	10	10	10	10	8	2	
	3	10	10	10	10	8	1	
	4	10	10	10	10	8	2	
Alopecia - Extremities/Snout	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	1	0	0	1
OCULAR								
Chromodacryorrhea - Unilateral	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
ORAL/BUCCAL								
Incisors Broken/Missing	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	1	0	0	0	1
	4	0	0	0	0	0	0	0
Nasal Discharge - Red	1	0	0	0	0	0	0	0
	2	0	0	0	1	0	0	1
	3	0	0	1	0	0	0	1
	4	0	0	0	1	0	0	1

TABLE 2

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY						
	GROUP#	-7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	7	3	
	2	10	10	10	10	7	3	
	3	10	10	10	10	7	3	
	4	10	10	10	10	7	3	
NORMAL								
WITHIN NORMAL LIMITS	1	10	10	10	10	0	0	10
	2	10	10	10	8	0	0	10
	3	10	10	9	9	0	0	10
	4	10	10	10	10	0	0	10
DEAD								
Terminal Sacrifice	1	0	0	0	0	7	3	10
	2	0	0	0	0	7	3	10
	3	0	0	0	0	7	3	10
	4	0	0	0	0	7	3	10
DERMAL GENERAL								
Alopecia - General	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	0	1	0	0	1
	4	0	0	0	0	0	0	0
Scab(s)	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	1	0	0	0	1
	4	0	0	0	0	0	0	0
Alopecia - Extremities/Snout	1	0	0	0	0	0	0	0
	2	0	0	0	1	0	0	1
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0

TABLE 2

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES — SUMMARY OF CLINICAL OBSERVATIONS

		DAY OF STUDY						
	GROUP#	-7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	7	3	
	2	10	10	10	10	7	3	
	3	10	10	10	10	7	3	
	4	10	10	10	10	7	3	
OCULAR								
Chromodacryorrhea -	1	0	0	0	0	0	0	0
Unilateral	2	0	0	0	1	0	0	1
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
ORAL/BUCCAL								
Incisors Maloccluded	1	0	0	0	0	0	0	0
	2	0	0	0	1	0	0	1
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0

TABLE 3

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — MEAN BODY WEIGHTS (GRAMS)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY	-7	MEAN	217	218	217	216
		S.D.	9.6	8.9	10.0	10.5
		N	10	10	10	10
DAY	0	MEAN	278	278	274	271
		S.D.	14.4	10.0	12.6	10.2
		N	10	10	10	10
DAY	7	MEAN	320	315	316	309
		S.D.	22.0	14.6	19.1	17.0
		N	10	10	10	10
DAY	13	MEAN	351	341	345	337
		S.D.	29.0	19.6	24.6	23.5
		N	10	10	9	10

No statistically significant differences

TABLE 3

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES — MEAN BODY WEIGHTS (GRAMS)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY	-7	MEAN	182	182	182	182
		S.D.	9.0	8.7	7.9	8.6
		N	10	10	10	10
DAY	0	MEAN	208	206	207	202
		S.D.	10.2	8.4	8.7	12.8
		N	10	10	10	10
DAY	7	MEAN	222	222	224	224
		S.D.	12.3	7.8	11.7	16.5
		N	10	10	10	10
DAY	13	MEAN	236	234	234	235
		S.D.	16.1	10.0	12.7	20.3
		N	10	10	10	10

No statistically significant differences

TABLE 4

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — MEAN BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY 0 TO 7		MEAN	42	37	42	38
		S.D.	9.5	8.0	9.2	11.3
		N	10	10	10	10
DAY 0 TO 13		MEAN	74	63	71	66
		S.D.	17.4	13.9	16.0	17.5
		N	10	10	9	10

No statistically significant differences

TABLE 4

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES — MEAN BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY 0 TO 7		MEAN	15	16	17	22
		S.D.	5.3	5.3	5.2	7.3
		N	10	10	10	10
DAY 0 TO 13		MEAN	28	28	27	33
		S.D.	12.5	7.4	9.4	12.5
		N	10	10	10	10

No statistically significant differences

TABLE 5

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — MEAN FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

	DOSE GROUP:	1	2	3	4
	DOSE LEVEL (PPM):	0	90	900	9000
DAY 0	MEAN	98	98	98	100
	S.D.	3.7	5.3	4.1	3.5
	N	10	10	10	10
DAY 7	MEAN	84	84	83	84
	S.D.	4.1	4.9	4.7	5.0
	N	10	10	10	10
DAY 13	MEAN	73	73	73	76
	S.D.	3.4	4.6	3.8	4.7
	N	10	10	9	10

No statistically significant differences

TABLE 5

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES — MEAN FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY	0	MEAN	90	94	93	91
		S.D.	6.8	4.9	4.1	2.9
		N	10	10	9	10
DAY	7	MEAN	80	83	82	84
		S.D.	3.7	3.8	5.4	3.8
		N	9	10	10	10
DAY	13	MEAN	81	83	82	85
		S.D.	4.0	3.5	3.2	2.8
		N	9	10	9	10

No statistically significant differences

	Mean Organ Weights Preface	Table 6

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Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observed

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	323.7	0.0611	2.1146	0.8813	1.2886	3.2673	11.6054	1.9605
Standard deviation:	25.5	0.0117	0.1954	0.0849	0.1068	0.5419	1.3625	0.4828
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	315.7	0.0583	2.0792	0.9150	1.2703	3.1185	11.3465	2.0957
Standard deviation:	19.0	0.0101	0.1682	0.1119	0.0658	0.2748	1.4651	0.5466
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	318.7	0.0600	2.0757	0.9077	1.2590	3.1841	11.0660	1.8407
Standard deviation:	19.5	0.0121	0.1081	0.0956	0.1283	0.3573	0.4142	0.1434
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
4								
Mean:	309.8	0.0628	2.0675	0.9150	1.2374	3.1412	10.9280	1.9451
Standard deviation:	19.3	0.0139	0.0996	0.1234	0.1165	0.3611	1.1373	0.2265
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

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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
			Male Animals			
1						
Mean:	323.7	0.0099	1.2849	0.6915	3.2707	0.5299
Standard deviation:	25.5	0.0021	0.1544	0.1354	0.2016	0.1093
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	315.7	0.0099	1.2515	0.6983	3.1284	0.5507
Standard deviation:	19.0	0.0015	0.2480	0.1394	0.3335	0.1307
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	318.7	0.0099	1.1158	0.7225	3.2499	0.5140
Standard deviation:	19.5	0.0019	0.1936	0.0538	0.1562	0.0481
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)
4						
Mean:	309.8	0.0100	1.2375	0.6546	3.0946	0.6064
Standard deviation:	19.3	0.0021	0.2355	0.0821	0.1654	0.1988
Number of observ. :	(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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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
				Female Animals				
1								
Mean:	217.5	0.0676	2.0334	0.8631	2.0933	7.7371	1.4582	0.1119
Standard deviation:	10.9	0.0059	0.0999	0.0797	0.2995	0.8167	0.2191	0.0212
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	213.5	0.0733	1.9777	0.8876	2.1801	8.4194	1.4006	0.0999
Standard deviation:	7.9	0.0164	0.1475	0.0664	0.1665	1.1764	0.2085	0.0156
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	215.9	0.0744	1.9857	0.9004	2.1712	8.1312	1.4736	0.1018
Standard deviation:	10.6	0.0108	0.0922	0.0625	0.3014	1.0694	0.2090	0.0201
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	217.0	0.0741	1.9935	0.8881	2.1373	8.2259	1.5086	0.1038
Standard deviation:	17.2	0.0099	0.1283	0.1140	0.2799	0.9745	0.1889	0.0132
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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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
			Female Animals		
1					
Mean:	217.5	0.0128	0.5363	0.4846	0.5841
Standard deviation:	10.9	0.0036	0.0661	0.0893	0.1886
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	213.5	0.0126	0.5055	0.4577	0.6610
Standard deviation:	7.9	0.0035	0.0658	0.0688	0.2468
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	215.9	0.0122	0.5284	0.4980	0.5756
Standard deviation:	10.6	0.0023	0.0768	0.0946	0.1277
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	217.0	0.0124	0.5268	0.4862	0.5823
Standard deviation:	17.2	0.0025	0.0736	0.1005	0.1121
Number of observ. :	(10)	(10)	(10)	(10)	(10)

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	323.7	0.0189	0.6550	0.2734	0.3985	1.0058	3.5816	0.6024
Standard deviation:	25.5	0.0036	0.0575	0.0312	0.0202	0.0999	0.2250	0.1117
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	315.7	0.0186	0.6601	0.2913	0.4028	0.9890	3.5939	0.6618
Standard deviation:	19.0	0.0037	0.0590	0.0429	0.0168	0.0824	0.4077	0.1599
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	318.7	0.0188	0.6531	0.2855	0.3950	1.0014	3.4799	0.5791
Standard deviation:	19.5	0.0038	0.0476	0.0335	0.0335	0.1206	0.1832	0.0543
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
4								
Mean:	309.8	0.0202	0.6688	0.2952	0.3991	1.0139	3.5228	0.6270
Standard deviation:	19.3	0.0039	0.0390	0.0336	0.0229	0.0952	0.2343	0.0510
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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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
			Male Animals			
1						
Mean:	323.7	0.0031	0.3995	0.2126	1.0165	0.1630
Standard deviation:	25.5	0.0007	0.0589	0.0282	0.1048	0.0254
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	315.7	0.0032	0.3965	0.2213	0.9930	0.1749
Standard deviation:	19.0	0.0006	0.0757	0.0427	0.1133	0.0435
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	318.7	0.0031	0.3508	0.2274	1.0233	0.1616
Standard deviation:	19.5	0.0005	0.0631	0.0222	0.0817	0.0157
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)
4						
Mean:	309.8	0.0032	0.4007	0.2108	1.0020	0.1956
Standard deviation:	19.3	0.0006	0.0808	0.0187	0.0801	0.0608
Number of observ. :	(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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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
				Female Animals				
1								
Mean:	217.5	0.0311	0.9358	0.3973	0.9604	3.5528	0.6704	0.0512
Standard deviation:	10.9	0.0026	0.0419	0.0372	0.1124	0.2664	0.0941	0.0077
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	213.5	0.0342	0.9263	0.4156	1.0207	3.9349	0.6569	0.0468
Standard deviation:	7.9	0.0070	0.0585	0.0247	0.0592	0.4406	0.1004	0.0070
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	215.9	0.0344	0.9213	0.4174	1.0052	3.7625	0.6827	0.0471
Standard deviation:	10.6	0.0043	0.0546	0.0274	0.1248	0.4281	0.0924	0.0088
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	217.0	0.0341	0.9223	0.4084	0.9841	3.7824	0.6963	0.0478
Standard deviation:	17.2	0.0034	0.0756	0.0320	0.0910	0.2335	0.0790	0.0037
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

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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
			Female Animals		
1					
Mean:	217.5	0.0059	0.2469	0.2227	0.2678
Standard deviation:	10.9	0.0015	0.0322	0.0406	0.0849
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	213.5	0.0059	0.2366	0.2141	0.3091
Standard deviation:	7.9	0.0015	0.0270	0.0280	0.1128
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	215.9	0.0057	0.2455	0.2296	0.2670
Standard deviation:	10.6	0.0011	0.0394	0.0362	0.0587
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	217.0	0.0057	0.2426	0.2246	0.2690
Standard deviation:	17.2	0.0010	0.0274	0.0448	0.0500
Number of observ. :	(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

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
				Male Animals				
1								
Mean:	323.7	2.8979	100.0000	42.0258	61.1911	154.1615	549.0490	92.6791
Standard deviation:	25.5	0.5497	0.0000	5.8219	5.5082	15.6197	38.7561	19.6753
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	315.7	2.8075	100.0000	44.1630	61.3029	150.0173	545.5922	99.7505
Standard deviation:	19.0	0.4457	0.0000	5.5093	3.8503	6.4330	54.4550	17.9694
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	318.7	2.8923	100.0000	43.8971	60.7454	153.4010	534.6950	88.8373
Standard deviation:	19.5	0.5820	0.0000	5.7525	6.5187	15.2802	38.6614	7.5705
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)
4								
Mean:	309.8	3.0357	100.0000	44.2044	59.7993	151.6690	528.1927	94.0074
Standard deviation:	19.3	0.6366	0.0000	5.1076	4.0738	11.8192	44.5221	9.1148
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

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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
			Male Animals			
1						
Mean:	323.7	0.4758	61.3436	32.7090	155.5544	25.0706
Standard deviation:	25.5	0.1173	10.3699	5.4278	13.7689	4.7540
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	315.7	0.4795	60.2599	33.5319	150.9738	26.3776
Standard deviation:	19.0	0.0827	11.6189	5.6387	17.7578	5.5406
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	318.7	0.4785	53.5511	34.9089	156.9726	24.7740
Standard deviation:	19.5	0.0871	7.5651	3.3040	11.6937	2.0484
Number of observ. :	(9)	(9)	(9)	(9)	(9)	(9)
4						
Mean:	309.8	0.4810	59.8534	31.6745	149.8308	29.3304
Standard deviation:	19.3	0.0942	11.0088	3.8275	8.0877	9.2378
Number of observ. :	(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

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
			Female Animals					
1								
Mean:	217.5	3.3275	100.0000	42.4200	102.6308	380.1178	71.5027	5.5085
Standard deviation:	10.9	0.3114	0.0000	3.0650	10.7350	30.2687	8.0714	1.0443
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	213.5	3.7151	100.0000	44.9367	110.3498	426.1762	71.0627	5.0717
Standard deviation:	7.9	0.8336	0.0000	2.4482	5.6924	52.7284	11.1762	0.8520
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	215.9	3.7322%	100.0000	45.3859	109.1050	409.4227	74.2145	5.1173
Standard deviation:	10.6	0.3889	0.0000	3.0842	11.3943	48.2172	10.2049	0.9289
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	217.0	3.7253	100.0000	44.5444	106.9473	412.2143	75.5838	5.2027
Standard deviation:	17.2	0.5164	0.0000	4.9631	8.9811	37.2721	6.8800	0.5258
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
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice

Summary Statistics for % Organ to Brain Weight
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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
			Female Animals		
1					
Mean:	217.5	0.6296	26.3799	23.7726	28.6247
Standard deviation:	10.9	0.1692	3.0690	4.0202	8.8442
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	213.5	0.6353	25.5441	23.2059	33.7381
Standard deviation:	7.9	0.1583	2.4717	3.4213	13.7272
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	215.9	0.6139	26.6371	25.0393	29.1359
Standard deviation:	10.6	0.1090	3.9337	4.3395	7.3297
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	217.0	0.6216	26.3672	24.4469	29.1245
Standard deviation:	17.2	0.1223	2.6722	5.0514	4.8584
Number of observ. :	(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

	Incidence Summary Report for Gross Necropsy Observations Preface	Table 7

Key to Abbreviations

LN = Lymph Node
Submandib/Max = Submandibular/Submaxillary

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice

Incidence Summary Report for Gross Necropsy Observations
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	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	10	10	9	10	10	10	10	10
Within normal limits	9	8	8	8	8	6	9	9
Adrenal Glands								
Discolored	0	0	0	0	1	0	1	0
Lungs								
Discolored	0	1	1	1	0	0	0	0
Abnormal Contents	0	1	0	1	0	0	0	0
Mediastinal LN								
Enlarged	0	0	0	0	0	1	0	0
Seminal vesicles								
Small	0	0	0	1	0	0	0	0
Submandib/Max LN								
Enlarged	0	0	0	0	1	1	1	0
Thymus								
Discolored	0	0	0	0	1	0	0	1
Trachea								
Abnormal Contents	1	1	0	1	0	0	0	0
Uterus								
Distended	0	0	0	0	0	2	0	0
Skin (other)								
Hair Thin/Absent	0	0	0	1	0	0	1	0
Lymph Node,other								
Enlarged	0	0	0	0	0	1	0	0

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Humane Sacrificed

Incidence Summary Report for Gross Necropsy Observations
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	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	0	0	1	0	0	0	0	0
Within normal limits	0	0	0	0	0	0	0	0
Bone								
Fracture	0	0	1	0	0	0	0	0

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 ppm (air only)

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment	
			Nominal (ppm)	Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Mean Temperature (°C)	Humidity (%)
0	12-Aug-03	1	-	0.00	0.00	0.00	0.00	0.00	-	-	-	24	57
1	13-Aug-03	2	-	0.00	0.00	0.00	0.00	0.00	0.8698	2.629	1.95E-02	23	58
2	14-Aug-03	3	-	0.00	0.00	0.00	0.00	0.00	0.8881	2.122	3.10E-03	23	57
3	15-Aug-03	4	-	0.00	0.00	0.00	0.00	0.00	0.8575	1.939	2.57E-03	23	58
4	16-Aug-03	5	-	0.00	0.00	0.00	0.00	0.00	0.9147	2.543	9.12E-03	23	56
5	17-Aug-03	6	-	0.00	0.00	0.00	0.00	0.00	0.7929	1.685	7.05E-03	23	57
6	18-Aug-03	7	-	0.00	0.00	0.00	0.00	0.00	0.9397	1.981	2.29E-03	23	57
7	19-Aug-03	8	-	0.00	0.00	0.00	0.00	0.00	0.9774	2.091	2.50E-03	23	56
8	20-Aug-03	9	-	0.00	0.00	0.00	0.00	0.00	0.9054	2.093	5.10E-03	23	56
9	21-Aug-03	10	-	0.00	0.00	0.00	0.00	0.00	0.8330	1.752	8.82E-03	23	57
10	22-Aug-03	11	-	0.00	0.00	0.00	0.00	0.00	0.8146	1.591	1.52E-03	23	59
11	23-Aug-03	12	-	0.00	0.00	0.00	0.00	0.00	2.953	2.141	1.84E-03	23	54
12	24-Aug-03	13	-	0.00	0.00	0.00	0.00	0.00	2.471	1.815	1.02E-03	24	56
13	25-Aug-03	14	-	0.00	0.00	0.00	0.00	0.00	2.080	1.931	1.08E-03	23	55
14	26-Aug-03	15	-	0.00	0.00	0.00	0.00	0.00	0.8897	1.981	2.39E-03	22	57
		Mean	-		**0.00**				**1.228**	**2.021**	**4.85E-03**	**23**	**57**
		S.D.	-		**0.00**				**0.713**	**0.292**	**5.03E-03**	**0**	**1**

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 90 ppm

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment Mean	
			Nominal (ppm)	Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	12-Aug-03	1	84.9	89.55	86.8	91.7	88.0	91.7	-	-	-	23	58
1	13-Aug-03	2	84.9	91.73	96.6	89.3	89.3	91.7	0.8626	2.052	1.90E-02	23	59
2	14-Aug-03	3	84.9	90.80	90.5	94.2	86.8	91.7	0.9185	1.908	3.20E-03	23	57
3	15-Aug-03	4	84.9	88.95	88.0	90.5	91.7	85.6	1.258	2.569	3.36E-03	23	57
4	16-Aug-03	5	84.9	90.48	97.8	83.1	89.3	91.7	0.7854	1.514	5.69E-03	23	57
5	17-Aug-03	6	84.9	88.05	90.5	84.4	85.6	91.7	0.7770	1.333	6.06E-03	23	58
6	18-Aug-03	7	84.9	89.90	91.7	84.4	91.8	91.7	2.007	2.584	2.94E-03	23	57
7	19-Aug-03	8	84.9	91.38	92.9	92.9	81.9	97.8	0.8561	1.602	1.94E-03	23	56
8	20-Aug-03	9	84.9	92.03	94.2	91.7	91.7	90.5	0.8056	1.770	3.50E-03	23	57
9	21-Aug-03	10	84.9	93.88	94.2	99.1	91.7	90.5	0.8092	1.335	7.39E-03	23	57
10	22-Aug-03	11	84.9	91.73	96.6	90.5	95.4	84.4	0.8265	1.894	1.56E-02	23	60
11	23-Aug-03	12	84.9	92.03	91.7	95.4	90.5	90.5	1.256	1.787	9.65E-04	23	54
12	24-Aug-03	13	84.9	89.88	97.8	81.9	84.4	95.4	1.638	1.624	6.04E-04	24	56
13	25-Aug-03	14	84.9	88.03	88.0	95.4	83.1	85.6	1.316	1.699	8.02E-04	23	55
14	26-Aug-03	15	84.9	93.55	97.8	89.3	90.5	96.6	0.8431	1.707	2.11E-03	22	59
		Mean	**84.9**		**90.80**				**1.069**	**1.813**	**5.23E-03**	**23**	**57**
		S.D.	**0.0**		**4.30**				**0.378**	**0.382**	**5.33E-03**	**0**	**2**

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 900 ppm

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment Mean	
			Nominal (ppm)	Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	12-Aug-03	1	964	920.0	931	921	914	914	-	-	-	23	54
1	13-Aug-03	2	964	920.5	917	891	928	946	0.8421	1.796	1.68E-02	23	54
2	14-Aug-03	3	964	939.8	937	946	938	938	1.033	2.267	3.59E-03	23	54
3	15-Aug-03	4	964	947.3	939	963	939	948	0.8871	2.132	2.52E-03	23	54
4	16-Aug-03	5	964	888.0	946	863	873	870	0.7906	1.795	6.14E-03	23	54
5	17-Aug-03	6	964	909.5	975	858	926	879	0.7846	1.548	6.86E-03	23	54
6	18-Aug-03	7	964	937.0	947	938	936	927	1.099	2.273	2.43E-03	23	54
7	19-Aug-03	8	929	906.5	937	909	884	896	0.9040	1.893	2.30E-03	23	54
8	20-Aug-03	9	929	910.5	929	908	908	897	0.8607	2.084	4.55E-03	23	54
9	21-Aug-03	10	929	882.5	912	852	883	883	0.8220	1.584	7.82E-03	23	54
10	22-Aug-03	11	929	908.3	909	889	923	912	0.8345	1.943	1.65E-02	23	56
11	23-Aug-03	12	929	881.8	888	892	845	902	2.740	2.291	1.48E-03	23	52
12	24-Aug-03	13	929	897.0	882	883	877	946	1.748	1.815	7.16E-04	24	55
13	25-Aug-03	14	929	915.8	917	921	921	904	12.71	2.630	3.24E-03	23	53
14	26-Aug-03	15	929	909.3	965	837	917	918	0.8353	1.797	2.18E-03	22	55
		Mean	**945**		**911.6**				**1.921**	**1.989**	**5.51E-03**	**23**	**54**
		S.D.	**18**		**30.6**				**3.151**	**0.304**	**4.96E-03**	**0**	**1**

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 9000 ppm

Day	Date	Exposure Number	Analytical Chamber Concentration						Particle Size Determinations			Chamber Environment Mean	
			Nominal (ppm)	Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	12-Aug-03	1	8490	9090	8750	9240	9120	9250	-	-	-	23	55
1	13-Aug-03	2	8490	9185	9190	9170	9210	9170	0.8446	1.568	1.65E-02	23	56
2	14-Aug-03	3	8490	9190	9120	9150	9380	9110	8.810	3.328	7.12E-03	23	54
3	15-Aug-03	4	8490	9213	9090	9150	9320	9290	0.8802	1.882	2.66E-03	23	55
4	16-Aug-03	5	8490	9218	9250	9240	9070	9310	0.8033	1.789	7.17E-03	23	54
5	17-Aug-03	6	8490	9225	9170	9110	9310	9310	0.7964	1.562	7.26E-03	23	55
6	18-Aug-03	7	8490	9288	9210	9380	9290	9270	0.8716	1.999	2.08E-03	23	54
7	19-Aug-03	8	8490	9178	9290	9120	9150	9150	1.395	2.344	3.53E-03	23	55
8	20-Aug-03	9	8490	9310	9150	9180	9440	9470	0.8366	2.012	4.34E-03	23	55
9	21-Aug-03	10	8490	9320	9140	9280	9470	9390	0.8294	1.739	8.38E-03	23	55
10	22-Aug-03	11	8490	9408	9350	9410	9520	9350	0.8202	1.330	1.49E-02	23	58
11	23-Aug-03	12	8490	9233	9020	9220	9320	9370	1.939	2.049	1.37E-03	23	54
12	24-Aug-03	13	8490	9358	9270	9270	9420	9470	2.684	1.935	9.29E-04	24	55
13	25-Aug-03	14	8490	9240	9110	9250	9390	9210	1.731	2.094	9.20E-04	23	54
14	26-Aug-03	15	8490	9313	9210	9470	9150	9420	0.8679	1.996	2.46E-03	21	55
		Mean	**8490**		**9251**				**1.722**	**1.973**	**5.69E-03**	**23**	**55**
		S.D.	**0**		**136**				**2.119**	**0.468**	**4.77E-03**	**1**	**1**

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1001	Terminal Sacrifice	26-AUG-03	3	14
1002	Terminal Sacrifice	26-AUG-03	3	14
1003	Terminal Sacrifice	26-AUG-03	3	14
1004	Terminal Sacrifice	26-AUG-03	3	14
1005	Terminal Sacrifice	26-AUG-03	3	14
1006	Terminal Sacrifice	26-AUG-03	3	14
1007	Terminal Sacrifice	26-AUG-03	3	14
1008	Terminal Sacrifice	26-AUG-03	3	14
1009	Terminal Sacrifice	27-AUG-03	3	15
1010	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 2 90 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2001	Terminal Sacrifice	26-AUG-03	3	14
2002	Terminal Sacrifice	26-AUG-03	3	14
2003	Terminal Sacrifice	26-AUG-03	3	14
2004	Terminal Sacrifice	26-AUG-03	3	14
2005	Terminal Sacrifice	26-AUG-03	3	14
2006	Terminal Sacrifice	26-AUG-03	3	14
2007	Terminal Sacrifice	26-AUG-03	3	14
2008	Terminal Sacrifice	26-AUG-03	3	14
2009	Terminal Sacrifice	27-AUG-03	3	15
2010	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 3 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3001	Terminal Sacrifice	26-AUG-03	3	14
3002	Terminal Sacrifice	26-AUG-03	3	14
3003	Terminal Sacrifice	26-AUG-03	3	14
3004	Terminal Sacrifice	26-AUG-03	3	14
3005	Terminal Sacrifice	26-AUG-03	3	14
3006	Terminal Sacrifice	26-AUG-03	3	14
3007	Terminal Sacrifice	26-AUG-03	3	14
3008	Terminal Sacrifice	26-AUG-03	3	14
3009	Terminal Sacrifice	27-AUG-03	3	15
3010	Humane Sacrifice	22-AUG-03	2	10

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4001	Terminal Sacrifice	26-AUG-03	3	14
4002	Terminal Sacrifice	26-AUG-03	3	14
4003	Terminal Sacrifice	26-AUG-03	3	14
4004	Terminal Sacrifice	26-AUG-03	3	14
4005	Terminal Sacrifice	26-AUG-03	3	14
4006	Terminal Sacrifice	26-AUG-03	3	14
4007	Terminal Sacrifice	26-AUG-03	3	14
4008	Terminal Sacrifice	26-AUG-03	3	14
4009	Terminal Sacrifice	27-AUG-03	3	15
4010	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1501	Terminal Sacrifice	26-AUG-03	3	14
1502	Terminal Sacrifice	26-AUG-03	3	14
1503	Terminal Sacrifice	26-AUG-03	3	14
1504	Terminal Sacrifice	26-AUG-03	3	14
1505	Terminal Sacrifice	26-AUG-03	3	14
1506	Terminal Sacrifice	26-AUG-03	3	14
1507	Terminal Sacrifice	26-AUG-03	3	14
1508	Terminal Sacrifice	27-AUG-03	3	15
1509	Terminal Sacrifice	27-AUG-03	3	15
1510	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 90 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2501	Terminal Sacrifice	26-AUG-03	3	14
2502	Terminal Sacrifice	26-AUG-03	3	14
2503	Terminal Sacrifice	26-AUG-03	3	14
2504	Terminal Sacrifice	26-AUG-03	3	14
2505	Terminal Sacrifice	26-AUG-03	3	14
2506	Terminal Sacrifice	26-AUG-03	3	14
2507	Terminal Sacrifice	26-AUG-03	3	14
2508	Terminal Sacrifice	27-AUG-03	3	15
2509	Terminal Sacrifice	27-AUG-03	3	15
2510	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3501	Terminal Sacrifice	26-AUG-03	3	14
3502	Terminal Sacrifice	26-AUG-03	3	14
3503	Terminal Sacrifice	26-AUG-03	3	14
3504	Terminal Sacrifice	26-AUG-03	3	14
3505	Terminal Sacrifice	26-AUG-03	3	14
3506	Terminal Sacrifice	26-AUG-03	3	14
3507	Terminal Sacrifice	26-AUG-03	3	14
3508	Terminal Sacrifice	27-AUG-03	3	15
3509	Terminal Sacrifice	27-AUG-03	3	15
3510	Terminal Sacrifice	27-AUG-03	3	15

APPENDIX B

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4501	Terminal Sacrifice	26-AUG-03	3	14
4502	Terminal Sacrifice	26-AUG-03	3	14
4503	Terminal Sacrifice	26-AUG-03	3	14
4504	Terminal Sacrifice	26-AUG-03	3	14
4505	Terminal Sacrifice	26-AUG-03	3	14
4506	Terminal Sacrifice	26-AUG-03	3	14
4507	Terminal Sacrifice	26-AUG-03	3	14
4508	Terminal Sacrifice	27-AUG-03	3	15
4509	Terminal Sacrifice	27-AUG-03	3	15
4510	Terminal Sacrifice	27-AUG-03	3	15

	Individual Clinical Observations Preface	Appendix C

For summarization purposes, descriptive comments [i.e., location of scab(s) and sore(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
1001	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1002	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1003	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	OCULAR: Chromodacryorrhea - Unilateral				P	P	
	ORAL/BUCCAL: Incisors Broken/Missing				P	P	
1004	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1005	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1006	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1007	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - General				2	2	
	DERMAL GENERAL: Scab(s)				P		
1008	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1009	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
1010	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 90 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
2001	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2002	WITHIN NORMAL LIMITS	P	P	P			
	Terminal Sacrifice					P	
	ORAL/BUCCAL: Nasal Discharge - Red				P		
2003	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2004	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2005	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2006	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2007	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2008	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2009	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
2010	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
3001	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3002	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3003	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3004	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3005	WITHIN NORMAL LIMITS	P	P		P		
	Terminal Sacrifice					P	
	ORAL/BUCCAL: Incisors Broken/Missing			P			
3006	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3007	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3008	WITHIN NORMAL LIMITS	P	P		P		
	Terminal Sacrifice					P	
	ORAL/BUCCAL: Nasal Discharge - Red			P			
3009	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3010	WITHIN NORMAL LIMITS	P	P	P			
	Humane Sacrifice				P		

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
4001	WITHIN NORMAL LIMITS	P	P	P			
	Terminal Sacrifice						P
	DERMAL GENERAL: Alopecia - Extremities/Snout				3		
4002	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4003	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4004	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4005	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4006	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4007	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4008	WITHIN NORMAL LIMITS	P	P	P			
	Terminal Sacrifice						P
	ORAL/BUCCAL: Nasal Discharge - Red				P		
4009	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4010	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
1501	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1502	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1503	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1504	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1505	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1506	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1507	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1508	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1509	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1510	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 90 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
2501	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2502	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2503	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2504	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2505	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2506	WITHIN NORMAL LIMITS	P	P	P			
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - Extremities/Snout				3		
2507	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2508	WITHIN NORMAL LIMITS	P	P	P			
	Terminal Sacrifice						P
	OCULAR: Chromodacryorrhea - Unilateral				P		
	ORAL/BUCCAL: Incisors Maloccluded				P		
2509	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
2510	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	1 3	1 4	1 5
3501	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3502	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - General				2		
	DERMAL GENERAL: Scab(s)			P			
3503	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3504	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3505	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3506	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3507	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3508	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3509	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3510	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY - 7	0	7	3	4	11 5
4501	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4502	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4503	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4504	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4505	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4506	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4507	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4508	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4509	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4510	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
1001	205	267	302	327
1002	218	282	324	349
1003	205	259	296	323
1004	223	271	301	314
1005	228	290	327	369
1006	210	274	317	350
1007	221	278	321	353
1008	231	303	368	414
1009	223	292	339	374
1010	209	261	302	342
MEAN	217	278	320	351
S.D.	9.6	14.4	22.0	29.0
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 2 90 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
2001	220	274	316	335
2002	219	297	350	392
2003	229	284	313	337
2004	224	278	309	335
2005	208	267	314	347
2006	212	278	316	343
2007	230	281	313	329
2008	209	265	294	319
2009	221	285	318	342
2010	205	267	301	329
MEAN	218	278	315	341
S.D.	8.9	10.0	14.6	19.6
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 3 900 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
3001	230	291	343	371
3002	209	265	303	329
3003	201	254	295	321
3004	230	296	350	387
3005	219	266	310	341
3006	206	272	324	366
3007	226	276	308	338
3008	221	279	325	343
3009	216	271	297	312
3010	210	266	304	AD
MEAN	217	274	316	345
S.D.	10.0	12.6	19.1	24.6
N	10	10	10	9

AD=Animal Died

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 4 9000 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
4001	229	292	332	369
4002	221	273	304	321
4003	209	257	287	305
4004	205	268	328	364
4005	209	272	323	358
4006	231	278	324	358
4007	217	277	301	325
4008	220	271	305	334
4009	224	258	288	308
4010	199	263	294	325
MEAN	216	271	309	337
S.D.	10.5	10.2	17.0	23.5
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
1501	170	196	212	212
1502	173	208	226	259
1503	180	213	231	239
1504	184	193	206	230
1505	186	220	235	240
1506	176	206	217	224
1507	191	209	235	255
1508	187	210	219	229
1509	173	198	205	217
1510	198	225	238	252
MEAN	182	208	222	236
S.D.	9.0	10.2	12.3	16.1
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 2 90 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
2501	188	216	226	241
2502	172	209	218	225
2503	183	206	228	236
2504	171	197	216	222
2505	189	212	235	252
2506	187	216	229	238
2507	173	198	210	220
2508	185	197	218	234
2509	196	214	228	241
2510	174	195	216	228
MEAN	182	206	222	234
S.D.	8.7	8.4	7.8	10.0
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 900 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
3501	173	195	207	213
3502	183	216	237	239
3503	188	211	235	235
3504	184	208	227	246
3505	192	216	233	251
3506	174	202	215	216
3507	190	217	234	239
3508	169	197	205	221
3509	180	196	220	241
3510	187	211	224	237
MEAN	182	207	224	234
S.D.	7.9	8.7	11.7	12.7
N	10	10	10	10

APPENDIX D

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
4501	183	206	223	236
4502	173	187	198	213
4503	177	192	225	244
4504	194	214	238	263
4505	174	203	224	221
4506	184	209	221	226
4507	188	214	245	258
4508	168	176	194	199
4509	191	212	239	249
4510	185	206	229	244
MEAN	182	202	224	235
S.D.	8.6	12.8	16.5	20.3
N	10	10	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
1001	35	60
1002	42	68
1003	37	64
1004	30	43
1005	36	78
1006	43	77
1007	43	75
1008	65	111
1009	47	81
1010	42	81
MEAN	42	74
S.D.	9.5	17.4
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 2 90 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
2001	42	61
2002	53	95
2003	30	54
2004	32	57
2005	48	80
2006	38	65
2007	32	48
2008	30	55
2009	33	57
2010	34	62
MEAN	37	63
S.D.	8.0	13.9
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 3 900 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
3001	52	80
3002	38	64
3003	41	67
3004	54	91
3005	44	75
3006	52	94
3007	32	62
3008	46	64
3009	26	42
3010	38	AD
MEAN	42	71
S.D.	9.2	16.0
N	10	9

AD=Animal Died

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 4 9000 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
4001	40	78
4002	31	49
4003	30	48
4004	60	95
4005	51	86
4006	46	80
4007	25	49
4008	34	64
4009	30	50
4010	31	62
MEAN	38	66
S.D.	11.3	17.5
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
1501	16	16
1502	18	51
1503	18	26
1504	13	37
1505	14	20
1506	11	18
1507	26	46
1508	10	20
1509	7	19
1510	13	27
MEAN	15	28
S.D.	5.3	12.5
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 2 90 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
2501	10	25
2502	9	16
2503	22	30
2504	18	25
2505	23	41
2506	13	22
2507	12	22
2508	21	37
2509	14	27
2510	21	33
MEAN	16	28
S.D.	5.3	7.4
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 3 900 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
3501	12	19
3502	21	23
3503	24	24
3504	19	38
3505	17	35
3506	13	14
3507	17	22
3508	8	24
3509	24	44
3510	13	26
MEAN	17	27
S.D.	5.2	9.4
N	10	10

APPENDIX E

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
4501	17	30
4502	11	26
4503	32	51
4504	24	49
4505	21	18
4506	12	16
4507	31	44
4508	18	23
4509	27	37
4510	23	38
MEAN	22	33
S.D.	7.3	12.5
N	10	10

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 1 0 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
1001	103	85	75
1002	100	86	73
1003	96	79	75
1004	96	83	70
1005	95	76	75
1006	101	87	71
1007	91	82	67
1008	101	89	78
1009	100	89	73
1010	97	81	77
MEAN	98	84	73
S.D.	3.7	4.1	3.4
N	10	10	10

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 2 90 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
2001	100	84	74
2002	105	94	84
2003	92	78	68
2004	92	79	69
2005	97	89	76
2006	100	81	72
2007	92	85	72
2008	92	80	69
2009	104	87	70
2010	102	84	72
MEAN	98	84	73
S.D.	5.3	4.9	4.6
N	10	10	10

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 3 900 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
3001	99	86	75
3002	95	83	72
3003	100	82	72
3004	99	85	75
3005	94	83	75
3006	104	89	79
3007	92	73	71
3008	102	87	75
3009	92	78	65
3010	98	83	AD
MEAN	98	83	73
S.D.	4.1	4.7	3.8
N	10	10	9

AD=Animal Died

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
4001	103	85	77
4002	97	82	70
4003	97	78	69
4004	108	95	81
4005	100	87	77
4006	99	85	79
4007	101	76	71
4008	98	85	76
4009	97	85	82
4010	103	85	75
MEAN	100	84	76
S.D.	3.5	5.0	4.7
N	10	10	10

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
1501	93	84	81
1502	97	84	90
1503	94	80	80
1504	78	76	78
1505	95	83	84
1506	78	CF	CF
1507	92	85	80
1508	89	77	77
1509	87	77	78
1510	95	77	78
MEAN	90	80	81
S.D.	6.8	3.7	4.0
N	10	9	9

CF=Contaminated Feeder

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 2 90 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
2501	91	79	82
2502	98	84	86
2503	91	81	82
2504	95	83	83
2505	96	86	88
2506	99	86	81
2507	87	77	78
2508	85	82	79
2509	100	86	81
2510	95	90	88
MEAN	94	83	83
S.D.	4.9	3.8	3.5
N	10	10	10

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 3 900 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
3501	91	79	82
3502	93	81	76
3503	95	85	83
3504	91	81	80
3505	96	82	82
3506	CF	70	CF
3507	95	89	82
3508	101	90	88
3509	86	80	80
3510	92	82	83
MEAN	93	82	82
S.D.	4.1	5.4	3.2
N	9	10	9

CF=Contaminated Feeder

APPENDIX F

ISOBUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
4501	86	77	80
4502	88	77	86
4503	92	85	82
4504	93	85	89
4505	91	85	82
4506	91	81	86
4507	94	86	85
4508	89	86	88
4509	96	88	86
4510	93	86	85
MEAN	91	84	85
S.D.	2.9	3.8	2.8
N	10	10	10

	Individual Organ Weights Preface	Appendix G

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% Organ to Brain Weight Ratios 130

Key to Abbreviations:

g = Grams
wt. = Weight
observ. = Observed

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
				M a l e	A n i m a l s			
1001/M	1/1	293.8	0.0483	2.0882	0.7974	1.2813	3.0713	10.6342
1002/M	1/1	326.9	0.0424	1.8379	0.8584	1.3630	2.9269	10.7020
1003/M	1/1	300.4	0.0524	2.2107	0.7537	1.2190	2.8942	10.5258
1004/M	1/1	296.0	0.0680	2.0968	0.9651	1.1404	2.8465	11.5283
1005/M	1/1	343.7	0.0651	1.9761	0.8778	1.2733	3.3369	11.7854
1006/M	1/1	322.7	0.0800	2.1580	0.8869	1.3318	3.4209	11.0822
1007/M	1/1	323.0	0.0695	2.0103	1.0510	1.2519	2.9193	11.1002
1008/M	1/1	377.1	0.0686	2.5598	0.8502	1.5293	4.6876	14.9922
1009/M	1/1	340.3	0.0518	2.2193	0.9315	1.3009	3.3349	12.7530
1010/M	1/1	312.8	0.0651	1.9889	0.8405	1.1949	3.2343	10.9506
M e a n:		323.7	0.0611	2.1146	0.8813	1.2886	3.2673	11.6054
Standard deviation:		25.5	0.0117	0.1954	0.0849	0.1068	0.5419	1.3625
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	0.0708	2.0529	0.9638	1.2335	3.1319	11.0903
2002/M	2/1	364.3	0.0372	2.1108	0.7768	1.3669	3.3091	13.4361
2003/M	2/1	306.9	0.0570	1.8607	0.7716	1.2269	2.7619	10.4285
2004/M	2/1	314.4	0.0640	2.2771	1.1173	1.3287	3.4889	11.5244
2005/M	2/1	318.0	0.0727	2.4411	0.8449	1.3492	3.5763	13.3213
2006/M	2/1	317.3	0.0560	1.9962	0.8935	1.2700	3.1814	10.2972
2007/M	2/1	306.9	0.0512	2.0352	1.0580	1.3070	2.8006	10.5939
2008/M	2/1	291.4	0.0619	2.0463	0.9302	1.1785	3.0349	10.1575
2009/M	2/1	319.5	0.0577	1.9236	0.9360	1.2537	2.9540	9.4336
2010/M	2/1	305.4	0.0546	2.0479	0.8575	1.1882	2.9455	13.1826
M e a n:		315.7	0.0583	2.0792	0.9150	1.2703	3.1185	11.3465
Standard deviation:		19.0	0.0101	0.1682	0.1119	0.0658	0.2748	1.4651
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	0.0700	2.0646	1.0211	1.4150	2.7697	11.3009
3002/M	3/1	307.2	0.0498	2.1298	0.8221	1.3402	3.1870	11.2715
3003/M	3/1	296.8	0.0569	2.0900	0.7574	1.2712	3.6263	11.1211
3004/M	3/1	349.7	0.0665	2.0838	0.9225	1.2984	3.6367	11.4386
3005/M	3/1	303.9	0.0851	2.1002	1.0064	1.2222	3.2581	10.5030
3006/M	3/1	337.0	0.0600	1.9666	0.8255	1.4047	3.0612	11.7204
3007/M	3/1	317.9	0.0519	2.2297	0.8559	1.1297	2.9524	10.8992
3008/M	3/1	325.9	0.0524	2.1578	0.9605	1.2334	3.5036	10.5177
3009/M	3/1	294.5	0.0470	1.8584	0.9982	1.0159	2.6615	10.8216
M e a n:		318.7	0.0600	2.0757	0.9077	1.2590	3.1841	11.0660
Standard deviation:		19.5	0.0121	0.1081	0.0956	0.1283	0.3573	0.4142
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	0.0655	2.1662	0.9112	1.3680	3.3445	11.9640
4002/M	4/1	299.2	0.0602	2.1467	0.9221	1.2499	3.2850	10.6335
4003/M	4/1	277.2	0.0560	1.9682	0.8961	1.0845	2.8290	8.9376
4004/M	4/1	325.0	0.0893	2.2546	1.0999	1.4050	4.0377	12.5774

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
4005/M	4/1	320.4	0.0802	1.9302	0.8132	1.1376	3.0293	11.0420
4006/M	4/1	330.6	0.0645	2.0415	1.1304	1.3811	3.1097	12.0668
4007/M	4/1	303.6	0.0496	2.0983	0.9208	1.1343	2.7790	11.5656
4008/M	4/1	312.0	0.0542	2.0473	0.9235	1.2635	3.0414	9.7036
4009/M	4/1	291.9	0.0427	1.9869	0.7389	1.1313	2.9439	10.4771
4010/M	4/1	298.3	0.0661	2.0351	0.7943	1.2190	3.0123	10.3122
	M e a n:	309.8	0.0628	2.0675	0.9150	1.2374	3.1412	10.9280
Standard deviation:		19.3	0.0139	0.0996	0.1234	0.1165	0.3611	1.1373
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland Seminal vesicles	Spleen	Testes	Thymus
				Male Animals			
1001/M	1/1	293.8	1.8858	0.0095	1.2614	0.6386	3.2501	0.4370
1002/M	1/1	326.9	2.3980	0.0110	1.5409	0.6083	3.2581	0.4583
1003/M	1/1	300.4	1.7158	0.0087	1.2137	0.5853	3.4382	0.5233
1004/M	1/1	296.0	1.6527	0.0112	1.3491	0.5673	3.2201	0.5189
1005/M	1/1	343.7	1.8964	0.0123	1.1497	0.8530	3.0181	0.7209
1006/M	1/1	322.7	1.9729	0.0114	1.5679	0.7519	3.7282	0.4090
1007/M	1/1	323.0	1.6209	0.0094	1.2274	0.6936	3.1770	0.4638
1008/M	1/1	377.1	3.1504	0.0106	1.2318	0.9844	3.2174	0.6976
1009/M	1/1	340.3	1.5432	0.0048	1.1568	0.5865	3.3404	0.6056
1010/M	1/1	312.8	1.7691	0.0105	1.1498	0.6461	3.0589	0.4650
Mean:		323.7	1.9605	0.0099	1.2849	0.6915	3.2707	0.5299
Standard deviation:		25.5	0.4828	0.0021	0.1544	0.1354	0.2016	0.1093
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	1.9189	0.0101	1.2583	0.5977	2.9629	0.5719
2002/M	2/1	364.3	2.4796	0.0099	1.3425	0.7697	3.3593	0.5808
2003/M	2/1	306.9	1.6650	0.0103	1.0615	0.8406	2.3141	0.3973
2004/M	2/1	314.4	2.7391	0.0073	1.6345	0.6982	3.2062	0.5925
2005/M	2/1	318.0	3.2431	0.0108	1.2872	1.0155	3.0941	0.6963
2006/M	2/1	317.3	2.0243	0.0099	0.8296	0.5957	3.2033	0.6489
2007/M	2/1	306.9	1.8324	0.0108	1.3462	0.6263	3.0757	0.5938
2008/M	2/1	291.4	1.6145	0.0125	1.0834	0.6069	3.4784	0.7013
2009/M	2/1	319.5	1.7767	0.0095	1.5927	0.5905	3.4734	0.3781
2010/M	2/1	305.4	1.6635	0.0079	1.0792	0.6416	3.1168	0.3460
Mean:		315.7	2.0957	0.0099	1.2515	0.6983	3.1284	0.5507
Standard deviation:		19.0	0.5466	0.0015	0.2480	0.1394	0.3335	0.1307
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	1.6530	0.0125	1.1090	0.6727	3.2571	0.4524
3002/M	3/1	307.2	1.7804	0.0091	0.9498	0.6263	3.1871	0.5365
3003/M	3/1	296.8	1.9443	0.0097	1.2198	0.7906	3.0711	0.5585
3004/M	3/1	349.7	1.9480	0.0111	0.9777	0.7483	3.0765	0.5677
3005/M	3/1	303.9	2.0359	0.0085	1.2252	0.7467	3.1409	0.4506
3006/M	3/1	337.0	1.9686	0.0115	1.1296	0.7405	3.1928	0.5190
3007/M	3/1	317.9	1.7442	0.0101	1.3960	0.6804	3.4112	0.5320
3008/M	3/1	325.9	1.8503	0.0108	1.2747	0.7807	3.4942	0.5537
3009/M	3/1	294.5	1.6419	0.0062	0.7602	0.7164	3.4184	0.4559
Mean:		318.7	1.8407	0.0099	1.1158	0.7225	3.2499	0.5140
Standard deviation:		19.5	0.1434	0.0019	0.1936	0.0538	0.1562	0.0481
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	2.1923	0.0109	1.4051	0.7275	3.1754	0.5027
4002/M	4/1	299.2	1.8972	0.0103	1.4714	0.5533	3.2748	0.4191
4003/M	4/1	277.2	1.6350	0.0087	1.2573	0.5114	3.2200	0.5529
4004/M	4/1	325.0	2.3799	0.0120	1.0073	0.6886	3.1108	1.0391

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
4005/M	4/1	320.4	2.1120	0.0102	1.1030	0.6559	2.9292	0.8197
4006/M	4/1	330.6	1.9248	0.0120	1.0959	0.7663	3.1800	0.4322
4007/M	4/1	303.6	1.8916	0.0107	1.4638	0.6991	3.2296	0.5428
4008/M	4/1	312.0	1.7543	0.0098	1.4870	0.6540	3.1549	0.6487
4009/M	4/1	291.9	1.9316	0.0047	0.7822	0.5787	2.8501	0.6812
4010/M	4/1	298.3	1.7320	0.0104	1.3021	0.7114	2.8208	0.4257
M e a n:		309.8	1.9451	0.0100	1.2375	0.6546	3.0946	0.6064
Standard deviation:		19.3	0.2265	0.0021	0.2355	0.0821	0.1654	0.1988
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1501/F	1/1	204.6	0.0647	2.0057	0.9323	1.7435	7.3866	1.3824
1502/F	1/1	236.0	0.0688	2.1155	0.9388	2.3744	8.9409	1.3054
1503/F	1/1	221.5	0.0721	2.0781	0.9178	1.9908	9.0700	1.4960
1504/F	1/1	212.0	0.0616	2.0474	0.8793	2.2756	7.1273	1.5705
1505/F	1/1	220.4	0.0672	2.2252	0.9132	2.6360	8.2389	1.9175
1506/F	1/1	209.9	0.0655	2.0167	0.8710	1.9236	7.2837	1.4184
1507/F	1/1	231.3	0.0665	2.0381	0.7779	2.1920	8.2224	1.6834
1508/F	1/1	205.5	0.0722	1.8823	0.6843	1.6534	6.7724	1.2262
1509/F	1/1	209.1	0.0581	1.8914	0.8301	1.9404	7.1291	1.2017
1510/F	1/1	224.7	0.0789	2.0331	0.8862	2.2033	7.1995	1.3809
Mean:		217.5	0.0676	2.0334	0.8631	2.0933	7.7371	1.4582
Standard deviation:		10.9	0.0059	0.0999	0.0797	0.2995	0.8167	0.2191
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	0.0699	1.9893	0.9237	2.1883	8.2437	1.7944
2502/F	2/1	214.0	0.0699	2.2602	0.9356	2.3428	8.1951	1.5367
2503/F	2/1	210.2	0.0608	1.9707	0.9168	2.1073	8.6649	1.1647
2504/F	2/1	204.0	0.0686	1.8672	0.8298	1.8958	7.6957	1.6700
2505/F	2/1	226.6	0.1040	2.2059	1.0203	2.5311	11.1658	1.3159
2506/F	2/1	214.9	0.1020	1.8406	0.9168	2.2164	9.0983	1.4042
2507/F	2/1	198.9	0.0646	1.8751	0.8484	2.1460	6.7805	1.3520
2508/F	2/1	215.2	0.0737	1.8380	0.8021	2.0925	8.7242	1.1645
2509/F	2/1	217.4	0.0623	1.9992	0.8509	2.1511	7.4449	1.3499
2510/F	2/1	213.1	0.0571	1.9303	0.8313	2.1296	8.1804	1.2541
Mean:		213.5	0.0733	1.9777	0.8876	2.1801	8.4194	1.4006
Standard deviation:		7.9	0.0164	0.1475	0.0664	0.1665	1.1764	0.2085
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	0.0657	2.0272	0.7848	1.8767	6.3059	1.4324
3502/F	3/1	223.0	0.0958	2.1839	0.9392	2.9071	9.9957	1.4655
3503/F	3/1	219.5	0.0795	1.9784	0.8873	2.3361	7.2222	1.5654
3504/F	3/1	225.5	0.0843	2.0646	0.9766	2.1435	7.7627	1.6434
3505/F	3/1	227.6	0.0725	1.9652	0.9648	2.1969	8.8019	1.7992
3506/F	3/1	206.4	0.0719	1.9358	0.9507	2.2282	8.1959	1.7360
3507/F	3/1	220.1	0.0817	2.0134	0.9159	2.1329	9.4575	1.3818
3508/F	3/1	198.5	0.0650	1.9227	0.8965	1.9515	7.8284	1.2241
3509/F	3/1	222.7	0.0632	1.8705	0.8215	1.8552	8.0737	1.2036
3510/F	3/1	215.9	0.0639	1.8950	0.8669	2.0835	7.6677	1.2845
Mean:		215.9	0.0744	1.9857	0.9004	2.1712	8.1312	1.4736
Standard deviation:		10.6	0.0108	0.0922	0.0625	0.3014	1.0694	0.2090
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	0.0700	1.9923	0.9880	2.1550	8.6054	1.6745
4502/F	4/1	192.0	0.0729	2.0045	0.7241	2.0121	7.5224	1.2519
4503/F	4/1	224.3	0.0718	2.1259	0.9689	2.5166	8.6829	1.4926

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4504/F	4/1	238.3	0.0758	2.1712	0.9110	2.6568	9.8859	1.8102
4505/F	4/1	217.3	0.0678	1.8173	0.7954	1.8061	7.7594	1.4146
4506/F	4/1	210.3	0.0711	2.1377	0.9100	2.0815	8.3072	1.7718
4507/F	4/1	236.4	0.0870	2.0202	1.0775	2.2776	8.7353	1.5178
4508/F	4/1	185.2	0.0543	1.8254	0.7210	1.7877	6.1282	1.3903
4509/F	4/1	226.3	0.0861	1.8595	0.8859	2.0697	8.4634	1.3045
4510/F	4/1	220.5	0.0845	1.9810	0.8990	2.0097	8.1685	1.4576
	M e a n:	217.0	0.0741	1.9935	0.8881	2.1373	8.2259	1.5086
Standard deviation:		17.2	0.0099	0.1283	0.1140	0.2799	0.9745	0.1889
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
				Female Animals			
1501/F	1/1	204.6	0.1009	0.0048	0.6421	0.5096	0.3909
1502/F	1/1	236.0	0.1383	0.0186	0.5862	0.5033	0.7290
1503/F	1/1	221.5	0.1117	0.0137	0.6046	0.5544	0.5335
1504/F	1/1	212.0	0.0954	0.0099	0.5876	0.4725	1.0194
1505/F	1/1	220.4	0.0961	0.0154	0.5085	0.4774	0.5886
1506/F	1/1	209.9	0.0877	0.0148	0.4653	0.6280	0.5258
1507/F	1/1	231.3	0.1537	0.0131	0.5462	0.4971	0.6881
1508/F	1/1	205.5	0.0957	0.0122	0.4937	0.3484	0.4924
1509/F	1/1	209.1	0.1176	0.0133	0.4533	0.3279	0.3951
1510/F	1/1	224.7	0.1214	0.0125	0.4750	0.5274	0.4778
Mean:		217.5	0.1119	0.0128	0.5363	0.4846	0.5841
Standard deviation:		10.9	0.0212	0.0036	0.0661	0.0893	0.1886
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	0.1061	0.0148	0.5183	0.4032	0.5569
2502/F	2/1	214.0	0.0922	0.0121	0.5348	0.4166	0.5634
2503/F	2/1	210.2	0.0899	0.0067	0.4468	0.3530	0.6043
2504/F	2/1	204.0	0.1044	0.0115	0.5636	0.4339	0.5643
2505/F	2/1	226.6	0.1164	0.0201	0.6502	0.5840	0.6002
2506/F	2/1	214.9	0.1192	0.0131	0.4534	0.4815	0.5360
2507/F	2/1	198.9	0.1002	0.0146	0.4444	0.4264	0.5261
2508/F	2/1	215.2	0.0897	0.0103	0.4531	0.4789	1.2364
2509/F	2/1	217.4	0.1134	0.0110	0.5156	0.5491	0.9769
2510/F	2/1	213.1	0.0676	0.0117	0.4752	0.4500	0.4450
Mean:		213.5	0.0999	0.0126	0.5055	0.4577	0.6610
Standard deviation:		7.9	0.0156	0.0035	0.0658	0.0688	0.2468
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	0.0839	0.0110	0.5153	0.3849	0.5273
3502/F	3/1	223.0	0.1149	0.0144	0.6196	0.6043	0.5491
3503/F	3/1	219.5	0.1008	0.0130	0.4557	0.6194	0.4911
3504/F	3/1	225.5	0.1285	0.0134	0.5634	0.6217	0.5750
3505/F	3/1	227.6	0.1161	0.0085	0.4786	0.5152	0.5673
3506/F	3/1	206.4	0.1295	0.0158	0.6133	0.4752	0.5881
3507/F	3/1	220.1	0.1030	0.0129	0.4204	0.4364	0.5045
3508/F	3/1	198.5	0.0844	0.0111	0.5719	0.3651	0.6338
3509/F	3/1	222.7	0.0728	0.0127	0.6089	0.5198	0.8984
3510/F	3/1	215.9	0.0845	0.0092	0.4367	0.4377	0.4213
Mean:		215.9	0.1018	0.0122	0.5284	0.4980	0.5756
Standard deviation:		10.6	0.0201	0.0023	0.0768	0.0946	0.1277
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	0.1043	0.0136	0.5241	0.3076	0.7582
4502/F	4/1	192.0	0.0861	0.0132	0.4460	0.5360	0.5856
4503/F	4/1	224.3	0.1063	0.0140	0.6725	0.6260	0.6583

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Pituitary gland		Thymus		
			Ovaries		Spleen		Uterus
4504/F	4/1	238.3	0.1210	0.0161	0.5549	0.4495	0.5305
4505/F	4/1	217.3	0.0936	0.0148	0.4603	0.4370	0.4259
4506/F	4/1	210.3	0.1047	0.0109	0.5989	0.4233	0.6420
4507/F	4/1	236.4	0.1261	0.0097	0.5425	0.6188	0.7292
4508/F	4/1	185.2	0.0898	0.0078	0.4275	0.4306	0.4859
4509/F	4/1	226.3	0.0940	0.0126	0.5342	0.5749	0.4683
4510/F	4/1	220.5	0.1121	0.0112	0.5067	0.4587	0.5390
M e a n:		217.0	0.1038	0.0124	0.5268	0.4862	0.5823
Standard deviation:		17.2	0.0132	0.0025	0.0736	0.1005	0.1121
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
				Male Animals				
1001/M	1/1	293.8	0.0164	0.7108	0.2714	0.4361	1.0454	3.6195
1002/M	1/1	326.9	0.0130	0.5622	0.2626	0.4169	0.8954	3.2738
1003/M	1/1	300.4	0.0174	0.7359	0.2509	0.4058	0.9634	3.5039
1004/M	1/1	296.0	0.0230	0.7084	0.3260	0.3853	0.9617	3.8947
1005/M	1/1	343.7	0.0189	0.5749	0.2554	0.3705	0.9709	3.4290
1006/M	1/1	322.7	0.0248	0.6687	0.2748	0.4127	1.0601	3.4342
1007/M	1/1	323.0	0.0215	0.6224	0.3254	0.3876	0.9038	3.4366
1008/M	1/1	377.1	0.0182	0.6788	0.2255	0.4055	1.2431	3.9757
1009/M	1/1	340.3	0.0152	0.6522	0.2737	0.3823	0.9800	3.7476
1010/M	1/1	312.8	0.0208	0.6358	0.2687	0.3820	1.0340	3.5008
	Mean:	323.7	0.0189	0.6550	0.2734	0.3985	1.0058	3.5816
Standard deviation:		25.5	0.0036	0.0575	0.0312	0.0202	0.0999	0.2250
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	0.0226	0.6565	0.3082	0.3945	1.0016	3.5466
2002/M	2/1	364.3	0.0102	0.5794	0.2132	0.3752	0.9083	3.6882
2003/M	2/1	306.9	0.0186	0.6063	0.2514	0.3998	0.8999	3.3980
2004/M	2/1	314.4	0.0204	0.7243	0.3554	0.4226	1.1097	3.6655
2005/M	2/1	318.0	0.0229	0.7676	0.2657	0.4243	1.1246	4.1891
2006/M	2/1	317.3	0.0176	0.6291	0.2816	0.4003	1.0026	3.2453
2007/M	2/1	306.9	0.0167	0.6631	0.3447	0.4259	0.9125	3.4519
2008/M	2/1	291.4	0.0212	0.7022	0.3192	0.4044	1.0415	3.4858
2009/M	2/1	319.5	0.0181	0.6021	0.2930	0.3924	0.9246	2.9526
2010/M	2/1	305.4	0.0179	0.6706	0.2808	0.3891	0.9645	4.3165
	Mean:	315.7	0.0186	0.6601	0.2913	0.4028	0.9890	3.5939
Standard deviation:		19.0	0.0037	0.0590	0.0429	0.0168	0.0824	0.4077
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	0.0209	0.6152	0.3043	0.4216	0.8253	3.3674
3002/M	3/1	307.2	0.0162	0.6933	0.2676	0.4363	1.0374	3.6691
3003/M	3/1	296.8	0.0192	0.7042	0.2552	0.4283	1.2218	3.7470
3004/M	3/1	349.7	0.0190	0.5959	0.2638	0.3713	1.0399	3.2710
3005/M	3/1	303.9	0.0280	0.6911	0.3312	0.4022	1.0721	3.4561
3006/M	3/1	337.0	0.0178	0.5836	0.2450	0.4168	0.9084	3.4779
3007/M	3/1	317.9	0.0163	0.7014	0.2692	0.3554	0.9287	3.4285
3008/M	3/1	325.9	0.0161	0.6621	0.2947	0.3785	1.0751	3.2273
3009/M	3/1	294.5	0.0160	0.6310	0.3389	0.3450	0.9037	3.6746
	Mean:	318.7	0.0188	0.6531	0.2855	0.3950	1.0014	3.4799
Standard deviation:		19.5	0.0038	0.0476	0.0335	0.0335	0.1206	0.1832
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	0.0193	0.6369	0.2679	0.4022	0.9834	3.5178
4002/M	4/1	299.2	0.0201	0.7175	0.3082	0.4177	1.0979	3.5540
4003/M	4/1	277.2	0.0202	0.7100	0.3233	0.3912	1.0206	3.2242
4004/M	4/1	325.0	0.0275	0.6937	0.3384	0.4323	1.2424	3.8700

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
4005/M	4/1	320.4	0.0250	0.6024	0.2538	0.3551	0.9455	3.4463
4006/M	4/1	330.6	0.0195	0.6175	0.3419	0.4178	0.9406	3.6500
4007/M	4/1	303.6	0.0163	0.6911	0.3033	0.3736	0.9153	3.8095
4008/M	4/1	312.0	0.0174	0.6562	0.2960	0.4050	0.9748	3.1101
4009/M	4/1	291.9	0.0146	0.6807	0.2531	0.3876	1.0085	3.5893
4010/M	4/1	298.3	0.0222	0.6822	0.2663	0.4086	1.0098	3.4570
	M e a n:	309.8	0.0202	0.6688	0.2952	0.3991	1.0139	3.5228
Standard deviation:		19.3	0.0039	0.0390	0.0336	0.0229	0.0952	0.2343
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland Seminal vesicles		Spleen	Testes	Thymus
				Male Animals				
1001/M	1/1	293.8	0.6419	0.0032	0.4293	0.2174	1.1062	0.1487
1002/M	1/1	326.9	0.7336	0.0034	0.4714	0.1861	0.9967	0.1402
1003/M	1/1	300.4	0.5712	0.0029	0.4040	0.1948	1.1445	0.1742
1004/M	1/1	296.0	0.5583	0.0038	0.4558	0.1917	1.0879	0.1753
1005/M	1/1	343.7	0.5518	0.0036	0.3345	0.2482	0.8781	0.2097
1006/M	1/1	322.7	0.6114	0.0035	0.4859	0.2330	1.1553	0.1267
1007/M	1/1	323.0	0.5018	0.0029	0.3800	0.2147	0.9836	0.1436
1008/M	1/1	377.1	0.8354	0.0028	0.3267	0.2610	0.8532	0.1850
1009/M	1/1	340.3	0.4535	0.0014	0.3399	0.1723	0.9816	0.1780
1010/M	1/1	312.8	0.5656	0.0034	0.3676	0.2066	0.9779	0.1487
Mean:		323.7	0.6024	0.0031	0.3995	0.2126	1.0165	0.1630
Standard deviation:		25.5	0.1117	0.0007	0.0589	0.0282	0.1048	0.0254
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	0.6137	0.0032	0.4024	0.1911	0.9475	0.1829
2002/M	2/1	364.3	0.6806	0.0027	0.3685	0.2113	0.9221	0.1594
2003/M	2/1	306.9	0.5425	0.0034	0.3459	0.2739	0.7540	0.1295
2004/M	2/1	314.4	0.8712	0.0023	0.5199	0.2221	1.0198	0.1885
2005/M	2/1	318.0	1.0198	0.0034	0.4048	0.3193	0.9730	0.2190
2006/M	2/1	317.3	0.6380	0.0031	0.2615	0.1877	1.0095	0.2045
2007/M	2/1	306.9	0.5971	0.0035	0.4386	0.2041	1.0022	0.1935
2008/M	2/1	291.4	0.5540	0.0043	0.3718	0.2083	1.1937	0.2407
2009/M	2/1	319.5	0.5561	0.0030	0.4985	0.1848	1.0871	0.1183
2010/M	2/1	305.4	0.5447	0.0026	0.3534	0.2101	1.0206	0.1133
Mean:		315.7	0.6618	0.0032	0.3965	0.2213	0.9930	0.1749
Standard deviation:		19.0	0.1599	0.0006	0.0757	0.0427	0.1133	0.0435
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	0.4926	0.0037	0.3305	0.2004	0.9705	0.1348
3002/M	3/1	307.2	0.5796	0.0030	0.3092	0.2039	1.0375	0.1746
3003/M	3/1	296.8	0.6551	0.0033	0.4110	0.2664	1.0347	0.1882
3004/M	3/1	349.7	0.5570	0.0032	0.2796	0.2140	0.8798	0.1623
3005/M	3/1	303.9	0.6699	0.0028	0.4032	0.2457	1.0335	0.1483
3006/M	3/1	337.0	0.5842	0.0034	0.3352	0.2197	0.9474	0.1540
3007/M	3/1	317.9	0.5487	0.0032	0.4391	0.2140	1.0730	0.1673
3008/M	3/1	325.9	0.5678	0.0033	0.3911	0.2396	1.0722	0.1699
3009/M	3/1	294.5	0.5575	0.0021	0.2581	0.2433	1.1607	0.1548
Mean:		318.7	0.5791	0.0031	0.3508	0.2274	1.0233	0.1616
Standard deviation:		19.5	0.0543	0.0005	0.0631	0.0222	0.0817	0.0157
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	0.6446	0.0032	0.4131	0.2139	0.9337	0.1478
4002/M	4/1	299.2	0.6341	0.0034	0.4918	0.1849	1.0945	0.1401
4003/M	4/1	277.2	0.5898	0.0031	0.4536	0.1845	1.1616	0.1995
4004/M	4/1	325.0	0.7323	0.0037	0.3099	0.2119	0.9572	0.3197

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
4005/M	4/1	320.4	0.6592	0.0032	0.3443	0.2047	0.9142	0.2558
4006/M	4/1	330.6	0.5822	0.0036	0.3315	0.2318	0.9619	0.1307
4007/M	4/1	303.6	0.6231	0.0035	0.4821	0.2303	1.0638	0.1788
4008/M	4/1	312.0	0.5623	0.0031	0.4766	0.2096	1.0112	0.2079
4009/M	4/1	291.9	0.6617	0.0016	0.2680	0.1983	0.9764	0.2334
4010/M	4/1	298.3	0.5806	0.0035	0.4365	0.2385	0.9456	0.1427
M e a n:		309.8	0.6270	0.0032	0.4007	0.2108	1.0020	0.1956
Standard deviation:		19.3	0.0510	0.0006	0.0808	0.0187	0.0801	0.0608
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1501/F	1/1	204.6	0.0316	0.9803	0.4557	0.8522	3.6103	0.6757
1502/F	1/1	236.0	0.0292	0.8964	0.3978	1.0061	3.7885	0.5531
1503/F	1/1	221.5	0.0326	0.9382	0.4144	0.8988	4.0948	0.6754
1504/F	1/1	212.0	0.0291	0.9658	0.4148	1.0734	3.3619	0.7408
1505/F	1/1	220.4	0.0305	1.0096	0.4143	1.1960	3.7382	0.8700
1506/F	1/1	209.9	0.0312	0.9608	0.4150	0.9164	3.4701	0.6758
1507/F	1/1	231.3	0.0288	0.8812	0.3363	0.9477	3.5549	0.7278
1508/F	1/1	205.5	0.0351	0.9160	0.3330	0.8046	3.2956	0.5967
1509/F	1/1	209.1	0.0278	0.9045	0.3970	0.9280	3.4094	0.5747
1510/F	1/1	224.7	0.0351	0.9048	0.3944	0.9806	3.2041	0.6146
Mean:		217.5	0.0311	0.9358	0.3973	0.9604	3.5528	0.6704
Standard deviation:		10.9	0.0026	0.0419	0.0372	0.1124	0.2664	0.0941
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	0.0317	0.9018	0.4187	0.9920	3.7369	0.8134
2502/F	2/1	214.0	0.0327	1.0562	0.4372	1.0948	3.8295	0.7181
2503/F	2/1	210.2	0.0289	0.9375	0.4362	1.0025	4.1222	0.5541
2504/F	2/1	204.0	0.0336	0.9153	0.4068	0.9293	3.7724	0.8186
2505/F	2/1	226.6	0.0459	0.9735	0.4503	1.1170	4.9275	0.5807
2506/F	2/1	214.9	0.0475	0.8565	0.4266	1.0314	4.2337	0.6534
2507/F	2/1	198.9	0.0325	0.9427	0.4265	1.0789	3.4090	0.6797
2508/F	2/1	215.2	0.0342	0.8541	0.3727	0.9724	4.0540	0.5411
2509/F	2/1	217.4	0.0287	0.9196	0.3914	0.9895	3.4245	0.6209
2510/F	2/1	213.1	0.0268	0.9058	0.3901	0.9993	3.8388	0.5885
Mean:		213.5	0.0342	0.9263	0.4156	1.0207	3.9349	0.6569
Standard deviation:		7.9	0.0070	0.0585	0.0247	0.0592	0.4406	0.1004
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	0.0329	1.0141	0.3926	0.9388	3.1545	0.7166
3502/F	3/1	223.0	0.0430	0.9793	0.4212	1.3036	4.4824	0.6572
3503/F	3/1	219.5	0.0362	0.9013	0.4042	1.0643	3.2903	0.7132
3504/F	3/1	225.5	0.0374	0.9156	0.4331	0.9506	3.4424	0.7288
3505/F	3/1	227.6	0.0319	0.8634	0.4239	0.9652	3.8673	0.7905
3506/F	3/1	206.4	0.0348	0.9379	0.4606	1.0796	3.9709	0.8411
3507/F	3/1	220.1	0.0371	0.9148	0.4161	0.9691	4.2969	0.6278
3508/F	3/1	198.5	0.0327	0.9686	0.4516	0.9831	3.9438	0.6167
3509/F	3/1	222.7	0.0284	0.8399	0.3689	0.8330	3.6254	0.5405
3510/F	3/1	215.9	0.0296	0.8777	0.4015	0.9650	3.5515	0.5950
Mean:		215.9	0.0344	0.9213	0.4174	1.0052	3.7625	0.6827
Standard deviation:		10.6	0.0043	0.0546	0.0274	0.1248	0.4281	0.0924
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	0.0319	0.9068	0.4497	0.9809	3.9169	0.7622
4502/F	4/1	192.0	0.0380	1.0440	0.3771	1.0480	3.9179	0.6520
4503/F	4/1	224.3	0.0320	0.9478	0.4320	1.1220	3.8711	0.6654

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4504/F	4/1	238.3	0.0318	0.9111	0.3823	1.1149	4.1485	0.7596
4505/F	4/1	217.3	0.0312	0.8363	0.3660	0.8312	3.5708	0.6510
4506/F	4/1	210.3	0.0338	1.0165	0.4327	0.9898	3.9502	0.8425
4507/F	4/1	236.4	0.0368	0.8546	0.4558	0.9635	3.6951	0.6420
4508/F	4/1	185.2	0.0293	0.9856	0.3893	0.9653	3.3090	0.7507
4509/F	4/1	226.3	0.0380	0.8217	0.3915	0.9146	3.7399	0.5764
4510/F	4/1	220.5	0.0383	0.8984	0.4077	0.9114	3.7045	0.6610
M e a n:		217.0	0.0341	0.9223	0.4084	0.9841	3.7824	0.6963
Standard deviation:		17.2	0.0034	0.0756	0.0320	0.0910	0.2335	0.0790
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
				Female Animals			
1501/F	1/1	204.6	0.0493	0.0023	0.3138	0.2491	0.1911
1502/F	1/1	236.0	0.0586	0.0079	0.2484	0.2133	0.3089
1503/F	1/1	221.5	0.0504	0.0062	0.2730	0.2503	0.2409
1504/F	1/1	212.0	0.0450	0.0047	0.2772	0.2229	0.4808
1505/F	1/1	220.4	0.0436	0.0070	0.2307	0.2166	0.2671
1506/F	1/1	209.9	0.0418	0.0071	0.2217	0.2992	0.2505
1507/F	1/1	231.3	0.0665	0.0057	0.2361	0.2149	0.2975
1508/F	1/1	205.5	0.0466	0.0059	0.2402	0.1695	0.2396
1509/F	1/1	209.1	0.0562	0.0064	0.2168	0.1568	0.1890
1510/F	1/1	224.7	0.0540	0.0056	0.2114	0.2347	0.2126
Mean:		217.5	0.0512	0.0059	0.2469	0.2227	0.2678
Standard deviation:		10.9	0.0077	0.0015	0.0322	0.0406	0.0849
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	0.0481	0.0067	0.2350	0.1828	0.2524
2502/F	2/1	214.0	0.0431	0.0057	0.2499	0.1947	0.2633
2503/F	2/1	210.2	0.0428	0.0032	0.2126	0.1679	0.2875
2504/F	2/1	204.0	0.0512	0.0056	0.2763	0.2127	0.2766
2505/F	2/1	226.6	0.0514	0.0089	0.2869	0.2577	0.2649
2506/F	2/1	214.9	0.0555	0.0061	0.2110	0.2241	0.2494
2507/F	2/1	198.9	0.0504	0.0073	0.2234	0.2144	0.2645
2508/F	2/1	215.2	0.0417	0.0048	0.2105	0.2225	0.5745
2509/F	2/1	217.4	0.0522	0.0051	0.2372	0.2526	0.4494
2510/F	2/1	213.1	0.0317	0.0055	0.2230	0.2112	0.2088
Mean:		213.5	0.0468	0.0059	0.2366	0.2141	0.3091
Standard deviation:		7.9	0.0070	0.0015	0.0270	0.0280	0.1128
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	0.0420	0.0055	0.2578	0.1925	0.2638
3502/F	3/1	223.0	0.0515	0.0065	0.2778	0.2710	0.2462
3503/F	3/1	219.5	0.0459	0.0059	0.2076	0.2822	0.2237
3504/F	3/1	225.5	0.0570	0.0059	0.2498	0.2757	0.2550
3505/F	3/1	227.6	0.0510	0.0037	0.2103	0.2264	0.2493
3506/F	3/1	206.4	0.0627	0.0077	0.2971	0.2302	0.2849
3507/F	3/1	220.1	0.0468	0.0059	0.1910	0.1983	0.2292
3508/F	3/1	198.5	0.0425	0.0056	0.2881	0.1839	0.3193
3509/F	3/1	222.7	0.0327	0.0057	0.2734	0.2334	0.4034
3510/F	3/1	215.9	0.0391	0.0043	0.2023	0.2027	0.1951
Mean:		215.9	0.0471	0.0057	0.2455	0.2296	0.2670
Standard deviation:		10.6	0.0088	0.0011	0.0394	0.0362	0.0587
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	0.0475	0.0062	0.2386	0.1400	0.3451
4502/F	4/1	192.0	0.0448	0.0069	0.2323	0.2792	0.3050
4503/F	4/1	224.3	0.0474	0.0062	0.2998	0.2791	0.2935

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
4504/F	4/1	238.3	0.0508	0.0068	0.2329	0.1886	0.2226
4505/F	4/1	217.3	0.0431	0.0068	0.2118	0.2011	0.1960
4506/F	4/1	210.3	0.0498	0.0052	0.2848	0.2013	0.3053
4507/F	4/1	236.4	0.0533	0.0041	0.2295	0.2618	0.3085
4508/F	4/1	185.2	0.0485	0.0042	0.2308	0.2325	0.2624
4509/F	4/1	226.3	0.0415	0.0056	0.2361	0.2540	0.2069
4510/F	4/1	220.5	0.0508	0.0051	0.2298	0.2080	0.2444
M e a n:		217.0	0.0478	0.0057	0.2426	0.2246	0.2690
Standard deviation:		17.2	0.0037	0.0010	0.0274	0.0448	0.0500
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
				Male Animals				
1001/M	1/1	293.8	2.3130	100.0000	38.1860	61.3591	147.0788	509.2520
1002/M	1/1	326.9	2.3070	100.0000	46.7055	74.1607	159.2524	582.2950
1003/M	1/1	300.4	2.3703	100.0000	34.0933	55.1409	130.9178	476.1297
1004/M	1/1	296.0	3.2430	100.0000	46.0273	54.3876	135.7545	549.8045
1005/M	1/1	343.7	3.2944	100.0000	44.4208	64.4350	168.8629	596.3970
1006/M	1/1	322.7	3.7071	100.0000	41.0982	61.7146	158.5218	513.5403
1007/M	1/1	323.0	3.4572	100.0000	52.2808	62.2743	145.2171	552.1664
1008/M	1/1	377.1	2.6799	100.0000	33.2135	59.7430	183.1237	585.6786
1009/M	1/1	340.3	2.3341	100.0000	41.9727	58.6176	150.2681	574.6407
1010/M	1/1	312.8	3.2732	100.0000	42.2595	60.0784	162.6175	550.5858
Mean:		323.7	2.8979	100.0000	42.0258	61.1911	154.1615	549.0490
Standard deviation:		25.5	0.5497	0.0000	5.8219	5.5082	15.6197	38.7561
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	3.4488	100.0000	46.9482	60.0857	152.5598	540.2260
2002/M	2/1	364.3	1.7624	100.0000	36.8012	64.7574	156.7699	636.5406
2003/M	2/1	306.9	3.0634	100.0000	41.4683	65.9376	148.4334	560.4612
2004/M	2/1	314.4	2.8106	100.0000	49.0668	58.3505	153.2168	506.0999
2005/M	2/1	318.0	2.9782	100.0000	34.6115	55.2702	146.5036	545.7090
2006/M	2/1	317.3	2.8053	100.0000	44.7600	63.6209	159.3728	515.8402
2007/M	2/1	306.9	2.5157	100.0000	51.9851	64.2197	137.6081	520.5336
2008/M	2/1	291.4	3.0250	100.0000	45.4577	57.5918	148.3116	496.3838
2009/M	2/1	319.5	2.9996	100.0000	48.6588	65.1747	153.5663	490.4139
2010/M	2/1	305.4	2.6661	100.0000	41.8722	58.0204	143.8303	643.7131
Mean:		315.7	2.8075	100.0000	44.1630	61.3029	150.0173	545.5922
Standard deviation:		19.0	0.4457	0.0000	5.5093	3.8503	6.4330	54.4550
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	3.3905	100.0000	49.4575	68.5363	134.1519	547.3652
3002/M	3/1	307.2	2.3382	100.0000	38.5999	62.9261	149.6385	529.2281
3003/M	3/1	296.8	2.7225	100.0000	36.2392	60.8230	173.5072	532.1101
3004/M	3/1	349.7	3.1913	100.0000	44.2701	62.3092	174.5225	548.9299
3005/M	3/1	303.9	4.0520	100.0000	47.9193	58.1945	155.1329	500.0953
3006/M	3/1	337.0	3.0510	100.0000	41.9760	71.4279	155.6595	595.9728
3007/M	3/1	317.9	2.3277	100.0000	38.3863	50.6660	132.4124	488.8192
3008/M	3/1	325.9	2.4284	100.0000	44.5129	57.1601	162.3691	487.4271
3009/M	3/1	294.5	2.5291	100.0000	53.7129	54.6653	143.2146	582.3074
Mean:		318.7	2.8923	100.0000	43.8971	60.7454	153.4010	534.6950
Standard deviation:		19.5	0.5820	0.0000	5.7525	6.5187	15.2802	38.6614
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	3.0237	100.0000	42.0644	63.1521	154.3948	552.3036
4002/M	4/1	299.2	2.8043	100.0000	42.9543	58.2243	153.0256	495.3417
4003/M	4/1	277.2	2.8452	100.0000	45.5289	55.1011	143.7354	454.1003
4004/M	4/1	325.0	3.9608	100.0000	48.7847	62.3170	179.0872	557.8551

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
4005/M	4/1	320.4	4.1550	100.0000	42.1304	58.9369	156.9423	572.0651
4006/M	4/1	330.6	3.1594	100.0000	55.3710	67.6512	152.3243	591.0752
4007/M	4/1	303.6	2.3638	100.0000	43.8831	54.0581	132.4406	551.1891
4008/M	4/1	312.0	2.6474	100.0000	45.1082	61.7154	148.5566	473.9706
4009/M	4/1	291.9	2.1491	100.0000	37.1886	56.9380	148.1655	527.3090
4010/M	4/1	298.3	3.2480	100.0000	39.0300	59.8988	148.0173	506.7171
M e a n:		309.8	3.0357	100.0000	44.2044	59.7993	151.6690	528.1927
Standard deviation:		19.3	0.6366	0.0000	5.1076	4.0738	11.8192	44.5221
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland Seminal vesicles		Spleen	Testes	Thymus
				Male Animals				
1001/M	1/1	293.8	90.3074	0.4549	60.4061	30.5814	155.6412	20.9271
1002/M	1/1	326.9	130.4750	0.5985	83.8403	33.0976	177.2730	24.9361
1003/M	1/1	300.4	77.6134	0.3935	54.9012	26.4758	155.5254	23.6712
1004/M	1/1	296.0	78.8201	0.5341	64.3409	27.0555	153.5721	24.7472
1005/M	1/1	343.7	95.9668	0.6224	58.1803	43.1658	152.7301	36.4810
1006/M	1/1	322.7	91.4226	0.5283	72.6552	34.8424	172.7618	18.9527
1007/M	1/1	323.0	80.6298	0.4676	61.0556	34.5023	158.0361	23.0712
1008/M	1/1	377.1	123.0721	0.4141	48.1210	38.4561	125.6895	27.2521
1009/M	1/1	340.3	69.5354	0.2163	52.1245	26.4273	150.5159	27.2879
1010/M	1/1	312.8	88.9487	0.5279	57.8109	32.4853	153.7986	23.3798
Mean:		323.7	92.6791	0.4758	61.3436	32.7090	155.5544	25.0706
Standard deviation:		25.5	19.6753	0.1173	10.3699	5.4278	13.7689	4.7540
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2001/M	2/1	312.7	93.4726	0.4920	61.2938	29.1149	144.3275	27.8582
2002/M	2/1	364.3	117.4721	0.4690	63.6015	36.4648	159.1482	27.5156
2003/M	2/1	306.9	89.4825	0.5536	57.0484	45.1766	124.3672	21.3522
2004/M	2/1	314.4	120.2890	0.3206	71.7799	30.6618	140.8019	26.0199
2005/M	2/1	318.0	132.8540	0.4424	52.7303	41.6001	126.7502	28.5240
2006/M	2/1	317.3	101.4077	0.4959	41.5590	29.8417	160.4699	32.5068
2007/M	2/1	306.9	90.0354	0.5307	66.1458	30.7734	151.1252	29.1765
2008/M	2/1	291.4	78.8985	0.6109	52.9443	29.6584	169.9849	34.2716
2009/M	2/1	319.5	92.3633	0.4939	82.7979	30.6977	180.5677	19.6559
2010/M	2/1	305.4	81.2296	0.3858	52.6979	31.3297	152.1949	16.8954
Mean:		315.7	99.7505	0.4795	60.2599	33.5319	150.9738	26.3776
Standard deviation:		19.0	17.9694	0.0827	11.6189	5.6387	17.7578	5.5406
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3001/M	3/1	335.6	80.0639	0.6054	53.7150	32.5826	157.7594	21.9122
3002/M	3/1	307.2	83.5947	0.4273	44.5957	29.4065	149.6432	25.1902
3003/M	3/1	296.8	93.0287	0.4641	58.3636	37.8278	146.9426	26.7225
3004/M	3/1	349.7	93.4831	0.5327	46.9191	35.9104	147.6389	27.2435
3005/M	3/1	303.9	96.9384	0.4047	58.3373	35.5538	149.5524	21.4551
3006/M	3/1	337.0	100.1017	0.5848	57.4392	37.6538	162.3513	26.3907
3007/M	3/1	317.9	78.2258	0.4530	62.6093	30.5153	152.9892	23.8597
3008/M	3/1	325.9	85.7494	0.5005	59.0741	36.1804	161.9335	25.6604
3009/M	3/1	294.5	88.3502	0.3336	40.9062	38.5493	183.9432	24.5319
Mean:		318.7	88.8373	0.4785	53.5511	34.9089	156.9726	24.7740
Standard deviation:		19.5	7.5705	0.0871	7.5651	3.3040	11.6937	2.0484
Number of observ. :		(9)	(9)	(9)	(9)	(9)	(9)	(9)
4001/M	4/1	340.1	101.2049	0.5032	64.8647	33.5842	146.5885	23.2065
4002/M	4/1	299.2	88.3775	0.4798	68.5424	25.7744	152.5504	19.5230
4003/M	4/1	277.2	83.0708	0.4420	63.8807	25.9831	163.6013	28.0917
4004/M	4/1	325.0	105.5575	0.5322	44.6776	30.5420	137.9757	46.0880

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Pituitary gland Lungs	Seminal vesicles	Spleen	Testes	Thymus
4005/M	4/1	320.4	109.4187	0.5284	57.1443	33.9809	151.7563	42.4671
4006/M	4/1	330.6	94.2836	0.5878	53.6811	37.5361	155.7678	21.1707
4007/M	4/1	303.6	90.1492	0.5099	69.7612	33.3175	153.9151	25.8686
4008/M	4/1	312.0	85.6885	0.4787	72.6322	31.9445	154.1005	31.6856
4009/M	4/1	291.9	97.2168	0.2365	39.3679	29.1258	143.4446	34.2846
4010/M	4/1	298.3	85.1064	0.5110	63.9821	34.9565	138.6075	20.9179
	M e a n:	309.8	94.0074	0.4810	59.8534	31.6745	149.8308	29.3304
Standard deviation:		19.3	9.1148	0.0942	11.0088	3.8275	8.0877	9.2378
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1501/F	1/1	204.6	3.2258	100.0000	46.4825	86.9273	368.2804	68.9236
1502/F	1/1	236.0	3.2522	100.0000	44.3772	112.2382	422.6377	61.7065
1503/F	1/1	221.5	3.4695	100.0000	44.1653	95.7990	436.4564	71.9888
1504/F	1/1	212.0	3.0087	100.0000	42.9472	111.1459	348.1147	76.7070
1505/F	1/1	220.4	3.0200	100.0000	41.0390	118.4613	370.2544	86.1720
1506/F	1/1	209.9	3.2479	100.0000	43.1894	95.3835	361.1693	70.3327
1507/F	1/1	231.3	3.2628	100.0000	38.1679	107.5512	403.4346	82.5965
1508/F	1/1	205.5	3.8357	100.0000	36.3545	87.8393	359.7939	65.1437
1509/F	1/1	209.1	3.0718	100.0000	43.8881	102.5907	376.9219	63.5350
1510/F	1/1	224.7	3.8808	100.0000	43.5886	108.3715	354.1144	67.9209
Mean:		217.5	3.3275	100.0000	42.4200	102.6308	380.1178	71.5027
Standard deviation:		10.9	0.3114	0.0000	3.0650	10.7350	30.2687	8.0714
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	3.5138	100.0000	46.4334	110.0035	414.4021	90.2026
2502/F	2/1	214.0	3.0926	100.0000	41.3946	103.6545	362.5830	67.9896
2503/F	2/1	210.2	3.0852	100.0000	46.5215	106.9316	439.6864	59.1008
2504/F	2/1	204.0	3.6740	100.0000	44.4409	101.5317	412.1519	89.4387
2505/F	2/1	226.6	4.7146	100.0000	46.2532	114.7423	506.1789	59.6537
2506/F	2/1	214.9	5.5417	100.0000	49.8098	120.4173	494.3117	76.2903
2507/F	2/1	198.9	3.4451	100.0000	45.2456	114.4472	361.6074	72.1028
2508/F	2/1	215.2	4.0098	100.0000	43.6398	113.8466	474.6573	63.3569
2509/F	2/1	217.4	3.1162	100.0000	42.5620	107.5980	372.3940	67.5220
2510/F	2/1	213.1	2.9581	100.0000	43.0658	110.3248	423.7891	64.9692
Mean:		213.5	3.7151	100.0000	44.9367	110.3498	426.1762	71.0627
Standard deviation:		7.9	0.8336	0.0000	2.4482	5.6924	52.7284	11.1762
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	3.2409	100.0000	38.7135	92.5760	311.0645	70.6590
3502/F	3/1	223.0	4.3866	100.0000	43.0056	133.1151	457.6995	67.1047
3503/F	3/1	219.5	4.0184	100.0000	44.8494	118.0803	365.0526	79.1246
3504/F	3/1	225.5	4.0831	100.0000	47.3021	103.8216	375.9905	79.5990
3505/F	3/1	227.6	3.6892	100.0000	49.0942	111.7902	447.8883	91.5530
3506/F	3/1	206.4	3.7142	100.0000	49.1115	115.1049	423.3857	89.6787
3507/F	3/1	220.1	4.0578	100.0000	45.4902	105.9352	469.7278	68.6302
3508/F	3/1	198.5	3.3807	100.0000	46.6271	101.4979	407.1566	63.6657
3509/F	3/1	222.7	3.3788	100.0000	43.9187	99.1821	431.6333	64.3464
3510/F	3/1	215.9	3.3720	100.0000	45.7467	109.9472	404.6280	67.7837
Mean:		215.9	3.7322	100.0000	45.3859	109.1050	409.4227	74.2145
Standard deviation:		10.6	0.3889	0.0000	3.0842	11.3943	48.2172	10.2049
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	3.5135	100.0000	49.5909	108.1665	431.9330	84.0486
4502/F	4/1	192.0	3.6368	100.0000	36.1237	100.3792	375.2757	62.4545
4503/F	4/1	224.3	3.3774	100.0000	45.5760	118.3781	408.4341	70.2103

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4504/F	4/1	238.3	3.4912	100.0000	41.9584	122.3655	455.3196	83.3733
4505/F	4/1	217.3	3.7308	100.0000	43.7682	99.3837	426.9741	77.8408
4506/F	4/1	210.3	3.3260	100.0000	42.5691	97.3710	388.6046	82.8835
4507/F	4/1	236.4	4.3065	100.0000	53.3363	112.7413	432.3978	75.1312
4508/F	4/1	185.2	2.9747	100.0000	39.4982	97.9347	335.7182	76.1641
4509/F	4/1	226.3	4.6303	100.0000	47.6418	111.3041	455.1439	70.1533
4510/F	4/1	220.5	4.2655	100.0000	45.3811	101.4488	412.3423	73.5790
M e a n:		217.0	3.7253	100.0000	44.5444	106.9473	412.2143	75.5838
Standard deviation:		17.2	0.5164	0.0000	4.9631	8.9811	37.2721	6.8800
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Pituitary gland Ovaries	Thymus	Spleen		Uterus
				Female	Animals		
1501/F	1/1	204.6	5.0307	0.2393	32.0138	25.4076	19.4895
1502/F	1/1	236.0	6.5375	0.8792	27.7098	23.7911	34.4599
1503/F	1/1	221.5	5.3751	0.6593	29.0939	26.6782	25.6725
1504/F	1/1	212.0	4.6596	0.4835	28.6998	23.0781	49.7900
1505/F	1/1	220.4	4.3187	0.6921	22.8519	21.4543	26.4516
1506/F	1/1	209.9	4.3487	0.7339	23.0723	31.1400	26.0723
1507/F	1/1	231.3	7.5413	0.6428	26.7995	24.3904	33.7618
1508/F	1/1	205.5	5.0842	0.6481	26.2286	18.5093	26.1595
1509/F	1/1	209.1	6.2176	0.7032	23.9664	17.3364	20.8893
1510/F	1/1	224.7	5.9712	0.6148	23.3633	25.9407	23.5011
Mean:		217.5	5.5085	0.6296	26.3799	23.7726	28.6247
Standard deviation:		10.9	1.0443	0.1692	3.0690	4.0202	8.8442
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2501/F	2/1	220.6	5.3335	0.7440	26.0544	20.2684	27.9948
2502/F	2/1	214.0	4.0793	0.5354	23.6616	18.4320	24.9270
2503/F	2/1	210.2	4.5618	0.3400	22.6721	17.9124	30.6642
2504/F	2/1	204.0	5.5913	0.6159	30.1842	23.2380	30.2217
2505/F	2/1	226.6	5.2768	0.9112	29.4755	26.4745	27.2089
2506/F	2/1	214.9	6.4761	0.7117	24.6333	26.1600	29.1209
2507/F	2/1	198.9	5.3437	0.7786	23.7001	22.7401	28.0572
2508/F	2/1	215.2	4.8803	0.5604	24.6518	26.0555	67.2688
2509/F	2/1	217.4	5.6723	0.5502	25.7903	27.4660	48.8645
2510/F	2/1	213.1	3.5020	0.6061	24.6179	23.3124	23.0534
Mean:		213.5	5.0717	0.6353	25.5441	23.2059	33.7381
Standard deviation:		7.9	0.8520	0.1583	2.4717	3.4213	13.7272
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3501/F	3/1	199.9	4.1387	0.5426	25.4193	18.9868	26.0112
3502/F	3/1	223.0	5.2612	0.6594	28.3713	27.6707	25.1431
3503/F	3/1	219.5	5.0950	0.6571	23.0338	31.3081	24.8231
3504/F	3/1	225.5	6.2240	0.6490	27.2886	30.1124	27.8504
3505/F	3/1	227.6	5.9078	0.4325	24.3538	26.2162	28.8673
3506/F	3/1	206.4	6.6897	0.8162	31.6820	24.5480	30.3802
3507/F	3/1	220.1	5.1157	0.6407	20.8801	21.6748	25.0571
3508/F	3/1	198.5	4.3897	0.5773	29.7446	18.9889	32.9641
3509/F	3/1	222.7	3.8920	0.6790	32.5528	27.7894	48.0299
3510/F	3/1	215.9	4.4591	0.4855	23.0449	23.0976	22.2322
Mean:		215.9	5.1173	0.6139	26.6371	25.0393	29.1359
Standard deviation:		10.6	0.9289	0.1090	3.9337	4.3395	7.3297
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4501/F	4/1	219.7	5.2352	0.6826	26.3063	15.4394	38.0565
4502/F	4/1	192.0	4.2953	0.6585	22.2499	26.7398	29.2143
4503/F	4/1	224.3	5.0002	0.6585	31.6337	29.4464	30.9657

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Pituitary gland Ovaries		Spleen	Thymus	Uterus
4504/F	4/1	238.3	5.5730	0.7415	25.5573	20.7028	24.4335
4505/F	4/1	217.3	5.1505	0.8144	25.3288	24.0467	23.4359
4506/F	4/1	210.3	4.8978	0.5099	28.0161	19.8017	30.0323
4507/F	4/1	236.4	6.2420	0.4802	26.8538	30.6306	36.0954
4508/F	4/1	185.2	4.9195	0.4273	23.4195	23.5894	26.6188
4509/F	4/1	226.3	5.0551	0.6776	28.7282	30.9169	25.1842
4510/F	4/1	220.5	5.6588	0.5654	25.5780	23.1550	27.2085
M e a n:		217.0	5.2027	0.6216	26.3672	24.4469	29.1245
Standard deviation:		17.2	0.5258	0.1223	2.6722	5.0514	4.8584
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

	Raw Data Listing of Gross Observations	Appendix H

Key to Abbreviations

LN	=	Lymph Node
SC	=	Spinal Cord
Submandib/Max	=	Submandibular/Submaxillary

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
1001	M	1/1	26-Aug-03	Within normal limits
1002	M	1/1		Trachea
			26-Aug-03	Abnormal Contents, Lumen, White, Frothy fluid, , Moderate
				Tissues marked 'Within normal limits':
			26-Aug-03	Adrenal Glands, Aorta, Brain, Cecum, Colon, Duodenum, Epididymides, Esophagus, Eyes, Femur, Heart, Ileum, Jejunum, Kidneys, Lacrimal gland, Larynx, Liver, Lungs, Mammary-protocol, Mediastinal LN, Mesenteric LN, Nerve, Nose/Turbinates, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate, Rectum/Low Colon, Salivary glands, Seminal vesicles, Skeletal muscle, Skin-protocol, Cervical SC, Thoracic SC, Lumbar SC, Spleen, Sternum, Stomach, Submandib/Max LN, Testes, Thymus, Thyroid, Urinary bladder, Zymbal's gland
1003	M	1/1	26-Aug-03	Within normal limits
1004	M	1/1	26-Aug-03	Within normal limits
1005	M	1/1	26-Aug-03	Within normal limits
1006	M	1/1	26-Aug-03	Within normal limits
1007	M	1/1	26-Aug-03	Within normal limits
1008	M	1/1	26-Aug-03	Within normal limits
1009	M	1/1	27-Aug-03	Within normal limits
1010	M	1/1	27-Aug-03	Within normal limits
2001	M	2/1	26-Aug-03	Within normal limits
2002	M	2/1	26-Aug-03	Within normal limits
2003	M	2/1	26-Aug-03	Within normal limits
2004	M	2/1		Lungs
			26-Aug-03	Abnormal Contents, All lobes, , Fluid, , Moderate

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
				Trachea			
			26-Aug-03	Abnormal Contents, , Red, Frothy fluid, , Moderate			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx
				Liver	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Pancreas
				Parathyroid	Pituitary gland	Prostate	Rectum/Low Colon
				Salivary glands	Seminal vesicles	Skeletal muscle	Skin-protocol
				Cervical SC	Thoracic SC	Lumbar SC	Spleen
				Sternum	Stomach	Submandib/Max LN	Testes
				Thymus	Thyroid	Urinary bladder	Zymbal's gland
2005	M	2/1	26-Aug-03	Within normal limits			
2006	M	2/1		Lungs			
			26-Aug-03	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx
				Liver	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Pancreas
				Parathyroid	Pituitary gland	Prostate	Rectum/Low Colon
				Salivary glands	Seminal vesicles	Skeletal muscle	Skin-protocol
				Cervical SC	Thoracic SC	Lumbar SC	Spleen
				Sternum	Stomach	Submandib/Max LN	Testes
				Thymus	Thyroid	Trachea	Urinary bladder
				Zymbal's gland			
2007	M	2/1	26-Aug-03	Within normal limits			
2008	M	2/1	26-Aug-03	Within normal limits			
2009	M	2/1	27-Aug-03	Within normal limits			
2010	M	2/1	27-Aug-03	Within normal limits			
3001	M	3/1		Lungs			
			26-Aug-03	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight			

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
3001	M	3/1		Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx
				Liver	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Pancreas
				Parathyroid	Pituitary gland	Prostate	Rectum/Low Colon
				Salivary glands	Seminal vesicles	Skeletal muscle	Skin-protocol
				Cervical SC	Thoracic SC	Lumbar SC	Spleen
				Sternum	Stomach	Submandib/Max LN	Testes
				Thymus	Thyroid	Trachea	Urinary bladder
				Zymbal's gland			
3002	M	3/1	26-Aug-03	Within normal limits			
3003	M	3/1	26-Aug-03	Within normal limits			
3004	M	3/1	26-Aug-03	Within normal limits			
3005	M	3/1	26-Aug-03	Within normal limits			
3006	M	3/1	26-Aug-03	Within normal limits			
3007	M	3/1	26-Aug-03	Within normal limits			
3008	M	3/1	26-Aug-03	Within normal limits			
3009	M	3/1	27-Aug-03	Within normal limits			
4001	M	4/1		Lungs			
			26-Aug-03	Abnormal Contents, All lobes, , Fluid, , Moderate			
			26-Aug-03	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight			
				Trachea			
			26-Aug-03	Abnormal Contents, , , Frothy fluid, , Moderate			
				Skin (other)			
			26-Aug-03	Hair Thin/Absent, Forelegs, , , , Slight			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx

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Animal number	Sex	Group/ Subgroup	Date data taken		Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
4001	M	4/1	26-Aug-03	46	Tissues marked 'Within normal limits':			
					Liver	Mammary-protocol	Mediastinal LN	Mesenteric LN
					Nerve	Nose/Turbinates	Optic nerve	Pancreas
					Parathyroid	Pituitary gland	Prostate	Rectum/Low Colon
					Salivary glands	Seminal vesicles	Skeletal muscle	Skin-protocol
					Cervical SC	Thoracic SC	Lumbar SC	Spleen
					Sternum	Stomach	Submandib/Max LN	Testes
					Thymus	Thyroid	Urinary bladder	Zymbal's gland
4002	M	4/1	26-Aug-03		Within normal limits			
4003	M	4/1	26-Aug-03		Within normal limits			
4004	M	4/1	26-Aug-03		Within normal limits			
4005	M	4/1	26-Aug-03		Within normal limits			
4006	M	4/1	26-Aug-03		Within normal limits			
4007	M	4/1	26-Aug-03		Within normal limits			
4008	M	4/1	26-Aug-03		Within normal limits			
4009	M	4/1			Seminal vesicles			
			27-Aug-03		Small, Bilateral, , , , Moderate			
					Tissues marked 'Within normal limits':			
			27-Aug-03		Adrenal Glands	Aorta	Brain	Cecum
					Colon	Duodenum	Epididymides	Esophagus
					Eyes	Femur	Heart	Ileum
					Jejunum	Kidneys	Lacrimal gland	Larynx
					Liver	Lungs	Mammary-protocol	Mediastinal LN
					Mesenteric LN	Nerve	Nose/Turbinates	Optic nerve
					Pancreas	Parathyroid	Pituitary gland	Prostate
					Rectum/Low Colon	Salivary glands	Skeletal muscle	Skin-protocol
					Cervical SC	Thoracic SC	Lumbar SC	Spleen
					Sternum	Stomach	Submandib/Max LN	Testes
					Thymus	Thyroid	Trachea	Urinary bladder
					Zymbal's gland			
4010	M	4/1	27-Aug-03		Within normal limits			
1501	F	1/1	26-Aug-03		Within normal limits			

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1502	F	1/1		Adrenal Glands			
			26-Aug-03	Discolored, Bilateral, Pale, , , Moderate			
				Submandib/Max LN			
			26-Aug-03	Enlarged, , , , , Moderate			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Aorta	Brain	Cecum	Colon
				Duodenum	Esophagus	Eyes	Femur
				Heart	Ileum	Jejunum	Kidneys
				Lacrimal gland	Larynx	Liver	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nerve
				Nose/Turbinates	Optic nerve	Ovaries	Pancreas
				Parathyroid	Pituitary gland	Rectum/Low Colon	Salivary glands
				Skeletal muscle	Skin-protocol	Cervical SC	Thoracic SC
				Lumbar SC	Spleen	Sternum	Stomach
				Thymus	Thyroid	Trachea	Urinary bladder
				Uterus	Zymbal's gland	Lymph Node,other	
1503	F	1/1	26-Aug-03	Within normal limits			
1504	F	1/1	26-Aug-03	Within normal limits			
1505	F	1/1		Thymus			
			26-Aug-03	Discolored, Right lobe, Red, Foci, </= 0.1 cm, Moderate			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skeletal muscle	Skin-protocol	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Stomach	Submandib/Max LN	Thyroid	Trachea
				Urinary bladder	Uterus	Zymbal's gland	
1506	F	1/1	26-Aug-03	Within normal limits			
1507	F	1/1	26-Aug-03	Within normal limits			
1508	F	1/1	27-Aug-03	Within normal limits			
1509	F	1/1	27-Aug-03	Within normal limits			

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Terminal Sacrifice

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1510	F	1/1	27-Aug-03	Within normal limits			
2501	F	2/1	26-Aug-03	Within normal limits			
2502	F	2/1	26-Aug-03	Within normal limits			
2503	F	2/1		Lymph Node,other			
			26-Aug-03	Enlarged, Axillary, , , , Moderate			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skeletal muscle	Skin-protocol	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Stomach	Submandib/Max LN	Thymus	Thyroid
				Trachea	Urinary bladder	Uterus	Zymbal's gland
2504	F	2/1	26-Aug-03	Within normal limits			
2505	F	2/1		Mediastinal LN			
			26-Aug-03	Enlarged, , , , , Severe			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mesenteric LN	Nerve
				Nose/Turbinates	Optic nerve	Ovaries	Pancreas
				Parathyroid	Pituitary gland	Rectum/Low Colon	Salivary glands
				Skeletal muscle	Skin-protocol	Cervical SC	Thoracic SC
				Lumbar SC	Spleen	Sternum	Stomach
				Submandib/Max LN	Thymus	Thyroid	Trachea
				Urinary bladder	Uterus	Zymbal's gland	
2506	F	2/1	26-Aug-03	Within normal limits			
2507	F	2/1	26-Aug-03	Within normal limits			

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
2508	F	2/1		Submandib/Max LN			
			27-Aug-03	Enlarged, Bilateral, , , , Moderate			
				Uterus			
			27-Aug-03	Distended, Bilateral horns, , , , Moderate			
				Tissues marked 'Within normal limits':			
			27-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skeletal muscle	Skin-protocol	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Stomach	Thymus	Thyroid	Trachea
				Urinary bladder	Zymbal's gland		
2509	F	2/1		Uterus			
			27-Aug-03	Distended, Bilateral horns, , , , Slight			
				Tissues marked 'Within normal limits':			
			27-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skeletal muscle	Skin-protocol	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Stomach	Submandib/Max LN	Thymus	Thyroid
				Trachea	Urinary bladder	Zymbal's gland	
2510	F	2/1	27-Aug-03	Within normal limits			
3501	F	3/1	26-Aug-03	Within normal limits			
3502	F	3/1		Adrenal Glands			
			26-Aug-03	Discolored, Bilateral, Pale, , , Moderate			
				Submandib/Max LN			
			26-Aug-03	Enlarged, RIGHT, , , , Moderate			
				Skin (other)			
			26-Aug-03	Hair Thin/Absent, Thoracic, , , , Moderate			

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
3502	F	3/1		Tissues marked 'Within normal limits':			
			26-Aug-03	Aorta	Brain	Cecum	Colon
				Duodenum	Esophagus	Eyes	Femur
				Heart	Ileum	Jejunum	Kidneys
				Lacrimal gland	Larynx	Liver	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nerve
				Nose/Turbinates	Optic nerve	Ovaries	Pancreas
				Parathyroid	Pituitary gland	Rectum/Low Colon	Salivary glands
				Skeletal muscle	Skin-protocol	Cervical SC	Thoracic SC
				Lumbar SC	Spleen	Sternum	Stomach
				Thymus	Thyroid	Trachea	Urinary bladder
				Uterus	Zymbal's gland		
3503	F	3/1	26-Aug-03	Within normal limits			
3504	F	3/1	26-Aug-03	Within normal limits			
3505	F	3/1	26-Aug-03	Within normal limits			
3506	F	3/1	26-Aug-03	Within normal limits			
3507	F	3/1	26-Aug-03	Within normal limits			
3508	F	3/1	27-Aug-03	Within normal limits			
3509	F	3/1	27-Aug-03	Within normal limits			
3510	F	3/1	27-Aug-03	Within normal limits			
4501	F	4/1	26-Aug-03	Within normal limits			
4502	F	4/1	26-Aug-03	Within normal limits			
4503	F	4/1		Thymus			
			26-Aug-03	Discolored, , Red, Area, 0.6 - 0.9 cm, Slight			
				Tissues marked 'Within normal limits':			
			26-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Heart	Ileum	Jejunum
				Kidneys	Lacrimal gland	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nerve	Nose/Turbinates	Optic nerve	Ovaries

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Terminal Sacrifice

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
4503	F	4/1	26-Aug-03	Tissues marked 'Within normal limits':			
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skeletal muscle	Skin-protocol	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Stomach	Submandib/Max LN	Thyroid	Trachea
				Urinary bladder	Uterus	Zymbal's gland	
4504	F	4/1	26-Aug-03	Within normal limits			
4505	F	4/1	26-Aug-03	Within normal limits			
4506	F	4/1	26-Aug-03	Within normal limits			
4507	F	4/1	26-Aug-03	Within normal limits			
4508	F	4/1	27-Aug-03	Within normal limits			
4509	F	4/1	27-Aug-03	Within normal limits			
4510	F	4/1	27-Aug-03	Within normal limits			

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Humane Sacrificed

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
3010	M	3/1		Bone			
			22-Aug-03	Fracture, Snout, , , , Severe			
				Tissues marked 'Within normal limits':			
			22-Aug-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx
				Liver	Lungs	Mammary-protocol	Mediastinal LN
				Mesenteric LN	Nerve	Nose/Turbinates	Optic nerve
				Pancreas	Parathyroid	Pituitary gland	Prostate
				Rectum/Low Colon	Salivary glands	Seminal vesicles	Skeletal muscle
				Skin-protocol	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Stomach	Submandib/Max LN
				Testes	Thymus	Thyroid	Trachea
				Urinary bladder	Zymbal's gland		

	Equipment List	Appendix I

Exposure Chamber
1000 Liter glass and stainless steel chamber (Wahmann)

Flowmeters
Top Trak™ Mass Flow Meter, sizes 0 - 100 sccm, 0 - 1 and 0 - 10 Lpm, Model 821-1 (Sierra Instruments), calibrated prestudy with Gilian Gilibrator Generator, S/N 646-L and 569-S
Flowmeter, size 0 - 20 Lpm (Dwyer®)

Pressure/Vacuum Gauges
MG Industries backpressure gauges, P/N 10206 and 10201
GAST® vacuum gauge

Regulator
MG Industries, Series 300

Valve
Metering Valve, Model SS-4L Series (Nupro® Co.)

Tubing
Teflon® size ¼"
Plastic, sizes ¼" and ½" (Norton, Baxter)
Stainless steel, size ½"
Clear plastic 1/8" (Tygon)
"T"-tube

Vacuum Pump
Thomas Industries Inc., Model 707CM 50

Air Analyzer
MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter No. 22-195
Balston® Microfibre™ Disposable Filter Unit, Grade DQ, was attached in-line

	Equipment List	Appendix I

Particle Sizer

TSI Aerodynamic Particle Sizer, Model 331001 and a DELL computer, Model 486P/25, equipped with an Epson LQ-570+ Dot matrix printer, Model P630B

Environmental Monitoring

VWR Temperature and Humidity Gauge
Digital Sound Level Meter, Model 840029 (SPER Scientific)
Photometer 1 Light Meter (Quantum Instruments)
Oxygen/Gas Analyzer, Model 1214S, (Gastech)

Chamber Air Flow

Dwyer® Magnehelic® gauge, calibrated prestudy with Side Trak™ III, with Digital Meter, Model 831-N2 (Sierra Instruments Inc.)

Chamber Static Pressure

Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.); calibrated prestudy with a Dwyer® Mark II Manometer, Model 25 (Dwyer® Instruments Inc.) and gas tight syringe (Hamilton, Co.)

	MIRAN® Calibration	Appendix J

Methodology for Isobutane

Settings: The instrument settings for the unit are summarized below:

Wavelength, microns	10.9
Pathlength, dial setting	12.14
Slit width, mm	1
Range, absorbance	1
Response, seconds	1
Gain	High
Chart speed, cm/min	1
Chart volts	1

Calibrations: The MIRAN® was turned on and allowed to warm up for approximately 10 minutes. The cell was flushed with room air for approximately one minute. The loop was closed, the unit was zeroed and the calibration series was performed as shown below. The resultant data were plotted to obtain a calibration curve. Each operator used a separate syringe for calibration.

Injection Volume (µL)	Calculated Concentration[1] (ppm)	Absorbance Operator 1 (volts)	Absorbance Operator 2 (volts)	Absorbance Average (volts)
390	69	0.0056	0.0060	0.0058
510	90	0.0088	0.0091	0.0090
5000	887	0.0713	0.0720	0.0717
51,000	9043	0.679	0.684	0.682
61,000	10816	0.802	0.807	0.805

[1]Calculated Conc. (ppm) = $\frac{\text{Volume injected (µL)}}{5.64\text{L}}$

where: 5.64L = volume of MIRAN® closed-loop

	MIRAN® Calibration	Appendix J

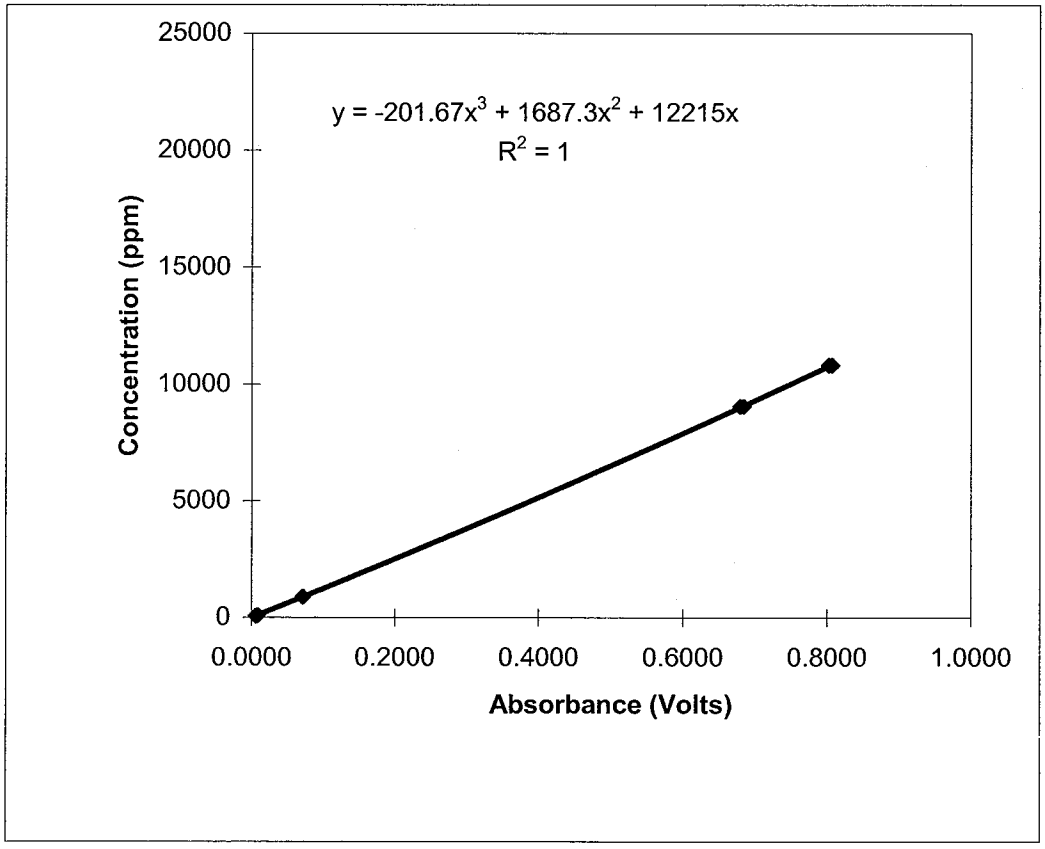
Calibration Checks: A three-point calibration check of the MIRAN® was performed prior to the exposure. The parameters are shown below:

Injection Volume (µL)	Calculated Concentration (ppm)	Expected Absorbance Reading (volts)	Acceptable Absorbance Range (volts)
510	90	0.0090	0.0077 – 0.0104
5000	887	0.0717	0.0609 – 0.0825
51000	9043	0.682	0.580 – 0.784

The absorbance was recorded after each injection. The absorbance was considered satisfactory if it was within 15% of the original calibration series. If the absorbance value fell outside the 15% range, the injection was rechecked as follows. The volume for the value that was out of range was reinjected twice. The closer pair of the three injections were averaged and the results were compared to the original curve. If the average of the pair was within the 15% range, the original was accepted. If the value of the average was outside the 15% range, the Study Director decided if a new graph was to be prepared.

	MIRAN® Calibration	Appendix J

Calibration Curve for Isobutane



	Chamber Distribution Results	Appendix K

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
2 (90 ppm)	5 August 2003	H-1	90.5	1.00
		H-2	90.5	1.00
		H-7	95.4	1.05
		H-8	89.3	0.99
3 (900 ppm)	5 August 2003	H-1	850	1.00
		H-2	858	1.01
		H-7	883	1.04
		H-8	861	1.01
4 (9000 ppm)	5 August 2003	H-1	9440	1.00
		H-2	9410	1.00
		H-7	9250	0.98
		H-8	9370	0.99

	Testing Room Environmental Monitoring	Appendix L

Interval	Location	Test Substance (ppm)[a]	Light (Ft Candles)	Noise (dB)	Oxygen (%)	Particle Sizing (mg/m^3)[b]
Pretest	Room	0	34.6	60.0	NM	NM
	Group 1	0	NM	NM	21	2.93×10^{-3}
	Group 2	89.3	NM	NM	21	2.39×10^{-3}
	Group 3	878	NM	NM	21	1.79×10^{-3}
	Group 4	9440	NM	NM	21	2.12×10^{-3}
Days 1 and 2	Room	0	32.0	61.9	NM	
	Group 1	0	NM	NM	21	
	Group 2	89.6	NM	NM	21	
	Group 3	920	NM	NM	21	
	Group 4	9090	NM	NM	21	
Day 8	Room	0	33.7	62.0	NM	
	Group 1	0	NM	NM	21	
	Group 2	91.4	NM	NM	21	
	Group 3	907	NM	NM	21	
	Group 4	9180	NM	NM	21	
Day 14	Room	0	35.4	62.0	NM	
	Group 1	0	NM	NM	21	
	Group 2	88.0	NM	NM	21	
	Group 3	916	NM	NM	21	
	Group 4	9240	NM	NM	21	

NM = Not measured

[a]Values presented are the daily average for the chamber samples and a single time point for the room air samples.

[b]Pretest results presented. For on-test results, see CMR (Table II).

Appendix M

PROTOCOL

ISOBUTANE

A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

CONFIDENTIAL

HLS Study No.:	**03-6145**
Protocol No.:	**Final**
Date:	**21 July 2003**

JUL 29 2003

PROTOCOL SIGNATURES / PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: Isobutane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures

HLS Study No.: 03-6145

This is the Final Protocol. It has been reviewed and approved by:

[redacted]

30 July 03
Date

Huntingdon Life Sciences (HLS)
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East Millstone, NJ 08875-2360
Phone No.: 732-873-2550 x2920
Fax No.: 732-873-3992
Email: [redacted]

[redacted]

July 29, 2003
Date

American Petroleum Institute (API)
Address: 1220 L Street, Northwest
Washington, D.C. 20005-4070
Phone No.: 202-682-8480
Fax No.: 202-682-8270
Email: [redacted]

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1. INTRODUCTION

HLS Study No.	03-6145
Study Title	Isobutane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures
Testing Facility	Huntingdon Life Sciences 100 Mettlers Road P.O. Box 2360 East Millstone, NJ 08875-2360
Purpose	This study is designed to provide a preliminary assessment of the toxicity of the test substance when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study 03-4244.

2. STUDY PERSONNEL

Study Director	Gary M. Hoffman, B.A., DABT
Alternate Contact	Keith P. Hazelden, BSc, CBiol, MIBiol Director of Reproductive Toxicology x2590

Additional personnel will be documented in the study file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation	Date Study Director signs protocol
Receipt of Test Animals	29 July 2003
First Day of Treatment	12 August 2003 (Experimental Start)
Last Day of Treatment	26 August 2003
Necropsy - Termination	26-27 August 2003
Experimental Termination	27 August 2003 (Date of last data collection)
Submission of Audited Draft Report	19 November 2003
Study Completion	Date final report is signed by Study Director

4. EXPERIMENTAL DESIGN

4.1. STUDY SUMMARY

Group	Test Substance	Exposure Level[a]	Number of Animals[b]	
		ppm	Males	Females
1	**Air Control**	0	10	10
2	**Isobutane**	90	10	10
3	**Isobutane**	900	10	10
4	**Isobutane**	9000	10	10

[a]Exposures will be 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Exposure levels are expressed as ppm of test substance. The exposures will be conducted via whole-body exposure.

[b]Complete postmortem evaluations will be performed on animals at termination of the study and on animals which are found dead or euthanized in a moribund condition during the course of the study.

The first day of exposures will be defined as Day 0 of the study.

4.2. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures are considered to be the minimum necessary for determining exposure levels for a subsequent OECD 422 Study 03-4244.

4.3. JUSTIFICATION FOR TEST ANIMAL SELECTION

The rat is an animal model commonly utilized in toxicity studies as recommended in OECD and EPA guidelines. In addition, a historical database is available for comparative evaluation.

4.4. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in the protocol is considered to be the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

4.5. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels were selected based on prior results of no toxicity up to 0.1% (1000 ppm). Therefore, the high exposure level was established (for safety reasons) as 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE: ISOBUTANE

Test Substance Category: industrial gas

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data. The Testing Facility will purchase the test substance from a Sponsor approved vendor (MG Industries, Malvern PA). The test substance will be stored (ambient conditions) in an outside solvent shed except when in use in the inhalation laboratory. The test substance will be handled as a flammable gas.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Supplier before its use in the study. This documentation will be maintained by the Supplier.

The Testing Facility will ensure that the location of the documentation of fabrication is provided in the report. Purity of the test substance will also be determined by the Testing Facility by assaying by GC before the study.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and stored in the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA 20166). If multiple studies are conducted with the same test substance, a common archival sample may be taken and appropriately labeled.

5.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered by whole-body inhalation exposure. The test substance will be administered as a gas (depending on the physical properties of the test substance) in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure levels. The method will be described in the raw data of the study and in the report.

The whole-body exposure chambers will each have a volume of approximately 1000 liters. Each chamber will be operated at a minimum flow rate of 200 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time of at most 23 minutes. This chamber size and air flowrate is considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals will remain in the chamber for a minimum of 30 minutes. During this time the chamber will be operated at approximately the same flow rate using clean air only.

5.5. EXPOSURE CONCENTRATION DETERMINATION

A nominal exposure concentration will be calculated daily, if possible. The flow of test substance into the chamber and the flow of air through the chamber will be monitored using appropriate calibrated equipment. The average test substance flow during the exposure will be divided by the average chamber airflow to give the nominal concentration.

During each exposure, measurements of airborne concentrations of test substance in the animal's breathing zone will be performed at least four times using an appropriate sampling procedure and infrared spectrophotometric analytical procedure. Also prior to initiation of animal exposures, additional samples will be taken to determine the distribution of the test substance in the exposure chamber.

If more than the normal amount of trial time is required because of test substance generation or monitoring problems (80 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

5.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each exposure, particle size determinations will be performed using a TSI Aerodynamic Particle Sizer to characterize the aerodynamic particle size distribution of any aerosol present.

5.7. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber temperature, humidity, airflow rate and static pressure will be monitored continuously and recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the maximum extent possible, between 20 to 24°C and 40 to 60%, respectively. Chamber oxygen levels (maintained at least 19%) will be measured pretest and at the beginning, middle and end of the study.

Air samples will be taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room will be measured pretest and at the beginning, middle and end of the study.

5.8. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/day
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate & Static Pressure	13X/day
Nominal Test Substance Concentration	1X/day
Rotation Pattern of Exposure Cages	1X/day
Loading/Unloading Verification	1X/day

5.9. FREQUENCY AND DURATION OF ADMINISTRATION

The test substance will be administered for 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Test substance administration will continue through the day prior to necropsy.

5.10. UNUSED TEST SUBSTANCE

The unused portion of the test substance as well as any empty test substance containers will be returned to the Supplier following completion of the in-life phase of the final study with this test substance.

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus®
Sprague-Dawley - derived (CD®)
Crl: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories

Documentation of the specific breeding facility will be maintained in the study file.

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. NUMBER OF ANIMALS ON STUDY

Total	Males	Females
80	40	40

6.3.2. AGE

Young adult (approximately 6 weeks at receipt; approximately 8 weeks (and no more than 9 weeks) at initiation of exposures.

6.3.3. WEIGHT

Approximately 200 to 300 grams (males) and 150 to 250 grams (females) at first exposure. Animals outside of this range may be used at the discretion of the Study Director.

6.4. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain suitability for study.

6.5. ANIMAL CARE AND HUSBANDRY

6.5.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry will be followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences Inc. is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.5.2. VETERINARY CARE

Animals will be monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.5.3. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5.4. HOUSING

Animals will be individually housed in suspended, stainless steel wire mesh cages during the study.

6.5.5. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, MO) *ad libitum.*

6.5.6. WATER

Elizabethtown Water Company, Westfield, NJ; *ad libitum,* via automated watering system.

6.5.7. FEED ANALYSIS

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.5.8. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file at the Testing Facility. There are

no known contaminants which are expected to interfere with the objectives of this study.

6.5.9. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Individual weights of animals placed on test shall be within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

6.5.10. IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. If the tag is lost, it will be replaced. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study number and animal number.

6.5.11. ANIMAL HUSBANDRY/EXPOSURE

Housing:	Individually in cages.
Feed:	None.
Water:	None.

7. IN-LIFE EVALUATIONS

7.1. CLINICAL OBSERVATIONS

7.1.1. VIABILITY CHECKS (CAGE-SIDE)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

7.1.2. PHYSICAL EXAMINATIONS

In-Chamber: All animals will be observed as a group at least once during each exposure.

Out-of-Chamber: Each animal will be removed from its cage and examined at least once pretest and once per week during the study period. Examinations will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded.

7.2. BODY WEIGHTS

Non-fasted body weights for each animal will be recorded at least once pretest, on the first day of exposures and once per week during the study period. Fasted weights will be obtained prior to necropsy.

7.3. FEED CONSUMPTION

Feed consumption will be measured (weighed) during the week prior to treatment initiation and once per week during the study period. Feed will be available without restriction 7 days/week except during exposures. Animals will be presented with weighed feeders at the scheduled intervals. After at least 5 days, the feeders will be reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal per day. The grams consumed per kilogram of body weight per day will then be calculated for each animal.

8. POSTMORTEM EVALUATIONS

8.1. MACROSCOPIC PATHOLOGY

A complete macroscopic examination will be performed on all animals, including animals euthanized in a moribund condition or found dead; all abnormal observations will be recorded. The necropsy will consist of a careful examination of the external surface of the body, all orifices and the cranial, thoracic and abdominal cavities and their contents. Special attention should be paid to the organs of the reproduction system.

8.1.1. MORIBUND ANIMALS

Animals showing signs of severe debility, particularly if death appears imminent, will be humanely euthanized to prevent loss of tissues through autolysis.

8.1.2. TERMINAL NECROPSY

Necropsy will be performed on 10 animals/sex/group after animals have been treated for at least 14 days. Necropsy schedules will be established in order to assure that approximately equal numbers of males and females from each group will be examined at similar times of the day of necropsy.

8.2. METHOD OF EUTHANASIA

Exsanguination following carbon dioxide inhalation.

8.3. ORGAN WEIGHTS

Organs indicated below will be taken from all survivors at the scheduled necropsies, weighed, recorded and organ/body and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition during the course of the study. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissues in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired organs will be weighed together.

adrenals	liver	seminal vesicles
brain	lungs	spleen
epididymides	ovaries	testes
heart	pituitary	thymus
kidneys		uterus

8.4. TISSUE PRESERVATION

Tissues listed in Appendix A will be obtained at necropsy and preserved for all animals.

Eyes – glutaraldehyde/paraformaldehyde initially and then 10% neutral buffered formalin

Testes and epididymides – modified Davidson's solution initially and then 10% neutral buffered formalin

All other tissues - 10% neutral buffered formalin

Note: Lungs and urinary bladder will be infused with formalin to ensure fixation.

8.5. MICROSCOPIC PATHOLOGY EVALUATIONS

No examinations are required. Authorization will be obtained from the Sponsor prior to performing any examinations. If tissues are examined, standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

9. ARCHIVING OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond one year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

10. STATISTICAL ANALYSIS

10.1. ITEMS TO BE ANALYZED

The following will be compared for control and test substance-treated groups.

mean body weight values
mean feed consumption values
mean terminal organ weights, organ/body and organ/brain weight ratios

10.2. PROCEDURES

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. Organ weight data will be analyzed only by parametric methods. The parametric method

will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977), Steel's test (Steel, 1959), or Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Armitage, P. 1971. *Statistical Methods in Medical Research.* Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. *Proceedings of the Royal Society, Series A,* 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. *Experimental Designs*, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. *Behav. Res. Methods and Instrumentations* 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. *Behav. Res. Methods and Instrumentation* 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. *Biometrics* 20-3: 482-491; Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. *Biometrics* 15: 560-572.; Williams, D.A. 1971.

A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

11. REPORTING

11.1. STATUS REPORTS

Periodic written (weekly) updates on study progress will be provided by the Study Director.

11.2. FINAL REPORT

One unbound hard copy and one electronic copy of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

Compliance Statement (including Sponsor signature line)
Quality Assurance Statement
Summary
Introduction
Experimental Design
Materials and Methods
Discussion of Study Results
Conclusion (including NOAEL statement, if applicable)
Tables of Exposure Data
Mortality Data
Individual animal termination history
Summary of daily animal observations (as appropriate)
Individual and summary tables of weekly physical examination data
Tables of mean and individual body weights
Tables of mean and individual feed consumption
Tables of mean and individual organ weights, organ/brain and organ/body weight ratios
Individual and summary tables of macroscopic pathology findings
References for experimental methodology
Senior personnel participating in the study
Copy of study protocol and associated amendments

12. REGULATORY REFERENCES

12.1. TESTING GUIDELINES

This study is not designed to meet regulatory requirements. It is designed to provide preliminary toxicity data for the test substance in order to determine appropriate exposure levels for a subsequent OECD 422 inhalation study 03-4244.

12.2. GOOD LABORATORY PRACTICES

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

12.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply 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. The Sponsor should make particular note of the following:

1. The Sponsor's signature on this protocol documents that, for the study described, there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments in regard to species, test substance, route of administration or duration of treatment.

2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or written laboratory standard operating procedures.

3. Any procedures outlined in this study which cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing by the Sponsor and the Study Director, in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain

or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review Form.

4. Animals experiencing more than momentary or slight pain or distress due to test substance or injury or illness will be treated by the Testing Facility's veterinary staff with approved analgesics or agents to relieve pain after consultation with the Study Director and Sponsor. However, in emergency situations, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

5. Methods of euthanasia used during this study are in conformance with the above-referenced regulations.

12.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with all appropriate regulations.

13. QUALITY ASSURANCE MONITORING

The Huntingdon Life Sciences Quality Assurance Unit will monitor the facilities, equipment, personnel, methods, practices, records and controls used in this study to assure that they are in conformance with this protocol, company SOPs, and the appropriate Good Laboratory Practice requirements.

14. ALTERATION IN STUDY DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by 2 members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A
Tissues Preserved

Tissue	Preserved
adrenal gland	X
aorta (thoracic)	X
bone (sternum/femur)	X
bone marrow (rib) [a]	X
brain (medulla/pons, cerebrum and cerebellum)	X
epididymides	X
esophagus	X
eye (with optic nerve)	X
heart	X
kidneys	X
large intestine (cecum, colon, and rectum)	X
lacrimal gland	X
larynx	X
liver	X
lungs (with mainstem bronchi)	X
lymph nodes (mediastinal and mesenteric)	X
mammary gland	X
muscle (biceps femoris)	X
nasopharyngeal tissue	X
nerve (sciatic)	X
ovaries	X
pancreas	X
pituitary	X
prostate	X

Tissue	Preserved
salivary gland with submandibular lymph node	X
seminal vesicles	X
skin	X
small intestine (duodenum, jejunum, ileum)	X
spinal cord (cervical, thoracic, lumbar)	X
spleen	X
stomach	X
testes	X
thymic region	X
thyroid (with parathyroids)	X
trachea	X
urinary bladder	X
uterus (body/horns with cervix)	X
Zymbal's gland	X
gross lesions and tissue masses	X
target organs[b]	X

[a]Bone marrow smears will be prepared. They will only be evaluated (Sponsor approval, additional cost) if needed.

[b]Target organs will be designated by the Study Director, Pathologist and/or Sponsor based on experimental findings.

Protocol Amendment No. 1

Study Title: Isobutane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures

Changes

1. Proposed Study Dates, page 1:

Revise: Receipt of Test Animals	29 July 2003 **(Experimental Start)**
First Day of Treatment	12 August 2003 ~~(Experimental Start)~~

2. Identification of Test Substance, page ~~5~~ 3 R 29oct03 mcochoT:
Add: ....Purity of the test substance will also be determined by the Testing Facility by assaying by GC before the study. **Stability of the test substance will also be determined by the Testing Facility by assaying by GC after the subsequent OECD 422 study 03-4244.**

3. Animal Requirements/Specifications, page 7:
Add: **Female rats will be nulliparous and non-pregnant.**

4. Statististical Analysis/Procedures, page 12:
Revise: Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. Organ weight data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (~~Armitage, 1971;~~ Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), ~~Williams (Williams, 1971, 1972),~~ or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, ~~Shirley's test (Shirley, 1977)~~, ~~Steel's test (Steel, 1959)~~, or Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

~~Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications;~~ Bartlett, M.S. 1937. Properties of sufficiency and statistical tests.

Protocol Amendment No. 1

Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. *Experimental Designs*, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. *Behav. Res. Methods and Instrumentations* 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. *Behav. Res. Methods and Instrumentation* 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. *Biometrics* 20-3: 482-491; Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; ~~Shirley, E.A.C. 1977. A non parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389;~~ Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; ~~Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.~~

Reasons for Changes

1. Correction of the Experimental Start Date as per OECD GLP's.
2. Clarification of how the stability of the test substance will be documented.
3. Oversight in original protocol.
4. Removal of statistical procedures and references not relevant to this study.

Amendment approved by:

[redacted]

28 Oct 03
Date

[redacted]

10/28/03
Date

STUDY TITLE

Analytical Report For:

Isobutane:
A "2-Week" Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures

AUTHOR

[redacted]

REPORT DATE

9 April 2010

STUDY NUMBER

03-6145

SIGNATURES

Written by: [redacted]
Formulation Chemistry Services
07 Apr 10
Date

Reviewed by: [redacted]
Formulation Chemistry Services
07 Apr 10
Date

Reviewed by: [redacted]
Formulation Chemistry Services
9 Apr 10
Date

Approved by: [redacted]
Analytical Services
9 Apr 10
Date

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II A Typical Gas Chromatogram of Isobutane Test Substance 7

1. Summary

The test substance and the analytical standard (Isobutane) were analyzed (pre-study) to determine the purity of the test substance by comparison to the analytical standard. The analytical method was validated at Huntingdon Life Sciences (HLS). The analytical method involved gas bag sampling of the test substance and the analytical standard and quantification using Gas Chromatography with Flame Ionization Detection (FID).

2. Experimental Procedures

The analytical method (HLS-013-03) was validated by Formulation Chemistry at HLS. Details of the analytical method and the validation are maintained in this study file.

Gas bag sampling of the test substance and the analytical standard was performed in the Inhalation Department at HLS. The test substance and the analytical standard were analyzed using a Gas Chromatograph equipped with a HP Plot Q (30 m x 0.32 mm, 20 µm) column and Flame Ionization Detector (FID) to determine the purity of Isobutane test substance. HP 3396A integrator was used for data collection and Excel was used for processing the data.

Date of sample analysis is listed as follows:

Interval	Date Analyzed
"Pre-Study" Characterization	28 May 03

3. Results and Discussion

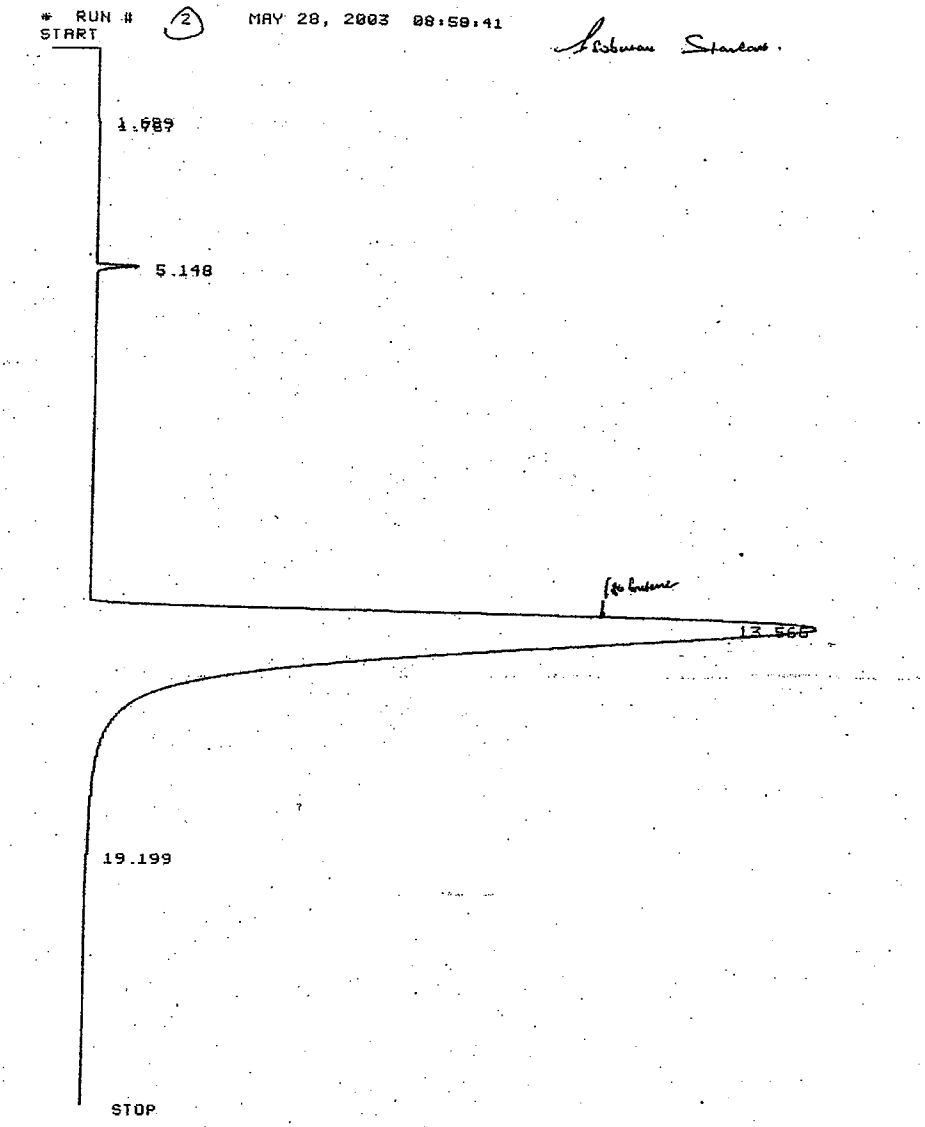
The test substance and analytical standard (Isobutane) were analyzed prior to the initiation of the study to determine the purity of the test substance. The results of the characterization are presented in Table I. A typical chromatogram of Isobutane standard is presented in Figure I. A typical chromatogram of Isobutane test substance is presented in Figure II.

Table I: Isobutane Characterization ("Pre-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % of other Impurities	Area % of Isobutane Standard	Mean Area % of Isobutane Standard
Isobutane Standard	0.00	0.53	0.00	0.02	99.45	99.51
Isobutane Standard	0.00	0.43	0.01	0.01	99.55	
Isobutane Standard	0.00	0.47	0.00	0.01	99.53	

Sample ID	Area % of Ethane	Area % of Propane	Area % of Butane	Area % Other Impurities	Area % of Isobutane Substance	Mean Area % of Isobutane Test Substance
Isobutane Test Substance	0.00	0.06	0.10	0.01	99.83	99.84
Isobutane Test Substance	0.01	0.07	0.11	0.01	99.81	
Isobutane Test Substance	0.00	0.06	0.06	0.01	99.87	

Figure I. A Typical Gas Chromatogram of Isobutane Analytical Standard



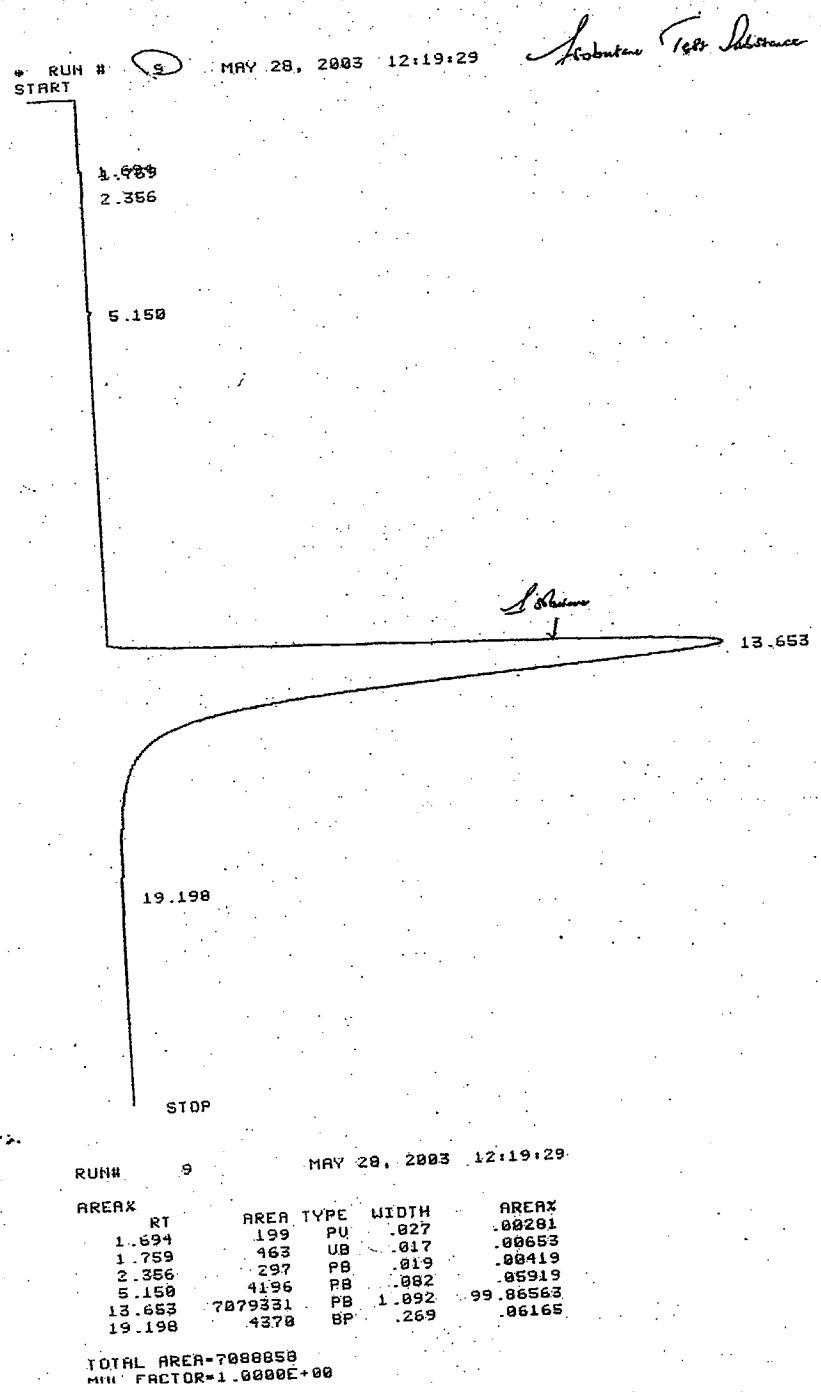
RUN# 2 MAY 28, 2003 08:58:41

AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.689	212	PB	.025	.00244
1.757	287	PB	.017	.00330
5.148	37515	PB	.083	.43199
13.565	8645011	PB	1.131	99.54944
19.199	1113	BP	.096	.01282

Response (mV) vs Time (minutes)

Figure II. A Typical Gas Chromatogram of Isobutane Test Substance



Response (mV) vs Time (minutes)

	Report Amendments	Appendix O

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	[redacted]
DIRECTOR OF REPRODUCTIVE TOXICOLOGY	[redacted]
DIRECTOR, ANALYTICAL SERVICES	[redacted]
DIRECTOR, TOXICOLOGY OPERATIONS	[redacted]
DIRECTOR, QUALITY ASSURANCE	[redacted]
STUDY DIRECTOR	[redacted]
STUDY MONITOR	[redacted]
VETERINARIAN	[redacted]
MANAGER/SUPERVISOR Inhalation Toxicology Pharmacy Analytical Services Necropsy	[redacted]

	Report Amendments	Appendix P

There are no amendments for this report at this time.

	Historical Control Data CD Rat - Mating, Fertility and Gestation Preface	Appendix OO

Data used for historical control purposes was obtained from inhalation studies run prior to this study (from April 2001 to August 2002).

	Historical Control Data CD Rat - Mating, Fertility and Gestation	Appendix OO

		Females						
Study ID	Initiation Date	Paired w/ Males No.	Mated No.	Mating Index %	Pregnant No.	Fertility Index %	No. with Liveborn No.	Gestation Index %
00-4208 P0	12-Jun-01	26	24	92.3	23	95.8	23	100.0
00-4208 F1		26	23	88.5	21	91.3	21	100.0
00-4207 P0	30-Apr-01	26	25	96.2	24	96.0	24	100.0
00-4207 F1		26	25	96.2	25	100.0	25	100.0
00-4206	20-Aug-02	26	24	92.3	21	87.5	21	100.0
00-4205	20-May-02	26	25	96.2	22	88.0	22	100.0
00-4204	19-Mar-02	26	26	100.0	25	96.2	25	100.0
00-4203	21-Jan-02	26	26	100.0	25	96.2	25	100.0
00-4202	22-Aug-01	26	26	100.0	24	92.3	24	100.0
	MEAN	**25**	**25**	**95.7**	**23**	**93.7**	**23**	**100.0**
	SD	**1.1**	**1.1**	**4.05**	**1.7**	**4.19**	**1.7**	**-**
	N	**9**	**9**	**9**	**9**	**9**	**9**	**9**
	MIN	**23**	**23**	**88.5**	**21**	**87.5**	**21**	**100.0**
	MAX	**26**	**26**	**100.0**	**25**	**100.0**	**25**	**100.0**

	Certificates of Analysis Preface	Appendix PP

Table of Contents

Feed Analysis 971
Water Analysis 985
Bedding Analysis 990

LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0323917-2
Lot Code: OCT 16 03 3B
Entered: 11/3/2003

Assay	Analysis	Units
PROTEIN	21.6	%
FAT ACID (HYDRO.)	6.11	%
FIBER (CRUDE)	3.93	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.052	PPM
CALCIUM	1.14	%
LEAD	0.19	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.670	%
SELENIUM	0.227	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" does not imply that traces of analyte were present.

LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0323917-1
Lot Code: OCT 16 03 3A
Entered: 11/3/2003

Assay	Analysis	Units
PROTEIN	21.2	%
FAT ACID (HYDRO.)	6.63	%
FIBER (CRUDE)	4.17	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.058	PPM
CALCIUM	1.13	%
LEAD	0.182	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.743	%
SELENIUM	0.271	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

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LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0325518-2
Lot Code: NOV 16 03 3B
Entered: 12/10/2003

Assay	Analysis	Units
PROTEIN	21.2	%
FAT ACID (HYDRO.)	5.86	%
FIBER (CRUDE)	4.02	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.052	PPM
CALCIUM	0.858	%
LEAD	0.163	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.649	%
SELENIUM	0.259	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

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LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0325123-1
Lot Code: NOV 08 03 2A
Entered: 11/25/2003

Assay	Analysis	Units
PROTEIN	21.5	%
FAT ACID (HYDRO.)	5.51	%
FIBER (CRUDE)	4.7	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.059	PPM
CALCIUM	0.774	%
LEAD	0.158	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.691	%
SELENIUM	0.207	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

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LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0322569-2
Lot Code: SEP 20 03 2B
Entered: 10/3/2003

Assay	Analysis	Units
PROTEIN	21.6	%
FAT ACID (HYDRO.)	6.07	%
FIBER (CRUDE)	4.48	%
ARSENIC	0.226	PPM
CADMIUM	0.061	PPM
CALCIUM	0.907	%
LEAD	0.146	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.660	%
SELENIUM	0.241	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" does not imply that traces of analyte were present.

LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0323129-3
Lot Code: OCT 01 03 1C
Entered: 10/14/2003

Assay	Analysis	Units
PROTEIN	21.8	%
FAT ACID (HYDRO.)	5.58	%
FIBER (CRUDE)	4.17	%
ARSENIC	0.611	PPM
CADMIUM	LESS THAN 0.05	PPM
CALCIUM	1.02	%
LEAD	0.131	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.622	%
SELENIUM	0.211	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 – for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 – for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 – all other questions

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LabDiet PMI NUTRITION

Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L0324455-1
Lot Code: NOV 01 03 1A
Entered: 11/10/2003

Assay	Analysis	Units
PROTEIN	21.2	%
FAT ACID (HYDRO.)	5.11	%
FIBER (CRUDE)	4.91	%
ARSENIC	0.222	PPM
CADMIUM	0.054	PPM
CALCIUM	1.04	%
LEAD	0.171	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.665	%
SELENIUM	0.235	PPM

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

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

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	Aflatoxins	LESS THAN 5 PPB	

No notes.
For additional information, please contact:
1) Customer Service at (314) 982-1310 -- for assay methodology
2) Dr. Dorrance Haught at (314) 768-4362 -- for nutritional interpretation
3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed. The use of the term "Less Than" does not imply that traces of analyte were present.

Elizabethtown Water Company
Physical & Chemical Analyses

Date December 2, 2003

General Source Raritan-Millstone Plant

Sample No. 1 Plant Delivered Water - 7:15 a.m. .12-2-03, DD

Sample No. 2

Sample No. 3

Sample No. 4

Sample No. 5

Sample No. 6

Sample No. 7

Sample No. 8

Parameter	MCL (mg/l)	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0
Temperature * F	-	48							
Turbidity (NTU)	0.5 NTU	0.10							
Color	10 *	1							
Threshold Odor 40 * C (1)	3 TON *	3.4/2cc							
Threshold Taste	3 TTN *	3.3							
Conductivity (micromhos / cm)	-	267							
Hardness, Total (as mg / l CaCO3)	250 mg / l *	82							
Alkalinity	-	38							
pH	6.5-8.5 *	6.9							
Chlorine, Free / Total (mg / l Cl)	-	<0.05/1.21							
[illegible]m (as mg / l CaCO3)	-	60							
Magnesium (as mg / l CaCO3)	-	22							
Iron, Total (mg / l Fe)	0.3 mg/ l *	<0.05							
Sulfates (mg / l SO4)	250 mg/ l *	31.6							
Chlorides (mg / l Cl)	250 mg/ l *	22.4							
Fluoride (mg / l F)	1.2 mg / l	<0.1							
Total Dissolved Solids (mg / l)	500 mg / l *	190							
Total Suspended Solids (mg / l)	-	<0.10							
Ammonia Nitrogen (mg / l N)	-	0.08							
Nitrate Nitrogen (mg / l N)	10 mg / l	1.80							
Dissolved Oxygen (mg / l O2)	-	11.9							
BOD 5 (mg / l O2)	-	-							
Langelier Index	+/- 1.0	-1.95							
Surfactants (mg / l LAS)	0.5 mg / l *	-							
Hydrogen Sulfide (mg / l H2S as S)	-	0							
Nitrite Nitrogen (mg / l N)	-	<0.010							
Phosphate (mg / l PO3)	-	<0.05							
Manganese (mg / l MN)	-	<0.05							
[illegible] (mg / l)	-	1.60							

REVIEWED
TM 19 Dec 03

* Secondary or Recommended MCL

Laboratory Analyst: KK

08/05/96

(1) Water odor/taste are not regulated parameters TM 19 Dec 03

Elizabethtown Water Company
Physical & Chemical Analyses

Date January 6, 2004

General Source **Raritan-Millstone Plant**

Sample No. 1 Plant Delivered Water - 7:15 a.m. .1-6-04, MT

Sample No. 2

Sample No. 3

Sample No. 4

Sample No. 5

Sample No. 6

Sample No. 7

Sample No. 8

Parameter	MCL (mg/l)	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0
Temperature ° F	-	44							
Turbidity (NTU)	0.3 NTU	0.11							
Color	10 *	1							
Threshold Odor 40 ° C	3 TON *	2.6/2cc							
Threshold Taste	3 TTN *	2.8							
Conductivity (micromhos / cm)	-	265							
Hardness, Total (as mg / l CaCO3)	250 mg / l *	78							
Alkalinity	-	30							
pH	6.5-8.5 *	6.9							
Chlorine, Free / Total (mg / l Cl)	-	<0.05/.74							
C[illegible]m (as mg / l CaCO3)	-	50							
Magnesium (as mg / l CaCO3)	-	28							
Iron, Total (mg / l Fe)	0.3 mg/ l *	<0.05							
Sulfates (mg / l SO4)	250 mg/ l *	33.3							
Chlorides (mg / l Cl)	250 mg/ l *	33.8							
Fluoride (mg / l F)	2 mg / l*	<0.10							
Total Dissolved Solids (mg / l)	500 mg / l *	114							
Total Suspended Solids (mg / l)	-	0.7							
Ammonia Nitrogen (mg / l N)	-	0.13							
Nitrate Nitrogen (mg / l N)	10 mg / l	1.49							
Dissolved Oxygen (mg / l O2)	-	16.1							
BOD 5 (mg / l O2)	-								
Langelier Index	+/- 1.0								
Surfactants (mg / l LAS)	0.5 mg / l *	<0.05							
Hydrogen Sulfide (mg / l H2S as S)	-	0							
Nitrite Nitrogen (mg / l N)	1 mg / l	<0.01							
Phosphate (mg / l PO3)	-	<0.05							
Manganese (mg / l MN)	0.05 mg / l *	<0.05							
T[illegible] (mg / l)	-	1.20							
	5 mg/l *								

REVIEWED
26 Jan 04

* Secondary or Recommended MCL

Laboratory Analyst: DSD

Any questions please call Water Quality Specialist- (908) 301-3163

Elizabethtown Water Company
Physical & Chemical Analyses

Date February 4, 2004

General Source Raritan-Millstone Plant

Sample No. 1 Plant Delivered Water - 7:15 a.m. .2-4-04, DD

Sample No. 2

Sample No. 3

Sample No. 4

Sample No. 5

Sample No. 6

Sample No. 7

Sample No. 8

Parameter	MCL (mg/l)	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0
Temperature * F	-	38							
Turbidity (NTU)	0.3 NTU	0.11							
Color ①	10 *	11 *							
Threshold Odor 40 * C	3 TON *	2.3/1cc							
Threshold Taste	3 TTN *	2.9							
Conductivity (micromhos / cm)	-	630							
Hardness, Total (as mg / l CaCO3)	250 mg / l *	100							
Alkalinity	-	34							
pH	6.5-8.5 *	6.6							
Chlorine, Free / Total (mg / l Cl)	-	<.05/0.52							
Calcium (as mg / l CaCO3)	-	72							
[illegible]esium (as mg / l CaCO3)	-	28							
Iron, Total (mg / l Fe)	0.3 mg/ l *	<0.05							
Sulfates (mg / l SO4)	250 mg/ l *	37.5							
Chlorides (mg / l Cl)	250 mg/ l *	135.9							
Fluoride (mg / l F)	2 mg / l*	<0.1							
Total Dissolved Solids (mg / l)	500 mg / l *	370							
Total Suspended Solids (mg / l)	-	0.3							
Ammonia Nitrogen (mg / l N)	-	0.07							
Nitrate Nitrogen (mg / l N)	10 mg / l	1.80							
Dissolved Oxygen (mg / l O2)	-	18.1							
BOD 5 (mg / l O2)	-								
Langelier Index	+/- 1.0	-2.39							
Surfactants (mg / l LAS)	0.5 mg / l *	-							
Hydrogen Sulfide (mg / l H2S as S)	-	0							
Nitrite Nitrogen (mg / l N)	1 mg / l	<0.10							
Phosphate (mg / l PO3)	-	<0.05							
Manganese (mg / l MN)	0.05 mg / l *	<0.05							
Zinc	5 mg/l *	0.21							
[illegible] (mg / l)	5 mg/l *	1.4							

Laboratory Analyst: KK

* Secondary or Recommended MCL

Any questions please call Water Quality Specialist- (908) 301-3163

① Color is not a regulated parameter by Elizabethtown Water, m 26 Feb 04

REVIEWED m 26 Feb 04

LAB ID# 39-401

BENCHMARK ANALYTICS
4777 SAUCON CREEK ROAD
CENTER VALLEY, PA 18034-9004

PHONE (610) 974-8100
FAX (610) 974-8104

SEND DATA TO:

NAME: Terry Kusznir
COMPANY: Huntingdon Life Sciences
ADDRESS: PO Box 2360, Mettlers Road
East Millstone, NJ 08875-2360

PHONE: (732) 873-2550 x 2100
FAX: (732) 873-3992

INV #: 318294,318298
381302
PAGE: 2 OF 6
PO #:
PWS ID#:

TEST REPORT

PROJECT NAME: ANIMAL DRINKING WATER
SAMPLED BY: ALLISON HAMMAR
LOCATION: SEE BELOW
DATE: 01/22/04
TIME: SEE BELOW

GRAB SAMPLES: 318294,298,302
COMPOSITE SAMPLES: NONE
DATE RECEIVED BY LAB: 01/23/04
TIME RECEIVED BY LAB: 0930
RECEIVED FOR LAB BY: J. ALTEMOSE

SAMPLE: SITE #4, L WING ROOM 456 TIME: 1555

TEST	RESULT	UNITS	METHOD	INV #	START DATE	START TIME	END DATE	INIT.
COPPER	0.019	MG/L	EPA 200.7	318294	01/26/04	0800	01/26/04	GR
LEAD	<0.002 *	MG/L	EPA 200.9	318294	01/26/04	0800	01/26/04	KFW

SAMPLE: SITE #5, V-1 ROOM 721 TIME: 1540

TEST	RESULT	UNITS	METHOD	INV #	START DATE	START TIME	END DATE	INIT.
COPPER	0.011	MG/L	EPA 200.7	318298	01/26/04	0800	01/26/04	GR
LEAD	<0.005 *	MG/L	EPA 200.9	318298	01/26/04	0800	01/26/04	KFW

SAMPLE: SITE #6, INHALATION ROOM 812 TIME: 1602

TEST	RESULT	UNITS	METHOD	INV #	START DATE	START TIME	END DATE	INIT.
COPPER	0.015	MG/L	EPA 200.7	318302	01/26/04	0800	01/26/04	GR
LEAD	<0.005 *	MG/L	EPA 200.9	318302	01/26/04	0800	01/26/04	KFW

REVIEWED
T 13 Feb 04

REMARKS:

* LIMIT OF DETECTION INCREASED DUE TO MATRIX INTERFERENCE AND SPIKE RECOVERY DATA.

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

MANAGER: Stephanie Olesa DATE: Feb 3, 2004

BENCHMARK ANALYTICS
4777 SAUCON CREEK ROAD
CENTER VALLEY, PA 18034-9004

PHONE (610) 974-8100
FAX (610) 974-8104

SEND DATA TO:

NAME:	Terry Kusznir	INV #:	318299-318301
COMPANY:	Huntingdon Life Sciences		318303-318305
ADDRESS:	PO Box 2360, Mettlers Road	PAGE:	5 OF 6
	East Millstone, NJ 08875-2360		
		PO #:	
PHONE:	(732) 873-2550 x2100		
FAX:	(732) 873-3992 **TEST REPORT**	PWS ID#:	

PROJECT NAME:	ANIMAL DRINKING WATER	GRAB SAMPLES:	318299-318301
SAMPLED BY:	ALLISON HAMMAR		318303-318305
LOCATION:	SEE BELOW	COMPOSITE SAMPLES:	NONE
DATE:	01/22/04	DATE RECEIVED BY LAB:	01/23/04
TIME:	SEE BELOW	TIME RECEIVED BY LAB:	0930
		RECEIVED FOR LAB BY:	J. ALTEMOSE

SAMPLE: SITE #5, V-1 ROOM 721 TIME: 1540

TEST	RESULT	UNITS	METHOD	INV #	START DATE	START TIME	END DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	318299	01/23/04	1420	01/24/04	DNG
STANDARD PLATE COUNT	46	CFU/ML	SM#19 9215 B	318300	01/23/04	1415	01/25/04	JLS
TOTAL COLIFORM	0	PER 100 ML	EPA 600-R-00-013	318301	01/23/04	1305	01/24/04	DNG
E. COLI	0	PER 100 ML	EPA 600-R-00-013	318301	01/23/04	1305	01/24/04	DNG

SAMPLE: SITE #6, INHALATION ROOM 812 TIME: 1602

TEST	RESULT	UNITS	METHOD	INV #	START DATE	START TIME	END DATE	INIT.
PSEUDOMONAS	<1	PER 100 ML	SM#19 9215 B	318303	01/23/04	1420	01/24/04	DNG
STANDARD PLATE COUNT	<1	CFU/ML	SM#19 9215 B	318304	01/23/04	1415	01/25/04	JLS
TOTAL COLIFORM	0	PER 100 ML	EPA 600-R-00-013	318305	01/23/04	1305	01/24/04	DNG
E. COLI	0	PER 100 ML	EPA 600-R-00-013	318305	01/23/04	1305	01/24/04	DNG

REMARKS:

REVIEWED
T 13 Feb 04

THE ABOVE TEST RESULTS MEET ALL THE REQUIREMENTS OF NELAC.

MANAGER: Stephanie Olsen DATE: Feb 3, 2004

NAMSA
Ensuring Medical Device Safety and Compliance™

Corp. Hdqtrs: 2261 Tracy Road, Northwood, OH 43619-1397 / 419.666.9455 / Fax 419.666.2954
3400 Cobb International Blvd., Kennesaw, GA 30152-7601 / 770.427.3101 / Fax 770.426.5692
9 Morgan, Irvine, CA 92618-2078 / 949.951.3110 / Fax 949.951.3280
Affiliates: France • Germany • Israel • Taiwan • United Kingdom

Confidential
MS005_00P

Ted Weaver
The Andersons
PO Box 119
Maumee , OH 43537

Lab No. 03T_22579_01
P.O. No. Ted Weaver
Test Facility: NAMSA
6750 Wales Road
Northwood, OH 43619

STERILITY TEST

Test Article: Bed O' Cobs 425RB
ID No. Lot: MK1703, Run #And6030036
Procedure/Test Method: S-20431-01-00/Immersion
Test Article Received: November 24, 2003
Test Start Date: November 24, 2003
Test Termination Date: December 8, 2003
Number of Products Tested:

STERILITY TEST RESULTS
Test Article Identity Maintained as Submitted by Client

Articles Tested	Number of Articles Tested	Type of Media	Incubation Temperature (Degrees C)	Number of Days Incubated	Number of Positive Articles
Product Section	1	SCDB-400 ml	20-25	14	0
Product Section	1	FTM-400 ml	30-35	14	0

SCDB = Soybean Casein Digest Broth FTM = Fluid Thioglycollate Medium

Results and conclusions apply only to the test article tested. No further evaluation of these results is made by NAMSA. Any extrapolation of these data to other samples is the responsibility of the sponsor. All procedures were conducted in conformance with good laboratory practice and ISO 17025.

Record Storage: All raw data pertaining to this study and a copy of the final report are to be retained in designated NAMSA archive files for a period of 5 years.

EXACT PHOTO COPY OF ORIGINAL
INIT. JMP DATE 12Feb04

cal Date Completed 12-8-03 Approved By

Michelle R. Pierce
Manager, Microbiology

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614-888-4077 * FAX 614-888-4223 * www.sterigenics.com

ARDIC
of the IDA Group

Certificate of Processing

acility: Westerville
ustomer Name: The Anderson Inc.
ustomer PO #:
un Date: 11/11/03
un Number: **AND01 AND 6030036**
otal Pallets: 22

Cell: Production A

Date Format: MM/DD/YY
Customer Ref:

ATERIALS PROCESSED:

Qty	Product	Description	Lot Number	LOT #
1,760	BED'O COB 1/4" BAG	10/TOTE 23.75 X 11.75 X 8"	425RB	MK1703
1	SAMPLE-506		425RB	MK1703
1,761 Bags		Total		

Minimum Dose: 27.4 kGy
Maximum Dose: 50.7 kGy

terigenics certifies that the materials listed above (as described by its anufacturer) received the indicated doses within the precision and accuracy f the dosimetry system employed:

Certified By: [signature]
Date: 11/13/03

ISO 9001:2000 REGISTERED

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9 Morgan, Irvine, CA 92618-2078 / 949.951.3110 / Fax 949.951.3280
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MS005-FEE

Lab No. 03T 10650 00
P.O. No. TED WEAVER

ID No. Lot: DH143

TED WEAVER
THE ANDERSONS INC.
PO BOX 119
MAUMEE, OH 43537-1639

STERILITY TEST

Test Article: ¼" Bed O'Cobs 425URB Run #6030024
Procedure/Test Method: S-00165-01-00/Immersion
Test Article Received: 8-28-03
Test Start Date: 8-29-03
Test Termination Date: 9-12-03
Number of Products Tested: 1

STERILITY TEST RESULTS

Test Article Identity Maintained as Submitted by Client

Articles Tested	Number of Articles Tested	Type of Media	Incubation Temperature (Degrees C)	Number of Days Incubated	Number of Positive Articles
Product Section	1	SCDB-400 ml	20-25	14	0
Product Section	1	FTM-400 ml	30-35	14	0

SCDB = Soybean Casein Digest Broth FTM = Fluid Thioglycollate Medium

Results and conclusions apply only to the test article tested. No further evaluation of these results is made by NAMSA. Any extrapolation of these data to other samples is the responsibility of the sponsor. All procedures were conducted in conformance with good laboratory practice and ISO 17025.

Record Storage: All raw data pertaining to this study and a copy of the final report are to be retained in designated NAMSA archive files.

Test Facility: NAMSA, 2261 Tracy Road, Northwood, OH 43619-1397.

cal Date Completed 9-12-03 Approved By _____
Michelle R. Pierce

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614-888-4077 * FAX 614-888-4223 * www.sterigenics.com

Certificate of Processing

Facility: Westerville
Cell: Production A
Customer Name: The Anderson Inc.
Customer PO #:
Run Date: 08/22/03
Date Format: MM/DD/YY
Run Number: **AND01 AND 6030024**
Customer Ref:
Total Pallets: 21

MATERIALS PROCESSED:

Qty	Product	Description	Lot Number	LOT #
400	BED'O COB 1/8" BAG	10/TOTE	DH133	825RB
80	BED'O COB 1/8" BAG	10/TOTE	DG033	825RB
1	SAMPLE-504		DH133	825RB
1,200	BED'O COB 1/4" BAG	10/TOTE 23.75 X 11.75 X 8"	DH143	425RB
1	SAMPLE-506		DH143	425RB
1,682 Bags	Total			

Minimum Dose: 29.2 kGy
Maximum Dose: 50.3 kGy

IBA certifies that the materials listed above (as described by its Manufacturer) received the indicated doses within the precision and accuracy of the dosimetry system employed:

Certified By:

Date: 08/25/03

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	Report Amendments	Appendix QQ

There are no amendments for this report at this time.