

**Data Requirement**

EPA OPPTS 870.3650  
OECD 422

STUDY NO. 03-4242

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

**Amended Final Report**

VOLUME I of III

[REDACTED]

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

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

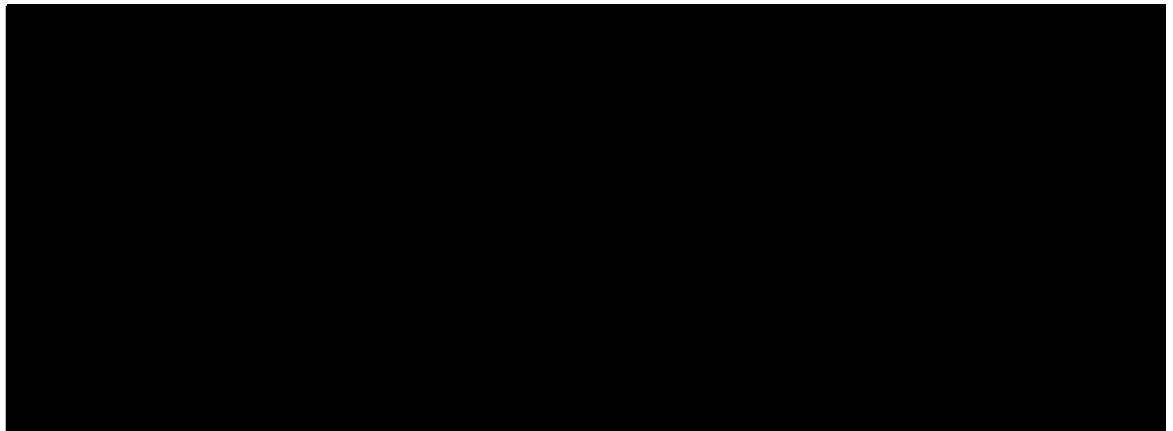
[REDACTED]

Date: 15 August 2008  
Amended Date: 14 May 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:

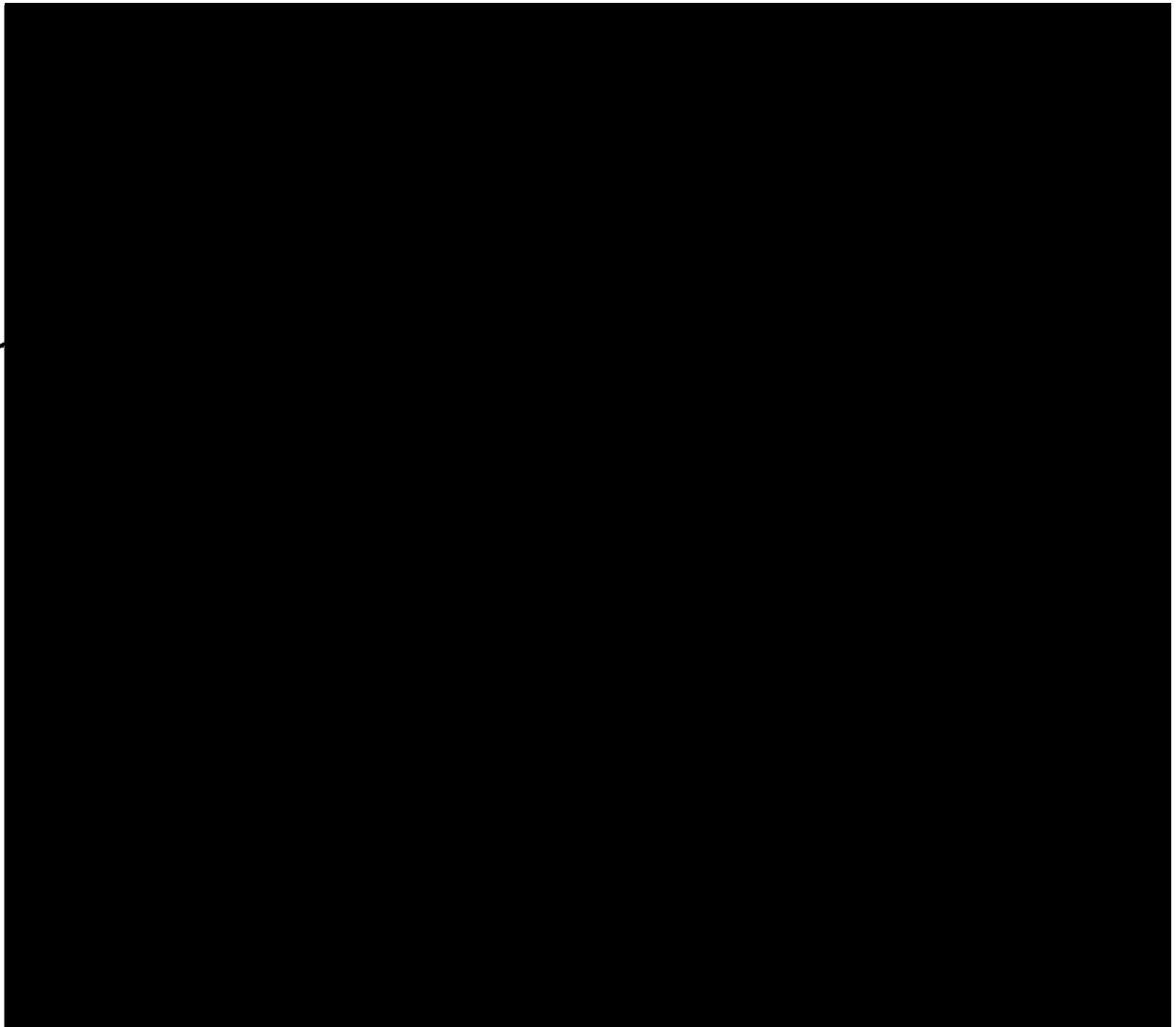
- 1) The supplier was responsible for the identity and stability of the test substance and those tests were not performed in compliance with GLP regulations.
- 2) A lot number for the test substance was not available.



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**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).



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<sup>1</sup> 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.

**QUALITY ASSURANCE STATEMENT<sup>a</sup>**

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. This report reflects the raw data as far as can be reasonably established.

| <b>Type of Inspection</b>                                                     | <b>Date(s) of Inspection</b>        | <b>Reported to Study Director and Management</b> |
|-------------------------------------------------------------------------------|-------------------------------------|--------------------------------------------------|
| GLP Protocol Review                                                           | 15 Sep 03                           | 15 Sep 03                                        |
| Exposure, Monitoring & Equipment Records                                      | 29 Sep 03                           | 01 Oct 03                                        |
| Functional Observational Battery, Training Records & Protocol Amendment No. 1 | 22 Oct 03                           | 22 Oct 03                                        |
| Terminal Blood Collection & Necropsy                                          | 29 Oct 03                           | 29 Oct 03                                        |
| Lactation Day 4 Necropsy                                                      | 10 & 11 Nov 03                      | 18 Nov 03                                        |
| Purity and Stability Analysis Report & Study Data & Protocol Amendment No. 2  | 21 Jan 04                           | 21 Jan 04                                        |
| Draft Report & Study Data                                                     | 24, 25, 29 Feb & 1, 3, 8 & 9 Mar 04 | 9 Mar 04                                         |
| Protocol Amendment No. 3                                                      | 21 Jan 08                           | 21 Jan 08                                        |
| Report Amendment No. 1 & Protocol Amendment No. 4                             | 12 May 10                           | 12 May 10                                        |

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<sup>a</sup>Quality Assurance Statement originally signed on 30 Jan 08; re-signed as a result of additional auditing performed on Protocol Amendment No. 4 and Report Amendment.

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

**SUMMARY**

This study was designed to assess the potential toxicity, including neurotoxicity and reproductive performance in male and female rats when butane 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 can detect effects on conception, development of the conceptus and parturition and pup survival to lactation 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 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 females were evaluated for subchronic effects and satellite females for reproductive effects only. 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), seven days/week for 4 weeks (28 days). Satellite female rats were exposed once daily (6 hours/day), seven 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). For satellite female rats without evidence of mating that appeared to be pregnant, exposure was terminated on the estimated gestation day 19. The following parameters were evaluated in all animals: viability, clinical observations, body weights, feed consumption, functional observational battery (FOB) and motor activity. Clinical pathology and 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 99.23% butane before the study and 99.98% butane 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 ( $\pm$  standard deviation) analytical (IR) concentrations for the control and the respective exposure groups were as follows:  $0 \pm 0$ ,  $930.6 \pm 28.1$ ,  $3022 \pm 58$  and  $9157 \pm 269$  ppm. Chamber environmental conditions

## SUMMARY

averaged 24°C temperature and 56% 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.

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 butane.

All mated female animals were found pregnant and delivered live pups. Mating indices for the male rats treated with the test substance were comparable to the air control group. Mating, fertility and gestation indices for the female rats treated with the test substance were comparable to the air control group. Most of the 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. There were no treatment-related differences in all parturition parameters including the total number of pups delivered, the number of pups dying, the viability (4 day survival) index, the number of implantation sites and corpora lutea per dam, the pup sex ratio and the number of live pups/litter, when compared to the air control group. The pups were unremarkable during the lactation period. There were no exposure-related differences in body weights or weight gains in the pups feeding from test substance exposed animals compared to the pups feeding from air control animals. There were no exposure-related differences in macroscopic postmortem evaluations in the pups feeding from test substance exposed animals compared to the pups feeding from air control animals.

In conclusion, exposure of male and female rats to target concentrations of 900, 3000 and 9000 ppm of Butane resulted in no general systemic effects, no effects on fertility and reproductive performance and no effects on pup survival and development to postnatal day 4. Therefore, a no observed adverse effect level (NOAEL) of 9000 ppm was determined for this study's systemic, reproductive/developmental, and neonatal endpoints.

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**1. INTRODUCTION**

This study was designed to assess the potential toxicity, including neurotoxicity and reproductive performance in male and female rats when butane 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**

22 September 2003 (date Study Director signed the protocol)

**2.2.2. DATE OF ANIMAL RECEIPT**

16 September 2003 (experimental start date, per OECD GLP's)

**2.2.3. EXPOSURE INITIATION**

29 September 2003 (experimental start date, per EPA GLP's)

**2.2.4. MATING INITIATION**

13 October 2003

**2.2.5. MATING TERMINATION**

27 October 2003

**2.2.6. EXPOSURE TERMINATIONS**

28 October 2003 (main study)

8 November 2003 (satellite female)

**2.2.7. TERMINAL SACRIFICES**

29 and 30 October 2003 (main study)

8-12, 14 and 15 November 2003 (satellite female)

**2.2.8. EXPERIMENTAL TERMINATION**

26 April 2006 (Date of last data collection)

**2.2.9. STUDY COMPLETION**

15 August 2008 (Date Final Report is signed by the Study Director)

### 2.3. EXPERIMENTAL OUTLINE

| Group | Group Designation        | Exposure Levels (ppm) | Treatment Schedule<br>Pre-mating Period |                                                     | Number of Animals    |                                       |
|-------|--------------------------|-----------------------|-----------------------------------------|-----------------------------------------------------|----------------------|---------------------------------------|
|       |                          |                       | Main Study Male Rats <sup>b</sup>       | Main Study and Satellite Female Rats <sup>b,c</sup> | Main Study Male Rats | Main Study and Satellite Female Rats* |
| 1     | Air Control <sup>a</sup> | 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

<sup>a</sup>Control animals were treated with air only with the same treatment regimen as the treated groups.

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

<sup>c</sup>Satellite female rats (12/group) for the reproduction/developmental study were exposed once daily (6 hours/day), seven 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). For satellite female rats without evidence of mating that appeared to be pregnant, exposure was terminated on an estimated gestation day 19.

The first day of exposure was designated day 0.

### 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 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.

#### **2.4.2. EXPOSURE LEVEL SELECTION**

The exposure levels were based on results of a 2-week range-finding study (HLS Study No. 03-6143, see Appendix NN, 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 is 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, a historical database 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 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 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.

### **2.5. TEST SUBSTANCE**

Butane

#### **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**

99.5% 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, 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. Indicate that documentation of the identity, strength, composition, and stability were also confirmed by the test facility.

**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 was initially shipped to ChevronTexaco on 13 August 2003 and then was delivered to EPL Archives. A common archival sample was taken for this study and the preceding range-finding study.

**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 report with this test substance.

**2.6. TEST ANIMALS****2.6.1. SPECIES**

Albino Rats (Outbred) VAF/Plus<sup>®</sup>  
Sprague-Dawley Derived (CD<sup>®</sup>)  
CrI:CD<sup>®</sup> (SD) IGS BR

**2.6.2. SUPPLIER**

Charles River Laboratories  
Raleigh, North Carolina 27610

**2.6.3. NUMBER OF ANIMALS**

Received:  
159 total (53 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)**

|         | <b>Mean</b> | <b>Range</b> |
|---------|-------------|--------------|
| Male:   | 261         | 241 - 280    |
| Female: | 200         | 174 - 229    |

Individual weights of animals placed on test were within  $\pm 20\%$  of the mean weight for each sex.

**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 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 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. Clean feeder jars and fresh feed were provided at least weekly. From day 18 of gestation and during lactation, the dam was housed with her litter in plastic "shoebox" cages with bedding. Clean feed jars and fresh feed were provided at least weekly for periods when feed consumption was not recorded and at each interval when feed consumption was recorded.

### **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.

### **2.10.4. FEED ANALYSIS**

Analysis of each 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, which were expected to interfere with the results of this study. Feed, Water, and Bedding Analyses: Please include these in the report as appendices.

**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, which 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, OH) was provided for each mated female rat on dayday 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 provided by the supplier, is maintained on file at the testing facility. 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: 20.7 to 22.4°C  
Daily Average Range: 21.0 to 22.1°C

**Relative Humidity**

Relative humidity was monitored in accordance with 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: 24.28 to 77.36%  
Daily Average Range: 44.91 to 54.96 %

**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 (1:1) until evidence of mating was seen, or for 2 consecutive weeks. During mating, cohabitation of male and female littermates was prohibited. 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 dayday 0 of gestation. Once mated, the satellite female rats were removed from the mating cages and housed individually for the remainder of the study. After the mating period was over, satellite female rats without evidence of copulation were removed from the mating cages and housed individually and monitored for visible signs of pregnancy with corresponding body weight gain.

## **2.13. EXPERIMENTAL EVALUATIONS**

### **2.13.1. VIABILITY EXAMINATION (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**

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

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 continuing throughout the study. Satellite female rats were observed weekly during the pre-mating period and on gestation daydays 0, 7, 14, 20 and Lactation days 0 (except if parturition didn't complete on the same day as it initiated), 1 and 4. The group 4 satellite female rat 4553 without evidence of mating continued to be observed weekly during the mating and post-mating period until it was determined (by body weight gain) that it appeared to be pregnant.

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. The Group 4 female satellite female rat 4553 without evidence of mating was weighed twice weekly during the mating and post-mating period until she delivered.

#### 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 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) =

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

<sup>a</sup>The average of the current and first weight of the week was used.

### **2.13.5. PARTURITION AND LACTATION**

On day 18 of gestation, several days prior to expected parturition, satellite female rats were transferred to solid, plastic cages with bedding article provided. Thereafter, examination for signs of parturition were made twice daily (morning and afternoon). The duration of gestation was documented. Evidence of difficult or prolonged parturition or bizarre behavior (including but not limited to self-mutilation, walking backwards), 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. Unusual observations and the absence of milk in the stomach was noted.

### **2.13.6. F<sub>1</sub> PUP EVALUATIONS**

#### **Physical Examinations**

Each F<sub>1</sub> pup was examined on lactation days 0 and 4. Pups were also observed for any abnormal behavior.

#### **Body Weights**

Individual F<sub>1</sub> 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.

### **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 functional observational battery was performed for all animals before evaluation of motor activity.

#### **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.

Desired: 18 to 26°C

Actual: 20 to 21°C

**Relative Humidity**

Relative humidity 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: 30 to 70%

Actual: 26 to 51%

**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: 54.5 to 63.2 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: <54.3 to 63.9 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. Positive historical control data demonstrating the sensitivity of the procedure is documented in Appendix KK.

**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: 20 to 21°C

**Relative Humidity**

Relative humidity 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: 30 to 70%

Actual: 25 to 54%

**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. Excursions outside the specified range were considered not to have affected the integrity of the study.

Desired: 55 to 65 dB

Actual: 50.7 to 61.6 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: <52.1 to 61.4 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<sub>2</sub>/O<sub>2</sub>) 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 Hematology Analyzer, 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<sup>1</sup>

##### **Other**

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

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<sup>1</sup>When questionable values were obtained, manual differential leukocyte counts (*Henry, 1991*) and an absolute value calculations were performed for verification.

### 2.15.2. COAGULATION

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

Blood samples were analyzed as follows:

**Mechanical clot detection system, STA Compact<sup>®</sup>,  
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:

**Olympus AU640, Olympus America 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 Wahlefeld 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 day 4 pups) were euthanized by exsanguination following an overexposure of carbon dioxide inhalation. Lactation day 4 pups were euthanized using an intraperitoneal injection of sodium pentobarbital.

**2.16.2. EUTHANASIA SCHEDULE****Main Study Male and Female Rats**

Main study male rats 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 day 4.

**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 (pre-fixation and/or post-fixation) were recorded for each satellite female rat.

**2.16.5. ORGAN WEIGHTS**

Organs indicated in Table I (page 31 – may change with revisions) 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) may change following revisions) 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**

| <b>ORGAN NAME</b>                             | <b>WEIGHED</b> | <b>PRESERVED<br/>Main and<br/>Satellite Study</b> | <b>EXAMINED<br/>MICROSCOPICALLY<br/>Main Study<br/>(Groups 1 and 4)</b> |
|-----------------------------------------------|----------------|---------------------------------------------------|-------------------------------------------------------------------------|
| Adrenal glands                                | X              | X                                                 | X                                                                       |
| Bone (sternum/femur) <sup>a</sup>             |                | X                                                 | X                                                                       |
| Bone marrow (rib)                             |                | X                                                 | <sup>b</sup>                                                            |
| 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)                       |                | X                                                 | X                                                                       |
| Lymph node (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                                                                       |

| ORGAN NAME                                | WEIGHED | PRESERVED                   | EXAMINED<br>MICROSCOPICALLY    |
|-------------------------------------------|---------|-----------------------------|--------------------------------|
|                                           |         | Main and<br>Satellite Study | Main Study<br>(Groups 1 and 4) |
| Uterus with vagina                        | X       | X                           | X                              |
| All macroscopic lesions and tissue masses |         | X                           | X                              |

<sup>a</sup>Qualitative examination (no differential count).

<sup>b</sup>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 10% neutral buffered formalin. Lungs and urinary bladder were infused with 10% formalin for optimal preservation.

### Processing

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

#### 2.16.7. MACROSCOPIC POSTMORTEM EXAMINATION - F<sub>1</sub> PUPS

Macroscopic postmortem examinations (internal and external) were performed on all F<sub>1</sub> pups found dead during lactation. Unusual observations, including gross abnormalities and the absence of milk in the stomach, were noted and then the carcasses discarded. F<sub>1</sub> pups found dead at birth were identified (lung floatation test) as stillborn or alive but found dead. Macroscopic postmortem examinations (external only) were performed on all F<sub>1</sub> pups on lactation day 4 for pups surviving to that interval.

## 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
- Hematology
- Coagulation
- Clinical Chemistry
- Gestation length
- Corpora lutea
- F<sub>1</sub> pup weights (each weighing interval during lactation)
- Number of pups (F<sub>1</sub> 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 to Brain weight ratios
- Grip Strength measurements

#### 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 (Snedecor and Cochran, 1967; Bartlett, 1937; 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 (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; Siegel, 1956) and if differences were indicated, Shirley's test (Shirley, 1977), Steel's test (Steel, 1959) or Pairwise Comparison (Siegel, 1956) 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 (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 problems with the white noise generator (low batteries), the room environment noise level was below protocol specified range for the first set of FOB and motor activity evaluated animals.
2. Due to equipment malfunction, Group 2 temperature and humidity could not be recorded from 2.5 to 6.0 hours during the Day 12 exposure.
3. Due to oversight, the lung floatation test was not performed on pup 2542-01, which was found dead on Study day 40, and therefore this death was categorized as stillborn by default.
4. Due to oversight, one adrenal was lost for main study male animal 4037 at the time of necropsy. Therefore, the adrenals were unable to be weighed as per protocol for this animal.

### 3. RESULTS AND DISCUSSION

#### 3.1. TEST SUBSTANCE ANALYSIS

##### (Appendix JJ)

Pre-study GC analysis of the test substance showed a purity of 99.23% for butane. This value compared closely to the purity of 99.96% for the analytical standard of butane and the 99.5% purity as guaranteed by the supplier of the test substance. Post-study GC analysis of the test substance showed a purity of 99.98% for butane. This value compared closely to the purity of 99.98% for the analytical standard of butane and the 99.23% 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.

The target and mean ( $\pm$  standard deviation) analytical (IR) and nominal concentrations (by volume of gas consumed) are summarized as follows:

| Group | Test Substance | Target Concentration (ppm) | Analytical Concentration (ppm) | Nominal Concentration (ppm) |
|-------|----------------|----------------------------|--------------------------------|-----------------------------|
| 1     | Air Control    | 0                          | $0 \pm 0$                      | $0 \pm 0$                   |
| 2     | Butane         | 900                        | $930.6 \pm 28.1$               | $930 \pm 12$                |
| 3     | Butane         | 3000                       | $3022 \pm 58$                  | $2950 \pm 0$                |
| 4     | Butane         | 9000                       | $9157 \pm 269$                 | $9829 \pm 142$              |

The analytically measured exposure levels of the airborne test substance were reasonably close to the targeted exposure levels and nominal concentrations (as calculated by volume of gas consumed, see above, and by weight of gas consumed, see pages 9-10 of Table II in Appendix II). Chamber environmental conditions averaged 24°C temperature and 56% relative humidity.

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

| Group | Test Substance | Mass Median Aerodynamic Diameter ( $\mu\text{m}$ ) | Geometric Standard Deviation | Total Mass Concentration ( $\text{mg}/\text{m}^3$ ) |
|-------|----------------|----------------------------------------------------|------------------------------|-----------------------------------------------------|
| 1     | Air Control    | 4.335                                              | 2.124                        | $3.62 \times 10^{-3}$                               |
| 2     | Butane         | 4.737                                              | 2.100                        | $3.45 \times 10^{-3}$                               |
| 3     | Butane         | 2.455                                              | 1.989                        | $2.94 \times 10^{-3}$                               |
| 4     | Butane         | 3.503                                              | 2.028                        | $3.18 \times 10^{-3}$                               |

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 chromodacryorrhea or transient red nasal discharge among males exposed to 9000 ppm, between the 7th and 28th days of exposure.

**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 exposure-related differences in feed consumption in the test substance exposed animals as compared to the air control animals. A couple of statistically significant increases were seen but these were not in an exposure-level related pattern and increases in feed consumption are not usually considered an adverse effect.

**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. Minor, but statistically significant, decreases in male forelimb grip strength and increases in female forelimb grip strength occurred at 9000 ppm, but were not suggestive of an adverse effect of treatment since there was a decrease in males and an increase in females for the same parameter. Inter-group differences of a similar magnitude occurred among hindlimb results for both sexes, without any apparent exposure-level relationship.

**3.3.5.2. MOTOR ACTIVITY****(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. A statistically significant increase in platelet count in all of the test substance exposed males was seen but was not in an exposure-related pattern (the highest count was seen in the 900 ppm exposed males) and there were no similar differences in the females. In isolation, these minor inter-group differences were not considered to indicate an effect of the exposures.

#### **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. A statistically significant decrease in total bilirubin concentration in the 3000 and 9000 ppm exposed males was seen but this was not in an exposure-related pattern and there were no similar differences in the females. 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 3000 ppm exposed male group showed the highest terminal body weight of all the groups, and therefore the mean absolute organ weights in this group were also generally the highest, such that statistically significant differences from air control animals occurred for absolute brain, heart, kidney and testis weight. These statistical results were resolved by analysis of organ weights relative to body or brain weight. Testis weight, however, is only weakly correlated with body weight and particularly in cases where there is only a small difference from air control in terminal body weight (as here) it is normally most appropriate to analyze inter-group differences by considering absolute testis weight.

### **3.3.8. MACROSCOPIC POSTMORTEM EVALUATIONS**

**(Table 11; Appendix L)**

There were no exposure-related differences in macroscopic postmortem evaluations in the test substance exposed animals as compared to the air control animals. Slight to moderate discoloration of the lungs occurred in all groups, including the air control, and there were sporadic incidences of other findings that were not related to treatment with the test substance.

### **3.3.9. HISTOPATHOLOGICAL EVALUATIONS**

**(Table 12; Appendix L)**

There were no exposure-related differences in microscopic postmortem evaluations in the test substance exposed animals as compared to the air control animals. The slight to moderate red discoloration of lungs in animals of all test groups represented nonspecific minimal to moderate multifocal congestion, hemorrhage, and edema. The slight renal pelvic dilatation and hair loss or thinning, noted at necropsy, were confirmed microscopically. Abnormal ileal contents could not be confirmed histologically. Microscopically, hair loss or hair thinning in the two air control animals were associated with a few hair follicles that contained an abundance of keratin and/or follicles which were devoid of hair shafts. Other changes were observed in most if not all groups or randomly in individual animals and were thus

considered incidental findings, and not related to the administration of the test substance.

Testes - Stages of Spermatogenesis: With the exception of slight, multifocal degenerative and/or necrotic changes in seminiferous tubules of 2 of 12 air controls, no abnormality was evident in any test animal.

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 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 incidences of findings that are common to this strain of rat: predominantly localized patchy alopecia or staining, occasional scabs and broken 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. A statistically significant increase in body weight gain in the 3000 ppm exposed females was seen during the gestation period which was not explained by notable

differences in litter size. This did not appear to be an exposure-related pattern and was considered incidental.

#### **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 INDICES**

**(Tables 26 and 27; Appendices Z and AA)**

Mating and fertility indices for the male rats treated with the test substance were optimal and comparable to the air control group. Mating, fertility and gestation indices for the female rats treated with the test substance were also optimal. Most of the females in each group mated at the first opportunity. There were also no exposure-related differences in the other reproductive parameters up to the time of parturition including the percent of females completing delivery, the duration of gestation and the proportion with live litters and/or stillborn pups, when compared to the air control group.

#### **3.4.6. PARTURITION AND LITTER SURVIVAL DATA**

**(Table 27; Appendices BB and CC)**

Parturition data for the female rats treated with the test substance were comparable to the air control group. There were no exposure-related differences in any of the parturition parameters including the total number of pups delivered, the number of pups dying, the viability (4 day survival) index, the number of implantation sites and corpora lutea per dam, the pup sex ratio and the number of live pups/litter, when compared to the air control group. The only statistically significant difference that was noted was an increased number of pups per litter at the 900 ppm exposure level - this was not in an exposure-related pattern, was not an adverse outcome, and was considered incidental.

### **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 single occurrences of discolored kidneys and enlarged mesenteric lymph nodes 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 few statistically significant differences (increased thymus weights in 3000 ppm exposed females and increased right ovary and spleen and thymus weights/ratios in 3000 and/or 9000 ppm exposed females) were sporadically seen but were not in an exposure-related pattern and there were no corresponding findings in the organ weights or the histopathology findings in the main study females. The differences were 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 lactation period.

### **3.5.2. BODY WEIGHT DATA**

**(Tables 31 and 32; Appendix GG)**

There were no exposure-related differences in body weights or weight gains 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. Scattered observations, such as no milk in stomach, were noted but were not considered exposure-related.

## **4. CONCLUSION**

Exposure of male and female rats to target concentrations of 900, 3000 and 9000 ppm of butane resulted in no general systemic effects, no effects on fertility and reproductive performance and no effects on pup survival and development to postnatal day 4. Therefore, a no observed adverse effect level (NOAEL) of 9000 ppm was determined for this study's systemic, reproductive/developmental, and neonatal endpoints.

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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

|  |                 |  |
|--|-----------------|--|
|  | 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 “Butane: 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.

|  |                                                           |         |
|--|-----------------------------------------------------------|---------|
|  | Summary of Clinical Observations<br>Main Study<br>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

| MALES | SUMMARY OF CLINICAL OBSERVATIONS |
|-------|----------------------------------|
|-------|----------------------------------|

[illegible]

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MAIN STUDY

TABLE 1

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

## SUMMARY OF CLINICAL OBSERVATIONS

[illegible]



TABLE 2

MALES

MEAN BODY WEIGHT VALUES (GRAMS)

No statistically significant differences

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TABLE 2

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

| FEMALES                        |      |  | MEAN BODY WEIGHT VALUES (GRAMS) |          |           |           |
|--------------------------------|------|--|---------------------------------|----------|-----------|-----------|
| DOSE GROUP<br>DOSE LEVEL (PPM) |      |  | 1<br>0                          | 2<br>900 | 3<br>3000 | 4<br>9000 |
| DAY -7                         | MEAN |  | 163                             | 163      | 165       | 163       |
|                                | S.D. |  | 6.6                             | 6.7      | 8.3       | 7.0       |
|                                | N    |  | 12                              | 12       | 12        | 12        |
| DAY 0                          | MEAN |  | 200                             | 197      | 204       | 200       |
|                                | S.D. |  | 9.8                             | 10.1     | 12.7      | 13.0      |
|                                | N    |  | 12                              | 12       | 12        | 12        |
| DAY 7                          | MEAN |  | 216                             | 213      | 223       | 215       |
|                                | S.D. |  | 10.4                            | 10.1     | 16.2      | 13.2      |
|                                | N    |  | 12                              | 12       | 12        | 12        |
| DAY 14                         | MEAN |  | 233                             | 232      | 241       | 231       |
|                                | S.D. |  | 16.0                            | 11.5     | 11.0      | 15.1      |
|                                | N    |  | 12                              | 12       | 12        | 12        |
| DAY 21                         | MEAN |  | 246                             | 248      | 258       | 244       |
|                                | S.D. |  | 13.7                            | 11.8     | 18.3      | 15.3      |
|                                | N    |  | 12                              | 12       | 12        | 12        |
| DAY 28                         | MEAN |  | 256                             | 258      | 268       | 254       |
|                                | S.D. |  | 16.6                            | 13.4     | 22.9      | 18.9      |
|                                | N    |  | 12                              | 12       | 12        | 12        |

No statistically significant differences

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MAIN STUDY

TABLE 3

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

| MALES                           |       |    | MEAN BODY WEIGHT GAIN (GRAMS) |          |           |           |      |
|---------------------------------|-------|----|-------------------------------|----------|-----------|-----------|------|
| DOSE GROUP<br>DOSE LEVEL (PPM)  |       |    | 1<br>0                        | 2<br>900 | 3<br>3000 | 4<br>9000 |      |
| DAY                             | -7 TO | 0  | MEAN                          | 65       | 69        | 76**      | 69   |
|                                 |       |    | S.D.                          | 4.8      | 6.6       | 5.9       | 6.2  |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| DAY                             | 0 TO  | 7  | MEAN                          | 41       | 41        | 44        | 40   |
|                                 |       |    | S.D.                          | 9.5      | 6.7       | 8.9       | 10.0 |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| DAY                             | 7 TO  | 14 | MEAN                          | 33       | 36        | 41        | 35   |
|                                 |       |    | S.D.                          | 7.9      | 9.6       | 9.3       | 9.1  |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| DAY                             | 14 TO | 21 | MEAN                          | 34       | 30        | 35        | 29   |
|                                 |       |    | S.D.                          | 6.5      | 9.7       | 6.3       | 5.7  |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| DAY                             | 21 TO | 28 | MEAN                          | 25       | 23        | 25        | 22   |
|                                 |       |    | S.D.                          | 7.0      | 5.8       | 5.7       | 7.8  |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| DAY                             | 0 TO  | 28 | MEAN                          | 133      | 130       | 146       | 126  |
|                                 |       |    | S.D.                          | 21.0     | 19.9      | 21.2      | 23.7 |
|                                 |       |    | N                             | 12       | 12        | 12        | 12   |
| Statistical key:    ** = p<0.01 |       |    |                               |          |           |           |      |

Statistical key: \*\* = p<0.01

BUTANE: 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 | 38                            | 34  | 40   | 37   |
|                  |       |    | S.D. | 5.4                           | 7.7 | 7.5  | 7.8  |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |
| DAY              | 0 TO  | 7  | MEAN | 15                            | 17  | 19   | 15   |
|                  |       |    | S.D. | 6.1                           | 8.7 | 8.2  | 7.3  |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |
| DAY              | 7 TO  | 14 | MEAN | 18                            | 18  | 18   | 16   |
|                  |       |    | S.D. | 7.7                           | 6.7 | 9.8  | 5.0  |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |
| DAY              | 14 TO | 21 | MEAN | 13                            | 17  | 16   | 13   |
|                  |       |    | S.D. | 6.6                           | 7.1 | 11.9 | 8.1  |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |
| DAY              | 21 TO | 28 | MEAN | 10                            | 10  | 10   | 11   |
|                  |       |    | S.D. | 5.0                           | 7.4 | 9.9  | 6.7  |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |
| DAY              | 0 TO  | 28 | MEAN | 55                            | 62  | 64   | 55   |
|                  |       |    | S.D. | 8.9                           | 9.2 | 13.4 | 11.1 |
|                  |       |    | N    | 12                            | 12  | 12   | 12   |

No statistically significant differences

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MAIN STUDY

TABLE 4

BUTANE: 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 | 103                                  | 103 | 109* | 103  |
|                  | S.D. | 6.2                                  | 5.4 | 7.7  | 5.6  |
|                  | N    | 12                                   | 12  | 12   | 12   |
| DAY 7            | MEAN | 85                                   | 86  | 89   | 87   |
|                  | S.D. | 3.3                                  | 4.5 | 5.4  | 4.0  |
|                  | N    | 12                                   | 12  | 12   | 12   |
| DAY 14           | MEAN | 75                                   | 76  | 78   | 76   |
|                  | S.D. | 3.7                                  | 3.4 | 5.5  | 3.9  |
|                  | N    | 12                                   | 12  | 12   | 12   |

Statistical key: \* =  $p < 0.05$

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MAIN STUDY

TABLE 4

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

| FEMALES                        |      |  | MEAN FEED CONSUMPTION (GRAMS/KG/DAY) |          |           |           |
|--------------------------------|------|--|--------------------------------------|----------|-----------|-----------|
| DOSE GROUP<br>DOSE LEVEL (PPM) |      |  | 1<br>0                               | 2<br>900 | 3<br>3000 | 4<br>9000 |
| DAY 0                          | MEAN |  | 100                                  | 102      | 99        | 101       |
|                                | S.D. |  | 6.5                                  | 4.9      | 9.2       | 4.5       |
|                                | N    |  | 11                                   | 11       | 12        | 12        |
| DAY 7                          | MEAN |  | 82                                   | 85       | 85        | 82        |
|                                | S.D. |  | 4.3                                  | 5.1      | 4.8       | 3.3       |
|                                | N    |  | 11                                   | 11       | 11        | 12        |
| DAY 14                         | MEAN |  | 80                                   | 86**     | 80        | 82        |
|                                | S.D. |  | 4.8                                  | 4.0      | 2.4       | 4.9       |
|                                | N    |  | 12                                   | 11       | 12        | 12        |
| DAY 21                         | MEAN |  | 75                                   | 80       | 77        | 76        |
|                                | S.D. |  | 5.2                                  | 4.1      | 5.6       | 3.8       |
|                                | N    |  | 12                                   | 12       | 12        | 12        |
| DAY 28                         | MEAN |  | 75                                   | 77       | 73        | 74        |
|                                | S.D. |  | 3.9                                  | 2.3      | 3.0       | 3.9       |
|                                | N    |  | 11                                   | 12       | 12        | 12        |

Statistical key: \*\* = p<0.01

|       |                                                                                         |         |
|-------|-----------------------------------------------------------------------------------------|---------|
| Males | Summary of Functional Observational<br>Battery Evaluations<br>Main Study<br>Termination | Table 5 |
|-------|-----------------------------------------------------------------------------------------|---------|

| Exposure Level (ppm):                                      | Group 1<br>0 | Group 2<br>900 | Group 3<br>3000 | Group 4<br>9000 |
|------------------------------------------------------------|--------------|----------------|-----------------|-----------------|
| <b>Forelimb Grip Strength (grams of force)<sup>1</sup></b> |              |                |                 |                 |
| Mean                                                       | 1007.7       | 957.5          | 930.0           | 876.0*          |
| S.D.                                                       | 133.9        | 140.9          | 102.8           | 147.5           |
| N                                                          | 12           | 12             | 12              | 12              |
| <b>Hindlimb Grip Strength (grams of force)<sup>1</sup></b> |              |                |                 |                 |
| Mean                                                       | 768.1        | 700.4          | 713.3           | 696.5           |
| S.D.                                                       | 107.2        | 63.9           | 73.1            | 109.8           |
| N                                                          | 12           | 12             | 12              | 12              |
| <b>Rectal Temperature (°C)</b>                             |              |                |                 |                 |
| Mean                                                       | 36.8         | 36.4           | 36.4            | 36.5            |
| S.D.                                                       | 1.3          | 1.7            | 1.5             | 1.5             |
| N                                                          | 12           | 12             | 12              | 12              |
| <b>Reflex Assessments</b>                                  |              |                |                 |                 |
| Number of Animals Examined                                 | 12           | 12             | 12              | 12              |
| <b>Audition Assessment</b>                                 |              |                |                 |                 |
| Normal                                                     | 12           | 12             | 12              | 12              |
| No Reaction                                                | 0            | 0              | 0               | 0               |
| Exaggerated, Jumps, Flips, Bites                           | 0            | 0              | 0               | 0               |
| <b>Pain Perception</b>                                     |              |                |                 |                 |
| Normal                                                     | 10           | 11             | 7               | 9               |
| No Reaction                                                | 2            | 1              | 5               | 3               |
| Increased Pain                                             | 0            | 0              | 0               | 0               |

<sup>1</sup> The means of Trials 1 and 2 were calculated and statistically evaluated.

\*Significantly different from control mean;  $p \leq 0.05$ .

\*\*Significantly different from control mean;  $p \leq 0.01$ .

If no asterisks, no statistically significant differences from control mean.

|         |                                                                                         |         |
|---------|-----------------------------------------------------------------------------------------|---------|
| Females | Summary of Functional Observational<br>Battery Evaluations<br>Main Study<br>Termination | Table 5 |
|---------|-----------------------------------------------------------------------------------------|---------|

| Exposure Level (ppm):                                      | Group 1<br>0 | Group 2<br>300 | Group 3<br>900 | Group 4<br>9000 |
|------------------------------------------------------------|--------------|----------------|----------------|-----------------|
| <b>Forelimb Grip Strength (grams of force)<sup>1</sup></b> |              |                |                |                 |
| Mean                                                       | 778.1        | 850.6          | 849.2          | 884.4 *         |
| S.D.                                                       | 75.6         | 88.0           | 113.7          | 115.5           |
| N                                                          | 12           | 12             | 12             | 12              |
| <b>Hindlimb Grip Strength (grams of force)<sup>1</sup></b> |              |                |                |                 |
| Mean                                                       | 595.8        | 701.3          | 632.9          | 618.5           |
| S.D.                                                       | 44.6         | 159.9          | 80.9           | 71.2            |
| N                                                          | 12           | 12             | 12             | 12              |
| <b>Rectal Temperature (°C)</b>                             |              |                |                |                 |
| Mean                                                       | 37.8         | 37.4           | 37.1           | 37.9            |
| S.D.                                                       | 1.2          | 1.5            | 1.9            | 1.0             |
| N                                                          | 12           | 12             | 12             | 12              |
| <b>Reflex Assessments</b>                                  |              |                |                |                 |
| Number of Animals Examined                                 | 12           | 12             | 12             | 12              |
| <b>Audition Assessment</b>                                 |              |                |                |                 |
| Normal                                                     | 12           | 12             | 12             | 12              |
| No Reaction                                                | 0            | 0              | 0              | 0               |
| Exaggerated, Jumps, Flips, Bites                           | 0            | 0              | 0              | 0               |
| <b>Pain Perception</b>                                     |              |                |                |                 |
| Normal                                                     | 11           | 11             | 11             | 12              |
| No Reaction                                                | 1            | 1              | 1              | 0               |
| Increased Pain                                             | 0            | 0              | 0              | 0               |

<sup>1</sup> The means of Trials 1 and 2 were calculated and statistically evaluated.

\*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.

|  |                                       |         |
|--|---------------------------------------|---------|
|  | Mean Motor Activity Values<br>Preface | Table 6 |
|--|---------------------------------------|---------|

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|  |                                                                              |         |
|--|------------------------------------------------------------------------------|---------|
|  | Mean Motor Activity Values<br>Main Study<br>4 <sup>th</sup> Week of Exposure | Table 6 |
|--|------------------------------------------------------------------------------|---------|

## Overview

The following is a brief summary of the statistical analysis of the motor activity data for Study 03-4242. 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. The inhalation exposure levels to the test substance, Butane, were 0 (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<sup>®</sup> 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<br>Main Study<br>4 <sup>th</sup> 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 |
|----------------------------------|----------|-------------------------------|----------------------------|------------------------------|
| 4 <sup>th</sup> Week of Exposure | Male     | 0.3533                        | 0.7561                     | NA                           |
|                                  | Female   | 0.6997                        | 0.7378                     | NA                           |
|                                  | Combined | 0.6005                        | 0.6546                     | NA                           |

NA: not applicable

**Discussion**

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

Analysis Performed By:

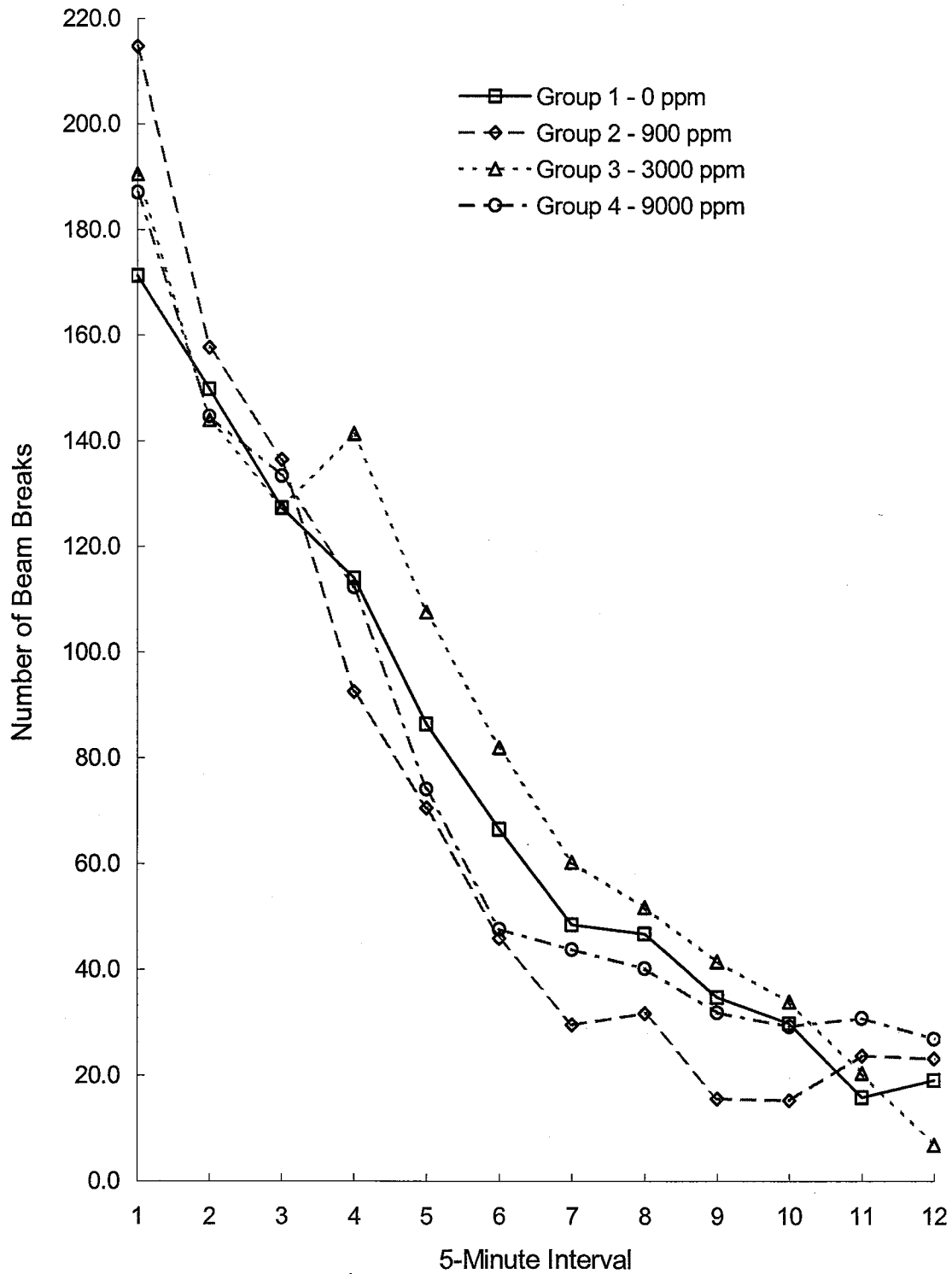
Thomas Soeder  
for Raymond Buck

Raymond D. Buck, Ph.D.

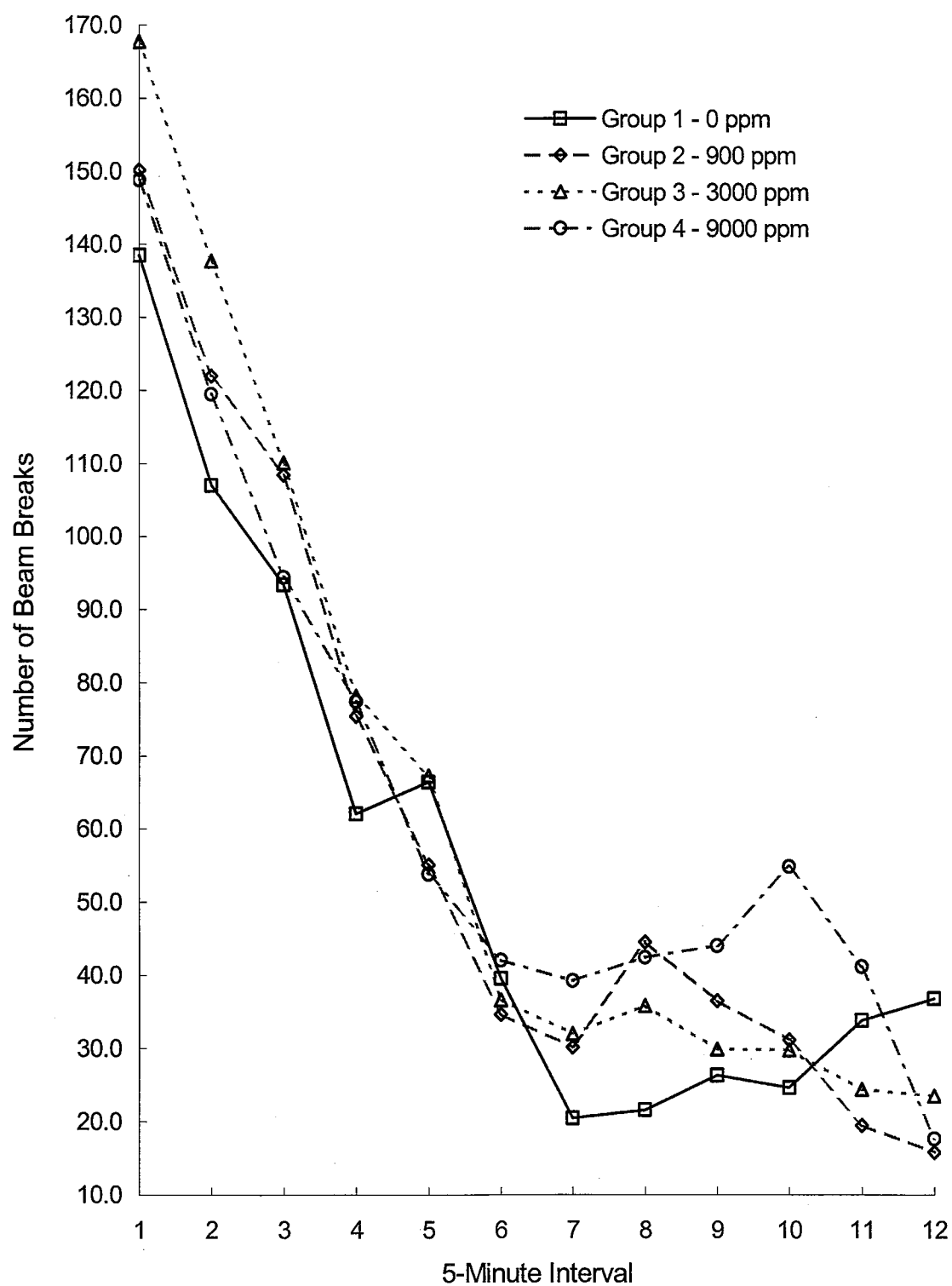
Cato Research Ltd.

26 April 2006  
Date

| Males | Mean Motor Activity<br>Termination | Figure 1 |
|-------|------------------------------------|----------|
|-------|------------------------------------|----------|



|         |                                    |          |
|---------|------------------------------------|----------|
| Females | Mean Motor Activity<br>Termination | Figure 2 |
|---------|------------------------------------|----------|



| Males | Mean Motor Activity Values <sup>a</sup><br>Termination |  |  |  |  |  |  |  |  |  |  | Table 6 |
|-------|--------------------------------------------------------|--|--|--|--|--|--|--|--|--|--|---------|
|-------|--------------------------------------------------------|--|--|--|--|--|--|--|--|--|--|---------|

|                    | Interval |       |       |       |       |       |       |       |       |       |       |       |
|--------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                    | 1        | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    |
| Group 1 – 0 ppm    |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 171.3    | 149.8 | 127.3 | 114.1 | 86.4  | 66.6  | 48.5  | 46.8  | 34.8  | 29.8  | 15.8  | 19.1  |
| SD                 | 24.29    | 31.13 | 34.49 | 61.45 | 56.05 | 61.77 | 58.13 | 51.26 | 52.23 | 53.12 | 39.64 | 30.62 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 2 – 900 ppm  |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 214.8    | 157.8 | 136.5 | 92.6  | 70.6  | 45.9  | 29.6  | 31.8  | 15.6  | 15.3  | 23.8  | 23.2  |
| SD                 | 73.98    | 59.64 | 58.92 | 51.11 | 50.41 | 50.60 | 42.26 | 53.78 | 42.37 | 23.29 | 41.83 | 43.54 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 3 – 3000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 190.6    | 144.0 | 127.4 | 141.4 | 107.7 | 82.0  | 60.3  | 51.8  | 41.5  | 33.9  | 20.4  | 6.8   |
| SD                 | 37.31    | 45.96 | 56.53 | 35.54 | 57.93 | 62.39 | 64.05 | 43.88 | 53.70 | 50.11 | 33.51 | 11.15 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 4 – 9000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 187.1    | 144.7 | 133.4 | 112.3 | 74.2  | 47.7  | 43.8  | 40.3  | 31.9  | 29.3  | 30.8  | 26.9  |
| SD                 | 46.97    | 29.11 | 33.75 | 51.80 | 50.93 | 33.93 | 41.93 | 54.35 | 50.12 | 39.34 | 48.57 | 44.96 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |

<sup>a</sup>Number of beam breaks per interval.

| Females | Mean Motor Activity Values <sup>a</sup><br>Termination |  |  |  |  |  |  |  |  |  |  | Table 6 |
|---------|--------------------------------------------------------|--|--|--|--|--|--|--|--|--|--|---------|
|---------|--------------------------------------------------------|--|--|--|--|--|--|--|--|--|--|---------|

|                    | Interval |       |       |       |       |       |       |       |       |       |       |       |
|--------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                    | 1        | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    |
| Group 1 – 0 ppm    |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 138.5    | 107.0 | 93.4  | 62.1  | 66.4  | 39.6  | 20.5  | 21.6  | 26.3  | 24.7  | 33.8  | 36.8  |
| SD                 | 28.93    | 28.08 | 27.60 | 33.23 | 42.33 | 41.61 | 31.36 | 28.24 | 41.27 | 34.10 | 46.76 | 29.07 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 2 – 900 ppm  |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 150.2    | 122.0 | 108.4 | 75.4  | 55.1  | 34.7  | 30.2  | 44.5  | 36.5  | 31.2  | 19.5  | 15.8  |
| SD                 | 17.08    | 19.83 | 30.65 | 38.74 | 38.03 | 39.67 | 35.82 | 47.47 | 34.75 | 36.67 | 25.57 | 22.63 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 3 – 3000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 167.8    | 137.8 | 110.1 | 78.2  | 67.3  | 36.7  | 32.0  | 35.8  | 29.9  | 29.8  | 24.4  | 23.5  |
| SD                 | 34.26    | 39.14 | 32.65 | 49.38 | 69.24 | 35.52 | 39.55 | 41.29 | 39.03 | 48.62 | 48.29 | 37.82 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 4 – 9000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| Mean               | 148.8    | 119.5 | 94.4  | 77.4  | 53.8  | 42.1  | 39.3  | 42.4  | 44.0  | 54.8  | 41.2  | 17.7  |
| SD                 | 23.22    | 22.13 | 43.05 | 43.31 | 47.78 | 44.51 | 42.80 | 57.63 | 46.30 | 57.13 | 45.94 | 16.31 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |

<sup>a</sup>Number of beam breaks per interval.

|  |                                                 |         |
|--|-------------------------------------------------|---------|
|  | Mean Hematology Values<br>Main Study<br>Preface | Table 7 |
|--|-------------------------------------------------|---------|

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

**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. 03-4242

Table 7 - Main Study

### Mean Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242

Table 7 - Main Study

Mean Hematology Values - Termination

| Group    |      | ANEU                 | ALYM                 | AMONO                | AEOS                 | ABASO                | ALUC                 |
|----------|------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|          |      | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL |
| 1M       |      |                      |                      |                      |                      |                      |                      |
| 0 ppm    | Mean | 2.42                 | 12.13                | 0.28                 | 0.21                 | 0.16                 | 0.10                 |
|          | SD   | 0.834                | 2.976                | 0.090                | 0.088                | 0.048                | 0.035                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 2M       |      |                      |                      |                      |                      |                      |                      |
| 900 ppm  | Mean | 2.48                 | 13.36                | 0.37                 | 0.16                 | 0.17                 | 0.13                 |
|          | SD   | 0.713                | 2.504                | 0.106                | 0.060                | 0.043                | 0.050                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 3M       |      |                      |                      |                      |                      |                      |                      |
| 3000 ppm | Mean | 2.40                 | 11.53                | 0.31                 | 0.19                 | 0.15                 | 0.10                 |
|          | SD   | 1.045                | 3.115                | 0.115                | 0.164                | 0.064                | 0.031                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 4M       |      |                      |                      |                      |                      |                      |                      |
| 9000 ppm | Mean | 2.49                 | 12.17                | 0.36                 | 0.22                 | 0.14                 | 0.09                 |
|          | SD   | 0.760                | 2.866                | 0.115                | 0.167                | 0.047                | 0.040                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |

Huntingdon Life Sciences Study No. 03-4242

Table 7 - Main Study

### Mean Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242

Table 7 - Main Study

Mean Hematology Values - Termination

| Group    |      | ANEU                 | ALYM                 | AMONO                | AEOS                 | ABASO                | ALUC                 |
|----------|------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|          |      | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL | x10 <sup>3</sup> /uL |
| 1F       |      |                      |                      |                      |                      |                      |                      |
| 0 ppm    | Mean | 2.18                 | 9.65                 | 0.26                 | 0.24                 | 0.13                 | 0.08                 |
|          | SD   | 0.488                | 2.756                | 0.070                | 0.090                | 0.045                | 0.033                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 2F       |      |                      |                      |                      |                      |                      |                      |
| 900 ppm  | Mean | 1.88                 | 10.91                | 0.26                 | 0.26                 | 0.14                 | 0.09                 |
|          | SD   | 0.397                | 2.407                | 0.083                | 0.116                | 0.040                | 0.043                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 3F       |      |                      |                      |                      |                      |                      |                      |
| 3000 ppm | Mean | 1.78                 | 9.82                 | 0.24                 | 0.23                 | 0.12                 | 0.08                 |
|          | SD   | 0.538                | 1.975                | 0.082                | 0.142                | 0.029                | 0.025                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |
| 4F       |      |                      |                      |                      |                      |                      |                      |
| 9000 ppm | Mean | 1.90                 | 8.49                 | 0.24                 | 0.28                 | 0.11                 | 0.06                 |
|          | SD   | 0.660                | 1.765                | 0.091                | 0.091                | 0.037                | 0.023                |
|          | n    | 12                   | 12                   | 12                   | 12                   | 12                   | 12                   |

|  |                                                  |         |
|--|--------------------------------------------------|---------|
|  | Mean Coagulation Values<br>Main Study<br>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. 03-4242

Table 8 - Main Study

Mean Coagulation Values - Termination

| Group    |      | PT      | APTT    |
|----------|------|---------|---------|
|          |      | Seconds | Seconds |
| 1M       |      |         |         |
| 0 ppm    | Mean | 13.7    | 22.3    |
|          | SD   | 0.87    | 1.93    |
|          | n    | 12      | 12      |
| 2M       |      |         |         |
| 900 ppm  | Mean | 13.6    | 23.4    |
|          | SD   | 0.81    | 1.81    |
|          | n    | 12      | 12      |
| 3M       |      |         |         |
| 3000 ppm | Mean | 13.8    | 22.8    |
|          | SD   | 0.90    | 1.72    |
|          | n    | 12      | 12      |
| 4M       |      |         |         |
| 9000 ppm | Mean | 13.6    | 23.3    |
|          | SD   | 0.90    | 2.04    |
|          | n    | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242

Table 8 - Main Study

Mean Coagulation Values - Termination

| Group    |      | PT      | APTT    |
|----------|------|---------|---------|
|          |      | Seconds | Seconds |
| 1F       |      |         |         |
| 0 ppm    | Mean | 12.0    | 19.8    |
|          | SD   | 0.62    | 1.54    |
|          | n    | 12      | 12      |
| 2F       |      |         |         |
| 900 ppm  | Mean | 12.1    | 20.0    |
|          | SD   | 0.82    | 2.32    |
|          | n    | 12      | 12      |
| 3F       |      |         |         |
| 3000 ppm | Mean | 11.8    | 20.1    |
|          | SD   | 0.50    | 1.73    |
|          | n    | 12      | 12      |
| 4F       |      |         |         |
| 9000 ppm | Mean | 11.9    | 20.7    |
|          | SD   | 0.55    | 2.46    |
|          | n    | 12      | 12      |

|  |                                                         |         |
|--|---------------------------------------------------------|---------|
|  | Mean Clinical Chemistry Values<br>Main Study<br>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 <sup>+</sup>  | Sodium                              | mEq/L           |
| K <sup>+</sup>   | Potassium                           | mEq/L           |
| Cl <sup>-</sup>  | Chloride                            | mEq/L           |
| Ca <sup>++</sup> | 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.

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Table 9 - Main Study  
Mean Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Table 9 - Main Study  
Mean Clinical Chemistry Values - Termination

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

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Table 9 - Main Study  
Mean Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Table 9 - Main Study  
Mean Clinical Chemistry Values - Termination

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

|  |                                             |          |
|--|---------------------------------------------|----------|
|  | Mean Organ Weights<br>Main Study<br>Preface | Table 10 |
|--|---------------------------------------------|----------|

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| % Organ to Brain Weight Ratios ..... | 93 |

**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 |

Huntingdon Life Sciences  
Princeton Research Center  
East Millstone, New Jersey

Summary statistics for absolute organ weights (g)  
Study number: 034242

Printed: 16-Mar-04  
Page: 1  
Version 4.2.2

## Terminal Sacrifice - Main Study

| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain<br>Epididymis Left | Epididymis Right | Heart  | Kidneys  | Liver   |
|---------------------|--------------------------|----------------|--------------------------|------------------|--------|----------|---------|
|                     |                          |                | Male                     | Animals          |        |          |         |
| 1                   |                          |                |                          |                  |        |          |         |
| Mean:               | 368.0                    | 0.0662         | 2.0631                   | 0.6029           | 0.6022 | 1.2755   | 3.1552  |
| Standard deviation: | 25.0                     | 0.0098         | 0.0865                   | 0.0724           | 0.0584 | 0.0637   | 0.2346  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)   | (12)     | (12)    |
| 2                   |                          |                |                          |                  |        |          |         |
| Mean:               | 369.6                    | 0.0721         | 2.0607                   | 0.6213           | 0.6377 | 1.2789   | 3.2459  |
| Standard deviation: | 24.5                     | 0.0141         | 0.0788                   | 0.0554           | 0.0559 | 0.1252   | 0.3172  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)   | (12)     | (12)    |
| 3                   |                          |                |                          |                  |        |          |         |
| Mean:               | 388.7                    | 0.0751         | 2.1650*                  | 0.6408           | 0.6478 | 1.3900\$ | 3.4607* |
| Standard deviation: | 23.0                     | 0.0120         | 0.0897                   | 0.0452           | 0.0408 | 0.0793   | 0.2814  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)   | (12)     | (12)    |
| 4                   |                          |                |                          |                  |        |          |         |
| Mean:               | 368.2                    | 0.0703         | 2.0788                   | 0.6125           | 0.6244 | 1.2939   | 3.2854  |
| Standard deviation: | 25.6                     | 0.0125         | 0.0755                   | 0.0682           | 0.0624 | 0.1421   | 0.2595  |
| Number of observ. : | (12)                     | (11)           | (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<br>Body wt. (g) | Lungs  | Spleen | Testis Left | Testis Right | Thymus |
|---------------------|--------------------------|--------|--------|-------------|--------------|--------|
| -----               |                          |        |        |             |              |        |
| Male Animals        |                          |        |        |             |              |        |
| 1                   |                          |        |        |             |              |        |
| Mean:               | 368.0                    | 1.9052 | 0.7028 | 1.5517      | 1.5398       | 0.5526 |
| Standard deviation: | 25.0                     | 0.2600 | 0.0941 | 0.1071      | 0.1105       | 0.1218 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |
| 2                   |                          |        |        |             |              |        |
| Mean:               | 369.6                    | 1.8961 | 0.7340 | 1.6114      | 1.6196       | 0.5813 |
| Standard deviation: | 24.5                     | 0.2383 | 0.0711 | 0.1141      | 0.1104       | 0.1235 |
| Number of observ. : | (12)                     | (11)   | (12)   | (12)        | (12)         | (12)   |
| 3                   |                          |        |        |             |              |        |
| Mean:               | 388.7                    | 1.9639 | 0.7950 | 1.6850+     | 1.6922+      | 0.6401 |
| Standard deviation: | 23.0                     | 0.1930 | 0.1005 | 0.0839      | 0.0915       | 0.1458 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |
| 4                   |                          |        |        |             |              |        |
| Mean:               | 368.2                    | 1.9802 | 0.7484 | 1.5808      | 1.5926       | 0.5747 |
| Standard deviation: | 25.6                     | 0.3602 | 0.1123 | 0.0799      | 0.0768       | 0.1166 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |

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| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain       | Heart         | Kidneys | Liver  | Lungs  | Ovary Left |
|---------------------|--------------------------|----------------|-------------|---------------|---------|--------|--------|------------|
| -----               |                          |                |             |               |         |        |        |            |
|                     |                          |                | F e m a l e | A n i m a l s |         |        |        |            |
| 1                   |                          |                |             |               |         |        |        |            |
| Mean:               | 235.9                    | 0.0742         | 2.0063      | 0.9227        | 2.1120  | 8.1589 | 1.6023 | 0.0754     |
| Standard deviation: | 14.2                     | 0.0079         | 0.0907      | 0.1030        | 0.2495  | 1.0008 | 0.2453 | 0.0102     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 2                   |                          |                |             |               |         |        |        |            |
| Mean:               | 239.7                    | 0.0800         | 1.9678      | 0.9481        | 2.1743  | 8.5485 | 1.4933 | 0.0698     |
| Standard deviation: | 11.1                     | 0.0120         | 0.0931      | 0.1147        | 0.1634  | 0.6893 | 0.1962 | 0.0163     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 3                   |                          |                |             |               |         |        |        |            |
| Mean:               | 249.7                    | 0.0761         | 2.0152      | 0.9666        | 2.2625  | 8.6244 | 1.5863 | 0.0765     |
| Standard deviation: | 19.7                     | 0.0071         | 0.1063      | 0.0934        | 0.1684  | 0.8292 | 0.2374 | 0.0135     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 4                   |                          |                |             |               |         |        |        |            |
| Mean:               | 236.4                    | 0.0758         | 1.9746      | 0.9253        | 2.1007  | 8.2600 | 1.5432 | 0.0763     |
| Standard deviation: | 16.9                     | 0.0086         | 0.0711      | 0.0662        | 0.1629  | 0.9688 | 0.1588 | 0.0188     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |

-----  
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| Group               | Terminal<br>Body wt. (g) | Ovary Right | Spleen      | Uterus w/vagina<br>Thymus |        |
|---------------------|--------------------------|-------------|-------------|---------------------------|--------|
| -----               |                          |             |             |                           |        |
|                     |                          |             | F e m a l e | A n i m a l s             |        |
| 1                   |                          |             |             |                           |        |
| M e a n:            | 235.9                    | 0.0712      | 0.5616      | 0.4489                    | 0.9799 |
| Standard deviation: | 14.2                     | 0.0093      | 0.0829      | 0.1139                    | 0.2977 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 2                   |                          |             |             |                           |        |
| M e a n:            | 239.7                    | 0.0681      | 0.5572      | 0.4776                    | 0.9303 |
| Standard deviation: | 11.1                     | 0.0101      | 0.0532      | 0.0891                    | 0.3015 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 3                   |                          |             |             |                           |        |
| M e a n:            | 249.7                    | 0.0737      | 0.5782      | 0.4874                    | 0.8965 |
| Standard deviation: | 19.7                     | 0.0137      | 0.0766      | 0.0988                    | 0.1846 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 4                   |                          |             |             |                           |        |
| M e a n:            | 236.4                    | 0.0715      | 0.5457      | 0.4721                    | 0.9756 |
| Standard deviation: | 16.9                     | 0.0128      | 0.0597      | 0.0882                    | 0.1843 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |

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| Terminal Sacrifice - Main Study |                          |                |         |                 |                  |        |         |        |  |
|---------------------------------|--------------------------|----------------|---------|-----------------|------------------|--------|---------|--------|--|
| Group                           | Terminal<br>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:                        | 368.0                    | 0.0180         | 0.5625  | 0.1642          | 0.1640           | 0.3480 | 0.8580  | 3.2796 |  |
| Standard deviation:             | 25.0                     | 0.0023         | 0.0369  | 0.0195          | 0.0156           | 0.0286 | 0.0441  | 0.3483 |  |
| Number of observ. :             | (12)                     | (12)           | (12)    | (12)            | (12)             | (12)   | (12)    | (12)   |  |
| 2                               |                          |                |         |                 |                  |        |         |        |  |
| M e a n:                        | 369.6                    | 0.0196         | 0.5592  | 0.1683          | 0.1728           | 0.3456 | 0.8779  | 3.2049 |  |
| Standard deviation:             | 24.5                     | 0.0042         | 0.0341  | 0.0133          | 0.0140           | 0.0174 | 0.0581  | 0.2466 |  |
| Number of observ. :             | (12)                     | (12)           | (12)    | (12)            | (12)             | (12)   | (12)    | (12)   |  |
| 3                               |                          |                |         |                 |                  |        |         |        |  |
| M e a n:                        | 388.7                    | 0.0193         | 0.5579  | 0.1655          | 0.1670           | 0.3583 | 0.8900  | 3.3258 |  |
| Standard deviation:             | 23.0                     | 0.0029         | 0.0225  | 0.0166          | 0.0122           | 0.0223 | 0.0444  | 0.2886 |  |
| Number of observ. :             | (12)                     | (12)           | (12)    | (12)            | (12)             | (12)   | (12)    | (12)   |  |
| 4                               |                          |                |         |                 |                  |        |         |        |  |
| M e a n:                        | 368.2                    | 0.0190         | 0.5663  | 0.1662          | 0.1697           | 0.3510 | 0.8930  | 3.2742 |  |
| Standard deviation:             | 25.6                     | 0.0027         | 0.0319  | 0.0126          | 0.0130           | 0.0232 | 0.0506  | 0.1937 |  |
| Number of observ. :             | (12)                     | (11)           | (12)    | (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 Dunnett's test of significance

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## Terminal Sacrifice - Main Study

| Group               | Terminal<br>Body wt. (g) | Lungs  | Spleen | Testis Left | Testis Right | Thymus |
|---------------------|--------------------------|--------|--------|-------------|--------------|--------|
| -----               |                          |        |        |             |              |        |
| Male Animals        |                          |        |        |             |              |        |
| 1                   |                          |        |        |             |              |        |
| Mean:               | 368.0                    | 0.5168 | 0.1914 | 0.4239      | 0.4205       | 0.1502 |
| Standard deviation: | 25.0                     | 0.0507 | 0.0260 | 0.0456      | 0.0438       | 0.0326 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |
| 2                   |                          |        |        |             |              |        |
| Mean:               | 369.6                    | 0.5115 | 0.1993 | 0.4373      | 0.4395       | 0.1589 |
| Standard deviation: | 24.5                     | 0.0465 | 0.0228 | 0.0377      | 0.0366       | 0.0399 |
| Number of observ. : | (12)                     | (11)   | (12)   | (12)        | (12)         | (12)   |
| 3                   |                          |        |        |             |              |        |
| Mean:               | 388.7                    | 0.5055 | 0.2046 | 0.4351      | 0.4367       | 0.1640 |
| Standard deviation: | 23.0                     | 0.0415 | 0.0234 | 0.0365      | 0.0343       | 0.0315 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |
| 4                   |                          |        |        |             |              |        |
| Mean:               | 368.2                    | 0.5364 | 0.2028 | 0.4308      | 0.4343       | 0.1565 |
| Standard deviation: | 25.6                     | 0.0822 | 0.0227 | 0.0322      | 0.0347       | 0.0322 |
| Number of observ. : | (12)                     | (12)   | (12)   | (12)        | (12)         | (12)   |

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| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain       | Heart         | Kidneys | Liver  | Lungs  | Ovary Left |
|---------------------|--------------------------|----------------|-------------|---------------|---------|--------|--------|------------|
| -----               |                          |                |             |               |         |        |        |            |
|                     |                          |                | F e m a l e | A n i m a l s |         |        |        |            |
| 1                   |                          |                |             |               |         |        |        |            |
| M e a n:            | 235.9                    | 0.0315         | 0.8523      | 0.3906        | 0.8935  | 3.4541 | 0.6787 | 0.0321     |
| Standard deviation: | 14.2                     | 0.0035         | 0.0455      | 0.0288        | 0.0655  | 0.2983 | 0.0852 | 0.0045     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 2                   |                          |                |             |               |         |        |        |            |
| M e a n:            | 239.7                    | 0.0335         | 0.8217      | 0.3955        | 0.9088  | 3.5725 | 0.6223 | 0.0293     |
| Standard deviation: | 11.1                     | 0.0054         | 0.0395      | 0.0451        | 0.0813  | 0.3346 | 0.0727 | 0.0077     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 3                   |                          |                |             |               |         |        |        |            |
| M e a n:            | 249.7                    | 0.0306         | 0.8109      | 0.3870        | 0.9096  | 3.4523 | 0.6335 | 0.0306     |
| Standard deviation: | 19.7                     | 0.0029         | 0.0666      | 0.0187        | 0.0816  | 0.1557 | 0.0597 | 0.0046     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |
| 4                   |                          |                |             |               |         |        |        |            |
| M e a n:            | 236.4                    | 0.0322         | 0.8379      | 0.3925        | 0.8897  | 3.4932 | 0.6534 | 0.0322     |
| Standard deviation: | 16.9                     | 0.0040         | 0.0457      | 0.0310        | 0.0494  | 0.3172 | 0.0572 | 0.0072     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)   | (12)   | (12)       |

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| Group               | Terminal<br>Body wt. (g) | Ovary Right | Spleen      | Uterus w/vagina<br>Thymus |        |
|---------------------|--------------------------|-------------|-------------|---------------------------|--------|
| -----               |                          |             |             |                           |        |
|                     |                          |             | F e m a l e | A n i m a l s             |        |
| 1                   |                          |             |             |                           |        |
| Mean:               | 235.9                    | 0.0301      | 0.2376      | 0.1900                    | 0.4154 |
| Standard deviation: | 14.2                     | 0.0027      | 0.0273      | 0.0440                    | 0.1221 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 2                   |                          |             |             |                           |        |
| Mean:               | 239.7                    | 0.0284      | 0.2326      | 0.1999                    | 0.3902 |
| Standard deviation: | 11.1                     | 0.0043      | 0.0222      | 0.0397                    | 0.1335 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 3                   |                          |             |             |                           |        |
| Mean:               | 249.7                    | 0.0294      | 0.2310      | 0.1945                    | 0.3639 |
| Standard deviation: | 19.7                     | 0.0040      | 0.0164      | 0.0321                    | 0.0926 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 4                   |                          |             |             |                           |        |
| Mean:               | 236.4                    | 0.0302      | 0.2310      | 0.1989                    | 0.4170 |
| Standard deviation: | 16.9                     | 0.0049      | 0.0213      | 0.0307                    | 0.0955 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |

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| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain<br>Epididymis Left | Epididymis Right | Heart   | Kidneys | Liver    |
|---------------------|--------------------------|----------------|--------------------------|------------------|---------|---------|----------|
| -----               |                          |                |                          |                  |         |         |          |
|                     |                          |                | M a l e                  | A n i m a l s    |         |         |          |
| 1                   |                          |                |                          |                  |         |         |          |
| M e a n:            | 368.0                    | 3.2172         | 100.0000                 | 29.2521          | 29.2379 | 61.8648 | 584.1524 |
| Standard deviation: | 25.0                     | 0.5207         | 0.0000                   | 3.5822           | 3.1837  | 2.9114  | 60.5683  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)    | (12)    | (12)     |
| 2                   |                          |                |                          |                  |         |         |          |
| M e a n:            | 369.6                    | 3.4979         | 100.0000                 | 30.1346          | 30.9427 | 62.0135 | 574.6399 |
| Standard deviation: | 24.5                     | 0.6546         | 0.0000                   | 2.2235           | 2.4201  | 4.9632  | 50.9548  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)    | (12)    | (12)     |
| 3                   |                          |                |                          |                  |         |         |          |
| M e a n:            | 388.7                    | 3.4767         | 100.0000                 | 29.6411          | 29.9599 | 64.2260 | 597.0335 |
| Standard deviation: | 23.0                     | 0.5909         | 0.0000                   | 2.3713           | 2.0916  | 3.0647  | 55.7252  |
| Number of observ. : | (12)                     | (12)           | (12)                     | (12)             | (12)    | (12)    | (12)     |
| 4                   |                          |                |                          |                  |         |         |          |
| M e a n:            | 368.2                    | 3.3753         | 100.0000                 | 29.4613          | 30.0312 | 62.1942 | 580.4666 |
| Standard deviation: | 25.6                     | 0.5641         | 0.0000                   | 3.0499           | 2.6808  | 5.7926  | 54.8955  |
| Number of observ. : | (12)                     | (11)           | (12)                     | (12)             | (12)    | (12)    | (12)     |

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| Group                      | Terminal<br>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:                   | 368.0                    | 92.4635 | 34.1077 | 75.3175     | 74.7137      | 26.7922 |
| Standard deviation:        | 25.0                     | 12.8475 | 4.7553  | 5.7673      | 5.5475       | 5.9555  |
| Number of observ. :        | (12)                     | (12)    | (12)    | (12)        | (12)         | (12)    |
| 2                          |                          |         |         |             |              |         |
| M e a n:                   | 369.6                    | 92.5803 | 35.7086 | 78.1924     | 78.5639      | 28.3305 |
| Standard deviation:        | 24.5                     | 11.4837 | 4.1782  | 4.6403      | 3.8681       | 6.5882  |
| Number of observ. :        | (12)                     | (11)    | (12)    | (12)        | (12)         | (12)    |
| 3                          |                          |         |         |             |              |         |
| M e a n:                   | 388.7                    | 90.6519 | 36.6645 | 78.0459     | 78.3823      | 29.4563 |
| Standard deviation:        | 23.0                     | 7.1794  | 3.7585  | 6.5544      | 6.7679       | 5.9068  |
| Number of observ. :        | (12)                     | (12)    | (12)    | (12)        | (12)         | (12)    |
| 4                          |                          |         |         |             |              |         |
| M e a n:                   | 368.2                    | 95.2561 | 35.9231 | 76.0970     | 76.6812      | 27.6399 |
| Standard deviation:        | 25.6                     | 16.8843 | 4.5793  | 4.0217      | 4.2542       | 5.4451  |
| Number of observ. :        | (12)                     | (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 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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Princeton Research Center  
East Millstone, New Jersey  
Terminal Sacrifice - Main Study

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

Printed: 16-Mar-04

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| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain       | Heart         | Kidneys  | Liver    | Lungs   | Ovary Left |
|---------------------|--------------------------|----------------|-------------|---------------|----------|----------|---------|------------|
| -----               |                          |                |             |               |          |          |         |            |
|                     |                          |                | F e m a l e | A n i m a l s |          |          |         |            |
| 1                   |                          |                |             |               |          |          |         |            |
| M e a n:            | 235.9                    | 3.7070         | 100.0000    | 45.9504       | 105.1337 | 406.2604 | 79.7636 | 3.7634     |
| Standard deviation: | 14.2                     | 0.4309         | 0.0000      | 4.1421        | 9.8509   | 41.1419  | 10.4229 | 0.5006     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)     | (12)     | (12)    | (12)       |
| 2                   |                          |                |             |               |          |          |         |            |
| M e a n:            | 239.7                    | 4.0766         | 100.0000    | 48.1266       | 110.7048 | 434.8648 | 75.7820 | 3.5550     |
| Standard deviation: | 11.1                     | 0.6538         | 0.0000      | 4.7793        | 9.6804   | 36.1015  | 8.3517  | 0.8568     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)     | (12)     | (12)    | (12)       |
| 3                   |                          |                |             |               |          |          |         |            |
| M e a n:            | 249.7                    | 3.7797         | 100.0000    | 47.9691       | 112.4532 | 428.8374 | 78.6186 | 3.8144     |
| Standard deviation: | 19.7                     | 0.3292         | 0.0000      | 3.8570        | 9.0692   | 43.7950  | 10.0412 | 0.7397     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)     | (12)     | (12)    | (12)       |
| 4                   |                          |                |             |               |          |          |         |            |
| M e a n:            | 236.4                    | 3.8401         | 100.0000    | 46.8566       | 106.4217 | 418.4969 | 78.1138 | 3.8622     |
| Standard deviation: | 16.9                     | 0.4455         | 0.0000      | 2.8581        | 7.7081   | 48.8393  | 7.2716  | 0.9298     |
| 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  
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East Millstone, New Jersey

Summary Statistics for % Organ to Brain Weight  
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Terminal Sacrifice - Main Study

| Group               | Terminal<br>Body wt. (g) | Ovary Right | Spleen      | Uterus w/vagina<br>Thymus |         |
|---------------------|--------------------------|-------------|-------------|---------------------------|---------|
| -----               |                          |             |             |                           |         |
|                     |                          |             | F e m a l e | A n i m a l s             |         |
| 1                   |                          |             |             |                           |         |
| Mean:               | 235.9                    | 3.5497      | 28.0095     | 22.3527                   | 48.9533 |
| Standard deviation: | 14.2                     | 0.4131      | 4.1045      | 5.3053                    | 15.3454 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)    |
| 2                   |                          |             |             |                           |         |
| Mean:               | 239.7                    | 3.4610      | 28.3171     | 24.3087                   | 47.5602 |
| Standard deviation: | 11.1                     | 0.4991      | 2.3132      | 4.5453                    | 16.3115 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)    |
| 3                   |                          |             |             |                           |         |
| Mean:               | 249.7                    | 3.6629      | 28.7288     | 24.1813                   | 44.7351 |
| Standard deviation: | 19.7                     | 0.6786      | 3.7279      | 4.7337                    | 10.3195 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)    |
| 4                   |                          |             |             |                           |         |
| Mean:               | 236.4                    | 3.6211      | 27.5938     | 23.8460                   | 49.6675 |
| Standard deviation: | 16.9                     | 0.6423      | 2.4519      | 4.0926                    | 10.7335 |
| 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<br>for Gross Necropsy Observations<br>Main Study<br>Preface | Table 11 |
|--|--------------------------------------------------------------------------------------|----------|

**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  
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 Terminal Sacrifice - Main Study

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:           | 12          | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Within normal limits ..... | 7           | 6  | 7  | 6  | 9             | 11 | 7  | 10 |
| Femur                      |             |    |    |    |               |    |    |    |
| Fracture .....             | 0           | 1  | 0  | 0  | 0             | 0  | 0  | 0  |
| Ileum                      |             |    |    |    |               |    |    |    |
| Abnormal Contents .....    | 1           | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| Kidneys                    |             |    |    |    |               |    |    |    |
| Dilated Pelvis .....       | 0           | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| Lungs                      |             |    |    |    |               |    |    |    |
| Discolored .....           | 4           | 5  | 5  | 6  | 1             | 1  | 3  | 2  |
| Extremity                  |             |    |    |    |               |    |    |    |
| hair thin/absent .....     | 0           | 0  | 0  | 0  | 2             | 0  | 2  | 0  |
| Skin (other)               |             |    |    |    |               |    |    |    |
| Hair Thin/Absent .....     | 0           | 0  | 0  | 0  | 1             | 0  | 0  | 0  |

|  |                                                                                            |          |
|--|--------------------------------------------------------------------------------------------|----------|
|  | Incidence Summary of Microscopic<br>Findings with Severity Levels<br>Main Study<br>Preface | Table 12 |
|--|--------------------------------------------------------------------------------------------|----------|

**Key to Abbreviations**

|      |   |                       |
|------|---|-----------------------|
| Ctls | = | Controls              |
| LN   | = | Lymph Node            |
| NAD  | = | No abnormal diagnoses |
| No.  | = | Number                |
| 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 |

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

Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                 |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|-------------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
|                                                 |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Controls from group(s): 1                       |  |               |    |    |    |               |    |    |    |
| Animal sex:                                     |  |               |    |    |    |               |    |    |    |
| Dosage group:                                   |  |               |    |    |    |               |    |    |    |
| Tissues With Diagnoses                          |  |               |    |    |    |               |    |    |    |
| No. in group:                                   |  |               |    |    |    |               |    |    |    |
| Number examined:                                |  |               |    |    |    |               |    |    |    |
| Adrenal Glands .....                            |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| INTERSTITIAL MONONUCLEAR CELL AGGREGATES        |  |               |    |    |    |               |    |    |    |
| 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  |
| CORTICAL VACUOLATION                            |  |               |    |    |    |               |    |    |    |
| 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  |
| Brain .....                                     |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEMORRHAGE                                      |  |               |    |    |    |               |    |    |    |
| Nad>                                            |  | 11            | 0  | 0  | 12 | 11            | 0  | 0  | 12 |
| Minimal>                                        |  | 1             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:       |  | 1             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| HEMORRHAGE/HEMATOCYST WITH FIBROUS ORGANIZATION |  |               |    |    |    |               |    |    |    |
| 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  |
| Cecum .....                                     |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| DILATED GLAND WITH CELLULAR DEBRIS              |  |               |    |    |    |               |    |    |    |
| Nad>                                            |  | 12            | 0  | 0  | 12 | 11            | 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  |
| CONGESTION/HEMORRHAGE                           |  |               |    |    |    |               |    |    |    |
| 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  |
| Cervical SC .....                               |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Number examined:                                |  |               |    |    |    |               |    |    |    |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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

Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                               |       | -- A n i m a l s -- |                 |    |    | A f f e c t e d --  |    |    |    |    |
|---------------------------------------------------------------|-------|---------------------|-----------------|----|----|---------------------|----|----|----|----|
| Controls from group(s): 1                                     |       | Animal sex:         | -- M a l e s -- |    |    | -- F e m a l e s -- |    |    |    |    |
| Dosage group:                                                 |       | Ctls                | 2               | 3  | 4  | Ctls 2 3 4          |    |    |    |    |
| T i s s u e s   W i t h   D i a g n o s e s                   |       | No. in group:       | 12              | 12 | 12 | 12                  | 12 | 12 | 12 |    |
| Colon                                                         | ..... | Number examined:    | 12              | 0  | 0  | 12                  | 12 | 0  | 0  | 12 |
| CONGESTION/HEMORRHAGE                                         |       |                     |                 |    |    |                     |    |    |    |    |
|                                                               |       | 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  |
| Duodenum                                                      | ..... | Number examined:    | 12              | 0  | 0  | 12                  | 12 | 0  | 0  | 12 |
| Epididymides                                                  | ..... | Number examined:    | 12              | 0  | 0  | 12                  |    |    |    |    |
| INTERSTITIAL MONONUCLEAR CELL AGGREGATES                      |       |                     |                 |    |    |                     |    |    |    |    |
|                                                               |       | Nad>                | 12              | 0  | 0  | 11                  |    |    |    |    |
|                                                               |       | Minimal>            | 0               | 0  | 0  | 1                   |    |    |    |    |
| .....Total Incidence of Finding Observed:                     |       |                     | 0               | 0  | 0  | 1                   |    |    |    |    |
| Extremity                                                     | ..... | Number examined:    | 1               | 0  | 0  | 0                   | 2  | 0  | 0  | 1  |
| FOLLICULAR HYPERKERATOSIS/HAIR SHAFT ABSENT/DECREASED IN SIZE |       |                     |                 |    |    |                     |    |    |    |    |
|                                                               |       | Nad>                | 1               | 0  | 0  | 0                   | 1  | 0  | 0  | 1  |
|                                                               |       | Slight>             | 0               | 0  | 0  | 0                   | 1  | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                     |       |                     | 0               | 0  | 0  | 0                   | 1  | 0  | 0  | 0  |
| EMPTY HAIR FOLLICLES/HAIR SHAFT ABSENT                        |       |                     |                 |    |    |                     |    |    |    |    |
|                                                               |       | Nad>                | 1               | 0  | 0  | 0                   | 1  | 0  | 0  | 1  |
|                                                               |       | Slight>             | 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                  | 11 | 0  | 0  | 12 |
| Femur                                                         | ..... | Number examined:    | 12              | 0  | 0  | 11                  | 11 | 0  | 0  | 12 |
| METAPHYSEAL CARTILAGINOUS ISLAND(S)                           |       |                     |                 |    |    |                     |    |    |    |    |
|                                                               |       | Nad>                | 12              | 0  | 0  | 10                  | 11 | 0  | 0  | 12 |
|                                                               |       | Slight>             | 0               | 0  | 0  | 1                   | 0  | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                     |       |                     | 0               | 0  | 0  | 1                   | 0  | 0  | 0  | 0  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                       |                  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|-------------------------------------------------------|------------------|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                             |                  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Tissues With Diagnoses                                |                  | Ctls          | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| No. in group:                                         |                  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Femur                                                 | Number examined: | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
| EPIPHYSEAL CARTILAGINOUS ISLAND(S)                    |                  |               |    |    |    |               |    |    |    |
|                                                       | Nad>             | 12            | 0  | 0  | 10 | 11            | 0  | 0  | 12 |
|                                                       | Slight>          | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:             |                  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Heart                                                 | Number examined: | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| INFLAMMATORY CELL FOCI                                |                  |               |    |    |    |               |    |    |    |
|                                                       | Nad>             | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
|                                                       | Minimal>         | 0             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:             |                  | 0             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| Ileum                                                 | Number examined: | 11            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Jejunum                                               | Number examined: | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Kidneys                                               | Number examined: | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| MEDULLA: MINERAL DEPOSIT(S)                           |                  |               |    |    |    |               |    |    |    |
|                                                       | Nad>             | 12            | 0  | 0  | 12 | 8             | 0  | 0  | 9  |
|                                                       | Minimal>         | 0             | 0  | 0  | 0  | 4             | 0  | 0  | 3  |
| .....Total Incidence of Finding Observed:             |                  | 0             | 0  | 0  | 0  | 4             | 0  | 0  | 3  |
| CORTEX/CORTICO-MEDULLARY JUNCTION: MINERAL DEPOSIT(S) |                  |               |    |    |    |               |    |    |    |
|                                                       | Nad>             | 12            | 0  | 0  | 12 | 10            | 0  | 0  | 9  |
|                                                       | Minimal>         | 0             | 0  | 0  | 0  | 1             | 0  | 0  | 2  |
|                                                       | Slight>          | 0             | 0  | 0  | 0  | 1             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:             |                  | 0             | 0  | 0  | 0  | 2             | 0  | 0  | 3  |
| CORTICAL TUBULAR MINERALIZATION                       |                  |               |    |    |    |               |    |    |    |
|                                                       | Nad>             | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 11 |
|                                                       | Minimal>         | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:             |                  | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                  |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|--------------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                        |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Animal sex:                                      |  | Ctl's         |    |    |    | Ctl's         |    |    |    |
| Dosage group:                                    |  | 2             | 3  | 4  |    | 2             | 3  | 4  |    |
| Tissues With Diagnoses                           |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| No. in group:                                    |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Kidneys .....                                    |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| CORTEX: CONVOLUTED TUBULAR EPITHELIUM-BASOPHILIC |  |               |    |    |    |               |    |    |    |
| Nad>                                             |  | 7             | 0  | 0  | 6  | 10            | 0  | 0  | 11 |
| Minimal>                                         |  | 5             | 0  | 0  | 6  | 2             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:        |  | 5             | 0  | 0  | 6  | 2             | 0  | 0  | 1  |
| INTERSTITIAL MONONUCLEAR CELL AGGREGATES         |  |               |    |    |    |               |    |    |    |
| Nad>                                             |  | 8             | 0  | 0  | 6  | 7             | 0  | 0  | 3  |
| Minimal>                                         |  | 3             | 0  | 0  | 5  | 5             | 0  | 0  | 8  |
| Slight>                                          |  | 1             | 0  | 0  | 1  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:        |  | 4             | 0  | 0  | 6  | 5             | 0  | 0  | 9  |
| EOSINOPHILIC TUBULAR CASTS                       |  |               |    |    |    |               |    |    |    |
| Nad>                                             |  | 12            | 0  | 0  | 9  | 12            | 0  | 0  | 10 |
| Minimal>                                         |  | 0             | 0  | 0  | 3  | 0             | 0  | 0  | 2  |
| .....Total Incidence of Finding Observed:        |  | 0             | 0  | 0  | 3  | 0             | 0  | 0  | 2  |
| DILATED PELVIS                                   |  |               |    |    |    |               |    |    |    |
| Nad>                                             |  | 12            | 0  | 0  | 12 | 11            | 0  | 0  | 12 |
| Present>                                         |  | 0             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:        |  | 0             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| Liver .....                                      |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEPATOCELLULAR NECROSIS/HEMORRHAGE               |  |               |    |    |    |               |    |    |    |
| 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  |
| SUBACUTE/CHRONIC INFLAMMATORY CELL FOCUS/FOCI    |  |               |    |    |    |               |    |    |    |
| Nad>                                             |  | 2             | 0  | 0  | 2  | 3             | 0  | 0  | 2  |
| Minimal>                                         |  | 9             | 0  | 0  | 10 | 9             | 0  | 0  | 10 |
| Slight>                                          |  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:        |  | 10            | 0  | 0  | 10 | 9             | 0  | 0  | 10 |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                            |               | -- Animals -- |    |    |    | Affected --   |    |    |    |
|------------------------------------------------------------|---------------|---------------|----|----|----|---------------|----|----|----|
|                                                            |               | -- Males --   |    |    |    | -- Females -- |    |    |    |
|                                                            |               | 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 |
| CENTRIOBULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE |               |               |    |    |    |               |    |    |    |
|                                                            | Nad>          | 3             | 0  | 0  | 3  | 1             | 0  | 0  | 1  |
|                                                            | Minimal>      | 9             | 0  | 0  | 8  | 10            | 0  | 0  | 11 |
|                                                            | Slight>       | 0             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                  |               | 9             | 0  | 0  | 9  | 11            | 0  | 0  | 11 |
| PERIPORTAL MONONUCLEAR CELL AGGREGATES                     |               |               |    |    |    |               |    |    |    |
|                                                            | Nad>          | 1             | 0  | 0  | 4  | 7             | 0  | 0  | 8  |
|                                                            | Minimal>      | 11            | 0  | 0  | 8  | 5             | 0  | 0  | 4  |
| .....Total Incidence of Finding Observed:                  |               | 11            | 0  | 0  | 8  | 5             | 0  | 0  | 4  |
| PERIPORTAL MICROGRANULOMA                                  |               |               |    |    |    |               |    |    |    |
|                                                            | Nad>          | 10            | 0  | 0  | 10 | 12            | 0  | 0  | 12 |
|                                                            | Slight>       | 1             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
|                                                            | Moderate>     | 1             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                  |               | 2             | 0  | 0  | 2  | 0             | 0  | 0  | 0  |
| SUBCAPSULAR SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE  |               |               |    |    |    |               |    |    |    |
|                                                            | 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  |
| FIBROUS TAGS                                               |               |               |    |    |    |               |    |    |    |
|                                                            | Nad>          | 11            | 0  | 0  | 9  | 12            | 0  | 0  | 10 |
|                                                            | Minimal>      | 1             | 0  | 0  | 3  | 0             | 0  | 0  | 1  |
|                                                            | Slight>       | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:                  |               | 1             | 0  | 0  | 3  | 0             | 0  | 0  | 2  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

Butane: Combined Repeated-Exposure Toxicity, Reproduction and  
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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                      |               | -- Animals -- |    |    |    | Affected --   |    |    |    |
|------------------------------------------------------|---------------|---------------|----|----|----|---------------|----|----|----|
|                                                      |               | -- Males --   |    |    |    | -- Females -- |    |    |    |
|                                                      |               | Ctls          | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| Tissues With Diagnoses                               | No. in group: | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Liver ..... SUBCAPSULAR HEMORRHAGE                   |               | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
|                                                      | 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  |
| Lumbar SC .....Number examined:                      |               | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Lungs .....Number examined:                          |               | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEMORRHAGE/CONGESTION/EDEMA                          |               |               |    |    |    |               |    |    |    |
|                                                      | Nad>          | 5             | 0  | 0  | 8  | 7             | 0  | 0  | 6  |
|                                                      | Minimal>      | 1             | 0  | 0  | 4  | 3             | 0  | 0  | 3  |
|                                                      | Slight>       | 5             | 0  | 0  | 0  | 1             | 0  | 0  | 3  |
|                                                      | Moderate>     | 1             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:            |               | 7             | 0  | 0  | 4  | 5             | 0  | 0  | 6  |
| SUBPLEURAL HEMORRHAGE/SUBACUTE INFLAMMATION/FIBROSIS |               |               |    |    |    |               |    |    |    |
|                                                      | Nad>          | 4             | 0  | 0  | 9  | 9             | 0  | 0  | 5  |
|                                                      | Minimal>      | 7             | 0  | 0  | 3  | 3             | 0  | 0  | 7  |
|                                                      | Slight>       | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:            |               | 8             | 0  | 0  | 3  | 3             | 0  | 0  | 7  |
| ARTERIAL MEDIAL HYPERTROPHY                          |               |               |    |    |    |               |    |    |    |
|                                                      | Nad>          | 0             | 0  | 0  | 2  | 1             | 0  | 0  | 1  |
|                                                      | Minimal>      | 8             | 0  | 0  | 8  | 8             | 0  | 0  | 7  |
|                                                      | Slight>       | 3             | 0  | 0  | 2  | 2             | 0  | 0  | 3  |
|                                                      | Moderate>     | 1             | 0  | 0  | 0  | 1             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:            |               | 12            | 0  | 0  | 10 | 11            | 0  | 0  | 11 |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                           |                                                                               | -- Animals --    |    |    |    | Affected --   |    |    |    |
|---------------------------|-------------------------------------------------------------------------------|------------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1 |                                                                               | -- Males --      |    |    |    | -- Females -- |    |    |    |
|                           |                                                                               | Ctlrs            |    |    |    | Ctlrs         |    |    |    |
| Tissues                   | With Diagnoses                                                                | No. in group     | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Lungs                     | PERIVASCULAR/PERIALVEOLAR SUBACUTE/CHRONIC INFLAMMATORY<br>-CELL FOCI         | Number examined: | 12 | 0  | 0  | 12            | 12 | 0  | 0  |
|                           | Nad>                                                                          |                  | 4  | 0  | 0  | 3             | 3  | 0  | 0  |
|                           | Minimal>                                                                      |                  | 7  | 0  | 0  | 9             | 8  | 0  | 0  |
|                           | Slight>                                                                       |                  | 1  | 0  | 0  | 0             | 0  | 0  | 0  |
|                           | Moderate>                                                                     |                  | 0  | 0  | 0  | 0             | 1  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                                          |                  | 8  | 0  | 0  | 9             | 9  | 0  | 0  |
|                           | PERIVASCULAR/SUBPLEURAL MICROGRANULOMA                                        |                  |    |    |    |               |    |    |    |
|                           | Nad>                                                                          |                  | 7  | 0  | 0  | 8             | 9  | 0  | 0  |
|                           | Minimal>                                                                      |                  | 5  | 0  | 0  | 4             | 3  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                                          |                  | 5  | 0  | 0  | 4             | 3  | 0  | 0  |
|                           | ALVEOLAR/INTRAALVEOLAR MACROPHAGES/GOLDEN BROWN<br>-PIGMENT-LADEN MACROPHAGES |                  |    |    |    |               |    |    |    |
|                           | Nad>                                                                          |                  | 0  | 0  | 0  | 2             | 0  | 0  | 0  |
|                           | Minimal>                                                                      |                  | 10 | 0  | 0  | 10            | 12 | 0  | 0  |
|                           | Slight>                                                                       |                  | 1  | 0  | 0  | 0             | 0  | 0  | 0  |
|                           | Moderate>                                                                     |                  | 1  | 0  | 0  | 0             | 0  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                                          |                  | 12 | 0  | 0  | 10            | 12 | 0  | 0  |
|                           | PERIBRONCHIAL/PERIVASCULAR LYMPHOID AGGREGATES                                |                  |    |    |    |               |    |    |    |
|                           | Nad>                                                                          |                  | 2  | 0  | 0  | 0             | 0  | 0  | 0  |
|                           | Minimal>                                                                      |                  | 3  | 0  | 0  | 3             | 4  | 0  | 0  |
|                           | Slight>                                                                       |                  | 6  | 0  | 0  | 7             | 7  | 0  | 0  |
|                           | Moderate>                                                                     |                  | 1  | 0  | 0  | 2             | 1  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                                          |                  | 10 | 0  | 0  | 12            | 12 | 0  | 0  |
|                           | VASCULAR MINERALIZATION                                                       |                  |    |    |    |               |    |    |    |
|                           | Nad>                                                                          |                  | 2  | 0  | 0  | 1             | 5  | 0  | 0  |
|                           | Minimal>                                                                      |                  | 10 | 0  | 0  | 11            | 6  | 0  | 0  |
|                           | Slight>                                                                       |                  | 0  | 0  | 0  | 0             | 1  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                                          |                  | 10 | 0  | 0  | 11            | 7  | 0  | 0  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                      |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|------------------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                            |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Animal sex:                                          |  |               |    |    |    |               |    |    |    |
| Dosage group:                                        |  |               |    |    |    |               |    |    |    |
| Tissues With Diagnoses                               |  | Ctl's 2 3 4   |    |    |    | Ctl's 2 3 4   |    |    |    |
| No. in group:                                        |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Mammary-protocol                                     |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| PROMINENT LUMINAL EOSINOPHILIC/BASOPHILIC SECRETIONS |  |               |    |    |    |               |    |    |    |
| Nad>                                                 |  | 5             | 0  | 0  | 6  | 12            | 0  | 0  | 12 |
| Present>                                             |  | 7             | 0  | 0  | 6  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:            |  | 7             | 0  | 0  | 6  | 0             | 0  | 0  | 0  |
| ACINAR EPITHELIAL VACUOLAR CHANGE                    |  |               |    |    |    |               |    |    |    |
| Nad>                                                 |  | 11            | 0  | 0  | 10 | 12            | 0  | 0  | 12 |
| Minimal>                                             |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Slight>                                              |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Moderate>                                            |  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:            |  | 1             | 0  | 0  | 2  | 0             | 0  | 0  | 0  |
| MONONUCLEAR CELL AGGREGATES                          |  |               |    |    |    |               |    |    |    |
| 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  |
| Mediastinal LN                                       |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 11 |
| HEMORRHAGE                                           |  |               |    |    |    |               |    |    |    |
| Nad>                                                 |  | 6             | 0  | 0  | 10 | 9             | 0  | 0  | 9  |
| Minimal>                                             |  | 0             | 0  | 0  | 0  | 1             | 0  | 0  | 0  |
| Slight>                                              |  | 2             | 0  | 0  | 0  | 0             | 0  | 0  | 2  |
| Moderate>                                            |  | 4             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:            |  | 6             | 0  | 0  | 1  | 2             | 0  | 0  | 2  |
| CONGESTION                                           |  |               |    |    |    |               |    |    |    |
| Nad>                                                 |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 10 |
| Slight>                                              |  | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:            |  | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                           |  | -- Animals -- |  |  |  | Affected --   |  |  |  |
|-------------------------------------------|--|---------------|--|--|--|---------------|--|--|--|
| Controls from group(s): 1                 |  | -- Males --   |  |  |  | -- Females -- |  |  |  |
| Animal sex:                               |  | Ctl's         |  |  |  | Ctl's         |  |  |  |
| Dosage group:                             |  | 2             |  |  |  | 2             |  |  |  |
| No. in group:                             |  | 12            |  |  |  | 12            |  |  |  |
| Tissues With Diagnoses                    |  | 12            |  |  |  | 12            |  |  |  |
| Mediastinal LN                            |  | 12            |  |  |  | 11            |  |  |  |
| FOLLICULAR LYMPHOID ACTIVITY              |  | 0             |  |  |  | 0             |  |  |  |
| Nad>                                      |  | 0             |  |  |  | 0             |  |  |  |
| Minimal>                                  |  | 10            |  |  |  | 4             |  |  |  |
| Slight>                                   |  | 2             |  |  |  | 4             |  |  |  |
| Moderate>                                 |  | 0             |  |  |  | 3             |  |  |  |
| .....Total Incidence of Finding Observed: |  | 12            |  |  |  | 11            |  |  |  |
| PARACORTICAL LYMPHOID ACTIVITY            |  | 3             |  |  |  | 3             |  |  |  |
| Minimal>                                  |  | 4             |  |  |  | 0             |  |  |  |
| Slight>                                   |  | 1             |  |  |  | 6             |  |  |  |
| Moderate>                                 |  | 4             |  |  |  | 2             |  |  |  |
| Marked>                                   |  | 0             |  |  |  | 0             |  |  |  |
| Severe>                                   |  | 12            |  |  |  | 11            |  |  |  |
| .....Total Incidence of Finding Observed: |  | 12            |  |  |  | 11            |  |  |  |
| SINUS HISTIOCYTES                         |  | 1             |  |  |  | 0             |  |  |  |
| Nad>                                      |  | 3             |  |  |  | 9             |  |  |  |
| Minimal>                                  |  | 6             |  |  |  | 2             |  |  |  |
| Slight>                                   |  | 2             |  |  |  | 0             |  |  |  |
| Moderate>                                 |  | 11            |  |  |  | 11            |  |  |  |
| .....Total Incidence of Finding Observed: |  | 11            |  |  |  | 11            |  |  |  |
| FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS     |  | 2             |  |  |  | 2             |  |  |  |
| Nad>                                      |  | 4             |  |  |  | 2             |  |  |  |
| Minimal>                                  |  | 5             |  |  |  | 6             |  |  |  |
| Slight>                                   |  | 1             |  |  |  | 1             |  |  |  |
| Moderate>                                 |  | 10            |  |  |  | 9             |  |  |  |
| .....Total Incidence of Finding Observed: |  | 10            |  |  |  | 9             |  |  |  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|------------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                      |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Animal sex:                                    |  |               |    |    |    |               |    |    |    |
| Dosage group:                                  |  |               |    |    |    |               |    |    |    |
| Tissues With Diagnoses                         |  |               |    |    |    |               |    |    |    |
| No. in group:                                  |  | Ctls          | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| Mediastinal LN                                 |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Number examined:                               |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 11 |
| RETICULOENDOTHELIAL CELL: GOLDEN-BROWN PIGMENT |  |               |    |    |    |               |    |    |    |
| Nad>                                           |  | 12            | 0  | 0  | 11 | 7             | 0  | 0  | 9  |
| Slight>                                        |  | 0             | 0  | 0  | 0  | 4             | 0  | 0  | 2  |
| Total Incidence of Finding Observed:           |  | 0             | 0  | 0  | 0  | 4             | 0  | 0  | 2  |
| SINUS EDEMA                                    |  |               |    |    |    |               |    |    |    |
| Nad>                                           |  | 5             | 0  | 0  | 4  | 6             | 0  | 0  | 5  |
| Minimal>                                       |  | 4             | 0  | 0  | 2  | 0             | 0  | 0  | 3  |
| Slight>                                        |  | 3             | 0  | 0  | 5  | 5             | 0  | 0  | 3  |
| Total Incidence of Finding Observed:           |  | 7             | 0  | 0  | 7  | 5             | 0  | 0  | 6  |
| MEDULLARY PLASMACYTOSIS                        |  |               |    |    |    |               |    |    |    |
| Nad>                                           |  | 3             | 0  | 0  | 4  | 6             | 0  | 0  | 6  |
| Minimal>                                       |  | 1             | 0  | 0  | 1  | 1             | 0  | 0  | 2  |
| Slight>                                        |  | 7             | 0  | 0  | 3  | 3             | 0  | 0  | 3  |
| Moderate>                                      |  | 1             | 0  | 0  | 3  | 1             | 0  | 0  | 0  |
| Total Incidence of Finding Observed:           |  | 9             | 0  | 0  | 7  | 5             | 0  | 0  | 5  |
| LYMPHOID DEPLETION                             |  |               |    |    |    |               |    |    |    |
| Nad>                                           |  | 12            | 0  | 0  | 10 | 11            | 0  | 0  | 11 |
| Moderate>                                      |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Total Incidence of Finding Observed:           |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Mesenteric LN                                  |  |               |    |    |    |               |    |    |    |
| Number examined:                               |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| FOLLICULAR LYMPHOID ACTIVITY                   |  |               |    |    |    |               |    |    |    |
| Minimal>                                       |  | 2             | 0  | 0  | 5  | 3             | 0  | 0  | 3  |
| Slight>                                        |  | 5             | 0  | 0  | 5  | 6             | 0  | 0  | 6  |
| Moderate>                                      |  | 3             | 0  | 0  | 1  | 2             | 0  | 0  | 3  |
| Marked>                                        |  | 2             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| Total Incidence of Finding Observed:           |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                |  | -- A n i m a l s -- |   |   |    | A f f e c t e d --  |   |   |    |
|------------------------------------------------|--|---------------------|---|---|----|---------------------|---|---|----|
| Controls from group(s): 1                      |  | -- M a l e s --     |   |   |    | -- F e m a l e s -- |   |   |    |
| T i s s u e s   W i t h   D i a g n o s e s    |  | C t l s   2   3   4 |   |   |    | C t l s   2   3   4 |   |   |    |
| Mesenteric LN .....                            |  | 12   12   12   12   |   |   |    | 12   12   12   12   |   |   |    |
| PARACORTICAL LYMPHOID ACTIVITY                 |  |                     |   |   |    |                     |   |   |    |
| .....Number examined:                          |  | 12                  | 0 | 0 | 12 | 12                  | 0 | 0 | 12 |
| Minimal>                                       |  | 1                   | 0 | 0 | 2  | 3                   | 0 | 0 | 3  |
| Slight>                                        |  | 2                   | 0 | 0 | 0  | 0                   | 0 | 0 | 0  |
| Moderate>                                      |  | 5                   | 0 | 0 | 5  | 2                   | 0 | 0 | 2  |
| Marked>                                        |  | 4                   | 0 | 0 | 5  | 7                   | 0 | 0 | 7  |
| .....Total Incidence of Finding Observed:      |  | 12                  | 0 | 0 | 12 | 12                  | 0 | 0 | 12 |
| SINUS HISTIOCYTES                              |  |                     |   |   |    |                     |   |   |    |
| Minimal>                                       |  | 1                   | 0 | 0 | 4  | 1                   | 0 | 0 | 1  |
| Slight>                                        |  | 8                   | 0 | 0 | 5  | 9                   | 0 | 0 | 7  |
| Moderate>                                      |  | 3                   | 0 | 0 | 3  | 2                   | 0 | 0 | 4  |
| .....Total Incidence of Finding Observed:      |  | 12                  | 0 | 0 | 12 | 12                  | 0 | 0 | 12 |
| SINUS EDEMA                                    |  |                     |   |   |    |                     |   |   |    |
| Nad>                                           |  | 4                   | 0 | 0 | 3  | 1                   | 0 | 0 | 1  |
| Minimal>                                       |  | 1                   | 0 | 0 | 0  | 2                   | 0 | 0 | 0  |
| Slight>                                        |  | 7                   | 0 | 0 | 8  | 7                   | 0 | 0 | 9  |
| Moderate>                                      |  | 0                   | 0 | 0 | 1  | 2                   | 0 | 0 | 2  |
| .....Total Incidence of Finding Observed:      |  | 8                   | 0 | 0 | 9  | 11                  | 0 | 0 | 11 |
| RETICULOENDOTHELIAL CELL: GOLDEN-BROWN PIGMENT |  |                     |   |   |    |                     |   |   |    |
| Nad>                                           |  | 10                  | 0 | 0 | 5  | 11                  | 0 | 0 | 10 |
| Minimal>                                       |  | 1                   | 0 | 0 | 3  | 1                   | 0 | 0 | 1  |
| Slight>                                        |  | 1                   | 0 | 0 | 4  | 0                   | 0 | 0 | 1  |
| .....Total Incidence of Finding Observed:      |  | 2                   | 0 | 0 | 7  | 1                   | 0 | 0 | 2  |
| FREE ERYTHROCYTES/ERYTHROPHAGOCYTOSIS          |  |                     |   |   |    |                     |   |   |    |
| Nad>                                           |  | 7                   | 0 | 0 | 7  | 11                  | 0 | 0 | 10 |
| Minimal>                                       |  | 4                   | 0 | 0 | 5  | 1                   | 0 | 0 | 2  |
| Moderate>                                      |  | 1                   | 0 | 0 | 0  | 0                   | 0 | 0 | 0  |
| .....Total Incidence of Finding Observed:      |  | 5                   | 0 | 0 | 5  | 1                   | 0 | 0 | 2  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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

Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                  |  | -- A n i m a l s -- |    |    |    | A f f e c t e d --  |    |    |    |
|--------------------------------------------------|--|---------------------|----|----|----|---------------------|----|----|----|
| Controls from group(s): 1                        |  | -- M a l e s --     |    |    |    | -- F e m a l e s -- |    |    |    |
| T i s s u e s   W i t h   D i a g n o s e s      |  | Ctls                | 2  | 3  | 4  | Ctls                | 2  | 3  | 4  |
| Mesenteric LN .....                              |  | 12                  | 12 | 12 | 12 | 12                  | 12 | 12 | 12 |
| MEDULLARY PLASMACYTOSIS                          |  |                     |    |    |    |                     |    |    |    |
| Number examined:                                 |  | 12                  | 0  | 0  | 12 | 12                  | 0  | 0  | 12 |
| Nad>                                             |  | 2                   | 0  | 0  | 6  | 9                   | 0  | 0  | 8  |
| Minimal>                                         |  | 5                   | 0  | 0  | 2  | 2                   | 0  | 0  | 3  |
| Slight>                                          |  | 4                   | 0  | 0  | 3  | 0                   | 0  | 0  | 1  |
| Moderate>                                        |  | 1                   | 0  | 0  | 1  | 1                   | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:        |  | 10                  | 0  | 0  | 6  | 3                   | 0  | 0  | 4  |
| Ovaries .....                                    |  |                     |    |    |    | 12                  | 0  | 0  | 12 |
| CONGESTION                                       |  |                     |    |    |    |                     |    |    |    |
| Nad>                                             |  |                     |    |    |    | 8                   | 0  | 0  | 7  |
| Slight>                                          |  |                     |    |    |    | 4                   | 0  | 0  | 2  |
| Moderate>                                        |  |                     |    |    |    | 0                   | 0  | 0  | 3  |
| .....Total Incidence of Finding Observed:        |  |                     |    |    |    | 4                   | 0  | 0  | 5  |
| Oviducts/Fallop .....                            |  |                     |    |    |    | 12                  | 0  | 0  | 12 |
| Number examined:                                 |  |                     |    |    |    |                     |    |    |    |
| Pancreas .....                                   |  | 1                   | 0  | 0  | 0  | 0                   | 0  | 0  | 0  |
| ISLETS: MONONUCLEAR CELL INFLAMMATORY INFILTRATE |  |                     |    |    |    |                     |    |    |    |
| Slight>                                          |  | 1                   | 0  | 0  | 0  | 0                   | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:        |  | 1                   | 0  | 0  | 0  | 0                   | 0  | 0  | 0  |
| Parathyroid .....                                |  | 12                  | 0  | 0  | 12 | 9                   | 0  | 0  | 11 |
| Number examined:                                 |  |                     |    |    |    |                     |    |    |    |
| Prostate .....                                   |  | 12                  | 0  | 0  | 12 |                     |    |    |    |
| LUMINAL CELLULAR DEBRIS                          |  |                     |    |    |    |                     |    |    |    |
| Nad>                                             |  | 11                  | 0  | 0  | 10 |                     |    |    |    |
| Minimal>                                         |  | 1                   | 0  | 0  | 1  |                     |    |    |    |
| Slight>                                          |  | 0                   | 0  | 0  | 1  |                     |    |    |    |
| .....Total Incidence of Finding Observed:        |  | 1                   | 0  | 0  | 2  |                     |    |    |    |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

Butane: Combined Repeated-Exposure Toxicity, Reproduction and  
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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                            |                  | -- Animals --   |    |    |    | A f f e c t e d --  |    |    |    |
|------------------------------------------------------------|------------------|-----------------|----|----|----|---------------------|----|----|----|
| Controls from group(s): 1                                  |                  | -- M a l e s -- |    |    |    | -- F e m a l e s -- |    |    |    |
| T i s s u e s   W i t h   D i a g n o s e s                |                  | Ctls            | 2  | 3  | 4  | Ctls                | 2  | 3  | 4  |
| No. in group:                                              |                  | 12              | 12 | 12 | 12 | 12                  | 12 | 12 | 12 |
| Prostate .....                                             | Number examined: | 12              | 0  | 0  | 12 |                     |    |    |    |
| INTERSTITIAL SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE |                  |                 |    |    |    |                     |    |    |    |
|                                                            | Nad>             | 7               | 0  | 0  | 8  |                     |    |    |    |
|                                                            | Minimal>         | 1               | 0  | 0  | 2  |                     |    |    |    |
|                                                            | Slight>          | 4               | 0  | 0  | 0  |                     |    |    |    |
|                                                            | Moderate>        | 0               | 0  | 0  | 2  |                     |    |    |    |
| .....Total Incidence of Finding Observed:                  |                  | 5               | 0  | 0  | 4  |                     |    |    |    |
| Rectum/Low Colon .....                                     | Number examined: | 12              | 0  | 0  | 12 | 12                  | 0  | 0  | 12 |
| CONGESTION/HEMORRHAGE                                      |                  |                 |    |    |    |                     |    |    |    |
|                                                            | 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  |
| Seminal vesicles .....                                     | Number examined: | 12              | 0  | 0  | 12 |                     |    |    |    |
| Skin (other) .....                                         | Number examined: | 0               | 0  | 0  | 0  | 1                   | 0  | 0  | 0  |
| EMPTY HAIR FOLLICLE                                        |                  |                 |    |    |    |                     |    |    |    |
|                                                            | Slight>          | 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  | 12 | 12                  | 0  | 0  | 12 |
| SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE              |                  |                 |    |    |    |                     |    |    |    |
|                                                            | Nad>             | 11              | 0  | 0  | 12 | 11                  | 0  | 0  | 12 |
|                                                            | Minimal>         | 1               | 0  | 0  | 0  | 1                   | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                  |                  | 1               | 0  | 0  | 0  | 1                   | 0  | 0  | 0  |
| Spleen .....                                               | Number examined: | 12              | 0  | 0  | 12 | 12                  | 0  | 0  | 12 |
| GOLDEN-BROWN PIGMENT                                       |                  |                 |    |    |    |                     |    |    |    |
|                                                            | Nad>             | 9               | 0  | 0  | 9  | 3                   | 0  | 0  | 1  |
|                                                            | Minimal>         | 3               | 0  | 0  | 3  | 9                   | 0  | 0  | 11 |
| .....Total Incidence of Finding Observed:                  |                  | 3               | 0  | 0  | 3  | 9                   | 0  | 0  | 11 |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                        |                  | -- Animals -- |   |   |    | Affected --   |   |   |    |
|----------------------------------------|------------------|---------------|---|---|----|---------------|---|---|----|
| Controls from group(s): 1              |                  | -- Males --   |   |   |    | -- Females -- |   |   |    |
| Tissues With Diagnoses                 |                  | Dosage group: |   |   |    | Dosage group: |   |   |    |
|                                        |                  | No. in group: |   |   |    | No. in group: |   |   |    |
|                                        |                  | Ctls          | 2 | 3 | 4  | Ctls          | 2 | 3 | 4  |
| Spleen                                 | Number examined: | 12            | 0 | 0 | 12 | 12            | 0 | 0 | 12 |
| EXTRAMEDULLARY HEMATOPOIESIS           |                  |               |   |   |    |               |   |   |    |
|                                        | Nad>             | 2             | 0 | 0 | 1  | 2             | 0 | 0 | 0  |
|                                        | Minimal>         | 10            | 0 | 0 | 11 | 10            | 0 | 0 | 12 |
| Total Incidence of Finding Observed:   |                  | 10            | 0 | 0 | 11 | 10            | 0 | 0 | 12 |
| CAPSULE FIBROSIS                       |                  |               |   |   |    |               |   |   |    |
|                                        | Nad>             | 10            | 0 | 0 | 12 | 12            | 0 | 0 | 11 |
|                                        | Slight>          | 2             | 0 | 0 | 0  | 0             | 0 | 0 | 1  |
| Total Incidence of Finding Observed:   |                  | 2             | 0 | 0 | 0  | 0             | 0 | 0 | 1  |
| Sternal Marrow                         | Number examined: | 12            | 0 | 0 | 12 | 12            | 0 | 0 | 12 |
| Sternum                                | Number examined: | 12            | 0 | 0 | 12 | 12            | 0 | 0 | 12 |
| PROMINENT CORTICAL HAVERSIAN SYSTEMS   |                  |               |   |   |    |               |   |   |    |
|                                        | Nad>             | 12            | 0 | 0 | 11 | 12            | 0 | 0 | 12 |
|                                        | Present>         | 0             | 0 | 0 | 1  | 0             | 0 | 0 | 0  |
| Total Incidence of Finding Observed:   |                  | 0             | 0 | 0 | 1  | 0             | 0 | 0 | 0  |
| Stomach                                | Number examined: | 12            | 0 | 0 | 12 | 12            | 0 | 0 | 12 |
| DILATED GLANDS                         |                  |               |   |   |    |               |   |   |    |
|                                        | Nad>             | 10            | 0 | 0 | 9  | 12            | 0 | 0 | 12 |
|                                        | Minimal>         | 2             | 0 | 0 | 3  | 0             | 0 | 0 | 0  |
| Total Incidence of Finding Observed:   |                  | 2             | 0 | 0 | 3  | 0             | 0 | 0 | 0  |
| Testes                                 | Number examined: | 12            | 0 | 0 | 12 |               |   |   |    |
| TUBULAR CELLULAR DEGENERATION/NECROSIS |                  |               |   |   |    |               |   |   |    |
|                                        | Nad>             | 10            | 0 | 0 | 12 |               |   |   |    |
|                                        | Slight>          | 2             | 0 | 0 | 0  |               |   |   |    |
| Total Incidence of Finding Observed:   |                  | 2             | 0 | 0 | 0  |               |   |   |    |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                           |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|-------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                 |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Animal sex:                               |  |               |    |    |    |               |    |    |    |
| Dosage group:                             |  | Ctl           |    |    |    | Ctl           |    |    |    |
| No. in group:                             |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Tissues With Diagnoses                    |  |               |    |    |    |               |    |    |    |
| Thoracic SC                               |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEMORRHAGE                                |  |               |    |    |    |               |    |    |    |
| Nad>                                      |  | 12            | 0  | 0  | 12 | 11            | 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  |
| Thymus                                    |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEMORRHAGE                                |  |               |    |    |    |               |    |    |    |
| Nad>                                      |  | 8             | 0  | 0  | 5  | 8             | 0  | 0  | 7  |
| Minimal>                                  |  | 3             | 0  | 0  | 6  | 4             | 0  | 0  | 4  |
| Slight>                                   |  | 1             | 0  | 0  | 1  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed: |  | 4             | 0  | 0  | 7  | 4             | 0  | 0  | 5  |
| Thyroid                                   |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| HEMORRHAGE/CONGESTION                     |  |               |    |    |    |               |    |    |    |
| Nad>                                      |  | 9             | 0  | 0  | 11 | 12            | 0  | 0  | 9  |
| Minimal>                                  |  | 3             | 0  | 0  | 1  | 0             | 0  | 0  | 2  |
| Slight>                                   |  | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed: |  | 3             | 0  | 0  | 1  | 0             | 0  | 0  | 3  |
| MONONUCLEAR CELL AGGREGATES               |  |               |    |    |    |               |    |    |    |
| Nad>                                      |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
| Minimal>                                  |  | 0             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed: |  | 0             | 0  | 0  | 1  | 1             | 0  | 0  | 0  |
| LYMPHOID NODULE                           |  |               |    |    |    |               |    |    |    |
| Nad>                                      |  | 12            | 0  | 0  | 11 | 12            | 0  | 0  | 12 |
| Slight>                                   |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed: |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                                           |  | -- Animals -- |    |    |    | Affected --   |    |    |    |
|-----------------------------------------------------------|--|---------------|----|----|----|---------------|----|----|----|
| Controls from group(s): 1                                 |  | -- Males --   |    |    |    | -- Females -- |    |    |    |
| Animal sex:                                               |  |               |    |    |    |               |    |    |    |
| Dosage group:                                             |  |               |    |    |    |               |    |    |    |
| No. in group:                                             |  | Ctls          | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| Tissues With Diagnoses                                    |  | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Tibia .....Number examined:                               |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
| SUBCHONDRAL/SUBFIBROUS BONE: FIBROUS CYST                 |  |               |    |    |    |               |    |    |    |
| Nad>                                                      |  | 9             | 0  | 0  | 9  | 9             | 0  | 0  | 10 |
| Minimal>                                                  |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 0  |
| Moderate>                                                 |  | 3             | 0  | 0  | 0  | 2             | 0  | 0  | 1  |
| Marked>                                                   |  | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 1  |
| .....Total Incidence of Finding Observed:                 |  | 3             | 0  | 0  | 2  | 2             | 0  | 0  | 2  |
| PROMINENT LARGE SUBCHONDRAL ARTERIES                      |  |               |    |    |    |               |    |    |    |
| Nad>                                                      |  | 11            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
| Marked>                                                   |  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| .....Total Incidence of Finding Observed:                 |  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| Tibial Marrow .....Number examined:                       |  | 12            | 0  | 0  | 11 | 11            | 0  | 0  | 12 |
| Tibial Nerve .....Number examined:                        |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Trachea .....Number examined:                             |  | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| MUCOSAL EPITHELIAL EOSINOPHILIC DROPLETS/INCLUSION BODIES |  |               |    |    |    |               |    |    |    |
| Nad>                                                      |  | 12            | 0  | 0  | 10 | 10            | 0  | 0  | 7  |
| Minimal>                                                  |  | 0             | 0  | 0  | 2  | 2             | 0  | 0  | 3  |
| Slight>                                                   |  | 0             | 0  | 0  | 0  | 0             | 0  | 0  | 2  |
| .....Total Incidence of Finding Observed:                 |  | 0             | 0  | 0  | 2  | 2             | 0  | 0  | 5  |
| GLANDULAR DILATATION                                      |  |               |    |    |    |               |    |    |    |
| Nad>                                                      |  | 2             | 0  | 0  | 4  | 2             | 0  | 0  | 4  |
| Minimal>                                                  |  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| Slight>                                                   |  | 6             | 0  | 0  | 4  | 7             | 0  | 0  | 6  |
| Moderate>                                                 |  | 3             | 0  | 0  | 4  | 3             | 0  | 0  | 2  |
| .....Total Incidence of Finding Observed:                 |  | 10            | 0  | 0  | 8  | 10            | 0  | 0  | 8  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                           |                                                          | -- Animals -- |    |    |    | Affected --   |    |    |    |
|---------------------------|----------------------------------------------------------|---------------|----|----|----|---------------|----|----|----|
|                           |                                                          | -- Males --   |    |    |    | -- Females -- |    |    |    |
|                           |                                                          | Ctls          | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| Tissues With Diagnoses    | Dosage group:<br>No. in group:                           | 12            | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| Controls from group(s): 1 | Animal sex:                                              |               |    |    |    |               |    |    |    |
|                           | Number examined:                                         | 12            | 0  | 0  | 12 | 12            | 0  | 0  | 12 |
| Trachea                   | SUBMUCOSAL SUBACUTE/CHRONIC INFLAMMATORY CELL INFILTRATE |               |    |    |    |               |    |    |    |
|                           | Nad>                                                     | 5             | 0  | 0  | 6  | 6             | 0  | 0  | 6  |
|                           | Minimal>                                                 | 7             | 0  | 0  | 3  | 4             | 0  | 0  | 3  |
|                           | Slight>                                                  | 0             | 0  | 0  | 2  | 2             | 0  | 0  | 2  |
|                           | Moderate>                                                | 0             | 0  | 0  | 1  | 0             | 0  | 0  | 1  |
|                           | Total Incidence of Finding Observed:                     | 7             | 0  | 0  | 6  | 6             | 0  | 0  | 6  |
|                           | SUBMUCOSAL FIBROUS/CART EMBOLUS                          |               |    |    |    |               |    |    |    |
|                           | 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  |
| Urinary bladder           | Number examined:                                         | 12            | 0  | 0  | 12 | 11            | 0  | 0  | 12 |
|                           | MINERAL DEPOSIT                                          |               |    |    |    |               |    |    |    |
|                           | Nad>                                                     | 11            | 0  | 0  | 12 | 11            | 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  |
|                           | LUMENAL DISTENSION                                       |               |    |    |    |               |    |    |    |
|                           | Nad>                                                     | 11            | 0  | 0  | 12 | 11            | 0  | 0  | 12 |
|                           | Marked>                                                  | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                     | 1             | 0  | 0  | 0  | 0             | 0  | 0  | 0  |
| Uterus                    | Number examined:                                         |               |    |    |    | 12            | 0  | 0  | 12 |
|                           | LUMENAL DISTENSION                                       |               |    |    |    |               |    |    |    |
|                           | Nad>                                                     |               |    |    |    | 11            | 0  | 0  | 10 |
|                           | Moderate>                                                |               |    |    |    | 0             | 0  | 0  | 2  |
|                           | Marked>                                                  |               |    |    |    | 1             | 0  | 0  | 0  |
|                           | Total Incidence of Finding Observed:                     |               |    |    |    | 1             | 0  | 0  | 2  |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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Incidence Summary of Microscopic Findings with Severity Levels  
Terminal Sacrifice

|                                           |  | -- Animals       |    |    |    | Affected --   |    |    |    |
|-------------------------------------------|--|------------------|----|----|----|---------------|----|----|----|
|                                           |  | -- Males --      |    |    |    | -- Females -- |    |    |    |
|                                           |  | Dosage group:    |    |    |    | Dosage group: |    |    |    |
| Tissues With Diagnoses                    |  | No. in group:    |    |    |    | No. in group: |    |    |    |
|                                           |  | Ctls             | 2  | 3  | 4  | Ctls          | 2  | 3  | 4  |
| Uterus .....                              |  | 12               | 12 | 12 | 12 | 12            | 12 | 12 | 12 |
| GLANDULAR DILATATION                      |  | Number examined: |    |    |    | 12            | 0  | 0  | 12 |
|                                           |  | Nad>             |    |    |    | 11            | 0  | 0  | 10 |
|                                           |  | Slight>          |    |    |    | 1             | 0  | 0  | 2  |
| .....Total Incidence of Finding Observed: |  |                  |    |    |    | 1             | 0  | 0  | 2  |
| Vagina .....                              |  | Number examined: |    |    |    | 12            | 0  | 0  | 12 |

All Diagnoses; Phases: P2; Death types: All; Date of death range: 29-Oct-03 To 30-Oct-03

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SATELLITE STUDY

TABLE 13

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

## SUMMARY OF SURVIVAL AND PREGNANCY

| DOSE GROUP<br>DOSE LEVEL (PPM) |   | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|--------------------------------|---|--------|----------|-----------|-----------|
| No. of females cohabitated     | N | 12     | 12       | 12        | 12        |
| - Without evidence of mating   | N | 0      | 0        | 0         | 1         |
| Pregnant                       | N | 0      | 0        | 0         | 1         |
| Nonpregnant                    | N | 0      | 0        | 0         | 0         |
| Pregnant                       | N | 12     | 12       | 12        | 12        |
| - 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      | 0        | 0         | 0         |
| - 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     | 12       | 12        | 12        |
| - With liveborn pups           | N | 12     | 12       | 12        | 12        |
|                                | % | 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<br>Satellite Study<br>Preface | Table 14 |
|--|----------------------------------------------------------------|----------|

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

Note: Observations for all animals in groups 1-3 and most of group 4, for study Days 21-35, can be found in gestation observation tables.

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TABLE 14

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

FEMALES SUMMARY OF CLINICAL OBSERVATIONS

|                       | GROUP# | DAY OF STUDY |    |    |    |    |    |    | TOTAL |
|-----------------------|--------|--------------|----|----|----|----|----|----|-------|
|                       |        | -7           | 0  | 7  | 14 | 21 | 28 | 35 |       |
| # OF ANIMALS EXAMINED | 1      | 12           | 12 | 12 | 12 | 0  | 0  | 0  |       |
|                       | 2      | 12           | 12 | 12 | 12 | 0  | 0  | 0  |       |
|                       | 3      | 12           | 12 | 12 | 12 | 0  | 0  | 0  |       |
|                       | 4      | 12           | 12 | 12 | 12 | 1  | 1  | 1  |       |
| Normal                |        |              |    |    |    |    |    |    |       |
| WITHIN NORMAL LIMITS  | 1      | 12           | 12 | 12 | 10 | 0  | 0  | 0  | 12    |
|                       | 2      | 12           | 12 | 12 | 9  | 0  | 0  | 0  | 12    |
|                       | 3      | 12           | 12 | 12 | 11 | 0  | 0  | 0  | 12    |
|                       | 4      | 12           | 12 | 12 | 10 | 1  | 1  | 1  | 12    |
| Dermal-General        |        |              |    |    |    |    |    |    |       |
| ALOPECIA -            | 1      | 0            | 0  | 0  | 2  | 0  | 0  | 0  | 2     |
| EXTREMITIES/SNOUT     | 2      | 0            | 0  | 0  | 3  | 0  | 0  | 0  | 3     |
|                       | 3      | 0            | 0  | 0  | 1  | 0  | 0  | 0  | 1     |
|                       | 4      | 0            | 0  | 0  | 2  | 0  | 0  | 0  | 2     |

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TABLE 15

BUTANE: 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         | 40/10 | 35/ 9 | 41/11 | 36/ 9 |
| Dermal-General               |       |       |       |       |
| -----                        |       |       |       |       |
| ALOPECIA - EXTREMITIES/SNOUT | 8/ 2  | 12/ 3 | 4/ 1  | 8/ 2  |
| SCABS                        | 0/ 0  | 0/ 0  | 3/ 1  | 0/ 0  |
| ALOPECIA - GENERAL           | 0/ 0  | 0/ 0  | 0/ 0  | 5/ 2  |

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TABLE 16

BUTANE: 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<br>DOSE LEVEL (PPM)    | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|-----------------------------------|--------|----------|-----------|-----------|
| DAY 0 to 4                        |        |          |           |           |
| Normal                            |        |          |           |           |
| WITHIN NORMAL LIMITS              | 23/ 9  | 21/ 9    | 26/11     | 16/ 8     |
| TERMINAL SACRIFICE                | 12/12  | 12/12    | 12/12     | 12/12     |
| Gen. Appearance                   |        |          |           |           |
| RED EXUDATE FROM ANO-GENITAL AREA | 1/ 1   | 0/ 0     | 0/ 0      | 0/ 0      |
| Dermal-General                    |        |          |           |           |
| ALOPECIA - EXTREMITIES/SNOUT      | 6/ 3   | 9/ 4     | 2/ 1      | 10/ 5     |
| SCABS                             | 0/ 0   | 0/ 0     | 3/ 2      | 0/ 0      |
| ALOPECIA - GENERAL                | 0/ 0   | 0/ 0     | 0/ 0      | 8/ 3      |
| RED/BROWN STAINS AG AREA          | 0/ 0   | 2/ 2     | 1/ 1      | 3/ 3      |
| Oral/Buccal                       |        |          |           |           |
| INCISORS BROKEN/MISSING           | 0/ 0   | 0/ 0     | 0/ 0      | 2/ 1      |

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SATELLITE STUDY

TABLE 17

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

| FEMALES                        |  |      | PREMATING MEAN BODY WEIGHT VALUES (GRAMS) |          |           |           |
|--------------------------------|--|------|-------------------------------------------|----------|-----------|-----------|
| DOSE GROUP<br>DOSE LEVEL (PPM) |  |      | 1<br>0                                    | 2<br>900 | 3<br>3000 | 4<br>9000 |
| DAY -7                         |  | MEAN | 163                                       | 163      | 163       | 163       |
|                                |  | S.D. | 6.0                                       | 6.8      | 6.2       | 6.5       |
|                                |  | N    | 12                                        | 12       | 12        | 12        |
| DAY 0                          |  | MEAN | 198                                       | 202      | 197       | 204       |
|                                |  | S.D. | 11.9                                      | 10.6     | 9.8       | 11.7      |
|                                |  | N    | 12                                        | 12       | 12        | 12        |
| DAY 4                          |  | MEAN | 207                                       | 211      | 208       | 213       |
|                                |  | S.D. | 16.2                                      | 10.7     | 10.0      | 13.0      |
|                                |  | N    | 12                                        | 12       | 12        | 12        |
| DAY 7                          |  | MEAN | 214                                       | 216      | 217       | 221       |
|                                |  | S.D. | 15.5                                      | 13.1     | 9.1       | 13.0      |
|                                |  | N    | 12                                        | 12       | 12        | 12        |
| DAY 11                         |  | MEAN | 226                                       | 228      | 231       | 232       |
|                                |  | S.D. | 18.3                                      | 13.8     | 9.0       | 14.8      |
|                                |  | N    | 12                                        | 12       | 12        | 12        |
| DAY 14                         |  | MEAN | 228                                       | 236      | 235       | 237       |
|                                |  | S.D. | 17.9                                      | 14.4     | 9.2       | 16.9      |
|                                |  | N    | 12                                        | 12       | 12        | 12        |

No statistically significant differences

TABLE 18

## FEMALES

## PREMATING MEAN BODY WEIGHT GAIN (GRAMS)

No statistically significant differences

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TABLE 19

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

## SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

| DOSE GROUP<br>DOSE LEVEL (PPM) |      | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|--------------------------------|------|--------|----------|-----------|-----------|
| DAY 0                          | MEAN | 235    | 238      | 240       | 243       |
|                                | S.D. | 20.6   | 17.1     | 11.8      | 16.4      |
|                                | N    | 12     | 12       | 12        | 11        |
| DAY 7                          | MEAN | 269    | 274      | 281       | 279       |
|                                | S.D. | 22.4   | 17.8     | 17.4      | 20.9      |
|                                | N    | 12     | 12       | 12        | 11        |
| DAY 14                         | MEAN | 305    | 310      | 324       | 315       |
|                                | S.D. | 23.9   | 18.7     | 24.6      | 25.1      |
|                                | N    | 12     | 12       | 12        | 11        |
| DAY 20                         | MEAN | 372    | 380      | 401       | 385       |
|                                | S.D. | 27.9   | 27.6     | 28.9      | 27.5      |
|                                | N    | 12     | 12       | 12        | 11        |

-----  
No statistically significant differences

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TABLE 20

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

## SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)

| DOSE GROUP<br>DOSE LEVEL (PPM) |      | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|--------------------------------|------|--------|----------|-----------|-----------|
| DAYS 0 TO 7                    | MEAN | 35     | 36       | 41        | 36        |
|                                | S.D. | 8.0    | 6.5      | 8.7       | 7.1       |
|                                | N    | 12     | 12       | 12        | 11        |
| DAYS 7 TO 14                   | MEAN | 36     | 35       | 43*       | 35        |
|                                | S.D. | 5.3    | 4.9      | 8.5       | 6.3       |
|                                | N    | 12     | 12       | 12        | 11        |
| DAYS 14 TO 20                  | MEAN | 67     | 71       | 78        | 71        |
|                                | S.D. | 9.9    | 12.2     | 8.6       | 8.8       |
|                                | N    | 12     | 12       | 12        | 11        |
| DAYS 0 TO 20                   | MEAN | 137    | 142      | 161**     | 142       |
|                                | S.D. | 15.1   | 20.1     | 20.9      | 13.7      |
|                                | N    | 12     | 12       | 12        | 11        |

Statistical key: \* = p<0.05 \*\* = p<0.01

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TABLE 21

BUTANE: 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 | 269  | 273  | 287  | 284  |
|                  | S.D. | 24.0 | 23.1 | 21.7 | 18.5 |
|                  | N    | 12   | 12   | 12   | 12   |
| DAY 4            | MEAN | 283  | 291  | 295  | 291  |
|                  | S.D. | 22.5 | 20.4 | 25.5 | 21.2 |
|                  | N    | 12   | 12   | 12   | 12   |

No statistically significant differences

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TABLE 22

BUTANE: 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 | 14   | 18  | 8    | 6    |
|                  | S.D. | 10.8 | 8.6 | 13.7 | 7.5  |
|                  | N    | 12   | 12  | 12   | 12   |

No statistically significant differences

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TABLE 23

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

| FEMALES          |      |  | PREMATING MEAN FEED CONSUMPTION (GRAMS/KG/DAY) |     |      |      |
|------------------|------|--|------------------------------------------------|-----|------|------|
|                  |      |  | 1                                              | 2   | 3    | 4    |
| DOSE GROUP       |      |  | 0                                              | 900 | 3000 | 9000 |
| DOSE LEVEL (PPM) |      |  |                                                |     |      |      |
| DAY 0            | MEAN |  | 99                                             | 104 | 102  | 103  |
|                  | S.D. |  | 5.2                                            | 4.7 | 5.6  | 5.6  |
|                  | N    |  | 11                                             | 12  | 12   | 11   |
| DAY 7            | MEAN |  | 87                                             | 87  | 89   | 88   |
|                  | S.D. |  | 3.8                                            | 3.2 | 4.8  | 4.7  |
|                  | N    |  | 12                                             | 12  | 12   | 11   |
| DAY 14           | MEAN |  | 83                                             | 84  | 85   | 84   |
|                  | S.D. |  | 5.7                                            | 4.1 | 3.7  | 4.0  |
|                  | N    |  | 12                                             | 12  | 12   | 12   |

No statistically significant differences

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SATELLITE STUDY

TABLE 24

BUTANE: 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 | 84  | 79   | 87   | 86   |
|                  | S.D. | 6.3 | 19.9 | 7.8  | 4.8  |
|                  | N    | 12  | 11   | 12   | 11   |
| DAYS 7 TO 14     | MEAN | 79  | 80   | 83   | 81   |
|                  | S.D. | 3.0 | 4.3  | 3.8  | 4.9  |
|                  | N    | 12  | 12   | 11   | 11   |
| DAYS 14 TO 20    | MEAN | 68  | 69   | 71   | 69   |
|                  | S.D. | 3.5 | 4.5  | 3.9  | 3.0  |
|                  | N    | 12  | 12   | 12   | 10   |

No statistically significant differences

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TABLE 25

BUTANE: 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 | 110  | 118  | 104  | 103  |
|                  | S.D. | 14.0 | 17.5 | 13.7 | 19.7 |
|                  | N    | 12   | 12   | 12   | 12   |

No statistically significant differences

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TABLE 26

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

|                                            |      | SUMMARY OF COHABITATION DATA |       |       |       |
|--------------------------------------------|------|------------------------------|-------|-------|-------|
| DOSE GROUP                                 |      | 1                            | 2     | 3     | 4     |
| DOSE LEVEL (PPM)                           |      | 0                            | 900   | 3000  | 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                           | 12    | 12    | 12    |
| female fertility index                     | %    | 100.0                        | 100.0 | 100.0 | 100.0 |
| pregnancy index                            | %    | 100.0                        | 100.0 | 100.0 | 100.0 |
| 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                           | 12    | 12    | 12    |
| male fertility index                       | %    | 100.0                        | 100.0 | 100.0 | 100.0 |
| Females with defined<br>day 0 of Gestation | N    | 12                           | 12    | 12    | 11    |
| No. of days until Mating                   | MEAN | 3.0                          | 3.4   | 2.8   | 3.0   |
|                                            | S.D. | 1.35                         | 2.27  | 1.22  | 1.34  |
| Day 1 to 4                                 | N    | 11                           | 9     | 12    | 11    |
|                                            | %    | 91.7                         | 75.0  | 100.0 | 100.0 |
| Day 5 to 8                                 | N    | 1                            | 3     | 0     | 0     |
|                                            | %    | 8.3                          | 25.0  | 0.0   | 0.0   |
| Day 9 to 14                                | N    | 0                            | 0     | 0     | 0     |
|                                            | %    | 0.0                          | 0.0   | 0.0   | 0.0   |

No statistically significant differences

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TABLE 27

BUTANE: 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  |
| 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    | 12    | 12    | 12    |
| Female Fertility Index                      | %    | 100.0 | 100.0 | 100.0 | 100.0 |
| Females with Liveborn                       | N    | 12    | 12    | 12    | 12    |
| Gestation Index                             | %    | 100.0 | 100.0 | 100.0 | 100.0 |
| Females Completing Delivery                 | N    | 12    | 12    | 12    | 12    |
|                                             | %    | 100.0 | 100.0 | 100.0 | 100.0 |
| with Stillborn Pups                         | N    | 0     | 1     | 1     | 3     |
|                                             | %    | 0.0   | 8.3   | 8.3   | 25.0  |
| with all Stillborn                          | N    | 0     | 0     | 0     | 0     |
|                                             | %    | 0.0   | 0.0   | 0.0   | 0.0   |
| Litters with Liveborn,<br>but no Pups Alive |      |       |       |       |       |
| day 4                                       | N    | 0     | 0     | 0     | 0     |
|                                             | %    | 0.0   | 0.0   | 0.0   | 0.0   |
| Duration of Gestation                       | MEAN | 21.3  | 21.3  | 21.4  | 21.5  |
|                                             | S.D. | 0.49  | 0.65  | 0.51  | 0.52  |
|                                             | N    | 12    | 12    | 12    | 11    |

No statistically significant differences

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TABLE 27

BUTANE: 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    | 12    | 12   | 12   |
| Pups Delivered (total)                            | N    | 166   | 188   | 183  | 178  |
|                                                   | MEAN | 13.8  | 15.7* | 15.3 | 14.8 |
|                                                   | S.D. | 2.08  | 1.07  | 1.54 | 1.03 |
| Liveborn                                          | N    | 166   | 187   | 182  | 175  |
| Live Birth Index                                  | %    | 100.0 | 99.5  | 99.5 | 98.3 |
| Stillborn                                         | N    | 0     | 1     | 1    | 3    |
|                                                   | %    | 0.0   | 0.5   | 0.5  | 1.7  |
| Liveborn, not culled<br>prior to day 4            | N    | 166   | 187   | 182  | 175  |
| Pups Dying, Missing, and/or Cannibalized<br>day 0 | N    | 2     | 1     | 2    | 1    |
|                                                   | %    | 1.2   | 0.5   | 1.1  | 0.6  |
| days 1-4                                          | N    | 3     | 4     | 7    | 3    |
|                                                   | %    | 1.8   | 2.1   | 3.8  | 1.7  |
| Pups Surviving 4 days                             | N    | 161   | 182   | 173  | 171  |
| Viability Index                                   | %    | 97.0  | 97.3  | 95.1 | 97.7 |
| Statistical key: * = p<0.05                       |      |       |       |      |      |

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TABLE 27

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

## SUMMARY OF DELIVERY AND LITTER DATA

| DOSE GROUP<br>DOSE LEVEL (PPM)            |       | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|-------------------------------------------|-------|--------|----------|-----------|-----------|
| Implantation Sites<br>per Litter          | N     | 181    | 195      | 197       | 184       |
|                                           | MEAN  | 15.1   | 16.3     | 16.4      | 15.3      |
|                                           | S.D.  | 1.88   | 1.22     | 1.44      | 1.23      |
| Corpora Lutea                             | TOTAL | 199    | 209      | 210       | 194       |
|                                           | MEAN  | 16.6   | 17.4     | 17.5      | 16.2      |
|                                           | S.D.  | 2.27   | 1.73     | 1.98      | 1.47      |
| Live Pups/Litter<br>day 0                 | MEAN  | 13.8   | 15.6*    | 15.2      | 14.6      |
|                                           | S.D.  | 2.08   | 1.16     | 1.53      | 1.08      |
|                                           | N     | 12     | 12       | 12        | 12        |
| day 1                                     | MEAN  | 13.6   | 15.3*    | 14.8      | 14.4      |
|                                           | S.D.  | 1.83   | 1.15     | 1.71      | 1.16      |
|                                           | N     | 12     | 12       | 12        | 12        |
| day 4                                     | MEAN  | 13.4   | 15.2     | 14.4      | 14.3      |
|                                           | S.D.  | 1.62   | 1.34     | 1.83      | 1.22      |
|                                           | N     | 12     | 12       | 12        | 12        |
| Sex Ratio - Male Pups:Total Pups<br>day 0 | N     | 82     | 89       | 90        | 79        |
|                                           | %     | 49.7   | 47.6     | 49.5      | 45.1      |
|                                           |       |        |          |           |           |
| day 4                                     | N     | 82     | 87       | 88        | 77        |
|                                           | %     | 50.9   | 47.8     | 50.9      | 45.0      |
|                                           |       |        |          |           |           |

Statistical key: \* = p<0.05

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SATELLITE STUDY

TABLE 27

BUTANE: 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 |
| Pup Weight/Litter (grams)           |      |      |      |      |      |
| day 1                               | MEAN | 6.8  | 6.5  | 6.8  | 6.7  |
|                                     | S.D. | 0.59 | 0.56 | 0.55 | 0.67 |
|                                     | N    | 12   | 12   | 12   | 12   |
| day 4                               | MEAN | 9.7  | 9.1  | 9.5  | 9.5  |
|                                     | S.D. | 1.24 | 0.86 | 0.87 | 0.86 |
|                                     | N    | 12   | 12   | 12   | 12   |

No statistically significant differences

|  |                                                                                           |          |
|--|-------------------------------------------------------------------------------------------|----------|
|  | Incidence Summary Report<br>for Gross Necropsy Observations<br>Satellite Study<br>Preface | Table 28 |
|--|-------------------------------------------------------------------------------------------|----------|

**Note:**

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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Terminal Sacrifice - Satellite Animals

|                            |  | -- Females -- |    |    |    |
|----------------------------|--|---------------|----|----|----|
| Group:                     |  | 1             | 2  | 3  | 4  |
| Number in group:           |  | 12            | 12 | 12 | 12 |
| -----                      |  |               |    |    |    |
| Within normal limits ..... |  | 12            | 11 | 11 | 12 |
| Kidneys                    |  |               |    |    |    |
| Discolored .....           |  | 0             | 1  | 0  | 0  |
| Mesenteric LN              |  |               |    |    |    |
| Enlarged .....             |  | 0             | 0  | 1  | 0  |

|  |                                                                 |          |
|--|-----------------------------------------------------------------|----------|
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|--|-----------------------------------------------------------------|----------|

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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 | - | 900 ppm  |
| Group 3 | - | 3000 ppm |
| Group 4 | - | 9000 ppm |

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Summary statistics for absolute organ weights (g)  
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Terminal Sacrifice - Satellite Animals

| Group               | Terminal<br>Body wt. (g) | Adrenal Glands | Brain       | Heart         | Kidneys | Liver   | Lungs  | Ovary Left |
|---------------------|--------------------------|----------------|-------------|---------------|---------|---------|--------|------------|
| -----               |                          |                |             |               |         |         |        |            |
|                     |                          |                | F e m a l e | A n i m a l s |         |         |        |            |
| 1                   |                          |                |             |               |         |         |        |            |
| M e a n:            | 282.7                    | 0.0933         | 2.1271      | 1.0012        | 2.6158  | 13.0385 | 1.5771 | 0.0737     |
| Standard deviation: | 22.5                     | 0.0210         | 0.1411      | 0.1059        | 0.2371  | 1.4316  | 0.1498 | 0.0113     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)    | (12)   | (12)       |
| 2                   |                          |                |             |               |         |         |        |            |
| M e a n:            | 290.8                    | 0.0885         | 2.1242      | 0.9987        | 2.6088  | 13.1297 | 1.5435 | 0.0745     |
| Standard deviation: | 20.4                     | 0.0081         | 0.0864      | 0.0885        | 0.2446  | 1.0844  | 0.1630 | 0.0100     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)    | (12)   | (12)       |
| 3                   |                          |                |             |               |         |         |        |            |
| M e a n:            | 294.8                    | 0.1032         | 2.0992      | 1.0549        | 2.6929  | 12.9247 | 1.5412 | 0.0791     |
| Standard deviation: | 25.5                     | 0.0147         | 0.0910      | 0.1055        | 0.2631  | 0.8760  | 0.1469 | 0.0106     |
| Number of observ. : | (12)                     | (12)           | (12)        | (12)          | (12)    | (12)    | (12)   | (12)       |
| 4                   |                          |                |             |               |         |         |        |            |
| M e a n:            | 290.7                    | 0.0965         | 2.0477      | 1.0517        | 2.5992  | 12.7851 | 1.6046 | 0.0829     |
| Standard deviation: | 21.2                     | 0.0103         | 0.1180      | 0.1190        | 0.2674  | 1.3170  | 0.0981 | 0.0234     |
| 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<br>Body wt. (g) | Adrenal Glands | Brain  | Heart  | Kidneys | Liver  | Lungs  | Ovary Left |
|--------------------------------|--------------------------|----------------|--------|--------|---------|--------|--------|------------|
| F e m a l e      A n i m a l s |                          |                |        |        |         |        |        |            |
| 1                              |                          |                |        |        |         |        |        |            |
| M e a n:                       | 282.7                    | 0.0332         | 0.7560 | 0.3537 | 0.9285  | 4.6092 | 0.5605 | 0.0262     |
| Standard deviation:            | 22.5                     | 0.0076         | 0.0695 | 0.0175 | 0.0894  | 0.2801 | 0.0639 | 0.0042     |
| Number of observ. :            | (12)                     | (12)           | (12)   | (12)   | (12)    | (12)   | (12)   | (12)       |
| 2                              |                          |                |        |        |         |        |        |            |
| M e a n:                       | 290.8                    | 0.0306         | 0.7336 | 0.3435 | 0.9004  | 4.5237 | 0.5318 | 0.0257     |
| Standard deviation:            | 20.4                     | 0.0041         | 0.0558 | 0.0199 | 0.0990  | 0.3521 | 0.0547 | 0.0038     |
| Number of observ. :            | (12)                     | (12)           | (12)   | (12)   | (12)    | (12)   | (12)   | (12)       |
| 3                              |                          |                |        |        |         |        |        |            |
| M e a n:                       | 294.8                    | 0.0355         | 0.7160 | 0.3582 | 0.9145  | 4.3958 | 0.5238 | 0.0269     |
| Standard deviation:            | 25.5                     | 0.0071         | 0.0589 | 0.0251 | 0.0636  | 0.2438 | 0.0397 | 0.0036     |
| Number of observ. :            | (12)                     | (12)           | (12)   | (12)   | (12)    | (12)   | (12)   | (12)       |
| 4                              |                          |                |        |        |         |        |        |            |
| M e a n:                       | 290.7                    | 0.0334         | 0.7062 | 0.3626 | 0.8948  | 4.3996 | 0.5544 | 0.0287     |
| Standard deviation:            | 21.2                     | 0.0044         | 0.0430 | 0.0406 | 0.0775  | 0.3493 | 0.0509 | 0.0087     |
| 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<br>Body wt. (g) | Ovary Right | Spleen      | Uterus w/vagina<br>Thymus |        |
|---------------------|--------------------------|-------------|-------------|---------------------------|--------|
| -----               |                          |             |             |                           |        |
|                     |                          |             | F e m a l e | A n i m a l s             |        |
| 1                   |                          |             |             |                           |        |
| M e a n:            | 282.7                    | 0.0264      | 0.2211      | 0.0910                    | 0.4179 |
| Standard deviation: | 22.5                     | 0.0063      | 0.0386      | 0.0219                    | 0.0612 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 2                   |                          |             |             |                           |        |
| M e a n:            | 290.8                    | 0.0287      | 0.2464      | 0.0985                    | 0.4014 |
| Standard deviation: | 20.4                     | 0.0038      | 0.0230      | 0.0240                    | 0.0493 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 3                   |                          |             |             |                           |        |
| M e a n:            | 294.8                    | 0.0312      | 0.2417      | 0.1118                    | 0.4546 |
| Standard deviation: | 25.5                     | 0.0061      | 0.0263      | 0.0204                    | 0.0798 |
| Number of observ. : | (12)                     | (12)        | (12)        | (12)                      | (12)   |
| 4                   |                          |             |             |                           |        |
| M e a n:            | 290.7                    | 0.0271      | 0.2368      | 0.1031                    | 0.4270 |
| Standard deviation: | 21.2                     | 0.0028      | 0.0381      | 0.0169                    | 0.0799 |
| 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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## Terminal Sacrifice - Satellite Animals

| Group                          | Terminal<br>Body wt. (g) | Adrenal Glands | Brain    | Heart   | Kidneys  | Liver    | Lungs   | Ovary Left |
|--------------------------------|--------------------------|----------------|----------|---------|----------|----------|---------|------------|
| F e m a l e      A n i m a l s |                          |                |          |         |          |          |         |            |
| 1                              |                          |                |          |         |          |          |         |            |
| M e a n:                       | 282.7                    | 4.4130         | 100.0000 | 47.1973 | 122.9397 | 613.0333 | 74.1206 | 3.4860     |
| Standard deviation:            | 22.5                     | 1.0914         | 0.0000   | 5.3211  | 6.9491   | 52.9870  | 4.8535  | 0.6207     |
| Number of observ. :            | (12)                     | (12)           | (12)     | (12)    | (12)     | (12)     | (12)    | (12)       |
| 2                              |                          |                |          |         |          |          |         |            |
| M e a n:                       | 290.8                    | 4.1677         | 100.0000 | 47.0723 | 122.8263 | 618.8931 | 72.6098 | 3.5154     |
| Standard deviation:            | 20.4                     | 0.3388         | 0.0000   | 4.5351  | 10.6643  | 55.7727  | 6.3272  | 0.5245     |
| Number of observ. :            | (12)                     | (12)           | (12)     | (12)    | (12)     | (12)     | (12)    | (12)       |
| 3                              |                          |                |          |         |          |          |         |            |
| M e a n:                       | 294.8                    | 4.9259         | 100.0000 | 50.2944 | 128.1809 | 615.9839 | 73.3904 | 3.7739     |
| Standard deviation:            | 25.5                     | 0.7178         | 0.0000   | 4.9277  | 10.0633  | 36.8221  | 5.7329  | 0.5013     |
| Number of observ. :            | (12)                     | (12)           | (12)     | (12)    | (12)     | (12)     | (12)    | (12)       |
| 4                              |                          |                |          |         |          |          |         |            |
| M e a n:                       | 290.7                    | 4.7201         | 100.0000 | 51.3855 | 126.8281 | 624.8795 | 78.4982 | 4.0363     |
| Standard deviation:            | 21.2                     | 0.5034         | 0.0000   | 5.3165  | 9.5620   | 60.5752  | 5.2527  | 1.0493     |
| 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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## Terminal Sacrifice - Satellite Animals

| Group               | Terminal<br>Body wt. (g) | Ovary Right | Spleen   | Uterus w/vagina<br>Thymus |                                |
|---------------------|--------------------------|-------------|----------|---------------------------|--------------------------------|
|                     |                          |             |          |                           | F e m a l e      A n i m a l s |
| 1                   |                          |             |          |                           |                                |
| M e a n:            | 282.7                    | 3.4965      | 29.2662  | 12.0185                   | 55.5220                        |
| Standard deviation: | 22.5                     | 0.8178      | 4.1900   | 2.5088                    | 8.6270                         |
| Number of observ. : | (12)                     | (12)        | (12)     | (12)                      | (12)                           |
| 2                   |                          |             |          |                           |                                |
| M e a n:            | 290.8                    | 3.9351      | 33.6166  | 13.3950                   | 54.8320                        |
| Standard deviation: | 20.4                     | 0.6191      | 2.4371   | 2.9836                    | 6.4469                         |
| Number of observ. : | (12)                     | (12)        | (12)     | (12)                      | (12)                           |
| 3                   |                          |             |          |                           |                                |
| M e a n:            | 294.8                    | 4.3482+     | 33.9070* | 15.6683+                  | 63.5432                        |
| Standard deviation: | 25.5                     | 0.6768      | 4.2541   | 2.9188                    | 9.6675                         |
| Number of observ. : | (12)                     | (12)        | (12)     | (12)                      | (12)                           |
| 4                   |                          |             |          |                           |                                |
| M e a n:            | 290.7                    | 3.8416      | 33.7004* | 14.6424                   | 60.4483                        |
| Standard deviation: | 21.2                     | 0.3737      | 5.9775   | 2.4764                    | 10.4752                        |
| 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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TABLE 30

BUTANE: 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<br>DOSE LEVEL (PPM) | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|--------------------------------|--------|----------|-----------|-----------|
| DAY 0 to 4                     |        |          |           |           |
| Normal                         |        |          |           |           |
| -----                          |        |          |           |           |
| WITHIN NORMAL LIMITS           | 341/12 | 368/12   | 353/12    | 342/12    |
| Dermal-General                 |        |          |           |           |
| -----                          |        |          |           |           |
| SCABS                          | 0/ 0   | 0/ 0     | 0/ 0      | 3/ 1      |

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TABLE 31

BUTANE: 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 |  | 7.0  | 6.6  | 7.1  | 6.9  |
|                  | S.D. |  | 0.65 | 0.59 | 0.59 | 0.67 |
|                  | N    |  | 12   | 12   | 12   | 12   |
| 1 females        | MEAN |  | 6.6  | 6.4  | 6.6  | 6.6  |
|                  | S.D. |  | 0.54 | 0.53 | 0.56 | 0.69 |
|                  | N    |  | 12   | 12   | 12   | 12   |
| 1 males+females  | MEAN |  | 6.8  | 6.5  | 6.8  | 6.7  |
|                  | S.D. |  | 0.59 | 0.56 | 0.55 | 0.67 |
|                  | N    |  | 12   | 12   | 12   | 12   |
| day 4 males      | MEAN |  | 10.0 | 9.3  | 9.7  | 9.7  |
|                  | S.D. |  | 1.40 | 0.88 | 0.90 | 0.79 |
|                  | N    |  | 12   | 12   | 12   | 12   |
| 4 females        | MEAN |  | 9.4  | 8.9  | 9.2  | 9.4  |
|                  | S.D. |  | 1.09 | 0.83 | 0.88 | 0.94 |
|                  | N    |  | 12   | 12   | 12   | 12   |
| 4 males+females  | MEAN |  | 9.7  | 9.1  | 9.5  | 9.5  |
|                  | S.D. |  | 1.24 | 0.86 | 0.87 | 0.86 |
|                  | N    |  | 12   | 12   | 12   | 12   |

No statistically significant differences

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TABLE 32

BUTANE: 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 | 3.0  | 2.7  | 2.7  | 2.8  |
|                  | S.D. | 0.82 | 0.47 | 0.51 | 0.51 |
|                  | N    | 12   | 12   | 12   | 12   |
| females          | MEAN | 2.9  | 2.6  | 2.6  | 2.8  |
|                  | S.D. | 0.66 | 0.45 | 0.54 | 0.49 |
|                  | N    | 12   | 12   | 12   | 12   |
| males+females    | MEAN | 2.9  | 2.6  | 2.6  | 2.8  |
|                  | S.D. | 0.74 | 0.46 | 0.52 | 0.49 |
|                  | N    | 12   | 12   | 12   | 12   |

No statistically significant differences

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TABLE 33

BUTANE: 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  | 12             | 12   | 12   |
| Pups Evaluated                    | N | 164 | 185            | 178  | 178  |
| Live                              | N | 164 | 184            | 177  | 175  |
| Stillborn                         | N | 0   | 1              | 1    | 3    |
| GROSS EXAM                        |   |     |                |      |      |
| Litter Incidence                  | N | 1   | 0              | 0    | 1    |
| Pup Incidence                     | N | 1   | 0              | 0    | 1    |
| AUTOLYSIS                         |   |     |                |      |      |
| Pup Incidence                     | N | 1   | 0              | 0    | 1    |
|                                   | % | 0.6 | 0.0            | 0.0  | 0.6  |
| Litter Incidence                  | N | 1   | 0              | 0    | 1    |
|                                   | % | 8.3 | 0.0            | 0.0  | 8.3  |
| LUNGS                             |   |     |                |      |      |
| Litter Incidence                  | N | 1   | 2              | 3    | 3    |
| Pup Incidence                     | N | 1   | 2              | 4    | 4    |
| LUNG FLOATATION TEST - STILLBORN  |   |     |                |      |      |
| Pup Incidence                     | N | 0   | 0 <sup>a</sup> | 1    | 3    |
|                                   | % | 0.0 | 0.0            | 0.6  | 1.7  |
| Litter Incidence                  | N | 0   | 0              | 1    | 3    |
|                                   | % | 0.0 | 0.0            | 8.3  | 25.0 |
| LUNG FLOATATION TEST - FOUND DEAD |   |     |                |      |      |
| Pup Incidence                     | N | 1   | 2              | 3    | 1    |
|                                   | % | 0.6 | 1.1            | 1.7  | 0.6  |
| Litter Incidence                  | N | 1   | 2              | 2    | 1    |
|                                   | % | 8.3 | 16.7           | 16.7 | 8.3  |

No statistically significant differences

<sup>a</sup>Pup 2542-01 lung floatation test was not performed and the pup was categorized as stillborn by default.

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TABLE 33

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

## SUMMARY OF PUP NECROPSY OBSERVATIONS

| DOSE GROUP<br>DOSE LEVEL (PPM) |   | 1<br>0 | 2<br>900 | 3<br>3000 | 4<br>9000 |
|--------------------------------|---|--------|----------|-----------|-----------|
| Litters Evaluated              | N | 12     | 12       | 12        | 12        |
| Pups Evaluated                 | N | 164    | 185      | 178       | 178       |
| Live                           | N | 164    | 184      | 177       | 175       |
| Stillborn                      | N | 0      | 1        | 1         | 3         |
| STOMACH                        |   |        |          |           |           |
| -----                          |   |        |          |           |           |
| Litter Incidence               | N | 2      | 3        | 3         | 4         |
| Pup Incidence                  | N | 2      | 3        | 4         | 6         |
| NO MILK IN STOMACH             |   |        |          |           |           |
| Pup Incidence                  | N | 1      | 3        | 4         | 4         |
|                                | % | 0.6    | 1.6      | 2.2       | 2.2       |
| Litter Incidence               | N | 1      | 3        | 3         | 3         |
|                                | % | 8.3    | 25.0     | 25.0      | 25.0      |
| MILK IN STOMACH                |   |        |          |           |           |
| Pup Incidence                  | N | 1      | 0        | 0         | 2         |
|                                | % | 0.6    | 0.0      | 0.0       | 1.1       |
| Litter Incidence               | N | 1      | 0        | 0         | 1         |
|                                | % | 8.3    | 0.0      | 0.0       | 8.3       |
| LIMBS                          |   |        |          |           |           |
| -----                          |   |        |          |           |           |
| Litter Incidence               | N | 0      | 1        | 0         | 0         |
| Pup Incidence                  | N | 0      | 1        | 0         | 0         |
| EDEMA                          |   |        |          |           |           |
| Pup Incidence                  | N | 0      | 1        | 0         | 0         |
|                                | % | 0.0    | 0.5      | 0.0       | 0.0       |
| Litter Incidence               | N | 0      | 1        | 0         | 0         |
|                                | % | 0.0    | 8.3      | 0.0       | 0.0       |

No statistically significant differences

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INHALATION EXPOSURES

INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 1 0 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 1030    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1031    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1032    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1033    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1034    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1035    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1036    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1037    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1038    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1039    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1040    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1041    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 2 900 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 2030    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2031    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2032    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2033    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2034    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2035    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2036    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2037    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2038    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2039    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2040    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2041    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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INHALATION EXPOSURES

## INDIVIDUAL ANIMAL TERMINATION HISTORY

MALES GROUP 3 3000 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 3030    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3031    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3032    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3033    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3034    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3035    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3036    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3037    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3038    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3039    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3040    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3041    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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MALES GROUP 4 9000 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 4030    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4031    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4032    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4033    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4034    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4035    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4036    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4037    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4038    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4039    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4040    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4041    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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## INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 1530    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1531    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1532    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1533    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1534    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1535    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 1536    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1537    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1538    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1539    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1540    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 1541    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 900 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 2530    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2531    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2532    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2533    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2534    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2535    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 2536    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2537    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2538    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2539    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2540    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 2541    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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## INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 3000 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 3530    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3531    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3532    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3533    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3534    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3535    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 3536    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3537    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3554    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3539    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3540    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 3541    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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## INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

| ANIMAL# | TYPE OF<br>DEATH   | DATE OF<br>DEATH | STUDY<br>DAY |
|---------|--------------------|------------------|--------------|
| 4530    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4531    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4532    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4533    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4534    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4535    | TERMINAL SACRIFICE | 29-OCT-03        | 30           |
| 4536    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4537    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4538    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4539    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4540    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |
| 4541    | TERMINAL SACRIFICE | 30-OCT-03        | 31           |

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|  |                                                           |            |
|--|-----------------------------------------------------------|------------|
|  | Individual Clinical Observations<br>Main Study<br>Preface | Appendix B |
|--|-----------------------------------------------------------|------------|

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

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## INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

| ANIMAL# | OBSERVATIONS                 | DAY OF<br>STUDY | - 1 2 2 3 3 |   |   |   |   |   |   |
|---------|------------------------------|-----------------|-------------|---|---|---|---|---|---|
|         |                              |                 | 7           | 0 | 7 | 4 | 1 | 8 | 0 |
| 1030    | WITHIN NORMAL LIMITS         |                 | P           | P | P | P | P | P |   |
|         | TERMINAL SACRIFICE           |                 |             |   |   |   |   |   | P |
| 1031    | WITHIN NORMAL LIMITS         |                 | P           | P | P |   |   |   |   |
|         | TERMINAL SACRIFICE           |                 |             |   |   |   |   |   | P |
|         | ALOPECIA - GENERAL           |                 |             |   |   | 2 | 2 | 2 |   |
|         | ALOPECIA - EXTREMITIES/SNOUT |                 |             |   |   | 2 | 2 | 2 |   |
| 1032    | WITHIN NORMAL LIMITS         |                 | P           |   |   |   |   |   |   |
|         | TERMINAL SACRIFICE           |                 |             |   |   |   |   |   | P |
|         | ALOPECIA - GENERAL           |                 |             |   | 2 | 2 | 3 | 3 | 3 |
|         | SCABS                        |                 |             |   | P | P | P |   |   |
|         | CERVICAL                     |                 |             |   |   |   |   |   |   |
|         | ALOPECIA - EXTREMITIES/SNOUT |                 |             |   |   | 2 | 2 | 2 |   |
| 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 |

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

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INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

| ANIMAL# | OBSERVATIONS                               | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3     |
|---------|--------------------------------------------|-----------------|---|---|---|---|---|-------|
|         |                                            |                 | 7 | 0 | 7 | 4 | 1 | 8 0 1 |
| 1038    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P P   |
| 1039    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P P   |
| 1040    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P P   |
| 1041    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P P   |

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INHALATION EXPOSURES

## INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 900 PPM

| ANIMAL# | OBSERVATIONS                                                       | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|--------------------------------------------------------------------|-----------------|---|---|---|---|---|---|
|         |                                                                    |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 2030    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2031    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>SCABS<br>R FOREPAW   |                 | P | P | P | P | P | P |
| 2032    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>INCISORS MALOCCLUDED |                 | P | P | P | P | P | P |
| 2033    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2034    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2035    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2036    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2037    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |
| 2038    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                         |                 | P | P | P | P | P | P |

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 900 PPM

| ANIMAL# | OBSERVATIONS                               | DAY OF<br>STUDY | - |   |   |   |   |   |
|---------|--------------------------------------------|-----------------|---|---|---|---|---|---|
|         |                                            |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 2039    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 2040    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 2041    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | 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<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|--------------------------------------------|-----------------|---|---|---|---|---|---|
|         |                                            |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 3030    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3031    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3032    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3033    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3034    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3035    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3036    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3037    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3038    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 3039    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 3000 PPM

| ANIMAL# | OBSERVATIONS         | DAY OF | - | 1 | 2 | 2 | 3 | 3 |
|---------|----------------------|--------|---|---|---|---|---|---|
|         |                      | STUDY  | 7 | 0 | 7 | 4 | 1 | 8 |
| 3040    | WITHIN NORMAL LIMITS |        | P | P | P | P | P | P |
|         | TERMINAL SACRIFICE   |        |   |   |   |   |   | P |
| 3041    | WITHIN NORMAL LIMITS |        | P | P | P | P | P | P |
|         | TERMINAL SACRIFICE   |        |   |   |   |   |   | P |

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

| ANIMAL# | OBSERVATIONS                                                                 | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|------------------------------------------------------------------------------|-----------------|---|---|---|---|---|---|
|         |                                                                              |                 | 7 | 0 | 7 | 4 | 1 | 8 |
|         |                                                                              |                 | 0 | 1 | 8 | 0 | 1 |   |
| 4030    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4031    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4032    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4033    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4034    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4035    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4036    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                   |                 | P | P | P | P | P | P |
| 4037    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>CHROMODACRYORRHEA - UNILATERAL |                 | P | P | P | P | P | P |
| 4038    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>NASAL DISCHARGE - RED          |                 | P | P | P | P | P | P |

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INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

| ANIMAL# | OBSERVATIONS          | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|-----------------------|-----------------|---|---|---|---|---|---|
|         |                       |                 | 7 | 0 | 7 | 4 | 1 | 8 |
|         |                       |                 | 0 | 1 | 8 | 0 | 1 |   |
| 4039    | WITHIN NORMAL LIMITS  |                 | P | P | P | P | P |   |
|         | TERMINAL SACRIFICE    |                 |   |   |   |   |   | P |
|         | NASAL DISCHARGE - RED |                 |   |   |   | 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 |   |
|         | TERMINAL SACRIFICE    |                 |   |   |   |   |   | P |

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

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## APPENDIX B

BUTANE: 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<br>STUDY |   |   |   |   |   |   |   |   |  |  |
|---------|--------------------------------------------------------------------------------------------------|-----------------|---|---|---|---|---|---|---|---|--|--|
|         |                                                                                                  |                 | - | 1 | 2 | 2 | 3 | 3 |   |   |  |  |
|         |                                                                                                  |                 | 7 | 0 | 7 | 4 | 1 | 8 | 0 | 1 |  |  |
| 1530    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1531    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1532    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1533    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1534    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1535    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1536    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>ALOPECIA - EXTREMITIES/SNOUT                       |                 | P | P | P |   |   |   |   | P |  |  |
|         |                                                                                                  |                 |   |   |   | 2 | 2 | 2 |   |   |  |  |
| 1537    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE                                                       |                 | P | P | P | P | P | P |   | P |  |  |
| 1538    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE<br>ALOPECIA - GENERAL<br>ALOPECIA - EXTREMITIES/SNOUT |                 | P |   |   |   |   |   |   | P |  |  |
|         |                                                                                                  |                 |   |   |   | 2 | 2 | 2 | 2 |   |  |  |
|         |                                                                                                  |                 |   |   |   | 2 | 2 | 2 | 2 |   |  |  |

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<br>STUDY |   |   |   |   |   |   |   |
|---------|--------------------------------------|-----------------|---|---|---|---|---|---|---|
|         |                                      |                 | - | 1 | 2 | 2 | 3 | 3 |   |
|         |                                      |                 | 7 | 0 | 7 | 4 | 1 | 8 | 0 |
| 1539    | WITHIN NORMAL LIMITS                 |                 | P | P | P |   |   |   |   |
|         | TERMINAL SACRIFICE                   |                 |   |   |   |   |   | P |   |
|         | ALOPECIA - EXTREMITIES/SNOUT         |                 |   |   | 2 | 2 | 2 |   |   |
| 1540    | WITHIN NORMAL LIMITS                 |                 | P | P | P |   | P |   |   |
|         | TERMINAL SACRIFICE                   |                 |   |   |   |   |   | P |   |
|         | RED/BROWN STAINS - EXTREMITIES/SNOUT |                 |   |   | 1 | 1 |   |   |   |
| 1541    | 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<br>STUDY | - 1 2 2 3 3 |   |   |   |   |   |   |
|---------|--------------------------------------------|-----------------|-------------|---|---|---|---|---|---|
|         |                                            |                 | 7           | 0 | 7 | 4 | 1 | 8 | 0 |
| 2530    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2531    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2532    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2533    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2534    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2535    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2536    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2537    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2538    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |
| 2539    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P           | P | P | P | P | P | P |

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

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INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 900 PPM

| ANIMAL# | OBSERVATIONS         | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|----------------------|-----------------|---|---|---|---|---|---|
|         |                      |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 2540    | WITHIN NORMAL LIMITS |                 | P | P | P | P | P | P |
|         | TERMINAL SACRIFICE   |                 |   |   |   |   |   | P |
| 2541    | 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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INHALATION EXPOSURES

## INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

| ANIMAL# | OBSERVATIONS                 | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|------------------------------|-----------------|---|---|---|---|---|---|
|         |                              |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 3530    | WITHIN NORMAL LIMITS         |                 | P | P | P | P |   |   |
|         | TERMINAL SACRIFICE           |                 |   |   |   |   |   | P |
|         | ALOPECIA - EXTREMITIES/SNOUT |                 |   |   | 2 | 2 |   |   |
| 3531    | WITHIN NORMAL LIMITS         |                 | P | P | P | P | P | P |
|         | TERMINAL SACRIFICE           |                 |   |   |   |   |   | P |
| 3532    | WITHIN NORMAL LIMITS         |                 | P | P | P |   |   |   |
|         | TERMINAL SACRIFICE           |                 |   |   |   |   |   | P |
|         | ALOPECIA - GENERAL           |                 |   |   | 2 | 2 | 2 |   |
| 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 |   |   |   |
|         | TERMINAL SACRIFICE           |                 |   |   |   |   |   | P |
|         | ALOPECIA - EXTREMITIES/SNOUT |                 |   |   | 3 | 3 | 3 |   |
| 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 |
| 3554    | 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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INHALATION EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

| ANIMAL# | OBSERVATIONS                 | DAY OF | - | 1 | 2 | 2 | 3 | 3 |   |
|---------|------------------------------|--------|---|---|---|---|---|---|---|
|         |                              | STUDY  | 7 | 0 | 7 | 4 | 1 | 8 | 0 |
| 3539    | WITHIN NORMAL LIMITS         |        | P | P | P | P | P | P |   |
|         | TERMINAL SACRIFICE           |        |   |   |   |   |   |   | P |
| 3540    | WITHIN NORMAL LIMITS         |        | P | P | P |   |   |   |   |
|         | TERMINAL SACRIFICE           |        |   |   |   |   |   |   | P |
|         | ALOPECIA - EXTREMITIES/SNOUT |        |   |   |   | 3 | 3 | 3 |   |
| 3541    | 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 4 9000 PPM

| ANIMAL# | OBSERVATIONS                               | DAY OF<br>STUDY | - | 1 | 2 | 2 | 3 | 3 |
|---------|--------------------------------------------|-----------------|---|---|---|---|---|---|
|         |                                            |                 | 7 | 0 | 7 | 4 | 1 | 8 |
| 4530    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4531    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4532    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4533    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4534    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4535    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4536    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4537    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4538    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |
| 4539    | WITHIN NORMAL LIMITS<br>TERMINAL SACRIFICE |                 | P | P | P | P | P | P |

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

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

| ANIMAL# | OBSERVATIONS                 | DAY OF | - | 1 | 2 | 2 | 3 | 3 |
|---------|------------------------------|--------|---|---|---|---|---|---|
|         |                              | STUDY  | 7 | 0 | 7 | 4 | 1 | 8 |
| 4540    | WITHIN NORMAL LIMITS         |        | P | P | P | P | P | P |
|         | TERMINAL SACRIFICE           |        |   |   |   |   |   | P |
| 4541    | WITHIN NORMAL LIMITS         |        | P | P | P |   |   |   |
|         | TERMINAL SACRIFICE           |        |   |   |   |   |   | P |
|         | ALOPECIA - GENERAL           |        |   |   | 2 | 2 | 2 |   |
|         | ALOPECIA - EXTREMITIES/SNOUT |        |   |   | 2 | 2 | 2 |   |

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

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## APPENDIX C

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

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 1 0 PPM

| ANIMAL# | DAY OF STUDY |     |      |      |      |      |
|---------|--------------|-----|------|------|------|------|
|         | -7           | 0   | 7    | 14   | 21   | 28   |
| 1030    | 189          | 251 | 290  | 313  | 351  | 378  |
| 1031    | 193          | 249 | 312  | 347  | 388  | 430  |
| 1032    | 202          | 274 | 321  | 357  | 391  | 405  |
| 1033    | 200          | 269 | 311  | 348  | 387  | 405  |
| 1034    | 201          | 265 | 308  | 344  | 376  | 404  |
| 1035    | 187          | 248 | 272  | 295  | 313  | 337  |
| 1036    | 195          | 258 | 289  | 320  | 353  | 377  |
| 1037    | 195          | 265 | 312  | 358  | 384  | 408  |
| 1038    | 191          | 257 | 297  | 322  | 354  | 378  |
| 1039    | 185          | 251 | 296  | 337  | 370  | 393  |
| 1040    | 180          | 253 | 289  | 327  | 365  | 388  |
| 1041    | 183          | 245 | 279  | 300  | 340  | 372  |
| MEAN    | 192          | 257 | 298  | 331  | 364  | 389  |
| S.D.    | 7.2          | 9.2 | 14.7 | 21.1 | 23.2 | 23.6 |
| N       | 12           | 12  | 12   | 12   | 12   | 12   |

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## APPENDIX C

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

## INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 2 900 PPM

| ANIMAL# | DAY OF STUDY |      |      |      |      |      |
|---------|--------------|------|------|------|------|------|
|         | -7           | 0    | 7    | 14   | 21   | 28   |
| 2030    | 200          | 266  | 306  | 331  | 359  | 377  |
| 2031    | 195          | 261  | 297  | 328  | 353  | 369  |
| 2032    | 176          | 241  | 284  | 314  | 334  | 362  |
| 2033    | 201          | 270  | 306  | 354  | 375  | 407  |
| 2034    | 181          | 266  | 317  | 373  | 404  | 425  |
| 2035    | 189          | 262  | 306  | 337  | 379  | 407  |
| 2036    | 201          | 277  | 322  | 363  | 391  | 412  |
| 2037    | 194          | 259  | 301  | 333  | 362  | 393  |
| 2038    | 189          | 251  | 288  | 316  | 348  | 367  |
| 2039    | 183          | 246  | 281  | 312  | 340  | 366  |
| 2040    | 192          | 261  | 313  | 357  | 412  | 427  |
| 2041    | 185          | 259  | 288  | 316  | 340  | 363  |
| MEAN    | 191          | 260  | 301  | 336  | 366  | 390  |
| S.D.    | 8.1          | 10.1 | 13.3 | 20.8 | 25.9 | 25.0 |
| N       | 12           | 12   | 12   | 12   | 12   | 12   |

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND  
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INHALATION EXPOSURES

MALES      GROUP 3      3000 PPM      INDIVIDUAL BODY WEIGHTS (GRAMS)

| ANIMAL# | DAY OF STUDY |     |      |      |      |      |
|---------|--------------|-----|------|------|------|------|
|         | -7           | 0   | 7    | 14   | 21   | 28   |
| 3030    | 181          | 261 | 298  | 337  | 378  | 400  |
| 3031    | 201          | 271 | 321  | 370  | 398  | 413  |
| 3032    | 202          | 277 | 317  | 353  | 380  | 405  |
| 3033    | 198          | 272 | 310  | 341  | 370  | 391  |
| 3034    | 193          | 268 | 319  | 363  | 409  | 444  |
| 3035    | 193          | 262 | 293  | 315  | 348  | 376  |
| 3036    | 192          | 265 | 309  | 362  | 404  | 429  |
| 3037    | 197          | 280 | 338  | 384  | 421  | 450  |
| 3038    | 185          | 254 | 307  | 350  | 390  | 410  |
| 3039    | 188          | 263 | 296  | 329  | 364  | 388  |
| 3040    | 181          | 264 | 308  | 360  | 394  | 425  |
| 3041    | 183          | 271 | 326  | 375  | 402  | 432  |
| MEAN    | 191          | 267 | 312  | 353  | 388  | 413  |
| S.D.    | 7.5          | 7.1 | 13.1 | 19.8 | 20.7 | 22.9 |
| N       | 12           | 12  | 12   | 12   | 12   | 12   |

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INHALATION EXPOSURES

## INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 4 9000 PPM

| ANIMAL# | DAY OF STUDY |     |      |      |      |      |
|---------|--------------|-----|------|------|------|------|
|         | -7           | 0   | 7    | 14   | 21   | 28   |
| 4030    | 185          | 258 | 306  | 351  | 390  | 416  |
| 4031    | 198          | 262 | 307  | 339  | 361  | 383  |
| 4032    | 183          | 249 | 294  | 332  | 356  | 388  |
| 4033    | 204          | 279 | 326  | 369  | 397  | 424  |
| 4034    | 188          | 257 | 293  | 340  | 365  | 383  |
| 4035    | 197          | 265 | 303  | 327  | 361  | 367  |
| 4036    | 192          | 262 | 289  | 315  | 352  | 362  |
| 4037    | 194          | 259 | 303  | 335  | 362  | 381  |
| 4038    | 193          | 276 | 329  | 380  | 414  | 446  |
| 4039    | 181          | 245 | 278  | 306  | 336  | 361  |
| 4040    | 185          | 259 | 278  | 305  | 329  | 349  |
| 4041    | 200          | 261 | 305  | 338  | 365  | 387  |
| MEAN    | 192          | 261 | 301  | 336  | 366  | 387  |
| S.D.    | 7.3          | 9.4 | 16.2 | 22.8 | 24.3 | 28.3 |
| N       | 12           | 12  | 12   | 12   | 12   | 12   |

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INHALATION EXPOSURES

## FEMALES GROUP 1 0 PPM INDIVIDUAL BODY WEIGHTS (GRAMS)

| ANIMAL# | DAY OF STUDY |     |      |      |      |      |
|---------|--------------|-----|------|------|------|------|
|         | -7           | 0   | 7    | 14   | 21   | 28   |
| 1530    | 159          | 197 | 215  | 231  | 247  | 253  |
| 1531    | 166          | 200 | 212  | 217  | 246  | 260  |
| 1532    | 169          | 205 | 219  | 240  | 255  | 264  |
| 1533    | 153          | 191 | 204  | 224  | 238  | 247  |
| 1534    | 156          | 194 | 218  | 235  | 244  | 247  |
| 1535    | 162          | 197 | 216  | 233  | 242  | 252  |
| 1536    | 173          | 215 | 227  | 256  | 266  | 282  |
| 1537    | 175          | 222 | 239  | 268  | 272  | 289  |
| 1538    | 157          | 204 | 210  | 230  | 235  | 250  |
| 1539    | 161          | 193 | 219  | 237  | 250  | 252  |
| 1540    | 159          | 189 | 199  | 216  | 225  | 230  |
| 1541    | 164          | 200 | 209  | 213  | 230  | 241  |
| MEAN    | 163          | 200 | 216  | 233  | 246  | 256  |
| S.D.    | 6.6          | 9.8 | 10.4 | 16.0 | 13.7 | 16.6 |
| N       | 12           | 12  | 12   | 12   | 12   | 12   |

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND  
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INHALATION EXPOSURES

FEMALES GROUP 2 900 PPM INDIVIDUAL BODY WEIGHTS (GRAMS)

| ANIMAL# | DAY OF STUDY |      |      |      |      |      |
|---------|--------------|------|------|------|------|------|
|         | -7           | 0    | 7    | 14   | 21   | 28   |
| 2530    | 162          | 199  | 216  | 230  | 249  | 261  |
| 2531    | 175          | 198  | 234  | 259  | 272  | 278  |
| 2532    | 159          | 202  | 215  | 234  | 254  | 253  |
| 2533    | 170          | 203  | 210  | 239  | 263  | 272  |
| 2534    | 160          | 194  | 214  | 221  | 252  | 261  |
| 2535    | 154          | 175  | 201  | 217  | 232  | 235  |
| 2536    | 162          | 195  | 201  | 230  | 239  | 253  |
| 2537    | 163          | 200  | 216  | 234  | 256  | 269  |
| 2538    | 159          | 196  | 205  | 225  | 239  | 247  |
| 2539    | 165          | 188  | 213  | 228  | 243  | 259  |
| 2540    | 153          | 190  | 205  | 221  | 235  | 240  |
| 2541    | 172          | 218  | 229  | 242  | 246  | 274  |
| MEAN    | 163          | 197  | 213  | 232  | 248  | 258  |
| S.D.    | 6.7          | 10.1 | 10.1 | 11.5 | 11.8 | 13.4 |
| N       | 12           | 12   | 12   | 12   | 12   | 12   |

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

INDIVIDUAL BODY WEIGHTS (GRAMS)  
FEMALES GROUP 3 3000 PPM

| ANIMAL# | DAY OF STUDY |      |      |      |      |      |
|---------|--------------|------|------|------|------|------|
|         | -7           | 0    | 7    | 14   | 21   | 28   |
| 3530    | 163          | 206  | 226  | 252  | 275  | 266  |
| 3531    | 164          | 198  | 215  | 235  | 241  | 254  |
| 3532    | 154          | 195  | 213  | 236  | 243  | 252  |
| 3533    | 154          | 195  | 212  | 232  | 253  | 267  |
| 3534    | 175          | 229  | 266  | 256  | 303  | 324  |
| 3535    | 174          | 216  | 232  | 258  | 266  | 282  |
| 3536    | 161          | 201  | 220  | 232  | 259  | 269  |
| 3537    | 172          | 223  | 240  | 257  | 265  | 290  |
| 3554    | 178          | 211  | 215  | 238  | 253  | 265  |
| 3539    | 166          | 197  | 216  | 235  | 246  | 262  |
| 3540    | 159          | 197  | 210  | 227  | 234  | 235  |
| 3541    | 158          | 186  | 215  | 237  | 253  | 251  |
| MEAN    | 165          | 204  | 223  | 241  | 258  | 268  |
| S.D.    | 8.3          | 12.7 | 16.2 | 11.0 | 18.3 | 22.9 |
| N       | 12           | 12   | 12   | 12   | 12   | 12   |

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## APPENDIX C

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

INDIVIDUAL BODY WEIGHTS (GRAMS)  
FEMALES GROUP 4 9000 PPM

| ANIMAL# | DAY OF STUDY |      |      |      |      |      |
|---------|--------------|------|------|------|------|------|
|         | -7           | 0    | 7    | 14   | 21   | 28   |
| 4530    | 170          | 217  | 227  | 239  | 254  | 270  |
| 4531    | 162          | 200  | 216  | 234  | 250  | 256  |
| 4532    | 165          | 211  | 221  | 232  | 251  | 262  |
| 4533    | 161          | 187  | 211  | 221  | 230  | 242  |
| 4534    | 176          | 214  | 243  | 266  | 272  | 297  |
| 4535    | 157          | 185  | 191  | 210  | 214  | 223  |
| 4536    | 154          | 184  | 202  | 208  | 237  | 240  |
| 4537    | 154          | 194  | 212  | 227  | 230  | 244  |
| 4538    | 165          | 200  | 211  | 231  | 256  | 261  |
| 4539    | 173          | 219  | 225  | 242  | 250  | 266  |
| 4540    | 159          | 200  | 212  | 232  | 244  | 244  |
| 4541    | 160          | 186  | 207  | 225  | 236  | 245  |
| MEAN    | 163          | 200  | 215  | 231  | 244  | 254  |
| S.D.    | 7.0          | 13.0 | 13.2 | 15.1 | 15.3 | 18.9 |
| N       | 12           | 12   | 12   | 12   | 12   | 12   |

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## APPENDIX D

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

MALES      GROUP 1      0 PPM      INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 1030    | 62           | 39  | 23   | 38    | 27    | 127  |
| 1031    | 56           | 62  | 35   | 41    | 42    | 181  |
| 1032    | 72           | 47  | 36   | 34    | 14    | 131  |
| 1033    | 69           | 42  | 37   | 39    | 18    | 136  |
| 1034    | 64           | 43  | 36   | 32    | 29    | 139  |
| 1035    | 61           | 24  | 23   | 18    | 24    | 89   |
| 1036    | 63           | 31  | 31   | 33    | 24    | 119  |
| 1037    | 70           | 47  | 46   | 26    | 24    | 143  |
| 1038    | 65           | 40  | 25   | 32    | 25    | 122  |
| 1039    | 65           | 46  | 41   | 33    | 23    | 142  |
| 1040    | 72           | 37  | 38   | 38    | 23    | 135  |
| 1041    | 63           | 34  | 21   | 40    | 32    | 127  |
| MEAN    | 65           | 41  | 33   | 34    | 25    | 133  |
| S.D.    | 4.8          | 9.5 | 7.9  | 6.5   | 7.0   | 21.0 |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 2030    | 66           | 40  | 25   | 28    | 18    | 111  |
| 2031    | 66           | 36  | 31   | 25    | 16    | 108  |
| 2032    | 65           | 43  | 30   | 19    | 29    | 121  |
| 2033    | 70           | 35  | 49   | 21    | 32    | 137  |
| 2034    | 85           | 51  | 57   | 31    | 21    | 159  |
| 2035    | 73           | 44  | 32   | 41    | 28    | 144  |
| 2036    | 76           | 45  | 40   | 29    | 21    | 135  |
| 2037    | 65           | 42  | 32   | 29    | 31    | 134  |
| 2038    | 62           | 36  | 29   | 32    | 19    | 116  |
| 2039    | 62           | 36  | 31   | 28    | 26    | 121  |
| 2040    | 69           | 52  | 44   | 55    | 15    | 166  |
| 2041    | 74           | 29  | 28   | 23    | 23    | 103  |
| MEAN    | 69           | 41  | 36   | 30    | 23    | 130  |
| S.D.    | 6.6          | 6.7 | 9.6  | 9.7   | 5.8   | 19.9 |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 3030    | 80           | 37  | 39   | 41    | 22    | 139  |
| 3031    | 70           | 51  | 48   | 29    | 15    | 142  |
| 3032    | 75           | 40  | 36   | 27    | 25    | 128  |
| 3033    | 73           | 38  | 31   | 29    | 21    | 119  |
| 3034    | 76           | 50  | 44   | 46    | 36    | 176  |
| 3035    | 69           | 30  | 23   | 33    | 28    | 114  |
| 3036    | 73           | 44  | 53   | 41    | 25    | 164  |
| 3037    | 82           | 58  | 46   | 37    | 29    | 170  |
| 3038    | 69           | 53  | 43   | 40    | 20    | 156  |
| 3039    | 75           | 33  | 33   | 35    | 24    | 126  |
| 3040    | 83           | 43  | 52   | 35    | 30    | 160  |
| 3041    | 87           | 55  | 49   | 27    | 30    | 161  |
| MEAN    | 76           | 44  | 41   | 35    | 25    | 146  |
| S.D.    | 5.9          | 8.9 | 9.3  | 6.3   | 5.7   | 21.2 |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

BUTANE: 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

| ANIMAL# | DAY OF STUDY |      |      |       |       |      |
|---------|--------------|------|------|-------|-------|------|
|         | -7-0         | 0-7  | 7-14 | 14-21 | 21-28 | 0-28 |
| 4030    | 73           | 48   | 45   | 39    | 26    | 158  |
| 4031    | 64           | 46   | 32   | 22    | 22    | 122  |
| 4032    | 67           | 45   | 38   | 24    | 32    | 139  |
| 4033    | 76           | 47   | 43   | 27    | 27    | 145  |
| 4034    | 69           | 36   | 48   | 25    | 18    | 126  |
| 4035    | 67           | 39   | 24   | 34    | 6     | 103  |
| 4036    | 70           | 27   | 26   | 37    | 10    | 100  |
| 4037    | 66           | 43   | 33   | 26    | 20    | 122  |
| 4038    | 83           | 54   | 51   | 34    | 31    | 170  |
| 4039    | 64           | 33   | 28   | 30    | 25    | 116  |
| 4040    | 74           | 19   | 26   | 25    | 20    | 90   |
| 4041    | 60           | 45   | 32   | 27    | 23    | 126  |
| MEAN    | 69           | 40   | 35   | 29    | 22    | 126  |
| S.D.    | 6.2          | 10.0 | 9.1  | 5.7   | 7.8   | 23.7 |
| N       | 12           | 12   | 12   | 12    | 12    | 12   |

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## APPENDIX D

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 1530    | 38           | 19  | 15   | 16    | 6     | 56   |
| 1531    | 34           | 13  | 5    | 29    | 14    | 61   |
| 1532    | 36           | 14  | 21   | 15    | 9     | 60   |
| 1533    | 37           | 14  | 20   | 14    | 9     | 56   |
| 1534    | 37           | 24  | 17   | 10    | 3     | 54   |
| 1535    | 36           | 19  | 17   | 9     | 11    | 55   |
| 1536    | 43           | 11  | 29   | 10    | 17    | 67   |
| 1537    | 47           | 17  | 29   | 5     | 17    | 68   |
| 1538    | 47           | 6   | 21   | 5     | 15    | 46   |
| 1539    | 32           | 27  | 17   | 13    | 3     | 60   |
| 1540    | 29           | 10  | 17   | 9     | 4     | 41   |
| 1541    | 36           | 9   | 3    | 18    | 11    | 41   |
| MEAN    | 38           | 15  | 18   | 13    | 10    | 55   |
| S.D.    | 5.4          | 6.1 | 7.7  | 6.6   | 5.0   | 8.9  |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

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

FEMALES GROUP 2 900 PPM  
INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 2530    | 38           | 17  | 14   | 18    | 12    | 61   |
| 2531    | 23           | 36  | 26   | 13    | 6     | 81   |
| 2532    | 43           | 14  | 19   | 20    | -1    | 52   |
| 2533    | 33           | 7   | 29   | 23    | 9     | 68   |
| 2534    | 34           | 20  | 7    | 31    | 9     | 66   |
| 2535    | 21           | 25  | 16   | 15    | 4     | 60   |
| 2536    | 33           | 6   | 29   | 9     | 14    | 58   |
| 2537    | 37           | 16  | 18   | 22    | 13    | 68   |
| 2538    | 36           | 10  | 19   | 14    | 9     | 52   |
| 2539    | 24           | 25  | 15   | 15    | 16    | 71   |
| 2540    | 37           | 15  | 16   | 15    | 5     | 50   |
| 2541    | 45           | 11  | 13   | 4     | 28    | 56   |
| MEAN    | 34           | 17  | 18   | 17    | 10    | 62   |
| S.D.    | 7.7          | 8.7 | 6.7  | 7.1   | 7.4   | 9.2  |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 3530    | 43           | 20  | 26   | 23    | -9    | 60   |
| 3531    | 33           | 17  | 20   | 6     | 12    | 56   |
| 3532    | 41           | 18  | 23   | 7     | 9     | 57   |
| 3533    | 41           | 17  | 20   | 21    | 14    | 72   |
| 3534    | 54           | 38  | -11  | 47    | 22    | 96   |
| 3535    | 42           | 16  | 26   | 8     | 16    | 66   |
| 3536    | 40           | 19  | 13   | 27    | 10    | 68   |
| 3537    | 50           | 17  | 17   | 8     | 26    | 67   |
| 3554    | 33           | 4   | 23   | 16    | 12    | 54   |
| 3539    | 31           | 19  | 20   | 11    | 16    | 65   |
| 3540    | 38           | 13  | 17   | 6     | 2     | 38   |
| 3541    | 29           | 29  | 22   | 16    | -3    | 64   |
| MEAN    | 40           | 19  | 18   | 16    | 10    | 64   |
| S.D.    | 7.5          | 8.2 | 9.8  | 11.9  | 9.9   | 13.4 |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX D

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

FEMALES GROUP 4 9000 PPM INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

| ANIMAL# | DAY OF STUDY |     |      |       |       |      |
|---------|--------------|-----|------|-------|-------|------|
|         | -7-0         | 0-7 | 7-14 | 14-21 | 21-28 | 0-28 |
| 4530    | 47           | 11  | 12   | 15    | 16    | 54   |
| 4531    | 38           | 16  | 18   | 16    | 6     | 57   |
| 4532    | 46           | 10  | 10   | 19    | 11    | 51   |
| 4533    | 26           | 24  | 10   | 9     | 13    | 55   |
| 4534    | 39           | 29  | 23   | 6     | 25    | 83   |
| 4535    | 28           | 6   | 19   | 3     | 10    | 38   |
| 4536    | 29           | 19  | 6    | 28    | 3     | 56   |
| 4537    | 41           | 18  | 16   | 3     | 14    | 50   |
| 4538    | 35           | 11  | 20   | 25    | 5     | 62   |
| 4539    | 47           | 6   | 17   | 8     | 17    | 47   |
| 4540    | 41           | 12  | 20   | 12    | 0     | 44   |
| 4541    | 26           | 21  | 18   | 11    | 9     | 59   |
| MEAN    | 37           | 15  | 16   | 13    | 11    | 55   |
| S.D.    | 7.8          | 7.3 | 5.0  | 8.1   | 6.7   | 11.1 |
| N       | 12           | 12  | 12   | 12    | 12    | 12   |

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## APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |
|---------|--------------|-----|-----|
|         | 0            | 7   | 14  |
| 1030    | 101          | 81  | 76  |
| 1031    | 95           | 90  | 77  |
| 1032    | 110          | 88  | 78  |
| 1033    | 106          | 86  | 75  |
| 1034    | 93           | 80  | 71  |
| 1035    | 100          | 85  | 68  |
| 1036    | 98           | 80  | 73  |
| 1037    | 102          | 86  | 78  |
| 1038    | 101          | 84  | 70  |
| 1039    | 103          | 88  | 77  |
| 1040    | 117          | 87  | 80  |
| 1041    | 105          | 82  | 75  |
| MEAN    | 103          | 85  | 75  |
| S.D.    | 6.2          | 3.3 | 3.7 |
| N       | 12           | 12  | 12  |

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APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |
|---------|--------------|-----|-----|
|         | 0            | 7   | 14  |
| 2030    | 99           | 84  | 74  |
| 2031    | 93           | 78  | 69  |
| 2032    | 103          | 85  | 76  |
| 2033    | 101          | 86  | 76  |
| 2034    | 114          | 93  | 82  |
| 2035    | 107          | 86  | 76  |
| 2036    | 107          | 91  | 80  |
| 2037    | 97           | 89  | 78  |
| 2038    | 104          | 87  | 76  |
| 2039    | 100          | 85  | 73  |
| 2040    | 102          | 92  | 80  |
| 2041    | 103          | 80  | 75  |
| MEAN    | 103          | 86  | 76  |
| S.D.    | 5.4          | 4.5 | 3.4 |
| N       | 12           | 12  | 12  |

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## APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |
|---------|--------------|-----|-----|
|         | 0            | 7   | 14  |
| 3030    | 116          | 87  | 77  |
| 3031    | 98           | 86  | 76  |
| 3032    | 104          | 88  | 73  |
| 3033    | 104          | 85  | 70  |
| 3034    | 108          | 93  | 80  |
| 3035    | 99           | 79  | 69  |
| 3036    | 111          | 94  | 86  |
| 3037    | 113          | 91  | 80  |
| 3038    | 107          | 87  | 77  |
| 3039    | 106          | 88  | 76  |
| 3040    | 119          | 95  | 85  |
| 3041    | 123          | 99  | 83  |
| MEAN    | 109          | 89  | 78  |
| S.D.    | 7.7          | 5.4 | 5.5 |
| N       | 12           | 12  | 12  |

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APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |
|---------|--------------|-----|-----|
|         | 0            | 7   | 14  |
| 4030    | 108          | 89  | 76  |
| 4031    | 96           | 85  | 75  |
| 4032    | 101          | 86  | 78  |
| 4033    | 104          | 91  | 76  |
| 4034    | 107          | 91  | 82  |
| 4035    | 104          | 85  | 74  |
| 4036    | 102          | 80  | 70  |
| 4037    | 105          | 93  | 77  |
| 4038    | 116          | 92  | 83  |
| 4039    | 101          | 84  | 70  |
| 4040    | 95           | 82  | 73  |
| 4041    | 101          | 86  | 75  |
| MEAN    | 103          | 87  | 76  |
| S.D.    | 5.6          | 4.0 | 3.9 |
| N       | 12           | 12  | 12  |

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## APPENDIX E

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

FEMALES GROUP 1 0 PPM  
INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

| ANIMAL# | DAY OF STUDY |     |     |     |     |
|---------|--------------|-----|-----|-----|-----|
|         | 0            | 7   | 14  | 21  | 28  |
| 1530    | 99           | 82  | 76  | 72  | 71  |
| 1531    | 91           | 74  | 76  | 81  | 72  |
| 1532    | CF           | CF  | 69  | 63  | CF  |
| 1533    | 100          | 83  | 85  | 78  | 77  |
| 1534    | 101          | 88  | 81  | 76  | 77  |
| 1535    | 107          | 85  | 82  | 77  | 76  |
| 1536    | 103          | 87  | 88  | 83  | 82  |
| 1537    | 114          | 80  | 82  | 72  | 75  |
| 1538    | 99           | 76  | 80  | 75  | 79  |
| 1539    | 95           | 85  | 79  | 74  | 71  |
| 1540    | 93           | 80  | 79  | 72  | 69  |
| 1541    | 99           | 79  | 80  | 80  | 75  |
| MEAN    | 100          | 82  | 80  | 75  | 75  |
| S.D.    | 6.5          | 4.3 | 4.8 | 5.2 | 3.9 |
| N       | 11           | 11  | 12  | 12  | 11  |

CF=Contaminated Feeder

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## APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |     |     |
|---------|--------------|-----|-----|-----|-----|
|         | 0            | 7   | 14  | 21  | 28  |
| 2530    | 98           | 80  | 83  | 80  | 77  |
| 2531    | 95           | 88  | 82  | 76  | 76  |
| 2532    | 104          | 80  | 88  | 77  | 73  |
| 2533    | 102          | 85  | 90  | 84  | 75  |
| 2534    | 110          | 94  | 92  | 89  | 82  |
| 2535    | 101          | 87  | 84  | 78  | 78  |
| 2536    | 95           | 77  | 86  | 79  | 78  |
| 2537    | 101          | 82  | 88  | 86  | 76  |
| 2538    | 102          | 86  | 82  | 81  | 79  |
| 2539    | 101          | 91  | 89  | 80  | 78  |
| 2540    | SF           | SF  | SF  | 76  | 77  |
| 2541    | 109          | 84  | 79  | 77  | 78  |
| MEAN    | 102          | 85  | 86  | 80  | 77  |
| S.D.    | 4.9          | 5.1 | 4.0 | 4.1 | 2.3 |
| N       | 11           | 11  | 11  | 12  | 12  |

SF=Spilled Feeder

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## APPENDIX E

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

| FEMALES GROUP 3 |              | INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY) |     |     |     |  |
|-----------------|--------------|--------------------------------------------|-----|-----|-----|--|
|                 |              | 3000 PPM                                   |     |     |     |  |
| ANIMAL#         | DAY OF STUDY |                                            |     |     |     |  |
|                 | 0            | 7                                          | 14  | 21  | 28  |  |
| 3530            | 98           | 85                                         | 79  | 80  | 70  |  |
| 3531            | 107          | SF                                         | 81  | 88  | 72  |  |
| 3532            | 93           | 80                                         | 78  | 69  | 70  |  |
| 3533            | 96           | 80                                         | 78  | 76  | 71  |  |
| 3534            | 108          | 95                                         | 77  | 83  | 79  |  |
| 3535            | 101          | 84                                         | 85  | 78  | 73  |  |
| 3536            | 107          | 88                                         | 80  | 80  | 70  |  |
| 3537            | 103          | 84                                         | 78  | 75  | 75  |  |
| 3554            | 77           | 82                                         | 82  | 76  | 73  |  |
| 3539            | 98           | 83                                         | 80  | 77  | 78  |  |
| 3540            | 99           | 84                                         | 77  | 67  | 76  |  |
| 3541            | 101          | 93                                         | 82  | 76  | 74  |  |
| MEAN            | 99           | 85                                         | 80  | 77  | 73  |  |
| S.D.            | 8.4          | 4.8                                        | 2.4 | 5.6 | 3.0 |  |
| N               | 12           | 11                                         | 12  | 12  | 12  |  |

SF=Spilled Feeder

Huntingdon Life Sciences 03-4242  
MAIN STUDY

## APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |     |     |
|---------|--------------|-----|-----|-----|-----|
|         | 0            | 7   | 14  | 21  | 28  |
| 3530    | 98           | 85  | 79  | 80  | 70  |
| 3531    | 107          | SF  | 81  | 88  | 72  |
| 3532    | 93           | 80  | 78  | 69  | 70  |
| 3533    | 96           | 80  | 78  | 76  | 71  |
| 3534    | 108          | 95  | 77  | 83  | 79  |
| 3535    | 101          | 84  | 85  | 78  | 73  |
| 3536    | 107          | 88  | 80  | 80  | 70  |
| 3537    | 103          | 84  | 78  | 75  | 75  |
| 3554    | 77           | 82  | 82  | 76  | 73  |
| 3539    | 98           | 83  | 80  | 77  | 78  |
| 3540    | 99           | 84  | 77  | 67  | 76  |
| 3541    | 101          | 93  | 82  | 76  | 74  |
| MEAN    | 99           | 85  | 80  | 77  | 73  |
| S.D.    | 8.4          | 4.8 | 2.4 | 5.6 | 3.0 |
| N       | 12           | 11  | 12  | 12  | 12  |

SF=Spilled Feeder

Huntingdon Life Sciences 03-4242  
MAIN STUDY

## APPENDIX E

BUTANE: 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

| ANIMAL# | DAY OF STUDY |     |     |     |     |
|---------|--------------|-----|-----|-----|-----|
|         | 0            | 7   | 14  | 21  | 28  |
| 4530    | 101          | 80  | 77  | 72  | 71  |
| 4531    | 102          | 85  | 86  | 77  | 72  |
| 4532    | 103          | 78  | 79  | 78  | 72  |
| 4533    | 99           | 82  | 80  | 75  | 75  |
| 4534    | 99           | 80  | 74  | 68  | 73  |
| 4535    | 102          | 89  | 85  | 78  | 82  |
| 4536    | 102          | 83  | 81  | 83  | 67  |
| 4537    | 108          | 82  | 82  | 76  | 77  |
| 4538    | 102          | 86  | 92  | 79  | 77  |
| 4539    | 107          | 78  | 84  | 79  | 76  |
| 4540    | 99           | 82  | 83  | 74  | 73  |
| 4541    | 90           | 81  | 76  | 75  | 76  |
| MEAN    | 101          | 82  | 82  | 76  | 74  |
| S.D.    | 4.5          | 3.3 | 4.9 | 3.8 | 3.9 |
| N       | 12           | 12  | 12  | 12  | 12  |

|  |                                                                                     |            |
|--|-------------------------------------------------------------------------------------|------------|
|  | Individual Functional Observational<br>Battery Evaluations<br>Main Study<br>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<sup>1</sup>**

Forelimb and hindlimb grip strength measured in grams of force.

**RECTAL TEMPERATURE**

Measured in centigrade.

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<sup>1</sup>The means of Trials 1 and 2 were calculated and statistically evaluated in Table 6.

| Males           |                    | Individual Functional Observational Battery Evaluations Termination |                       |                  |             |         |                  |            | Appendix F              |
|-----------------|--------------------|---------------------------------------------------------------------|-----------------------|------------------|-------------|---------|------------------|------------|-------------------------|
| Animal Number   | Reflex Assessments |                                                                     | Grip Strength (grams) |                  |             |         |                  |            | Rectal Temperature (°C) |
|                 | Sound              | Pain                                                                | Trial 1               | Forelimb Trial 2 | Mean        | Trial 1 | Hindlimb Trial 2 | Mean       |                         |
| Group 1 – 0 ppm |                    |                                                                     |                       |                  |             |         |                  |            |                         |
| 1030            | 1                  | 1                                                                   | 855                   | 700              | <b>778</b>  | 610     | 750              | <b>680</b> | 38.5                    |
| 1031            | 1                  | 1                                                                   | 935                   | 945              | <b>940</b>  | 630     | 730              | <b>680</b> | 35.8                    |
| 1032            | 1                  | 1                                                                   | 1080                  | 990              | <b>1035</b> | 690     | 690              | <b>690</b> | 34.2                    |
| 1033            | 1                  | 1                                                                   | 1010                  | 835              | <b>923</b>  | 785     | 900              | <b>843</b> | 35.2                    |
| 1034            | 1                  | 2                                                                   | 1055                  | 1030             | <b>1043</b> | 865     | 870              | <b>868</b> | 37.3                    |
| 1035            | 1                  | 1                                                                   | 895                   | 1140             | <b>1018</b> | 810     | 950              | <b>880</b> | 37.4                    |
| 1036            | 1                  | 2                                                                   | 590                   | 955              | <b>773</b>  | 670     | 580              | <b>625</b> | 37.3                    |
| 1037            | 1                  | 1                                                                   | 1315                  | 1060             | <b>1188</b> | 870     | 865              | <b>868</b> | 35.4                    |
| 1038            | 1                  | 1                                                                   | 1180                  | 1065             | <b>1123</b> | 860     | 825              | <b>843</b> | 37.2                    |
| 1039            | 1                  | 1                                                                   | 925                   | 1110             | <b>1018</b> | 820     | 855              | <b>838</b> | 38.5                    |
| 1040            | 1                  | 1                                                                   | 1205                  | 1065             | <b>1135</b> | 835     | 805              | <b>820</b> | 37.2                    |
| 1041            | 1                  | 1                                                                   | 1195                  | 1050             | <b>1123</b> | 510     | 660              | <b>585</b> | 37.5                    |

|       |                                                                        |            |
|-------|------------------------------------------------------------------------|------------|
| Males | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|-------|------------------------------------------------------------------------|------------|

| Animal<br>Number  | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |             |         |                     |            | Rectal Temperature<br>(°C) |
|-------------------|-----------------------|------|--------------------------|---------------------|-------------|---------|---------------------|------------|----------------------------|
|                   | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean        | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 2 - 900 ppm |                       |      |                          |                     |             |         |                     |            |                            |
| 2030              | 1                     | 1    | 1050                     | 705                 | <b>878</b>  | 705     | 625                 | <b>665</b> | 33.3                       |
| 2031              | 1                     | 1    | 860                      | 780                 | <b>820</b>  | 820     | 650                 | <b>735</b> | 35.7                       |
| 2032              | 1                     | 1    | 680                      | 830                 | <b>755</b>  | 645     | 665                 | <b>655</b> | 32.9                       |
| 2033              | 1                     | 1    | 685                      | 1050                | <b>868</b>  | 560     | 600                 | <b>580</b> | 36.3                       |
| 2034              | 1                     | 1    | 900                      | 860                 | <b>880</b>  | 765     | 780                 | <b>773</b> | 37.1                       |
| 2035              | 1                     | 1    | 1060                     | 1180                | <b>1120</b> | 755     | 740                 | <b>748</b> | 38.0                       |
| 2036              | 1                     | 1    | 820                      | 1000                | <b>910</b>  | 715     | 605                 | <b>660</b> | 37.3                       |
| 2037              | 1                     | 2    | 1045                     | 865                 | <b>955</b>  | 745     | 830                 | <b>788</b> | 36.9                       |
| 2038              | 1                     | 1    | 945                      | 1010                | <b>978</b>  | 510     | 855                 | <b>683</b> | 36.1                       |
| 2039              | 1                     | 1    | 935                      | 1000                | <b>968</b>  | 690     | 805                 | <b>748</b> | 37.6                       |
| 2040              | 1                     | 1    | 1500                     | 1000                | <b>1250</b> | 710     | 550                 | <b>630</b> | 37.7                       |
| 2041              | 1                     | 1    | 1095                     | 1125                | <b>1110</b> | 705     | 780                 | <b>743</b> | 38.4                       |

| Males              |                    | Individual Functional Observational Battery Evaluations Termination |                       |                  |             |         |                  |            | Appendix F              |
|--------------------|--------------------|---------------------------------------------------------------------|-----------------------|------------------|-------------|---------|------------------|------------|-------------------------|
| Animal Number      | Reflex Assessments |                                                                     | Grip Strength (grams) |                  |             |         |                  |            | Rectal Temperature (°C) |
|                    | Sound              | Pain                                                                | Trial 1               | Forelimb Trial 2 | Mean        | Trial 1 | Hindlimb Trial 2 | Mean       |                         |
| Group 3 – 3000 ppm |                    |                                                                     |                       |                  |             |         |                  |            |                         |
| 3030               | 1                  | 1                                                                   | 730                   | 1055             | <b>893</b>  | 680     | 770              | <b>725</b> | 34.1                    |
| 3031               | 1                  | 2                                                                   | 1005                  | 900              | <b>953</b>  | 595     | 605              | <b>600</b> | 33.9                    |
| 3032               | 1                  | 1                                                                   | 775                   | 870              | <b>823</b>  | 760     | 875              | <b>818</b> | 35.8                    |
| 3033               | 1                  | 1                                                                   | 850                   | 985              | <b>918</b>  | 855     | 600              | <b>728</b> | 36.7                    |
| 3034               | 1                  | 1                                                                   | 945                   | 900              | <b>923</b>  | 980     | 660              | <b>820</b> | 35.8                    |
| 3035               | 1                  | 1                                                                   | 690                   | 780              | <b>735</b>  | 660     | 685              | <b>673</b> | 38.1                    |
| 3036               | 1                  | 2                                                                   | 810                   | 905              | <b>858</b>  | 715     | 815              | <b>765</b> | 37.0                    |
| 3037               | 1                  | 2                                                                   | 1045                  | 1095             | <b>1070</b> | 575     | 820              | <b>698</b> | 36.1                    |
| 3038               | 1                  | 1                                                                   | 900                   | 990              | <b>945</b>  | 590     | 665              | <b>628</b> | 36.7                    |
| 3039               | 1                  | 1                                                                   | 950                   | 1055             | <b>1003</b> | 640     | 935              | <b>788</b> | 38.1                    |
| 3040               | 1                  | 2                                                                   | 830                   | 1025             | <b>928</b>  | 640     | 660              | <b>650</b> | 38.6                    |
| 3041               | 1                  | 2                                                                   | 1040                  | 1190             | <b>1115</b> | 630     | 710              | <b>670</b> | 35.8                    |

|       |                                                                        |            |
|-------|------------------------------------------------------------------------|------------|
| Males | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|-------|------------------------------------------------------------------------|------------|

| Animal<br>Number   | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |             |         |                     |            | Rectal Temperature<br>(°C) |
|--------------------|-----------------------|------|--------------------------|---------------------|-------------|---------|---------------------|------------|----------------------------|
|                    | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean        | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 4 – 9000 ppm |                       |      |                          |                     |             |         |                     |            |                            |
| 4030               | 1                     | 1    | 680                      | 980                 | <b>830</b>  | 800     | 970                 | <b>885</b> | 37.1                       |
| 4031               | 1                     | 2    | 535                      | 555                 | <b>545</b>  | 435     | 490                 | <b>463</b> | 36.2                       |
| 4032               | 1                     | 2    | 805                      | 830                 | <b>818</b>  | 635     | 725                 | <b>680</b> | 36.8                       |
| 4033               | 1                     | 1    | 660                      | 1000                | <b>830</b>  | 850     | 855                 | <b>853</b> | 35.8                       |
| 4034               | 1                     | 1    | 1090                     | 1010                | <b>1050</b> | 730     | 795                 | <b>763</b> | 36.0                       |
| 4035               | 1                     | 1    | 920                      | 950                 | <b>935</b>  | 705     | 635                 | <b>670</b> | 36.1                       |
| 4036               | 1                     | 1    | 965                      | 1000                | <b>983</b>  | 655     | 640                 | <b>648</b> | 35.9                       |
| 4037               | 1                     | 1    | 995                      | 1050                | <b>1023</b> | 595     | 630                 | <b>613</b> | 36.0                       |
| 4038               | 1                     | 1    | 860                      | 920                 | <b>890</b>  | 785     | 675                 | <b>730</b> | 38.1                       |
| 4039               | 1                     | 1    | 1000                     | 1000                | <b>1000</b> | 705     | 600                 | <b>653</b> | 34.6                       |
| 4040               | 1                     | 2    | 985                      | 870                 | <b>928</b>  | 740     | 665                 | <b>703</b> | 37.5                       |
| 4041               | 1                     | 1    | 800                      | 565                 | <b>683</b>  | 560     | 840                 | <b>700</b> | 38.3                       |

|         |                                                                        |            |
|---------|------------------------------------------------------------------------|------------|
| Females | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|---------|------------------------------------------------------------------------|------------|

| Animal<br>Number | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |            |         |                     |            | Rectal Temperature<br>(°C) |
|------------------|-----------------------|------|--------------------------|---------------------|------------|---------|---------------------|------------|----------------------------|
|                  | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean       | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 1 – 0 ppm  |                       |      |                          |                     |            |         |                     |            |                            |
| 1530             | 1                     | 1    | 735                      | 790                 | <b>763</b> | 610     | 610                 | <b>610</b> | 36.6                       |
| 1531             | 1                     | 1    | 765                      | 780                 | <b>773</b> | 510     | 595                 | <b>553</b> | 38.1                       |
| 1532             | 1                     | 1    | 770                      | 770                 | <b>770</b> | 490     | 660                 | <b>575</b> | 35.3                       |
| 1533             | 1                     | 1    | 730                      | 805                 | <b>768</b> | 540     | 520                 | <b>530</b> | 38.4                       |
| 1534             | 1                     | 1    | 850                      | 835                 | <b>843</b> | 580     | 590                 | <b>585</b> | 37.6                       |
| 1535             | 1                     | 1    | 610                      | 625                 | <b>618</b> | 575     | 595                 | <b>585</b> | 38.0                       |
| 1536             | 1                     | 1    | 755                      | 740                 | <b>748</b> | 640     | 640                 | <b>640</b> | 38.5                       |
| 1537             | 1                     | 1    | 815                      | 830                 | <b>823</b> | 605     | 795                 | <b>700</b> | 38.3                       |
| 1538             | 1                     | 1    | 810                      | 725                 | <b>768</b> | 570     | 655                 | <b>613</b> | 39.0                       |
| 1539             | 1                     | 1    | 875                      | 1020                | <b>948</b> | 545     | 625                 | <b>585</b> | 39.2                       |
| 1540             | 1                     | 2    | 975                      | 535                 | <b>755</b> | 610     | 620                 | <b>615</b> | 36.1                       |
| 1541             | 1                     | 1    | 660                      | 870                 | <b>765</b> | 570     | 550                 | <b>560</b> | 38.9                       |

|         |                                                                        |            |
|---------|------------------------------------------------------------------------|------------|
| Females | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|---------|------------------------------------------------------------------------|------------|

| Animal<br>Number  | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |            |         |                     |            | Rectal Temperature<br>(°C) |
|-------------------|-----------------------|------|--------------------------|---------------------|------------|---------|---------------------|------------|----------------------------|
|                   | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean       | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 2 – 900 ppm |                       |      |                          |                     |            |         |                     |            |                            |
| 2530              | 1                     | 1    | 840                      | 845                 | <b>843</b> | 1000    | 860                 | <b>930</b> | 33.4                       |
| 2531              | 1                     | 1    | 940                      | 855                 | <b>898</b> | 1120    | 745                 | <b>933</b> | 36.4                       |
| 2532              | 1                     | 1    | 1000                     | 805                 | <b>903</b> | 815     | 640                 | <b>728</b> | 37.2                       |
| 2533              | 1                     | 1    | 900                      | 895                 | <b>898</b> | 710     | 555                 | <b>633</b> | 37.8                       |
| 2534              | 1                     | 1    | 855                      | 830                 | <b>843</b> | 700     | 850                 | <b>775</b> | 37.8                       |
| 2535              | 1                     | 1    | 760                      | 1000                | <b>880</b> | 780     | 765                 | <b>773</b> | 38.8                       |
| 2536              | 1                     | 1    | 955                      | 1035                | <b>995</b> | 570     | 750                 | <b>660</b> | 38.1                       |
| 2537              | 1                     | 1    | 810                      | 850                 | <b>830</b> | 650     | 525                 | <b>588</b> | 38.1                       |
| 2538              | 1                     | 1    | 745                      | 560                 | <b>653</b> | 350     | 380                 | <b>365</b> | 36.6                       |
| 2539              | 1                     | 1    | 765                      | 985                 | <b>875</b> | 710     | 665                 | <b>688</b> | 38.2                       |
| 2540              | 1                     | 1    | 840                      | 895                 | <b>868</b> | 635     | 955                 | <b>795</b> | 38.3                       |
| 2541              | 1                     | 2    | 890                      | 560                 | <b>725</b> | 500     | 600                 | <b>550</b> | 38.6                       |

|         |                                                                        |            |
|---------|------------------------------------------------------------------------|------------|
| Females | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|---------|------------------------------------------------------------------------|------------|

| Animal<br>Number   | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |            |         |                     |            | Rectal Temperature<br>(°C) |
|--------------------|-----------------------|------|--------------------------|---------------------|------------|---------|---------------------|------------|----------------------------|
|                    | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean       | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 3 – 3000 ppm |                       |      |                          |                     |            |         |                     |            |                            |
| 3530               | 1                     | 1    | 660                      | 665                 | <b>663</b> | 660     | 680                 | <b>670</b> | 38.2                       |
| 3531               | 1                     | 1    | 770                      | 890                 | <b>830</b> | 490     | 540                 | <b>515</b> | 37.8                       |
| 3532               | 1                     | 1    | 910                      | 860                 | <b>885</b> | 585     | 560                 | <b>573</b> | 37.2                       |
| 3533               | 1                     | 2    | 565                      | 740                 | <b>653</b> | 535     | 680                 | <b>608</b> | 38.2                       |
| 3534               | 1                     | 1    | 780                      | 895                 | <b>838</b> | 540     | 665                 | <b>603</b> | 36.4                       |
| 3535               | 1                     | 1    | 975                      | 940                 | <b>958</b> | 605     | 565                 | <b>585</b> | 38.5                       |
| 3536               | 1                     | 1    | 805                      | 850                 | <b>828</b> | 590     | 580                 | <b>585</b> | 36.7                       |
| 3537               | 1                     | 1    | 705                      | 795                 | <b>750</b> | 670     | 760                 | <b>715</b> | 31.7                       |
| 3554               | 1                     | 1    | 970                      | 950                 | <b>960</b> | 610     | 790                 | <b>700</b> | 38.7                       |
| 3539               | 1                     | 1    | 890                      | 870                 | <b>880</b> | 655     | 775                 | <b>715</b> | 35.5                       |
| 3540               | 1                     | 1    | 1000                     | 915                 | <b>958</b> | 525     | 570                 | <b>548</b> | 38.4                       |
| 3541               | 1                     | 1    | 935                      | 1045                | <b>990</b> | 660     | 900                 | <b>780</b> | 37.4                       |

|         |                                                                        |            |
|---------|------------------------------------------------------------------------|------------|
| Females | Individual Functional Observational Battery Evaluations<br>Termination | Appendix F |
|---------|------------------------------------------------------------------------|------------|

| Animal<br>Number   | Reflex<br>Assessments |      | Grip Strength<br>(grams) |                     |             |         |                     |            | Rectal Temperature<br>(°C) |
|--------------------|-----------------------|------|--------------------------|---------------------|-------------|---------|---------------------|------------|----------------------------|
|                    | Sound                 | Pain | Trial 1                  | Forelimb<br>Trial 2 | Mean        | Trial 1 | Hindlimb<br>Trial 2 | Mean       |                            |
| Group 4 – 9000 ppm |                       |      |                          |                     |             |         |                     |            |                            |
| 4530               | 1                     | 1    | 945                      | 930                 | <b>938</b>  | 470     | 730                 | <b>600</b> | 36.7                       |
| 4531               | 1                     | 1    | 850                      | 815                 | <b>833</b>  | 695     | 760                 | <b>728</b> | 36.9                       |
| 4532               | 1                     | 1    | 1000                     | 990                 | <b>995</b>  | 660     | 610                 | <b>635</b> | 38.1                       |
| 4533               | 1                     | 1    | 755                      | 840                 | <b>798</b>  | 570     | 620                 | <b>595</b> | 38.7                       |
| 4534               | 1                     | 1    | 805                      | 900                 | <b>853</b>  | 640     | 540                 | <b>590</b> | 37.7                       |
| 4535               | 1                     | 1    | 630                      | 780                 | <b>705</b>  | 580     | 560                 | <b>570</b> | 39.5                       |
| 4536               | 1                     | 1    | 995                      | 925                 | <b>960</b>  | 725     | 610                 | <b>668</b> | 37.5                       |
| 4537               | 1                     | 1    | 670                      | 810                 | <b>740</b>  | 425     | 470                 | <b>448</b> | 37.0                       |
| 4538               | 1                     | 1    | 990                      | 935                 | <b>963</b>  | 510     | 705                 | <b>608</b> | 36.5                       |
| 4539               | 1                     | 1    | 840                      | 700                 | <b>770</b>  | 690     | 580                 | <b>635</b> | 39.1                       |
| 4540               | 1                     | 1    | 1030                     | 1040                | <b>1035</b> | 745     | 550                 | <b>648</b> | 38.9                       |
| 4541               | 1                     | 1    | 990                      | 1060                | <b>1025</b> | 725     | 675                 | <b>700</b> | 38.3                       |

| Males | Individual Motor Activity Values <sup>a</sup> |  |  |  |  |  |  |  |  |  |  |
|-------|-----------------------------------------------|--|--|--|--|--|--|--|--|--|--|
|       | Main Study Termination                        |  |  |  |  |  |  |  |  |  |  |
|       | Appendix G                                    |  |  |  |  |  |  |  |  |  |  |

| Animal<br>Number | Interval |   |   |   |   |   |   |   |   |    |    |    |
|------------------|----------|---|---|---|---|---|---|---|---|----|----|----|
|                  | 1        | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |

## Group 1 – 0 ppm

|             |              |              |              |              |              |              |              |              |              |              |              |              |
|-------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| 1030        | 188          | 143          | 150          | 180          | 147          | 87           | 0            | 0            | 0            | 0            | 0            | 0            |
| 1031        | 210          | 108          | 114          | 161          | 182          | 143          | 122          | 110          | 122          | 116          | 7            | 41           |
| 1032        | 147          | 162          | 67           | 6            | 63           | 32           | 97           | 94           | 109          | 23           | 17           | 60           |
| 1033        | 186          | 167          | 160          | 164          | 72           | 163          | 39           | 92           | 5            | 6            | 2            | 1            |
| 1034        | 166          | 131          | 129          | 86           | 121          | 56           | 48           | 51           | 3            | 0            | 18           | 16           |
| 1035        | 155          | 87           | 92           | 24           | 0            | 0            | 0            | 0            | 0            | 0            | 0            | 10           |
| 1036        | 156          | 169          | 108          | 84           | 108          | 101          | 138          | 77           | 33           | 49           | 1            | 2            |
| 1037        | 199          | 207          | 190          | 172          | 150          | 154          | 135          | 131          | 128          | 159          | 140          | 95           |
| 1038        | 128          | 166          | 132          | 99           | 38           | 14           | 0            | 0            | 0            | 0            | 0            | 4            |
| 1039        | 155          | 148          | 107          | 69           | 28           | 0            | 1            | 0            | 15           | 1            | 0            | 0            |
| 1040        | 193          | 164          | 166          | 182          | 87           | 1            | 0            | 0            | 0            | 0            | 0            | 0            |
| 1041        | 173          | 146          | 113          | 142          | 41           | 48           | 2            | 6            | 2            | 4            | 5            | 0            |
| <b>Mean</b> | <b>171.3</b> | <b>149.8</b> | <b>127.3</b> | <b>114.1</b> | <b>86.4</b>  | <b>66.6</b>  | <b>48.5</b>  | <b>46.8</b>  | <b>34.8</b>  | <b>29.8</b>  | <b>15.8</b>  | <b>19.1</b>  |
| <b>SD</b>   | <b>24.29</b> | <b>31.13</b> | <b>34.49</b> | <b>61.45</b> | <b>56.05</b> | <b>61.77</b> | <b>58.13</b> | <b>51.26</b> | <b>52.23</b> | <b>53.12</b> | <b>39.64</b> | <b>30.62</b> |
| <b>N</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    |

## Group 2 – 900 ppm

|             |              |              |              |              |              |              |              |              |              |              |              |              |
|-------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| 2030        | 203          | 116          | 130          | 122          | 83           | 4            | 0            | 7            | 0            | 2            | 1            | 6            |
| 2031        | 141          | 120          | 125          | 43           | 0            | 0            | 5            | 15           | 0            | 1            | 1            | 0            |
| 2032        | 225          | 178          | 116          | 112          | 123          | 49           | 0            | 0            | 0            | 9            | 0            | 0            |
| 2033        | 323          | 245          | 164          | 58           | 62           | 75           | 54           | 65           | 13           | 53           | 3            | 8            |
| 2034        | 196          | 151          | 153          | 165          | 108          | 125          | 66           | 21           | 0            | 53           | 71           | 47           |
| 2035        | 190          | 191          | 120          | 80           | 7            | 0            | 0            | 0            | 0            | 1            | 117          | 144          |
| 2036        | 188          | 159          | 122          | 36           | 91           | 88           | 132          | 1            | 6            | 0            | 0            | 0            |
| 2037        | 153          | 73           | 38           | 51           | 82           | 0            | 10           | 1            | 1            | 1            | 7            | 2            |
| 2038        | 212          | 186          | 152          | 129          | 125          | 105          | 17           | 0            | 1            | 3            | 0            | 3            |
| 2039        | 195          | 147          | 157          | 142          | 138          | 105          | 71           | 102          | 16           | 55           | 85           | 65           |
| 2040        | 397          | 260          | 285          | 156          | 21           | 0            | 0            | 169          | 149          | 4            | 0            | 3            |
| 2041        | 154          | 67           | 76           | 17           | 7            | 0            | 0            | 0            | 1            | 1            | 0            | 0            |
| <b>Mean</b> | <b>214.8</b> | <b>157.8</b> | <b>136.5</b> | <b>92.6</b>  | <b>70.6</b>  | <b>45.9</b>  | <b>29.6</b>  | <b>31.8</b>  | <b>15.6</b>  | <b>15.3</b>  | <b>23.8</b>  | <b>23.2</b>  |
| <b>SD</b>   | <b>73.98</b> | <b>59.64</b> | <b>58.92</b> | <b>51.11</b> | <b>50.41</b> | <b>50.60</b> | <b>42.26</b> | <b>53.78</b> | <b>42.37</b> | <b>23.29</b> | <b>41.83</b> | <b>43.54</b> |
| <b>N</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    |

<sup>a</sup>Number of beam breaks per interval.

| Males | Individual Motor Activity Values <sup>a</sup> |  |  |  |  |  |  |  |  |  |  |
|-------|-----------------------------------------------|--|--|--|--|--|--|--|--|--|--|
|       | Main Study<br>Termination                     |  |  |  |  |  |  |  |  |  |  |
|       | Appendix G                                    |  |  |  |  |  |  |  |  |  |  |

| Animal<br>Number   | Interval     |              |              |              |              |              |              |              |              |              |              |              |
|--------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
|                    | 1            | 2            | 3            | 4            | 5            | 6            | 7            | 8            | 9            | 10           | 11           | 12           |
| Group 3 – 3000 ppm |              |              |              |              |              |              |              |              |              |              |              |              |
| 3030               | 235          | 180          | 177          | 119          | 177          | 117          | 156          | 125          | 53           | 124          | 102          | 22           |
| 3031               | 187          | 166          | 142          | 150          | 120          | 185          | 178          | 118          | 148          | 67           | 0            | 0            |
| 3032               | 119          | 151          | 36           | 169          | 154          | 51           | 13           | 27           | 2            | 0            | 2            | 0            |
| 3033               | 185          | 139          | 60           | 162          | 116          | 45           | 58           | 90           | 8            | 7            | 5            | 0            |
| 3034               | 194          | 34           | 94           | 46           | 2            | 0            | 0            | 2            | 1            | 3            | 4            | 1            |
| 3035               | 194          | 146          | 142          | 129          | 51           | 45           | 22           | 53           | 3            | 11           | 0            | 2            |
| 3036               | 159          | 120          | 48           | 148          | 167          | 32           | 7            | 2            | 0            | 1            | 0            | 3            |
| 3037               | 234          | 141          | 188          | 175          | 130          | 112          | 101          | 43           | 61           | 11           | 54           | 35           |
| 3038               | 140          | 124          | 154          | 146          | 96           | 90           | 58           | 47           | 76           | 44           | 11           | 6            |
| 3039               | 190          | 146          | 114          | 178          | 111          | 145          | 123          | 85           | 134          | 139          | 62           | 13           |
| 3040               | 238          | 235          | 199          | 125          | 13           | 0            | 3            | 0            | 0            | 0            | 5            | 0            |
| 3041               | 212          | 146          | 175          | 150          | 155          | 162          | 5            | 29           | 12           | 0            | 0            | 0            |
| <b>Mean</b>        | <b>190.6</b> | <b>144.0</b> | <b>127.4</b> | <b>141.4</b> | <b>107.7</b> | <b>82.0</b>  | <b>60.3</b>  | <b>51.8</b>  | <b>41.5</b>  | <b>33.9</b>  | <b>20.4</b>  | <b>6.8</b>   |
| <b>SD</b>          | <b>37.31</b> | <b>45.96</b> | <b>56.53</b> | <b>35.54</b> | <b>57.93</b> | <b>62.39</b> | <b>64.05</b> | <b>43.88</b> | <b>53.70</b> | <b>50.11</b> | <b>33.51</b> | <b>11.15</b> |
| <b>N</b>           | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    |
| Group 4 – 9000 ppm |              |              |              |              |              |              |              |              |              |              |              |              |
| 4030               | 212          | 153          | 131          | 135          | 81           | 69           | 135          | 42           | 0            | 3            | 0            | 0            |
| 4031               | 193          | 92           | 160          | 119          | 38           | 76           | 64           | 79           | 106          | 99           | 129          | 37           |
| 4032               | 169          | 157          | 76           | 34           | 11           | 34           | 0            | 0            | 0            | 2            | 17           | 6            |
| 4033               | 109          | 103          | 95           | 118          | 107          | 104          | 84           | 142          | 54           | 24           | 9            | 31           |
| 4034               | 94           | 122          | 122          | 179          | 12           | 0            | 6            | 0            | 0            | 0            | 0            | 0            |
| 4035               | 168          | 134          | 120          | 132          | 57           | 37           | 13           | 2            | 0            | 76           | 111          | 128          |
| 4036               | 179          | 139          | 107          | 6            | 1            | 3            | 61           | 148          | 134          | 8            | 0            | 1            |
| 4037               | 241          | 162          | 144          | 150          | 165          | 81           | 71           | 31           | 0            | 0            | 1            | 1            |
| 4038               | 222          | 193          | 189          | 111          | 103          | 57           | 35           | 29           | 88           | 100          | 89           | 110          |
| 4039               | 227          | 179          | 156          | 94           | 96           | 40           | 0            | 3            | 0            | 32           | 0            | 9            |
| 4040               | 196          | 155          | 121          | 91           | 93           | 3            | 4            | 7            | 1            | 1            | 6            | 0            |
| 4041               | 235          | 147          | 180          | 179          | 126          | 68           | 53           | 0            | 0            | 6            | 8            | 0            |
| <b>Mean</b>        | <b>187.1</b> | <b>144.7</b> | <b>133.4</b> | <b>112.3</b> | <b>74.2</b>  | <b>47.7</b>  | <b>43.8</b>  | <b>40.3</b>  | <b>31.9</b>  | <b>29.3</b>  | <b>30.8</b>  | <b>26.9</b>  |
| <b>SD</b>          | <b>46.97</b> | <b>29.11</b> | <b>33.75</b> | <b>51.80</b> | <b>50.93</b> | <b>33.93</b> | <b>41.93</b> | <b>54.35</b> | <b>50.12</b> | <b>39.34</b> | <b>48.57</b> | <b>44.96</b> |
| <b>N</b>           | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    | <b>12</b>    |

<sup>a</sup>Number of beam breaks per interval

|         |                                               |            |
|---------|-----------------------------------------------|------------|
|         | Individual Motor Activity Values <sup>a</sup> |            |
| Females | Main Study Termination                        | Appendix G |

| Animal Number     | Interval |       |       |       |       |       |       |       |       |       |       |       |
|-------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                   | 1        | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    |
| Group 1 – 0 ppm   |          |       |       |       |       |       |       |       |       |       |       |       |
| 1530              | 135      | 122   | 56    | 1     | 0     | 1     | 1     | 3     | 0     | 1     | 0     | 0     |
| 1531              | 116      | 74    | 57    | 52    | 32    | 30    | 0     | 0     | 0     | 0     | 17    | 75    |
| 1532              | 154      | 150   | 52    | 88    | 144   | 21    | 18    | 17    | 0     | 0     | 0     | 0     |
| 1533              | 149      | 106   | 123   | 98    | 67    | 61    | 24    | 0     | 0     | 6     | 4     | 22    |
| 1534              | 159      | 98    | 106   | 63    | 106   | 2     | 0     | 0     | 31    | 55    | 65    | 69    |
| 1535              | 105      | 45    | 110   | 86    | 48    | 0     | 0     | 0     | 2     | 0     | 0     | 25    |
| 1536              | 112      | 134   | 101   | 18    | 99    | 0     | 0     | 0     | 4     | 57    | 142   | 44    |
| 1537              | 199      | 112   | 134   | 57    | 88    | 108   | 96    | 24    | 0     | 0     | 1     | 45    |
| 1538              | 152      | 98    | 121   | 88    | 67    | 87    | 73    | 35    | 88    | 12    | 6     | 32    |
| 1539              | 121      | 118   | 85    | 104   | 87    | 75    | 7     | 29    | 76    | 86    | 81    | 83    |
| 1540              | 100      | 97    | 84    | 65    | 57    | 89    | 15    | 72    | 112   | 79    | 80    | 47    |
| 1541              | 160      | 130   | 92    | 25    | 2     | 1     | 12    | 79    | 3     | 0     | 10    | 0     |
| Mean              | 138.5    | 107.0 | 93.4  | 62.1  | 66.4  | 39.6  | 20.5  | 21.6  | 26.3  | 24.7  | 33.8  | 36.8  |
| SD                | 28.93    | 28.08 | 27.60 | 33.23 | 42.33 | 41.61 | 31.36 | 28.24 | 41.27 | 34.10 | 46.76 | 29.07 |
| N                 | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 2 – 900 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| 2530              | 140      | 107   | 54    | 47    | 17    | 7     | 0     | 33    | 56    | 0     | 0     | 0     |
| 2531              | 148      | 134   | 120   | 75    | 88    | 7     | 16    | 0     | 0     | 0     | 0     | 0     |
| 2532              | 144      | 109   | 157   | 12    | 0     | 0     | 10    | 0     | 5     | 27    | 25    | 0     |
| 2533              | 162      | 126   | 120   | 111   | 122   | 90    | 115   | 83    | 65    | 36    | 29    | 18    |
| 2534              | 143      | 132   | 114   | 55    | 95    | 12    | 8     | 1     | 104   | 96    | 25    | 37    |
| 2535              | 139      | 104   | 125   | 124   | 24    | 0     | 6     | 0     | 4     | 82    | 82    | 59    |
| 2536              | 126      | 109   | 116   | 16    | 48    | 0     | 83    | 60    | 0     | 0     | 0     | 0     |
| 2537              | 171      | 121   | 58    | 70    | 51    | 76    | 27    | 99    | 46    | 47    | 18    | 21    |
| 2538              | 160      | 145   | 121   | 135   | 89    | 99    | 20    | 6     | 35    | 2     | 0     | 0     |
| 2539              | 128      | 84    | 101   | 87    | 66    | 61    | 55    | 63    | 70    | 79    | 51    | 55    |
| 2540              | 183      | 148   | 136   | 78    | 11    | 0     | 5     | 146   | 53    | 5     | 4     | 0     |
| 2541              | 158      | 145   | 79    | 95    | 50    | 64    | 17    | 43    | 0     | 0     | 0     | 0     |
| Mean              | 150.2    | 122.0 | 108.4 | 75.4  | 55.1  | 34.7  | 30.2  | 44.5  | 36.5  | 31.2  | 19.5  | 15.8  |
| SD                | 17.08    | 19.83 | 30.65 | 38.74 | 38.03 | 39.67 | 35.82 | 47.47 | 34.75 | 36.67 | 25.57 | 22.63 |
| N                 | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |

<sup>a</sup>Number of beam breaks per interval

|         |                                               |  |  |  |  |  |  |  |  |  |  |            |
|---------|-----------------------------------------------|--|--|--|--|--|--|--|--|--|--|------------|
|         | Individual Motor Activity Values <sup>a</sup> |  |  |  |  |  |  |  |  |  |  |            |
|         | Main Study Termination                        |  |  |  |  |  |  |  |  |  |  |            |
| Females |                                               |  |  |  |  |  |  |  |  |  |  | Appendix G |

| Animal Number      | Interval |       |       |       |       |       |       |       |       |       |       |       |
|--------------------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                    | 1        | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    |
| Group 3 – 3000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| 3530               | 191      | 161   | 131   | 109   | 141   | 60    | 87    | 65    | 40    | 14    | 0     | 2     |
| 3531               | 170      | 91    | 120   | 56    | 25    | 23    | 86    | 101   | 38    | 11    | 0     | 0     |
| 3532               | 172      | 154   | 150   | 28    | 13    | 27    | 0     | 2     | 2     | 1     | 2     | 0     |
| 3533               | 134      | 85    | 85    | 89    | 21    | 0     | 1     | 95    | 72    | 122   | 74    | 57    |
| 3534               | 234      | 160   | 112   | 170   | 133   | 99    | 79    | 4     | 90    | 125   | 152   | 81    |
| 3535               | 223      | 153   | 110   | 125   | 74    | 19    | 0     | 46    | 12    | 9     | 0     | 5     |
| 3536               | 139      | 79    | 59    | 24    | 4     | 0     | 0     | 0     | 0     | 0     | 0     | 19    |
| 3537               | 178      | 207   | 173   | 147   | 218   | 63    | 11    | 6     | 0     | 0     | 0     | 8     |
| 3554               | 137      | 145   | 104   | 36    | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| 3539               | 158      | 111   | 123   | 47    | 62    | 68    | 82    | 90    | 105   | 76    | 65    | 110   |
| 3540               | 132      | 133   | 78    | 69    | 106   | 80    | 38    | 21    | 0     | 0     | 0     | 0     |
| 3541               | 145      | 174   | 76    | 38    | 10    | 1     | 0     | 0     | 0     | 0     | 0     | 0     |
| Mean               | 167.8    | 137.8 | 110.1 | 78.2  | 67.3  | 36.7  | 32.0  | 35.8  | 29.9  | 29.8  | 24.4  | 23.5  |
| SD                 | 34.26    | 39.14 | 32.65 | 49.38 | 69.24 | 35.52 | 39.55 | 41.29 | 39.03 | 48.62 | 48.29 | 37.82 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |
| Group 4 – 9000 ppm |          |       |       |       |       |       |       |       |       |       |       |       |
| 4530               | 136      | 101   | 61    | 27    | 17    | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| 4531               | 159      | 113   | 108   | 94    | 119   | 65    | 51    | 2     | 32    | 67    | 0     | 1     |
| 4532               | 99       | 74    | 105   | 68    | 45    | 119   | 55    | 50    | 43    | 65    | 118   | 26    |
| 4533               | 147      | 124   | 97    | 56    | 5     | 0     | 0     | 0     | 22    | 75    | 96    | 46    |
| 4534               | 175      | 138   | 29    | 157   | 117   | 50    | 5     | 8     | 70    | 139   | 55    | 15    |
| 4535               | 156      | 133   | 120   | 45    | 0     | 0     | 119   | 129   | 39    | 0     | 0     | 4     |
| 4536               | 183      | 124   | 11    | 18    | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 4     |
| 4537               | 139      | 133   | 102   | 75    | 55    | 68    | 53    | 3     | 1     | 0     | 0     | 31    |
| 4538               | 120      | 110   | 147   | 112   | 71    | 98    | 83    | 84    | 75    | 58    | 49    | 21    |
| 4539               | 149      | 115   | 123   | 125   | 118   | 88    | 95    | 68    | 99    | 84    | 89    | 45    |
| 4540               | 165      | 163   | 151   | 114   | 87    | 13    | 10    | 165   | 147   | 167   | 84    | 12    |
| 4541               | 158      | 106   | 79    | 38    | 12    | 4     | 0     | 0     | 0     | 3     | 3     | 7     |
| Mean               | 148.8    | 119.5 | 94.4  | 77.4  | 53.8  | 42.1  | 39.3  | 42.4  | 44.0  | 54.8  | 41.2  | 17.7  |
| SD                 | 23.22    | 22.13 | 43.05 | 43.31 | 47.78 | 44.51 | 42.80 | 57.63 | 46.30 | 57.13 | 45.94 | 16.31 |
| N                  | 12       | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    | 12    |

<sup>a</sup>Number of beam breaks per interval

|  |                                                       |            |
|--|-------------------------------------------------------|------------|
|  | Individual Hematology Values<br>Main Study<br>Preface | Appendix H |
|--|-------------------------------------------------------|------------|

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

**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 |
| NAN          | No abnormalities noted         |

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix H - Main Study

### Individual Hematology Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix H - Main Study

### Individual Hematology Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix H - Main Study

### Individual Hematology Values - Termination

[illegible]

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Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix H - Main Study

### Individual Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
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Individual Hematology Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix H - Main Study

### Individual Hematology Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix H - Main Study  
Individual Hematology Values - Termination

[illegible]

|  |                                                        |            |
|--|--------------------------------------------------------|------------|
|  | Individual Coagulation Values<br>Main Study<br>Preface | Appendix I |
|--|--------------------------------------------------------|------------|

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

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group       | Animal<br>Number | PT      | APTT    |
|-------------|------------------|---------|---------|
|             |                  | Seconds | Seconds |
| 1M<br>0 ppm | 1030             | 11.6    | 18.6    |
|             | 1031             | 13.8    | 21.9    |
|             | 1032             | 13.6    | 20.7    |
|             | 1033             | 14.1    | 21.4    |
|             | 1034             | 13.4    | 20.5    |
|             | 1035             | 13.1    | 21.8    |
|             | 1036             | 15.0    | 23.9    |
|             | 1037             | 13.9    | 23.9    |
|             | 1038             | 14.5    | 25.3    |
|             | 1039             | 13.2    | 22.8    |
|             | 1040             | 14.5    | 24.7    |
|             | 1041             | 14.0    | 22.5    |
|             | Mean             | 13.7    | 22.3    |
|             | SD               | 0.87    | 1.93    |
|             | n                | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group         | Animal<br>Number | PT      | APTT    |
|---------------|------------------|---------|---------|
|               |                  | Seconds | Seconds |
| 2M<br>900 ppm | 2030             | 15.0    | 24.6    |
|               | 2031             | 13.2    | 21.6    |
|               | 2032             | 13.3    | 21.1    |
|               | 2033             | 12.8    | 21.4    |
|               | 2034             | 13.3    | 22.2    |
|               | 2035             | 12.4    | 22.0    |
|               | 2036             | 13.3    | 22.6    |
|               | 2037             | 14.7    | 26.4    |
|               | 2038             | 14.8    | 25.7    |
|               | 2039             | 13.9    | 25.0    |
|               | 2040             | 13.4    | 23.5    |
|               | 2041             | 13.6    | 24.4    |
| Mean          |                  | 13.6    | 23.4    |
| SD            |                  | 0.81    | 1.81    |
| n             |                  | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group    | Animal<br>Number | PT      | APTT    |
|----------|------------------|---------|---------|
|          |                  | Seconds | Seconds |
| 3M       | 3030             | 13.4    | 22.0    |
| 3000 ppm | 3031             | 13.5    | 22.2    |
|          | 3032             | 13.4    | 22.1    |
|          | 3033             | 12.9    | 21.8    |
|          | 3034             | 12.5    | 21.4    |
|          | 3035             | 15.0    | 24.3    |
|          | 3036             | 13.0    | 19.7    |
|          | 3037             | 13.9    | 25.3    |
|          | 3038             | 13.1    | 22.1    |
|          | 3039             | 14.8    | 25.6    |
|          | 3040             | 14.8    | 23.6    |
|          | 3041             | 15.0    | 23.9    |
|          | Mean             | 13.8    | 22.8    |
|          | SD               | 0.90    | 1.72    |
|          | n                | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group          | Animal<br>Number | PT      | APTT    |
|----------------|------------------|---------|---------|
|                |                  | Seconds | Seconds |
| 4M<br>9000 ppm | 4030             | 13.5    | 21.0    |
|                | 4031             | 13.9    | 23.0    |
|                | 4032             | 12.8    | 21.9    |
|                | 4033             | 15.3    | 25.0    |
|                | 4034             | 12.5    | 24.3    |
|                | 4035             | 12.8    | 21.9    |
|                | 4036             | 13.1    | 24.0    |
|                | 4037             | 13.7    | 24.8    |
|                | 4038             | 13.3    | 19.6    |
|                | 4039             | 14.6    | 25.0    |
|                | 4040             | 15.0    | 26.9    |
|                | 4041             | 13.2    | 22.6    |
| Mean           |                  | 13.6    | 23.3    |
| SD             |                  | 0.90    | 2.04    |
| n              |                  | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group | Animal<br>Number | PT      | APTT    |
|-------|------------------|---------|---------|
|       |                  | Seconds | Seconds |
| 1F    | 1530             | 11.7    | 22.1    |
| 0 ppm | 1531             | 11.8    | 20.5    |
|       | 1532             | 11.5    | 19.4    |
|       | 1533             | 11.1    | 17.1    |
|       | 1534             | 11.6    | 18.2    |
|       | 1535             | 11.7    | 18.5    |
|       | 1536             | 11.8    | 20.7    |
|       | 1537             | 12.0    | 21.1    |
|       | 1538             | 12.8    | 19.5    |
|       | 1539             | 12.3    | 20.7    |
|       | 1540             | 13.4    | 21.3    |
|       | 1541             | 12.3    | 18.1    |
|       | Mean             | 12.0    | 19.8    |
|       | SD               | 0.62    | 1.54    |
|       | n                | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242

Appendix I - Main Study

Individual Coagulation Values - Termination

| Group         | Animal<br>Number | PT      | APTT    |
|---------------|------------------|---------|---------|
|               |                  | Seconds | Seconds |
| 2F<br>900 ppm | 2530             | 12.4    | 23.0    |
|               | 2531             | 11.6    | 18.7    |
|               | 2532             | 11.5    | 20.4    |
|               | 2533             | 11.6    | 19.5    |
|               | 2534             | 11.2    | 18.4    |
|               | 2535             | 11.5    | 17.7    |
|               | 2536             | 11.9    | 17.5    |
|               | 2537             | 14.3    | 25.1    |
|               | 2538             | 12.2    | 21.8    |
|               | 2539             | 12.2    | 18.8    |
|               | 2540             | 12.5    | 20.8    |
|               | 2541             | 11.7    | 18.3    |
|               | Mean             | 12.1    | 20.0    |
|               | SD               | 0.82    | 2.32    |
|               | n                | 12      | 12      |

Huntingdon Life Sciences Study No. 03-4242  
Appendix I - Main Study  
Individual Coagulation Values - Termination

| Group          | Animal<br>Number | PT      |         | APTT    |         |
|----------------|------------------|---------|---------|---------|---------|
|                |                  | Seconds | Seconds | Seconds | Seconds |
| 3F<br>3000 ppm | 3530             | 11.4    |         | 20.5    |         |
|                | 3531             | 11.4    |         | 22.5    |         |
|                | 3532             | 11.2    |         | 21.2    |         |
|                | 3533             | 11.6    |         | 20.0    |         |
|                | 3534             | 11.7    |         | 18.8    |         |
|                | 3535             | 11.5    |         | 21.9    |         |
|                | 3536             | 12.3    |         | 19.5    |         |
|                | 3537             | 11.7    |         | 18.8    |         |
|                | 3539             | 12.4    |         | 16.5    |         |
|                | 3540             | 11.4    |         | 22.4    |         |
|                | 3541             | 12.5    |         | 20.2    |         |
|                | 3554             | 12.6    |         | 19.4    |         |
|                | Mean             | 11.8    |         | 20.1    |         |
|                | SD               | 0.50    |         | 1.73    |         |
|                | n                | 12      |         | 12      |         |

Huntingdon Life Sciences Study No. 03-4242

Appendix I - Main Study

Individual Coagulation Values - Termination

| Group          | Animal<br>Number | PT      | APTT    |
|----------------|------------------|---------|---------|
|                |                  | Seconds | Seconds |
| 4F<br>9000 ppm | 4530             | 11.8    | 21.1    |
|                | 4531             | 12.0    | 22.8    |
|                | 4532             | 11.6    | 24.0    |
|                | 4533             | 11.1    | 21.2    |
|                | 4534             | 11.7    | 18.8    |
|                | 4535             | 11.3    | 21.0    |
|                | 4536             | 12.4    | 18.4    |
|                | 4537             | 13.0    | 25.0    |
|                | 4538             | 11.6    | 17.5    |
|                | 4539             | 12.6    | 20.5    |
|                | 4540             | 12.2    | 21.2    |
|                | 4541             | 12.0    | 17.1    |
|                | Mean             | 11.9    | 20.7    |
|                | SD               | 0.55    | 2.46    |
|                | n                | 12      | 12      |

|  |                                                               |            |
|--|---------------------------------------------------------------|------------|
|  | Individual Clinical Chemistry Values<br>Main Study<br>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 <sup>+</sup>  | Sodium                              | mEq/L           |
| K <sup>+</sup>   | Potassium                           | mEq/L           |
| Cl <sup>-</sup>  | Chloride                            | mEq/L           |
| Ca <sup>++</sup> | Calcium                             | mg/dL           |
| PHOS             | Inorganic Phosphorus                | mg/dL           |
| GGT              | Gamma-Glutamyl Transferase          | U/L             |

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

## Individual Clinical Chemistry Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242

Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

| Group       | Animal<br>Number | GGT |
|-------------|------------------|-----|
|             |                  | U/L |
| IM<br>0 ppm | 1030             | 0   |
|             | 1031             | 0   |
|             | 1032             | 0   |
|             | 1033             | 0   |
|             | 1034             | 0   |
|             | 1035             | 0   |
|             | 1036             | 0   |
|             | 1037             | 0   |
|             | 1038             | 0   |
|             | 1039             | 0   |
|             | 1040             | 0   |
|             | 1041             | 0   |
|             | Mean             | 0   |
|             | SD               | 0.0 |
|             | n                | 12  |

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242

Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

| Group   | Animal<br>Number | GGT |
|---------|------------------|-----|
|         |                  | U/L |
| 2M      | 2030             | 0   |
| 900 ppm | 2031             | 0   |
|         | 2032             | 0   |
|         | 2033             | 0   |
|         | 2034             | 0   |
|         | 2035             | 0   |
|         | 2036             | 0   |
|         | 2037             | 0   |
|         | 2038             | 0   |
|         | 2039             | 0   |
|         | 2040             | 0   |
|         | 2041             | 0   |
|         | Mean             | 0   |
|         | SD               | 0.0 |
|         | n                | 12  |

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group    | Animal<br>Number | GGT |
|----------|------------------|-----|
|          |                  | U/L |
| 3M       | 3030             | 0   |
| 3000 ppm | 3031             | 0   |
|          | 3032             | 0   |
|          | 3033             | 0   |
|          | 3034             | 0   |
|          | 3035             | 0   |
|          | 3036             | 0   |
|          | 3037             | 0   |
|          | 3038             | 0   |
|          | 3039             | 0   |
|          | 3040             | 0   |
|          | 3041             | 0   |
|          | Mean             | 0   |
|          | SD               | 0.0 |
|          | n                | 12  |

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

[illegible]

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group    | Animal<br>Number | GGT |
|----------|------------------|-----|
|          |                  | U/L |
| 4M       | 4030             | 0   |
| 9000 ppm | 4031             | 0   |
|          | 4032             | 0   |
|          | 4033             | 0   |
|          | 4034             | 0   |
|          | 4035             | 0   |
|          | 4036             | 0   |
|          | 4037             | 0   |
|          | 4038             | 0   |
|          | 4039             | 0   |
|          | 4040             | 0   |
|          | 4041             | 0   |
|          | Mean             | 0   |
|          | SD               | 0.0 |
|          | n                | 12  |

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group       | Animal<br>Number | GGT |
|-------------|------------------|-----|
|             |                  | U/L |
| 1F<br>0 ppm | 1530             | 0   |
|             | 1531             | 0   |
|             | 1532             | 0   |
|             | 1533             | 0   |
|             | 1534             | 0   |
|             | 1535             | 0   |
|             | 1536             | 0   |
|             | 1537             | 0   |
|             | 1538             | 0   |
|             | 1539             | 0   |
|             | 1540             | 0   |
|             | 1541             | 0   |
|             | Mean             | 0   |
|             | SD               | 0.0 |
|             | n                | 12  |

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

## Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group   | Animal<br>Number | GGT |
|---------|------------------|-----|
|         |                  | U/L |
| 2F      | 2530             | 0   |
| 900 ppm | 2531             | 0   |
|         | 2532             | 0   |
|         | 2533             | 0   |
|         | 2534             | 0   |
|         | 2535             | 0   |
|         | 2536             | 0   |
|         | 2537             | 0   |
|         | 2538             | 0   |
|         | 2539             | 0   |
|         | 2540             | 0   |
|         | 2541             | 0   |
|         | Mean             | 0   |
|         | SD               | 0.0 |
|         | n                | 12  |

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

## Individual Clinical Chemistry Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

## Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group    | Animal<br>Number | GGT |
|----------|------------------|-----|
|          |                  | U/L |
| 3F       | 3530             | 0   |
| 3000 ppm | 3531             | 0   |
|          | 3532             | 0   |
|          | 3533             | 0   |
|          | 3534             | 0   |
|          | 3535             | 0   |
|          | 3536             | 0   |
|          | 3537             | 0   |
|          | 3539             | 0   |
|          | 3540             | 0   |
|          | 3541             | 0   |
|          | 3554             | 0   |
|          | Mean             | 0   |
|          | SD               | 0.0 |
|          | n                | 12  |

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

[illegible]

## Huntingdon Life Sciences Study No. 03-4242

## Appendix J - Main Study

Individual Clinical Chemistry Values - Termination

[illegible]

Huntingdon Life Sciences Study No. 03-4242  
Appendix J - Main Study  
Individual Clinical Chemistry Values - Termination

| Group    | Animal<br>Number | GGT |
|----------|------------------|-----|
|          |                  | U/L |
| 4F       | 4530             | 0   |
| 9000 ppm | 4531             | 0   |
|          | 4532             | 0   |
|          | 4533             | 0   |
|          | 4534             | 0   |
|          | 4535             | 0   |
|          | 4536             | 0   |
|          | 4537             | 0   |
|          | 4538             | 0   |
|          | 4539             | 0   |
|          | 4540             | 0   |
|          | 4541             | 0   |
|          | Mean             | 0   |
|          | SD               | 0.0 |
|          | n                | 12  |

|  |                                                   |            |
|--|---------------------------------------------------|------------|
|  | Individual Organ Weights<br>Main Study<br>Preface | Appendix K |
|--|---------------------------------------------------|------------|

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| % Organ to Brain Weight Ratios ..... | 282 |

**Key to Abbreviations:**

|         |   |          |
|---------|---|----------|
| g       | = | Grams    |
| wt.     | = | Weight   |
| observ. | = | Observed |
| E       | = | Excluded |

**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:**

1. The lung weight for Main Study male animal 2031 was excluded because it was infused prior to being weighed.
2. One adrenal for Main Study male animal 4037 was lost at necropsy. Therefore, the adrenals were unable to be weighed as per protocol for this animal.

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

Summary statistics for absolute organ weights (g)  
Study number: 034242

Printed: 17-Mar-04  
Page: 1  
Version 4.2.2

| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Adrenal Glands | Brain  | Epididymis Left | Epididymis Right | Heart  | Kidneys |
|---------------------|-----------------|-----------------------|----------------|--------|-----------------|------------------|--------|---------|
|                     |                 |                       |                | Male   | Animals         |                  |        |         |
| 1030/M              | 1/1             | 355.9                 | 0.0684         | 1.9279 | 0.5782          | 0.5537           | 1.1315 | 3.1442  |
| 1031/M              | 1/1             | 406.9                 | 0.0710         | 2.0341 | 0.6234          | 0.6267           | 1.2755 | 3.3460  |
| 1032/M              | 1/1             | 384.1                 | 0.0592         | 2.0861 | 0.5608          | 0.5943           | 1.2284 | 3.2417  |
| 1033/M              | 1/1             | 383.0                 | 0.0663         | 2.1253 | 0.5192          | 0.5697           | 1.3236 | 3.3784  |
| 1034/M              | 1/1             | 381.8                 | 0.0770         | 2.0759 | 0.7575          | 0.6841           | 1.3143 | 3.0070  |
| 1035/M              | 1/1             | 311.3                 | 0.0519         | 1.9352 | 0.5034          | 0.5343           | 1.2893 | 2.5567  |
| 1036/M              | 1/1             | 360.9                 | 0.0589         | 2.0423 | 0.5494          | 0.5690           | 1.2446 | 3.1322  |
| 1037/M              | 1/1             | 396.0                 | 0.0719         | 2.1643 | 0.5595          | 0.5883           | 1.3484 | 3.4077  |
| 1038/M              | 1/1             | 353.1                 | 0.0609         | 2.1659 | 0.6139          | 0.5824           | 1.2463 | 3.1985  |
| 1039/M              | 1/1             | 367.9                 | 0.0836         | 1.9571 | 0.6711          | 0.7327           | 1.2995 | 3.0021  |
| 1040/M              | 1/1             | 361.9                 | 0.0731         | 2.0834 | 0.6387          | 0.5545           | 1.2369 | 3.0965  |
| 1041/M              | 1/1             | 353.2                 | 0.0523         | 2.1600 | 0.6594          | 0.6368           | 1.3679 | 3.3513  |
| Mean:               |                 | 368.0                 | 0.0662         | 2.0631 | 0.6029          | 0.6022           | 1.2755 | 3.1552  |
| Standard deviation: |                 | 25.0                  | 0.0098         | 0.0865 | 0.0724          | 0.0584           | 0.0637 | 0.2346  |
| Number of observ. : |                 | (12)                  | (12)           | (12)   | (12)            | (12)             | (12)   | (12)    |
|                     |                 |                       |                |        |                 |                  |        |         |
| 2030/M              | 2/1             | 362.3                 | 0.0689         | 1.9933 | 0.5618          | 0.5969           | 1.2299 | 3.3558  |
| 2031/M              | 2/1             | 362.8                 | 0.0558         | 2.1935 | 0.6084          | 0.6214           | 1.2773 | 3.1378  |
| 2032/M              | 2/1             | 348.5                 | 0.0826         | 2.0918 | 0.6012          | 0.6400           | 1.2616 | 2.9832  |
| 2033/M              | 2/1             | 387.7                 | 0.0572         | 1.9636 | 0.5810          | 0.5695           | 1.2679 | 3.2118  |
| 2034/M              | 2/1             | 408.2                 | 0.0759         | 2.1435 | 0.7062          | 0.7149           | 1.4663 | 3.4147  |
| 2035/M              | 2/1             | 384.9                 | 0.0659         | 2.0856 | 0.5935          | 0.6104           | 1.4600 | 3.7334  |
| 2036/M              | 2/1             | 392.8                 | 0.0624         | 2.0286 | 0.6686          | 0.7114           | 1.3467 | 3.6557  |
| 2037/M              | 2/1             | 359.1                 | 0.0780         | 2.0812 | 0.6984          | 0.6929           | 1.2089 | 2.8373  |
| 2038/M              | 2/1             | 344.5                 | 0.1012         | 2.0488 | 0.6439          | 0.5960           | 1.1883 | 3.3166  |
| 2039/M              | 2/1             | 338.2                 | 0.0707         | 1.9577 | 0.5833          | 0.6577           | 1.1333 | 2.7675  |
| 2040/M              | 2/1             | 402.4                 | 0.0897         | 2.1594 | 0.6726          | 0.6908           | 1.4285 | 3.5657  |
| 2041/M              | 2/1             | 343.7                 | 0.0571         | 1.9808 | 0.5363          | 0.5503           | 1.0780 | 2.9711  |
| Mean:               |                 | 369.6                 | 0.0721         | 2.0607 | 0.6213          | 0.6377           | 1.2789 | 3.2459  |
| Standard deviation: |                 | 24.5                  | 0.0141         | 0.0788 | 0.0554          | 0.0559           | 0.1252 | 0.3172  |
| Number of observ. : |                 | (12)                  | (12)           | (12)   | (12)            | (12)             | (12)   | (12)    |
|                     |                 |                       |                |        |                 |                  |        |         |
| 3030/M              | 3/1             | 378.8                 | 0.0696         | 2.1791 | 0.6815          | 0.5784           | 1.2856 | 3.4984  |
| 3031/M              | 3/1             | 385.0                 | 0.0893         | 2.1163 | 0.6647          | 0.6661           | 1.3750 | 3.2253  |
| 3032/M              | 3/1             | 379.0                 | 0.0729         | 2.0544 | 0.6423          | 0.6467           | 1.3411 | 3.2409  |
| 3033/M              | 3/1             | 361.0                 | 0.0825         | 2.1447 | 0.7309          | 0.6625           | 1.4598 | 2.9826  |
| 3034/M              | 3/1             | 415.5                 | 0.0777         | 2.2536 | 0.6464          | 0.6820           | 1.5523 | 3.6225  |
| 3035/M              | 3/1             | 351.2                 | 0.0568         | 2.0274 | 0.5797          | 0.6228           | 1.3105 | 3.1191  |
| 3036/M              | 3/1             | 402.8                 | 0.0995         | 2.0826 | 0.6165          | 0.6344           | 1.3509 | 3.7743  |
| 3037/M              | 3/1             | 425.2                 | 0.0795         | 2.3050 | 0.5876          | 0.6738           | 1.3625 | 3.6360  |
| 3038/M              | 3/1             | 389.0                 | 0.0786         | 2.1629 | 0.6876          | 0.7386           | 1.4284 | 3.3625  |
| 3039/M              | 3/1             | 365.4                 | 0.0612         | 2.1352 | 0.5936          | 0.6153           | 1.3216 | 3.4326  |
| 3040/M              | 3/1             | 400.5                 | 0.0673         | 2.2865 | 0.6417          | 0.6193           | 1.4875 | 3.8339  |
| 3041/M              | 3/1             | 411.0                 | 0.0668         | 2.2323 | 0.6170          | 0.6341           | 1.4043 | 3.8005  |
| Mean:               |                 | 388.7                 | 0.0751         | 2.1650 | 0.6408          | 0.6478           | 1.3900 | 3.4607  |

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| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Adrenal Glands | Brain  | Epididymis Left | Epididymis Right | Heart  | Kidneys |
|---------------------|-----------------|-----------------------|----------------|--------|-----------------|------------------|--------|---------|
| Standard deviation: |                 | 23.0                  | 0.0120         | 0.0897 | 0.0452          | 0.0408           | 0.0793 | 0.2814  |
| Number of observ. : |                 | (12)                  | (12)           | (12)   | (12)            | (12)             | (12)   | (12)    |
| 4030/M              | 4/1             | 396.0                 | 0.0925         | 2.1797 | 0.7059          | 0.7421           | 1.4581 | 3.4176  |
| 4031/M              | 4/1             | 366.0                 | 0.0584         | 1.9723 | 0.6042          | 0.6336           | 1.2909 | 3.0825  |
| 4032/M              | 4/1             | 369.9                 | 0.0804         | 2.1001 | 0.5672          | 0.5600           | 1.4446 | 3.2790  |
| 4033/M              | 4/1             | 390.3                 | 0.0770         | 2.1295 | 0.7333          | 0.7292           | 1.2993 | 3.1275  |
| 4034/M              | 4/1             | 359.7                 | 0.0560         | 2.0366 | 0.5550          | 0.5559           | 1.3148 | 3.3668  |
| 4035/M              | 4/1             | 346.5                 | 0.0655         | 2.0495 | 0.5922          | 0.5994           | 1.1188 | 3.3584  |
| 4036/M              | 4/1             | 351.1                 | 0.0665         | 2.0632 | 0.5446          | 0.5437           | 1.1991 | 3.2289  |
| 4037/M              | 4/1             | 359.1                 |                | 2.0558 | 0.5419          | 0.6112           | 1.0982 | 3.1787  |
| 4038/M              | 4/1             | 427.7                 | 0.0767         | 2.2152 | 0.6783          | 0.6583           | 1.5748 | 3.8602  |
| 4039/M              | 4/1             | 350.2                 | 0.0644         | 2.0446 | 0.6256          | 0.6114           | 1.2864 | 3.1393  |
| 4040/M              | 4/1             | 334.4                 | 0.0530         | 2.1311 | 0.5393          | 0.6102           | 1.1746 | 2.8311  |
| 4041/M              | 4/1             | 367.5                 | 0.0829         | 1.9684 | 0.6623          | 0.6381           | 1.2671 | 3.5544  |
| Mean:               |                 | 368.2                 | 0.0703         | 2.0788 | 0.6125          | 0.6244           | 1.2939 | 3.2854  |
| Standard deviation: |                 | 25.6                  | 0.0125         | 0.0755 | 0.0682          | 0.0624           | 0.1421 | 0.2595  |
| Number of observ. : |                 | (12)                  | (11)           | (12)   | (12)            | (12)             | (12)   | (12)    |

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Main Study

| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Liver                      | Lungs   | Spleen | Testis Left | Testis Right | Thymus |
|---------------------|-----------------|-----------------------|----------------------------|---------|--------|-------------|--------------|--------|
| -----               |                 |                       |                            |         |        |             |              |        |
|                     |                 |                       | M a l e      A n i m a l s |         |        |             |              |        |
| 1030/M              | 1/1             | 355.9                 | 10.3545                    | 1.7839  | 0.5560 | 1.6018      | 1.5554       | 0.3804 |
| 1031/M              | 1/1             | 406.9                 | 13.9234                    | 2.2531  | 0.8850 | 1.4939      | 1.4856       | 0.6131 |
| 1032/M              | 1/1             | 384.1                 | 13.2998                    | 2.1566  | 0.6992 | 1.5834      | 1.6086       | 0.4779 |
| 1033/M              | 1/1             | 383.0                 | 12.1031                    | 1.6979  | 0.7661 | 1.4806      | 1.4588       | 0.5490 |
| 1034/M              | 1/1             | 381.8                 | 10.8695                    | 2.3996  | 0.6312 | 1.5555      | 1.5029       | 0.4649 |
| 1035/M              | 1/1             | 311.3                 | 9.4840                     | 1.6384  | 0.7838 | 1.4606      | 1.4113       | 0.4199 |
| 1036/M              | 1/1             | 360.9                 | 13.0448                    | 1.7786  | 0.7447 | 1.5082      | 1.4747       | 0.6146 |
| 1037/M              | 1/1             | 396.0                 | 11.9257                    | 2.0826  | 0.7972 | 1.3608      | 1.3894       | 0.5537 |
| 1038/M              | 1/1             | 353.1                 | 11.8938                    | 1.8108  | 0.6122 | 1.7019      | 1.6369       | 0.4240 |
| 1039/M              | 1/1             | 367.9                 | 11.3616                    | 1.9493  | 0.6656 | 1.6286      | 1.6276       | 0.7370 |
| 1040/M              | 1/1             | 361.9                 | 12.0715                    | 1.6980  | 0.6372 | 1.5017      | 1.5458       | 0.7320 |
| 1041/M              | 1/1             | 353.2                 | 14.4440                    | 1.6139  | 0.6548 | 1.7434      | 1.7806       | 0.6643 |
| M e a n:            |                 | 368.0                 | 12.0646                    | 1.9052  | 0.7028 | 1.5517      | 1.5398       | 0.5526 |
| Standard deviation: |                 | 25.0                  | 1.4510                     | 0.2600  | 0.0941 | 0.1071      | 0.1105       | 0.1218 |
| Number of observ. : |                 | (12)                  | (12)                       | (12)    | (12)   | (12)        | (12)         | (12)   |
| -----               |                 |                       |                            |         |        |             |              |        |
| 2030/M              | 2/1             | 362.3                 | 12.6116                    | 1.8657  | 0.8115 | 1.4762      | 1.5248       | 0.8641 |
| 2031/M              | 2/1             | 362.8                 | 11.5164                    | 3.7371E | 0.6814 | 1.5610      | 1.6337       | 0.6604 |
| 2032/M              | 2/1             | 348.5                 | 10.1047                    | 1.8815  | 0.7464 | 1.6665      | 1.6691       | 0.5966 |
| 2033/M              | 2/1             | 387.7                 | 11.4195                    | 2.2601  | 0.7207 | 1.4384      | 1.4276       | 0.5494 |
| 2034/M              | 2/1             | 408.2                 | 12.0791                    | 2.1580  | 0.6736 | 1.6311      | 1.6910       | 0.4466 |
| 2035/M              | 2/1             | 384.9                 | 12.3501                    | 2.0623  | 0.7308 | 1.7072      | 1.6872       | 0.4583 |
| 2036/M              | 2/1             | 392.8                 | 12.5899                    | 1.8208  | 0.8515 | 1.7094      | 1.6471       | 0.5326 |
| 2037/M              | 2/1             | 359.1                 | 11.0439                    | 1.5634  | 0.6869 | 1.7167      | 1.7051       | 0.4627 |
| 2038/M              | 2/1             | 344.5                 | 12.8384                    | 1.6076  | 0.6693 | 1.7549      | 1.7443       | 0.5883 |
| 2039/M              | 2/1             | 338.2                 | 10.7305                    | 1.8977  | 0.8456 | 1.4904      | 1.5435       | 0.7424 |
| 2040/M              | 2/1             | 402.4                 | 13.9995                    | 2.1316  | 0.7551 | 1.6998      | 1.7285       | 0.5196 |
| 2041/M              | 2/1             | 343.7                 | 10.7622                    | 1.6082  | 0.6352 | 1.4848      | 1.4333       | 0.5549 |
| M e a n:            |                 | 369.6                 | 11.8372                    | 1.8961  | 0.7340 | 1.6114      | 1.6196       | 0.5813 |
| Standard deviation: |                 | 24.5                  | 1.1060                     | 0.2383  | 0.0711 | 0.1141      | 0.1104       | 0.1235 |
| Number of observ. : |                 | (12)                  | (12)                       | (11)    | (12)   | (12)        | (12)         | (12)   |
| -----               |                 |                       |                            |         |        |             |              |        |
| 3030/M              | 3/1             | 378.8                 | 12.0987                    | 1.9724  | 0.8366 | 1.5314      | 1.6112       | 0.4651 |
| 3031/M              | 3/1             | 385.0                 | 12.4725                    | 1.8443  | 0.6679 | 1.7386      | 1.7419       | 0.5581 |
| 3032/M              | 3/1             | 379.0                 | 11.7439                    | 1.8939  | 0.7675 | 1.8193      | 1.8389       | 0.5451 |
| 3033/M              | 3/1             | 361.0                 | 10.8826                    | 1.8767  | 0.7768 | 1.5994      | 1.5544       | 0.5279 |
| 3034/M              | 3/1             | 415.5                 | 13.8621                    | 2.1645  | 0.9509 | 1.6527      | 1.6835       | 0.9731 |
| 3035/M              | 3/1             | 351.2                 | 10.4964                    | 1.9912  | 0.6685 | 1.7844      | 1.7266       | 0.5535 |
| 3036/M              | 3/1             | 402.8                 | 13.7895                    | 1.7070  | 0.7489 | 1.7789      | 1.8499       | 0.5984 |
| 3037/M              | 3/1             | 425.2                 | 13.7849                    | 2.3915  | 0.7281 | 1.6483      | 1.6741       | 0.6174 |
| 3038/M              | 3/1             | 389.0                 | 14.4075                    | 2.1005  | 0.7933 | 1.7062      | 1.7350       | 0.7023 |
| 3039/M              | 3/1             | 365.4                 | 13.5452                    | 1.6957  | 0.7895 | 1.6672      | 1.6743       | 0.5795 |
| 3040/M              | 3/1             | 400.5                 | 15.4295                    | 1.9282  | 1.0074 | 1.6658      | 1.6066       | 0.8412 |
| 3041/M              | 3/1             | 411.0                 | 12.7789                    | 2.0008  | 0.8040 | 1.6272      | 1.6103       | 0.7191 |
| M e a n:            |                 | 388.7                 | 12.9410                    | 1.9639  | 0.7950 | 1.6850      | 1.6922       | 0.6401 |

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| Main Study                       |                          |                | Secondary Study |               |         |         |        |  |
|----------------------------------|--------------------------|----------------|-----------------|---------------|---------|---------|--------|--|
| Animal Group/<br>No/sex Subgroup | Terminal<br>Body wt. (g) | Adrenal Glands | Brain           | Heart         | Kidneys | Liver   | Lungs  |  |
|                                  |                          |                | F e m a l e     | A n i m a l s |         |         |        |  |
| 1530/F 1/1                       | 235.9                    | 0.0687         | 1.9444          | 0.8604        | 2.1518  | 8.3766  | 1.4087 |  |
| 1531/F 1/1                       | 239.4                    | 0.0588         | 2.0468          | 1.0709        | 2.0554  | 7.1709  | 1.6155 |  |
| 1532/F 1/1                       | 245.3                    | 0.0775         | 1.9379          | 0.8844        | 1.9730  | 7.6670  | 1.6628 |  |
| 1533/F 1/1                       | 230.3                    | 0.0683         | 1.9698          | 0.8785        | 1.9918  | 7.6238  | 1.5271 |  |
| 1534/F 1/1                       | 234.0                    | 0.0843         | 1.8535          | 0.9041        | 2.0997  | 8.1890  | 1.4753 |  |
| 1535/F 1/1                       | 232.8                    | 0.0702         | 1.9912          | 0.8944        | 2.1931  | 8.4633  | 1.5886 |  |
| 1536/F 1/1                       | 260.3                    | 0.0825         | 2.1361          | 1.1191        | 2.5221  | 10.6209 | 1.4316 |  |
| 1537/F 1/1                       | 259.8                    | 0.0733         | 2.1448          | 1.0365        | 2.6073  | 9.1456  | 2.2469 |  |
| 1538/F 1/1                       | 227.0                    | 0.0813         | 2.0255          | 0.9641        | 2.1226  | 8.1661  | 1.8065 |  |
| 1539/F 1/1                       | 234.4                    | 0.0845         | 2.0652          | 0.8497        | 1.9543  | 7.7290  | 1.7086 |  |
| 1540/F 1/1                       | 213.0                    | 0.0708         | 1.8961          | 0.8068        | 1.6794  | 6.6953  | 1.3667 |  |
| 1541/F 1/1                       | 218.2                    | 0.0706         | 2.0648          | 0.8031        | 1.9933  | 8.0592  | 1.3896 |  |
| M e a n:                         | 235.9                    | 0.0742         | 2.0063          | 0.9227        | 2.1120  | 8.1589  | 1.6023 |  |
| Standard deviation:              | 14.2                     | 0.0079         | 0.0907          | 0.1030        | 0.2495  | 1.0008  | 0.2453 |  |
| Number of observ. :              | (12)                     | (12)           | (12)            | (12)          | (12)    | (12)    | (12)   |  |
|                                  |                          |                |                 |               |         |         |        |  |
| 2530/F 2/1                       | 238.3                    | 0.0750         | 2.0060          | 0.9231        | 2.0609  | 9.0594  | 1.6222 |  |
| 2531/F 2/1                       | 265.7                    | 0.0621         | 2.0179          | 1.0370        | 2.0908  | 8.2953  | 1.6112 |  |
| 2532/F 2/1                       | 240.9                    | 0.0938         | 1.8252          | 0.8752        | 2.2489  | 8.3905  | 1.4434 |  |
| 2533/F 2/1                       | 250.4                    | 0.0948         | 2.0663          | 0.8880        | 2.2244  | 8.2658  | 1.6596 |  |
| 2534/F 2/1                       | 240.4                    | 0.0813         | 1.9080          | 1.0674        | 2.0070  | 8.6173  | 1.7057 |  |
| 2535/F 2/1                       | 225.1                    | 0.0660         | 1.7929          | 0.7450        | 1.9361  | 6.8621  | 1.2258 |  |
| 2536/F 2/1                       | 234.4                    | 0.0765         | 2.0914          | 1.1825        | 2.0552  | 8.2045  | 1.8032 |  |
| 2537/F 2/1                       | 243.1                    | 0.0612         | 2.0293          | 1.0090        | 2.1157  | 8.4608  | 1.5439 |  |
| 2538/F 2/1                       | 230.0                    | 0.0909         | 1.9615          | 0.8955        | 2.2415  | 9.1311  | 1.2097 |  |
| 2539/F 2/1                       | 234.1                    | 0.0904         | 2.0023          | 0.8638        | 2.2059  | 8.5553  | 1.4269 |  |
| 2540/F 2/1                       | 227.9                    | 0.0860         | 1.8985          | 0.9047        | 2.4905  | 9.6279  | 1.2565 |  |
| 2541/F 2/1                       | 246.3                    | 0.0822         | 2.0141          | 0.9865        | 2.4152  | 9.1121  | 1.4116 |  |
| M e a n:                         | 239.7                    | 0.0800         | 1.9678          | 0.9481        | 2.1743  | 8.5485  | 1.4933 |  |
| Standard deviation:              | 11.1                     | 0.0120         | 0.0931          | 0.1147        | 0.1634  | 0.6893  | 0.1962 |  |
| Number of observ. :              | (12)                     | (12)           | (12)            | (12)          | (12)    | (12)    | (12)   |  |
|                                  |                          |                |                 |               |         |         |        |  |
| 3530/F 3/1                       | 254.9                    | 0.0849         | 2.2520          | 1.0634        | 2.3183  | 8.4647  | 1.8522 |  |
| 3531/F 3/1                       | 232.3                    | 0.0621         | 2.0259          | 0.8418        | 1.9767  | 7.5553  | 1.4583 |  |
| 3532/F 3/1                       | 234.9                    | 0.0704         | 1.9659          | 0.9360        | 1.9867  | 8.2594  | 1.3729 |  |
| 3533/F 3/1                       | 246.8                    | 0.0768         | 1.8553          | 0.9424        | 2.2085  | 8.2176  | 1.6532 |  |
| 3534/F 3/1                       | 297.8                    | 0.0796         | 2.0926          | 1.1378        | 2.4156  | 10.0378 | 1.9708 |  |
| 3535/F 3/1                       | 258.6                    | 0.0850         | 2.0483          | 0.9736        | 2.2636  | 9.5423  | 1.5882 |  |
| 3536/F 3/1                       | 252.4                    | 0.0831         | 1.9430          | 0.9657        | 2.1235  | 8.9416  | 1.4640 |  |
| 3537/F 3/1                       | 267.4                    | 0.0757         | 2.0803          | 1.1223        | 2.4175  | 9.3657  | 2.0265 |  |
| 3539/F 3/1                       | 244.1                    | 0.0768         | 1.9546          | 0.9087        | 2.2165  | 8.3975  | 1.4614 |  |
| 3540/F 3/1                       | 219.9                    | 0.0797         | 2.0949          | 0.8913        | 2.3870  | 7.1422  | 1.3703 |  |
| 3541/F 3/1                       | 240.3                    | 0.0671         | 1.9176          | 0.9036        | 2.5058  | 8.3935  | 1.3871 |  |
| 3554/F 3/1                       | 246.5                    | 0.0722         | 1.9524          | 0.9125        | 2.3305  | 9.1755  | 1.4303 |  |
| M e a n:                         | 249.7                    | 0.0761         | 2.0152          | 0.9666        | 2.2625  | 8.6244  | 1.5863 |  |



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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 |        |                 |
| 1530/F              | 1/1             | 235.9                 | 0.0825     | 0.0719      | 0.6025        | 0.4984 | 0.6902          |
| 1531/F              | 1/1             | 239.4                 | 0.0776     | 0.0642      | 0.4692        | 0.4581 | 0.8281          |
| 1532/F              | 1/1             | 245.3                 | 0.0673     | 0.0735      | 0.6932        | 0.4700 | 1.6512          |
| 1533/F              | 1/1             | 230.3                 | 0.0741     | 0.0740      | 0.4741        | 0.3880 | 0.7143          |
| 1534/F              | 1/1             | 234.0                 | 0.0755     | 0.0718      | 0.5754        | 0.3739 | 0.8701          |
| 1535/F              | 1/1             | 232.8                 | 0.0738     | 0.0698      | 0.5341        | 0.3752 | 1.3729          |
| 1536/F              | 1/1             | 260.3                 | 0.0801     | 0.0965      | 0.6157        | 0.7074 | 0.9459          |
| 1537/F              | 1/1             | 259.8                 | 0.0901     | 0.0713      | 0.6841        | 0.3610 | 0.8128          |
| 1538/F              | 1/1             | 227.0                 | 0.0748     | 0.0705      | 0.6223        | 0.6283 | 1.0734          |
| 1539/F              | 1/1             | 234.4                 | 0.0487     | 0.0690      | 0.5192        | 0.3909 | 1.2340          |
| 1540/F              | 1/1             | 213.0                 | 0.0772     | 0.0573      | 0.4546        | 0.3985 | 0.7835          |
| 1541/F              | 1/1             | 218.2                 | 0.0834     | 0.0650      | 0.4943        | 0.3374 | 0.7821          |
| M e a n:            |                 | 235.9                 | 0.0754     | 0.0712      | 0.5616        | 0.4489 | 0.9799          |
| Standard deviation: |                 | 14.2                  | 0.0102     | 0.0093      | 0.0829        | 0.1139 | 0.2977          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)          | (12)   | (12)            |
| 2530/F              | 2/1             | 238.3                 | 0.0522     | 0.0647      | 0.6112        | 0.5783 | 0.8142          |
| 2531/F              | 2/1             | 265.7                 | 0.0584     | 0.0706      | 0.6111        | 0.4120 | 0.7416          |
| 2532/F              | 2/1             | 240.9                 | 0.0710     | 0.0692      | 0.5368        | 0.5471 | 1.1760          |
| 2533/F              | 2/1             | 250.4                 | 0.0592     | 0.0766      | 0.5598        | 0.4326 | 1.3026          |
| 2534/F              | 2/1             | 240.4                 | 0.0694     | 0.0796      | 0.5720        | 0.4193 | 0.6483          |
| 2535/F              | 2/1             | 225.1                 | 0.0566     | 0.0519      | 0.5179        | 0.4171 | 1.0020          |
| 2536/F              | 2/1             | 234.4                 | 0.0787     | 0.0779      | 0.6539        | 0.5623 | 1.0148          |
| 2537/F              | 2/1             | 243.1                 | 0.0548     | 0.0668      | 0.5078        | 0.6081 | 0.6967          |
| 2538/F              | 2/1             | 230.0                 | 0.1106     | 0.0731      | 0.5679        | 0.5395 | 0.8553          |
| 2539/F              | 2/1             | 234.1                 | 0.0753     | 0.0703      | 0.5763        | 0.3346 | 0.6137          |
| 2540/F              | 2/1             | 227.9                 | 0.0841     | 0.0708      | 0.4670        | 0.5022 | 1.5983          |
| 2541/F              | 2/1             | 246.3                 | 0.0669     | 0.0455      | 0.5048        | 0.3784 | 0.6999          |
| M e a n:            |                 | 239.7                 | 0.0698     | 0.0681      | 0.5572        | 0.4776 | 0.9303          |
| Standard deviation: |                 | 11.1                  | 0.0163     | 0.0101      | 0.0532        | 0.0891 | 0.3015          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)          | (12)   | (12)            |
| 3530/F              | 3/1             | 254.9                 | 0.0588     | 0.0656      | 0.6087        | 0.5944 | 0.8361          |
| 3531/F              | 3/1             | 232.3                 | 0.0796     | 0.0708      | 0.5165        | 0.3541 | 0.8540          |
| 3532/F              | 3/1             | 234.9                 | 0.0808     | 0.0709      | 0.5378        | 0.3583 | 0.8190          |
| 3533/F              | 3/1             | 246.8                 | 0.0874     | 0.0746      | 0.5292        | 0.5580 | 0.9974          |
| 3534/F              | 3/1             | 297.8                 | 0.1049     | 0.1088      | 0.7585        | 0.6516 | 0.6804          |
| 3535/F              | 3/1             | 258.6                 | 0.0693     | 0.0598      | 0.5322        | 0.5097 | 0.7773          |
| 3536/F              | 3/1             | 252.4                 | 0.0934     | 0.0742      | 0.6193        | 0.6113 | 0.7226          |
| 3537/F              | 3/1             | 267.4                 | 0.0707     | 0.0776      | 0.6233        | 0.4595 | 0.8024          |
| 3539/F              | 3/1             | 244.1                 | 0.0750     | 0.0656      | 0.5641        | 0.4106 | 0.7821          |
| 3540/F              | 3/1             | 219.9                 | 0.0648     | 0.0671      | 0.4505        | 0.4801 | 1.1162          |
| 3541/F              | 3/1             | 240.3                 | 0.0620     | 0.0600      | 0.5938        | 0.4128 | 1.2979          |
| 3554/F              | 3/1             | 246.5                 | 0.0712     | 0.0891      | 0.6042        | 0.4486 | 1.0722          |
| M e a n:            |                 | 249.7                 | 0.0765     | 0.0737      | 0.5782        | 0.4874 | 0.8965          |

Huntingdon Life Sciences  
Princeton Research Center  
East Millstone, New Jersey

Summary statistics for absolute organ weights (g)  
Study number: 034242

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## Main Study

| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Ovary Left | Ovary Right | Spleen | Thymus | Uterus w/vagina |
|---------------------|-----------------|-----------------------|------------|-------------|--------|--------|-----------------|
| <hr/>               |                 |                       |            |             |        |        |                 |
| Standard deviation: |                 | 19.7                  | 0.0135     | 0.0137      | 0.0766 | 0.0988 | 0.1846          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)   | (12)   | (12)            |
| 4530/F              | 4/1             | 247.1                 | 0.0536     | 0.0609      | 0.5666 | 0.5404 | 0.9407          |
| 4531/F              | 4/1             | 236.6                 | 0.0659     | 0.0737      | 0.5704 | 0.3883 | 1.0913          |
| 4532/F              | 4/1             | 241.9                 | 0.1106     | 0.1017      | 0.4929 | 0.5856 | 0.9821          |
| 4533/F              | 4/1             | 222.8                 | 0.0785     | 0.0720      | 0.5440 | 0.3678 | 0.8148          |
| 4534/F              | 4/1             | 269.8                 | 0.1130     | 0.0882      | 0.5538 | 0.5222 | 0.7349          |
| 4535/F              | 4/1             | 203.0                 | 0.0694     | 0.0568      | 0.4301 | 0.2899 | 1.0371          |
| 4536/F              | 4/1             | 222.9                 | 0.0880     | 0.0757      | 0.5828 | 0.5394 | 0.9485          |
| 4537/F              | 4/1             | 235.5                 | 0.0628     | 0.0628      | 0.5139 | 0.4799 | 1.1379          |
| 4538/F              | 4/1             | 244.8                 | 0.0759     | 0.0684      | 0.5576 | 0.5384 | 0.7696          |
| 4539/F              | 4/1             | 250.1                 | 0.0702     | 0.0666      | 0.6472 | 0.5278 | 0.8465          |
| 4540/F              | 4/1             | 237.4                 | 0.0614     | 0.0595      | 0.6120 | 0.4614 | 0.9984          |
| 4541/F              | 4/1             | 224.8                 | 0.0659     | 0.0716      | 0.4769 | 0.4244 | 1.4056          |
| M e a n:            |                 | 236.4                 | 0.0763     | 0.0715      | 0.5457 | 0.4721 | 0.9756          |
| Standard deviation: |                 | 16.9                  | 0.0188     | 0.0128      | 0.0597 | 0.0882 | 0.1843          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)   | (12)   | (12)            |

Huntingdon Life Sciences  
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Summary Statistics for % Organ to Body Weight  
Study number: 034242

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Terminal Sacrifice - Main Study

| Animal Group/<br>No/sex Subgroup | Terminal<br>Body wt. (g) | Adrenal Glands | Brain  | Epididymis Left | Epididymis Right | Heart  | Kidneys |
|----------------------------------|--------------------------|----------------|--------|-----------------|------------------|--------|---------|
| -----                            |                          |                |        |                 |                  |        |         |
|                                  |                          |                |        | M a l e         | A n i m a l s    |        |         |
| 1030/M                           | 1/1                      | 355.9          | 0.0192 | 0.5417          | 0.1625           | 0.1556 | 0.8835  |
| 1031/M                           | 1/1                      | 406.9          | 0.0174 | 0.4999          | 0.1532           | 0.1540 | 0.8223  |
| 1032/M                           | 1/1                      | 384.1          | 0.0154 | 0.5431          | 0.1460           | 0.1547 | 0.8440  |
| 1033/M                           | 1/1                      | 383.0          | 0.0173 | 0.5549          | 0.1356           | 0.1487 | 0.8821  |
| 1034/M                           | 1/1                      | 381.8          | 0.0202 | 0.5437          | 0.1984           | 0.1792 | 0.7876  |
| 1035/M                           | 1/1                      | 311.3          | 0.0167 | 0.6217          | 0.1617           | 0.1716 | 0.8213  |
| 1036/M                           | 1/1                      | 360.9          | 0.0163 | 0.5659          | 0.1522           | 0.1577 | 0.8679  |
| 1037/M                           | 1/1                      | 396.0          | 0.0182 | 0.5465          | 0.1413           | 0.1486 | 0.8605  |
| 1038/M                           | 1/1                      | 353.1          | 0.0172 | 0.6134          | 0.1739           | 0.1649 | 0.9058  |
| 1039/M                           | 1/1                      | 367.9          | 0.0227 | 0.5320          | 0.1824           | 0.1992 | 0.8160  |
| 1040/M                           | 1/1                      | 361.9          | 0.0202 | 0.5757          | 0.1765           | 0.1532 | 0.8556  |
| 1041/M                           | 1/1                      | 353.2          | 0.0148 | 0.6116          | 0.1867           | 0.1803 | 0.9488  |
| M e a n:                         | 368.0                    | 0.0180         | 0.5625 | 0.1642          | 0.1640           | 0.3480 | 0.8580  |
| Standard deviation:              | 25.0                     | 0.0023         | 0.0369 | 0.0195          | 0.0156           | 0.0286 | 0.0441  |
| Number of observ. :              | (12)                     | (12)           | (12)   | (12)            | (12)             | (12)   | (12)    |
| -----                            |                          |                |        |                 |                  |        |         |
| 2030/M                           | 2/1                      | 362.3          | 0.0190 | 0.5502          | 0.1551           | 0.1648 | 0.9262  |
| 2031/M                           | 2/1                      | 362.8          | 0.0154 | 0.6046          | 0.1677           | 0.1713 | 0.8649  |
| 2032/M                           | 2/1                      | 348.5          | 0.0237 | 0.6002          | 0.1725           | 0.1836 | 0.8560  |
| 2033/M                           | 2/1                      | 387.7          | 0.0148 | 0.5065          | 0.1499           | 0.1469 | 0.8284  |
| 2034/M                           | 2/1                      | 408.2          | 0.0186 | 0.5251          | 0.1730           | 0.1751 | 0.8365  |
| 2035/M                           | 2/1                      | 384.9          | 0.0171 | 0.5419          | 0.1542           | 0.1586 | 0.9700  |
| 2036/M                           | 2/1                      | 392.8          | 0.0159 | 0.5164          | 0.1702           | 0.1811 | 0.9307  |
| 2037/M                           | 2/1                      | 359.1          | 0.0217 | 0.5796          | 0.1945           | 0.1930 | 0.7901  |
| 2038/M                           | 2/1                      | 344.5          | 0.0294 | 0.5947          | 0.1869           | 0.1730 | 0.9627  |
| 2039/M                           | 2/1                      | 338.2          | 0.0209 | 0.5789          | 0.1725           | 0.1945 | 0.8183  |
| 2040/M                           | 2/1                      | 402.4          | 0.0223 | 0.5366          | 0.1671           | 0.1717 | 0.8861  |
| 2041/M                           | 2/1                      | 343.7          | 0.0166 | 0.5763          | 0.1560           | 0.1601 | 0.8644  |
| M e a n:                         | 369.6                    | 0.0196         | 0.5592 | 0.1683          | 0.1728           | 0.3456 | 0.8779  |
| Standard deviation:              | 24.5                     | 0.0042         | 0.0341 | 0.0133          | 0.0140           | 0.0174 | 0.0581  |
| Number of observ. :              | (12)                     | (12)           | (12)   | (12)            | (12)             | (12)   | (12)    |
| -----                            |                          |                |        |                 |                  |        |         |
| 3030/M                           | 3/1                      | 378.8          | 0.0184 | 0.5753          | 0.1799           | 0.1527 | 0.9235  |
| 3031/M                           | 3/1                      | 385.0          | 0.0232 | 0.5497          | 0.1726           | 0.1730 | 0.8377  |
| 3032/M                           | 3/1                      | 379.0          | 0.0192 | 0.5421          | 0.1695           | 0.1706 | 0.8551  |
| 3033/M                           | 3/1                      | 361.0          | 0.0229 | 0.5941          | 0.2025           | 0.1835 | 0.8262  |
| 3034/M                           | 3/1                      | 415.5          | 0.0187 | 0.5424          | 0.1556           | 0.1641 | 0.8718  |
| 3035/M                           | 3/1                      | 351.2          | 0.0162 | 0.5773          | 0.1651           | 0.1773 | 0.8881  |
| 3036/M                           | 3/1                      | 402.8          | 0.0247 | 0.5170          | 0.1531           | 0.1575 | 0.9370  |
| 3037/M                           | 3/1                      | 425.2          | 0.0187 | 0.5421          | 0.1382           | 0.1585 | 0.8551  |
| 3038/M                           | 3/1                      | 389.0          | 0.0202 | 0.5560          | 0.1768           | 0.1899 | 0.8644  |
| 3039/M                           | 3/1                      | 365.4          | 0.0167 | 0.5843          | 0.1625           | 0.1684 | 0.9394  |
| 3040/M                           | 3/1                      | 400.5          | 0.0168 | 0.5709          | 0.1602           | 0.1546 | 0.9573  |
| 3041/M                           | 3/1                      | 411.0          | 0.0163 | 0.5431          | 0.1501           | 0.1543 | 0.9247  |
| M e a n:                         | 388.7                    | 0.0193         | 0.5579 | 0.1655          | 0.1670           | 0.3583 | 0.8900  |

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

Summary Statistics for % Organ to Body Weight  
 Study number: 034242

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| Terminal Sacrifice - Main Study  |                          |                |                          |                  |        |         |        |
|----------------------------------|--------------------------|----------------|--------------------------|------------------|--------|---------|--------|
| Animal Group/<br>No/sex Subgroup | Terminal<br>Body wt. (g) | Adrenal Glands | Brain<br>Epididymis Left | Epididymis Right | Heart  | Kidneys |        |
| <hr/>                            |                          |                |                          |                  |        |         |        |
| Standard deviation:              | 23.0                     | 0.0029         | 0.0225                   | 0.0166           | 0.0122 | 0.0223  | 0.0444 |
| Number of observ. :              | (12)                     | (12)           | (12)                     | (12)             | (12)   | (12)    | (12)   |
| <hr/>                            |                          |                |                          |                  |        |         |        |
| 4030/M 4/1                       | 396.0                    | 0.0234         | 0.5504                   | 0.1783           | 0.1874 | 0.3682  | 0.8630 |
| 4031/M 4/1                       | 366.0                    | 0.0160         | 0.5389                   | 0.1651           | 0.1731 | 0.3527  | 0.8422 |
| 4032/M 4/1                       | 369.9                    | 0.0217         | 0.5677                   | 0.1533           | 0.1514 | 0.3905  | 0.8865 |
| 4033/M 4/1                       | 390.3                    | 0.0197         | 0.5456                   | 0.1879           | 0.1868 | 0.3329  | 0.8013 |
| 4034/M 4/1                       | 359.7                    | 0.0156         | 0.5662                   | 0.1543           | 0.1545 | 0.3655  | 0.9360 |
| 4035/M 4/1                       | 346.5                    | 0.0189         | 0.5915                   | 0.1709           | 0.1730 | 0.3229  | 0.9692 |
| 4036/M 4/1                       | 351.1                    | 0.0189         | 0.5876                   | 0.1551           | 0.1549 | 0.3415  | 0.9197 |
| 4037/M 4/1                       | 359.1                    |                | 0.5725                   | 0.1509           | 0.1702 | 0.3058  | 0.8852 |
| 4038/M 4/1                       | 427.7                    | 0.0179         | 0.5179                   | 0.1586           | 0.1539 | 0.3682  | 0.9025 |
| 4039/M 4/1                       | 350.2                    | 0.0184         | 0.5838                   | 0.1786           | 0.1746 | 0.3673  | 0.8964 |
| 4040/M 4/1                       | 334.4                    | 0.0158         | 0.6373                   | 0.1613           | 0.1825 | 0.3513  | 0.8466 |
| 4041/M 4/1                       | 367.5                    | 0.0226         | 0.5356                   | 0.1802           | 0.1736 | 0.3448  | 0.9672 |
| Mean:                            | 368.2                    | 0.0190         | 0.5663                   | 0.1662           | 0.1697 | 0.3510  | 0.8930 |
| Standard deviation:              | 25.6                     | 0.0027         | 0.0319                   | 0.0126           | 0.0130 | 0.0232  | 0.0506 |
| Number of observ. :              | (12)                     | (11)           | (12)                     | (12)             | (12)   | (12)    | (12)   |

Huntingdon Life Sciences  
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Terminal Sacrifice - Main Study

Summary Statistics for % Organ to Body Weight  
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| Animal<br>No/sex    | Group/<br>Subgroup | Terminal<br>Body wt. (g) | Liver        | Lungs   | Spleen | Testis Left | Testis Right | Thymus |
|---------------------|--------------------|--------------------------|--------------|---------|--------|-------------|--------------|--------|
| -----               |                    |                          |              |         |        |             |              |        |
|                     |                    |                          | Male Animals |         |        |             |              |        |
| 1030/M              | 1/1                | 355.9                    | 2.9094       | 0.5012  | 0.1562 | 0.4501      | 0.4370       | 0.1069 |
| 1031/M              | 1/1                | 406.9                    | 3.4218       | 0.5537  | 0.2175 | 0.3671      | 0.3651       | 0.1507 |
| 1032/M              | 1/1                | 384.1                    | 3.4626       | 0.5615  | 0.1820 | 0.4122      | 0.4188       | 0.1244 |
| 1033/M              | 1/1                | 383.0                    | 3.1601       | 0.4433  | 0.2000 | 0.3866      | 0.3809       | 0.1433 |
| 1034/M              | 1/1                | 381.8                    | 2.8469       | 0.6285  | 0.1653 | 0.4074      | 0.3936       | 0.1218 |
| 1035/M              | 1/1                | 311.3                    | 3.0466       | 0.5263  | 0.2518 | 0.4692      | 0.4534       | 0.1349 |
| 1036/M              | 1/1                | 360.9                    | 3.6145       | 0.4928  | 0.2063 | 0.4179      | 0.4086       | 0.1703 |
| 1037/M              | 1/1                | 396.0                    | 3.0115       | 0.5259  | 0.2013 | 0.3436      | 0.3509       | 0.1398 |
| 1038/M              | 1/1                | 353.1                    | 3.3684       | 0.5128  | 0.1734 | 0.4820      | 0.4636       | 0.1201 |
| 1039/M              | 1/1                | 367.9                    | 3.0882       | 0.5298  | 0.1809 | 0.4427      | 0.4424       | 0.2003 |
| 1040/M              | 1/1                | 361.9                    | 3.3356       | 0.4692  | 0.1761 | 0.4149      | 0.4271       | 0.2023 |
| 1041/M              | 1/1                | 353.2                    | 4.0895       | 0.4569  | 0.1854 | 0.4936      | 0.5041       | 0.1881 |
| Mean:               |                    | 368.0                    | 3.2796       | 0.5168  | 0.1914 | 0.4239      | 0.4205       | 0.1502 |
| Standard deviation: |                    | 25.0                     | 0.3483       | 0.0507  | 0.0260 | 0.0456      | 0.0438       | 0.0326 |
| Number of observ. : |                    | (12)                     | (12)         | (12)    | (12)   | (12)        | (12)         | (12)   |
| -----               |                    |                          |              |         |        |             |              |        |
| 2030/M              | 2/1                | 362.3                    | 3.4810       | 0.5150  | 0.2240 | 0.4075      | 0.4209       | 0.2385 |
| 2031/M              | 2/1                | 362.8                    | 3.1743       | 1.0301E | 0.1878 | 0.4303      | 0.4503       | 0.1820 |
| 2032/M              | 2/1                | 348.5                    | 2.8995       | 0.5399  | 0.2142 | 0.4782      | 0.4789       | 0.1712 |
| 2033/M              | 2/1                | 387.7                    | 2.9454       | 0.5830  | 0.1859 | 0.3710      | 0.3682       | 0.1417 |
| 2034/M              | 2/1                | 408.2                    | 2.9591       | 0.5287  | 0.1650 | 0.3996      | 0.4143       | 0.1094 |
| 2035/M              | 2/1                | 384.9                    | 3.2087       | 0.5358  | 0.1899 | 0.4435      | 0.4383       | 0.1191 |
| 2036/M              | 2/1                | 392.8                    | 3.2052       | 0.4635  | 0.2168 | 0.4352      | 0.4193       | 0.1356 |
| 2037/M              | 2/1                | 359.1                    | 3.0754       | 0.4354  | 0.1913 | 0.4781      | 0.4748       | 0.1288 |
| 2038/M              | 2/1                | 344.5                    | 3.7267       | 0.4666  | 0.1943 | 0.5094      | 0.5063       | 0.1708 |
| 2039/M              | 2/1                | 338.2                    | 3.1728       | 0.5611  | 0.2500 | 0.4407      | 0.4564       | 0.2195 |
| 2040/M              | 2/1                | 402.4                    | 3.4790       | 0.5297  | 0.1876 | 0.4224      | 0.4295       | 0.1291 |
| 2041/M              | 2/1                | 343.7                    | 3.1313       | 0.4679  | 0.1848 | 0.4320      | 0.4170       | 0.1614 |
| Mean:               |                    | 369.6                    | 3.2049       | 0.5115  | 0.1993 | 0.4373      | 0.4395       | 0.1589 |
| Standard deviation: |                    | 24.5                     | 0.2466       | 0.0465  | 0.0228 | 0.0377      | 0.0366       | 0.0399 |
| Number of observ. : |                    | (12)                     | (12)         | (11)    | (12)   | (12)        | (12)         | (12)   |
| -----               |                    |                          |              |         |        |             |              |        |
| 3030/M              | 3/1                | 378.8                    | 3.1940       | 0.5207  | 0.2209 | 0.4043      | 0.4253       | 0.1228 |
| 3031/M              | 3/1                | 385.0                    | 3.2396       | 0.4790  | 0.1735 | 0.4516      | 0.4524       | 0.1450 |
| 3032/M              | 3/1                | 379.0                    | 3.0987       | 0.4997  | 0.2025 | 0.4800      | 0.4852       | 0.1438 |
| 3033/M              | 3/1                | 361.0                    | 3.0146       | 0.5199  | 0.2152 | 0.4430      | 0.4306       | 0.1462 |
| 3034/M              | 3/1                | 415.5                    | 3.3362       | 0.5209  | 0.2289 | 0.3978      | 0.4052       | 0.2342 |
| 3035/M              | 3/1                | 351.2                    | 2.9887       | 0.5670  | 0.1903 | 0.5081      | 0.4916       | 0.1576 |
| 3036/M              | 3/1                | 402.8                    | 3.4234       | 0.4238  | 0.1859 | 0.4416      | 0.4593       | 0.1486 |
| 3037/M              | 3/1                | 425.2                    | 3.2420       | 0.5624  | 0.1712 | 0.3877      | 0.3937       | 0.1452 |
| 3038/M              | 3/1                | 389.0                    | 3.7037       | 0.5400  | 0.2039 | 0.4386      | 0.4460       | 0.1805 |
| 3039/M              | 3/1                | 365.4                    | 3.7070       | 0.4641  | 0.2161 | 0.4563      | 0.4582       | 0.1586 |
| 3040/M              | 3/1                | 400.5                    | 3.8526       | 0.4814  | 0.2515 | 0.4159      | 0.4011       | 0.2100 |
| 3041/M              | 3/1                | 411.0                    | 3.1092       | 0.4868  | 0.1956 | 0.3959      | 0.3918       | 0.1750 |
| Mean:               |                    | 388.7                    | 3.3258       | 0.5055  | 0.2046 | 0.4351      | 0.4367       | 0.1640 |

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

Summary Statistics for % Organ to Body Weight  
Study number: 034242

Printed: 17-Feb-04  
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| 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 |                 |                       |                |        |        |         |        |        |
| 1530/F                    | 1/1             | 235.9                 | 0.0291         | 0.8242 | 0.3647 | 0.9122  | 3.5509 | 0.5972 |
| 1531/F                    | 1/1             | 239.4                 | 0.0246         | 0.8550 | 0.4473 | 0.8586  | 2.9954 | 0.6748 |
| 1532/F                    | 1/1             | 245.3                 | 0.0316         | 0.7900 | 0.3605 | 0.8043  | 3.1256 | 0.6779 |
| 1533/F                    | 1/1             | 230.3                 | 0.0297         | 0.8553 | 0.3815 | 0.8649  | 3.3104 | 0.6631 |
| 1534/F                    | 1/1             | 234.0                 | 0.0360         | 0.7921 | 0.3864 | 0.8973  | 3.4996 | 0.6305 |
| 1535/F                    | 1/1             | 232.8                 | 0.0302         | 0.8553 | 0.3842 | 0.9421  | 3.6354 | 0.6824 |
| 1536/F                    | 1/1             | 260.3                 | 0.0317         | 0.8206 | 0.4299 | 0.9689  | 4.0803 | 0.5500 |
| 1537/F                    | 1/1             | 259.8                 | 0.0282         | 0.8256 | 0.3990 | 1.0036  | 3.5202 | 0.8649 |
| 1538/F                    | 1/1             | 227.0                 | 0.0358         | 0.8923 | 0.4247 | 0.9351  | 3.5974 | 0.7958 |
| 1539/F                    | 1/1             | 234.4                 | 0.0360         | 0.8811 | 0.3625 | 0.8337  | 3.2974 | 0.7289 |
| 1540/F                    | 1/1             | 213.0                 | 0.0332         | 0.8902 | 0.3788 | 0.7885  | 3.1433 | 0.6416 |
| 1541/F                    | 1/1             | 218.2                 | 0.0324         | 0.9463 | 0.3681 | 0.9135  | 3.6935 | 0.6368 |
| M e a n:                  |                 | 235.9                 | 0.0315         | 0.8523 | 0.3906 | 0.8935  | 3.4541 | 0.6787 |
| Standard deviation:       |                 | 14.2                  | 0.0035         | 0.0455 | 0.0288 | 0.0655  | 0.2983 | 0.0852 |
| Number of observ. :       |                 | (12)                  | (12)           | (12)   | (12)   | (12)    | (12)   | (12)   |
| 2530/F                    | 2/1             | 238.3                 | 0.0315         | 0.8418 | 0.3874 | 0.8648  | 3.8017 | 0.6807 |
| 2531/F                    | 2/1             | 265.7                 | 0.0234         | 0.7595 | 0.3903 | 0.7869  | 3.1221 | 0.6064 |
| 2532/F                    | 2/1             | 240.9                 | 0.0389         | 0.7577 | 0.3633 | 0.9335  | 3.4830 | 0.5992 |
| 2533/F                    | 2/1             | 250.4                 | 0.0379         | 0.8252 | 0.3546 | 0.8883  | 3.3010 | 0.6628 |
| 2534/F                    | 2/1             | 240.4                 | 0.0338         | 0.7937 | 0.4440 | 0.8349  | 3.5846 | 0.7095 |
| 2535/F                    | 2/1             | 225.1                 | 0.0293         | 0.7965 | 0.3310 | 0.8601  | 3.0485 | 0.5446 |
| 2536/F                    | 2/1             | 234.4                 | 0.0326         | 0.8922 | 0.5045 | 0.8768  | 3.5002 | 0.7693 |
| 2537/F                    | 2/1             | 243.1                 | 0.0252         | 0.8348 | 0.4151 | 0.8703  | 3.4804 | 0.6351 |
| 2538/F                    | 2/1             | 230.0                 | 0.0395         | 0.8528 | 0.3893 | 0.9746  | 3.9700 | 0.5260 |
| 2539/F                    | 2/1             | 234.1                 | 0.0386         | 0.8553 | 0.3690 | 0.9423  | 3.6545 | 0.6095 |
| 2540/F                    | 2/1             | 227.9                 | 0.0377         | 0.8330 | 0.3970 | 1.0928  | 4.2246 | 0.5513 |
| 2541/F                    | 2/1             | 246.3                 | 0.0334         | 0.8177 | 0.4005 | 0.9806  | 3.6996 | 0.5731 |
| M e a n:                  |                 | 239.7                 | 0.0335         | 0.8217 | 0.3955 | 0.9088  | 3.5725 | 0.6223 |
| Standard deviation:       |                 | 11.1                  | 0.0054         | 0.0395 | 0.0451 | 0.0813  | 0.3346 | 0.0727 |
| Number of observ. :       |                 | (12)                  | (12)           | (12)   | (12)   | (12)    | (12)   | (12)   |
| 3530/F                    | 3/1             | 254.9                 | 0.0333         | 0.8835 | 0.4172 | 0.9095  | 3.3208 | 0.7266 |
| 3531/F                    | 3/1             | 232.3                 | 0.0267         | 0.8721 | 0.3624 | 0.8509  | 3.2524 | 0.6278 |
| 3532/F                    | 3/1             | 234.9                 | 0.0300         | 0.8369 | 0.3985 | 0.8458  | 3.5161 | 0.5845 |
| 3533/F                    | 3/1             | 246.8                 | 0.0311         | 0.7517 | 0.3818 | 0.8949  | 3.3297 | 0.6699 |
| 3534/F                    | 3/1             | 297.8                 | 0.0267         | 0.7027 | 0.3821 | 0.8111  | 3.3707 | 0.6618 |
| 3535/F                    | 3/1             | 258.6                 | 0.0329         | 0.7921 | 0.3765 | 0.8753  | 3.6900 | 0.6142 |
| 3536/F                    | 3/1             | 252.4                 | 0.0329         | 0.7698 | 0.3826 | 0.8413  | 3.5426 | 0.5800 |
| 3537/F                    | 3/1             | 267.4                 | 0.0283         | 0.7780 | 0.4197 | 0.9041  | 3.5025 | 0.7579 |
| 3539/F                    | 3/1             | 244.1                 | 0.0315         | 0.8007 | 0.3723 | 0.9080  | 3.4402 | 0.5987 |
| 3540/F                    | 3/1             | 219.9                 | 0.0362         | 0.9527 | 0.4053 | 1.0855  | 3.2479 | 0.6231 |
| 3541/F                    | 3/1             | 240.3                 | 0.0279         | 0.7980 | 0.3760 | 1.0428  | 3.4929 | 0.5772 |
| 3554/F                    | 3/1             | 246.5                 | 0.0293         | 0.7920 | 0.3702 | 0.9454  | 3.7223 | 0.5802 |
| M e a n:                  |                 | 249.7                 | 0.0306         | 0.8109 | 0.3870 | 0.9096  | 3.4523 | 0.6335 |

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Huntingdon Life Sciences  
Princeton Research Center  
East Millstone, New Jersey

Summary Statistics for % Organ to Body Weight  
Study number: 034242

Printed: 17-Feb-04  
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## Main Study

| 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 |        |                 |
| 1530/F              | 1/1             | 235.9                 | 0.0350     | 0.0305      | 0.2554        | 0.2113 | 0.2926          |
| 1531/F              | 1/1             | 239.4                 | 0.0324     | 0.0268      | 0.1960        | 0.1914 | 0.3459          |
| 1532/F              | 1/1             | 245.3                 | 0.0274     | 0.0300      | 0.2826        | 0.1916 | 0.6731          |
| 1533/F              | 1/1             | 230.3                 | 0.0322     | 0.0321      | 0.2059        | 0.1685 | 0.3102          |
| 1534/F              | 1/1             | 234.0                 | 0.0323     | 0.0307      | 0.2459        | 0.1598 | 0.3718          |
| 1535/F              | 1/1             | 232.8                 | 0.0317     | 0.0300      | 0.2294        | 0.1612 | 0.5897          |
| 1536/F              | 1/1             | 260.3                 | 0.0308     | 0.0371      | 0.2365        | 0.2718 | 0.3634          |
| 1537/F              | 1/1             | 259.8                 | 0.0347     | 0.0274      | 0.2633        | 0.1390 | 0.3129          |
| 1538/F              | 1/1             | 227.0                 | 0.0330     | 0.0311      | 0.2741        | 0.2768 | 0.4729          |
| 1539/F              | 1/1             | 234.4                 | 0.0208     | 0.0294      | 0.2215        | 0.1668 | 0.5265          |
| 1540/F              | 1/1             | 213.0                 | 0.0362     | 0.0269      | 0.2134        | 0.1871 | 0.3678          |
| 1541/F              | 1/1             | 218.2                 | 0.0382     | 0.0298      | 0.2265        | 0.1546 | 0.3584          |
| M e a n:            |                 | 235.9                 | 0.0321     | 0.0301      | 0.2376        | 0.1900 | 0.4154          |
| Standard deviation: |                 | 14.2                  | 0.0045     | 0.0027      | 0.0273        | 0.0440 | 0.1221          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)          | (12)   | (12)            |
| 2530/F              | 2/1             | 238.3                 | 0.0219     | 0.0272      | 0.2565        | 0.2427 | 0.3417          |
| 2531/F              | 2/1             | 265.7                 | 0.0220     | 0.0266      | 0.2300        | 0.1551 | 0.2791          |
| 2532/F              | 2/1             | 240.9                 | 0.0295     | 0.0287      | 0.2228        | 0.2271 | 0.4882          |
| 2533/F              | 2/1             | 250.4                 | 0.0236     | 0.0306      | 0.2236        | 0.1728 | 0.5202          |
| 2534/F              | 2/1             | 240.4                 | 0.0289     | 0.0331      | 0.2379        | 0.1744 | 0.2697          |
| 2535/F              | 2/1             | 225.1                 | 0.0251     | 0.0231      | 0.2301        | 0.1853 | 0.4451          |
| 2536/F              | 2/1             | 234.4                 | 0.0336     | 0.0332      | 0.2790        | 0.2399 | 0.4329          |
| 2537/F              | 2/1             | 243.1                 | 0.0225     | 0.0275      | 0.2089        | 0.2501 | 0.2866          |
| 2538/F              | 2/1             | 230.0                 | 0.0481     | 0.0318      | 0.2469        | 0.2346 | 0.3719          |
| 2539/F              | 2/1             | 234.1                 | 0.0322     | 0.0300      | 0.2462        | 0.1429 | 0.2622          |
| 2540/F              | 2/1             | 227.9                 | 0.0369     | 0.0311      | 0.2049        | 0.2204 | 0.7013          |
| 2541/F              | 2/1             | 246.3                 | 0.0272     | 0.0185      | 0.2050        | 0.1536 | 0.2842          |
| M e a n:            |                 | 239.7                 | 0.0293     | 0.0284      | 0.2326        | 0.1999 | 0.3902          |
| Standard deviation: |                 | 11.1                  | 0.0077     | 0.0043      | 0.0222        | 0.0397 | 0.1335          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)          | (12)   | (12)            |
| 3530/F              | 3/1             | 254.9                 | 0.0231     | 0.0257      | 0.2388        | 0.2332 | 0.3280          |
| 3531/F              | 3/1             | 232.3                 | 0.0343     | 0.0305      | 0.2223        | 0.1524 | 0.3676          |
| 3532/F              | 3/1             | 234.9                 | 0.0344     | 0.0302      | 0.2289        | 0.1525 | 0.3487          |
| 3533/F              | 3/1             | 246.8                 | 0.0354     | 0.0302      | 0.2144        | 0.2261 | 0.4041          |
| 3534/F              | 3/1             | 297.8                 | 0.0352     | 0.0365      | 0.2547        | 0.2188 | 0.2285          |
| 3535/F              | 3/1             | 258.6                 | 0.0268     | 0.0231      | 0.2058        | 0.1971 | 0.3006          |
| 3536/F              | 3/1             | 252.4                 | 0.0370     | 0.0294      | 0.2454        | 0.2422 | 0.2863          |
| 3537/F              | 3/1             | 267.4                 | 0.0264     | 0.0290      | 0.2331        | 0.1718 | 0.3001          |
| 3539/F              | 3/1             | 244.1                 | 0.0307     | 0.0269      | 0.2311        | 0.1682 | 0.3204          |
| 3540/F              | 3/1             | 219.9                 | 0.0295     | 0.0305      | 0.2049        | 0.2183 | 0.5076          |
| 3541/F              | 3/1             | 240.3                 | 0.0258     | 0.0250      | 0.2471        | 0.1718 | 0.5401          |
| 3554/F              | 3/1             | 246.5                 | 0.0289     | 0.0361      | 0.2451        | 0.1820 | 0.4350          |
| M e a n:            |                 | 249.7                 | 0.0306     | 0.0294      | 0.2310        | 0.1945 | 0.3639          |

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

Summary Statistics for % Organ to Body Weight  
Study number: 034242

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| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Ovary Left | Ovary Right | Spleen | Thymus | Uterus w/vagina |
|---------------------|-----------------|-----------------------|------------|-------------|--------|--------|-----------------|
| <hr/>               |                 |                       |            |             |        |        |                 |
| Standard deviation: |                 | 19.7                  | 0.0046     | 0.0040      | 0.0164 | 0.0321 | 0.0926          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)   | (12)   | (12)            |
| 4530/F              | 4/1             | 247.1                 | 0.0217     | 0.0246      | 0.2293 | 0.2187 | 0.3807          |
| 4531/F              | 4/1             | 236.6                 | 0.0279     | 0.0311      | 0.2411 | 0.1641 | 0.4612          |
| 4532/F              | 4/1             | 241.9                 | 0.0457     | 0.0420      | 0.2038 | 0.2421 | 0.4060          |
| 4533/F              | 4/1             | 222.8                 | 0.0352     | 0.0323      | 0.2442 | 0.1651 | 0.3657          |
| 4534/F              | 4/1             | 269.8                 | 0.0419     | 0.0327      | 0.2053 | 0.1936 | 0.2724          |
| 4535/F              | 4/1             | 203.0                 | 0.0342     | 0.0280      | 0.2119 | 0.1428 | 0.5109          |
| 4536/F              | 4/1             | 222.9                 | 0.0395     | 0.0340      | 0.2615 | 0.2420 | 0.4255          |
| 4537/F              | 4/1             | 235.5                 | 0.0267     | 0.0267      | 0.2182 | 0.2038 | 0.4832          |
| 4538/F              | 4/1             | 244.8                 | 0.0310     | 0.0279      | 0.2278 | 0.2199 | 0.3144          |
| 4539/F              | 4/1             | 250.1                 | 0.0281     | 0.0266      | 0.2588 | 0.2110 | 0.3385          |
| 4540/F              | 4/1             | 237.4                 | 0.0259     | 0.0251      | 0.2578 | 0.1944 | 0.4206          |
| 4541/F              | 4/1             | 224.8                 | 0.0293     | 0.0319      | 0.2121 | 0.1888 | 0.6253          |
| M e a n:            |                 | 236.4                 | 0.0322     | 0.0302      | 0.2310 | 0.1989 | 0.4170          |
| Standard deviation: |                 | 16.9                  | 0.0072     | 0.0049      | 0.0213 | 0.0307 | 0.0955          |
| Number of observ. : |                 | (12)                  | (12)       | (12)        | (12)   | (12)   | (12)            |

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

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

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| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Adrenal Glands | Brain    | Epididymis Left | Epididymis Right | Heart   | Kidneys  |
|---------------------|-----------------|-----------------------|----------------|----------|-----------------|------------------|---------|----------|
|                     |                 |                       |                | Male     | Animals         |                  |         |          |
| 1030/M              | 1/1             | 355.9                 | 3.5479         | 100.0000 | 29.9912         | 28.7204          | 58.6908 | 163.0894 |
| 1031/M              | 1/1             | 406.9                 | 3.4905         | 100.0000 | 30.6475         | 30.8097          | 62.7059 | 164.4954 |
| 1032/M              | 1/1             | 384.1                 | 2.8378         | 100.0000 | 26.8827         | 28.4886          | 58.8850 | 155.3952 |
| 1033/M              | 1/1             | 383.0                 | 3.1196         | 100.0000 | 24.4295         | 26.8056          | 62.2783 | 158.9611 |
| 1034/M              | 1/1             | 381.8                 | 3.7092         | 100.0000 | 36.4902         | 32.9544          | 63.3123 | 144.8528 |
| 1035/M              | 1/1             | 311.3                 | 2.6819         | 100.0000 | 26.0128         | 27.6096          | 66.6236 | 132.1156 |
| 1036/M              | 1/1             | 360.9                 | 2.8840         | 100.0000 | 26.9010         | 27.8507          | 60.9411 | 153.3663 |
| 1037/M              | 1/1             | 396.0                 | 3.3221         | 100.0000 | 25.8513         | 27.1820          | 62.3019 | 157.4505 |
| 1038/M              | 1/1             | 353.1                 | 2.8118         | 100.0000 | 28.3439         | 26.8895          | 57.5419 | 147.6753 |
| 1039/M              | 1/1             | 367.9                 | 4.2716         | 100.0000 | 34.2905         | 37.4380          | 66.3993 | 153.3953 |
| 1040/M              | 1/1             | 361.9                 | 3.5087         | 100.0000 | 30.6566         | 26.6151          | 59.3693 | 148.6272 |
| 1041/M              | 1/1             | 353.2                 | 2.4213         | 100.0000 | 30.5278         | 29.4815          | 63.3287 | 155.1528 |
| Mean:               |                 | 368.0                 | 3.2172         | 100.0000 | 29.2521         | 29.2379          | 61.8648 | 152.8814 |
| Standard deviation: |                 | 25.0                  | 0.5207         | 0.0000   | 3.5822          | 3.1837           | 2.9114  | 8.7894   |
| Number of observ. : |                 | (12)                  | (12)           | (12)     | (12)            | (12)             | (12)    | (12)     |
| 2030/M              | 2/1             | 362.3                 | 3.4566         | 100.0000 | 28.1844         | 29.9453          | 61.7017 | 168.3540 |
| 2031/M              | 2/1             | 362.8                 | 2.5439         | 100.0000 | 27.7365         | 28.3292          | 58.2311 | 143.0499 |
| 2032/M              | 2/1             | 348.5                 | 3.9488         | 100.0000 | 28.7408         | 30.5957          | 60.3117 | 142.6140 |
| 2033/M              | 2/1             | 387.7                 | 2.9130         | 100.0000 | 29.5885         | 29.0029          | 64.5702 | 163.5669 |
| 2034/M              | 2/1             | 408.2                 | 3.5409         | 100.0000 | 32.9461         | 33.3520          | 68.4068 | 159.3049 |
| 2035/M              | 2/1             | 384.9                 | 3.1598         | 100.0000 | 28.4570         | 29.2674          | 70.0038 | 179.0085 |
| 2036/M              | 2/1             | 392.8                 | 3.0760         | 100.0000 | 32.9587         | 35.0685          | 66.3857 | 180.2080 |
| 2037/M              | 2/1             | 359.1                 | 3.7478         | 100.0000 | 33.5576         | 33.2933          | 58.0867 | 136.3300 |
| 2038/M              | 2/1             | 344.5                 | 4.9395         | 100.0000 | 31.4282         | 29.0902          | 57.9998 | 161.8801 |
| 2039/M              | 2/1             | 338.2                 | 3.6114         | 100.0000 | 29.7952         | 33.5956          | 57.8894 | 141.3649 |
| 2040/M              | 2/1             | 402.4                 | 4.1539         | 100.0000 | 31.1475         | 31.9904          | 66.1526 | 165.1246 |
| 2041/M              | 2/1             | 343.7                 | 2.8827         | 100.0000 | 27.0749         | 27.7817          | 54.4225 | 149.9950 |
| Mean:               |                 | 369.6                 | 3.4979         | 100.0000 | 30.1346         | 30.9427          | 62.0135 | 157.5667 |
| Standard deviation: |                 | 24.5                  | 0.6546         | 0.0000   | 2.2235          | 2.4201           | 4.9632  | 14.7975  |
| Number of observ. : |                 | (12)                  | (12)           | (12)     | (12)            | (12)             | (12)    | (12)     |
| 3030/M              | 3/1             | 378.8                 | 3.1940         | 100.0000 | 31.2744         | 26.5431          | 58.9968 | 160.5434 |
| 3031/M              | 3/1             | 385.0                 | 4.2196         | 100.0000 | 31.4086         | 31.4747          | 64.9719 | 152.4028 |
| 3032/M              | 3/1             | 379.0                 | 3.5485         | 100.0000 | 31.2646         | 31.4788          | 65.2794 | 157.7541 |
| 3033/M              | 3/1             | 361.0                 | 3.8467         | 100.0000 | 34.0794         | 30.8901          | 68.0655 | 139.0684 |
| 3034/M              | 3/1             | 415.5                 | 3.4478         | 100.0000 | 28.6830         | 30.2627          | 68.8809 | 160.7428 |
| 3035/M              | 3/1             | 351.2                 | 2.8016         | 100.0000 | 28.5933         | 30.7191          | 64.6395 | 153.8473 |
| 3036/M              | 3/1             | 402.8                 | 4.7777         | 100.0000 | 29.6024         | 30.4619          | 64.8660 | 181.2302 |
| 3037/M              | 3/1             | 425.2                 | 3.4490         | 100.0000 | 25.4924         | 29.2321          | 59.1106 | 157.7440 |
| 3038/M              | 3/1             | 389.0                 | 3.6340         | 100.0000 | 31.7907         | 34.1486          | 66.0410 | 155.4626 |
| 3039/M              | 3/1             | 365.4                 | 2.8662         | 100.0000 | 27.8007         | 28.8170          | 61.8958 | 160.7625 |
| 3040/M              | 3/1             | 400.5                 | 2.9434         | 100.0000 | 28.0647         | 27.0851          | 65.0558 | 167.6755 |
| 3041/M              | 3/1             | 411.0                 | 2.9924         | 100.0000 | 27.6397         | 28.4057          | 62.9082 | 170.2504 |
| Mean:               |                 | 388.7                 | 3.4767         | 100.0000 | 29.6411         | 29.9599          | 64.2260 | 159.7903 |

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

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

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| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Adrenal Glands | Brain    | Epididymis Left | Epididymis Right | Heart   | Kidneys  |
|---------------------|-----------------|-----------------------|----------------|----------|-----------------|------------------|---------|----------|
| <hr/>               |                 |                       |                |          |                 |                  |         |          |
| Standard deviation: |                 | 23.0                  | 0.5909         | 0.0000   | 2.3713          | 2.0916           | 3.0647  | 10.3574  |
| Number of observ. : |                 | (12)                  | (12)           | (12)     | (12)            | (12)             | (12)    | (12)     |
| <hr/>               |                 |                       |                |          |                 |                  |         |          |
| 4030/M              | 4/1             | 396.0                 | 4.2437         | 100.0000 | 32.3852         | 34.0460          | 66.8945 | 156.7922 |
| 4031/M              | 4/1             | 366.0                 | 2.9610         | 100.0000 | 30.6343         | 32.1249          | 65.4515 | 156.2896 |
| 4032/M              | 4/1             | 369.9                 | 3.8284         | 100.0000 | 27.0082         | 26.6654          | 68.7872 | 156.1354 |
| 4033/M              | 4/1             | 390.3                 | 3.6159         | 100.0000 | 34.4353         | 34.2428          | 61.0143 | 146.8655 |
| 4034/M              | 4/1             | 359.7                 | 2.7497         | 100.0000 | 27.2513         | 27.2955          | 64.5586 | 165.3147 |
| 4035/M              | 4/1             | 346.5                 | 3.1959         | 100.0000 | 28.8949         | 29.2462          | 54.5889 | 163.8644 |
| 4036/M              | 4/1             | 351.1                 | 3.2231         | 100.0000 | 26.3959         | 26.3523          | 58.1185 | 156.4996 |
| 4037/M              | 4/1             | 359.1                 |                | 100.0000 | 26.3596         | 29.7305          | 53.4196 | 154.6211 |
| 4038/M              | 4/1             | 427.7                 | 3.4624         | 100.0000 | 30.6203         | 29.7174          | 71.0907 | 174.2597 |
| 4039/M              | 4/1             | 350.2                 | 3.1498         | 100.0000 | 30.5977         | 29.9032          | 62.9170 | 153.5410 |
| 4040/M              | 4/1             | 334.4                 | 2.4870         | 100.0000 | 25.3062         | 28.6331          | 55.1171 | 132.8469 |
| 4041/M              | 4/1             | 367.5                 | 4.2115         | 100.0000 | 33.6466         | 32.4172          | 64.3721 | 180.5731 |
| Mean:               |                 | 368.2                 | 3.3753         | 100.0000 | 29.4613         | 30.0312          | 62.1942 | 158.1336 |
| Standard deviation: |                 | 25.6                  | 0.5641         | 0.0000   | 3.0499          | 2.6808           | 5.7926  | 12.2833  |
| Number of observ. : |                 | (12)                  | (11)           | (12)     | (12)            | (12)             | (12)    | (12)     |

Huntingdon Life Sciences  
Princeton Research Center  
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Main Study

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

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| Animal No/sex       | Group/ Subgroup | Terminal Body wt. (g) | Liver        | Lungs     | Spleen  | Testis Left | Testis Right | Thymus  |
|---------------------|-----------------|-----------------------|--------------|-----------|---------|-------------|--------------|---------|
| -----               |                 |                       |              |           |         |             |              |         |
|                     |                 |                       | Male Animals |           |         |             |              |         |
| 1030/M              | 1/1             | 355.9                 | 537.0870     | 92.5307   | 28.8397 | 83.0852     | 80.6785      | 19.7313 |
| 1031/M              | 1/1             | 406.9                 | 684.4993     | 110.7664  | 43.5082 | 73.4428     | 73.0348      | 30.1411 |
| 1032/M              | 1/1             | 384.1                 | 637.5438     | 103.3795  | 33.5171 | 75.9024     | 77.1104      | 22.9088 |
| 1033/M              | 1/1             | 383.0                 | 569.4773     | 79.8899   | 36.0467 | 69.6655     | 68.6397      | 25.8317 |
| 1034/M              | 1/1             | 381.8                 | 523.6042     | 115.5932  | 30.4061 | 74.9314     | 72.3975      | 22.3951 |
| 1035/M              | 1/1             | 311.3                 | 490.0786     | 84.6631   | 40.5023 | 75.4754     | 72.9279      | 21.6980 |
| 1036/M              | 1/1             | 360.9                 | 638.7309     | 87.0881   | 36.4638 | 73.8481     | 72.2078      | 30.0935 |
| 1037/M              | 1/1             | 396.0                 | 551.0189     | 96.2251   | 36.8341 | 62.8748     | 64.1963      | 25.5833 |
| 1038/M              | 1/1             | 353.1                 | 549.1390     | 83.6050   | 28.2654 | 78.5770     | 75.5760      | 19.5762 |
| 1039/M              | 1/1             | 367.9                 | 580.5325     | 99.6015   | 34.0095 | 83.2150     | 83.1639      | 37.6578 |
| 1040/M              | 1/1             | 361.9                 | 579.4135     | 81.5014   | 30.5846 | 72.0793     | 74.1960      | 35.1349 |
| 1041/M              | 1/1             | 353.2                 | 668.7037     | 74.7176   | 30.3148 | 80.7130     | 82.4352      | 30.7546 |
| Mean:               |                 | 368.0                 | 584.1524     | 92.4635   | 34.1077 | 75.3175     | 74.7137      | 26.7922 |
| Standard deviation: |                 | 25.0                  | 60.5683      | 12.8475   | 4.7553  | 5.7673      | 5.5475       | 5.9555  |
| Number of observ. : |                 | (12)                  | (12)         | (12)      | (12)    | (12)        | (12)         | (12)    |
| -----               |                 |                       |              |           |         |             |              |         |
| 2030/M              | 2/1             | 362.3                 | 632.6996     | 93.5986   | 40.7114 | 74.0581     | 76.4963      | 43.3502 |
| 2031/M              | 2/1             | 362.8                 | 525.0240     | 170.3716E | 31.0645 | 71.1648     | 74.4791      | 30.1071 |
| 2032/M              | 2/1             | 348.5                 | 483.0625     | 89.9465   | 35.6822 | 79.6682     | 79.7925      | 28.5209 |
| 2033/M              | 2/1             | 387.7                 | 581.5594     | 115.0998  | 36.7030 | 73.2532     | 72.7032      | 27.9792 |
| 2034/M              | 2/1             | 408.2                 | 563.5223     | 100.6765  | 31.4252 | 76.0952     | 78.8897      | 20.8351 |
| 2035/M              | 2/1             | 384.9                 | 592.1606     | 98.8828   | 35.0403 | 81.8566     | 80.8976      | 21.9745 |
| 2036/M              | 2/1             | 392.8                 | 620.6202     | 89.7565   | 41.9748 | 84.2650     | 81.1939      | 26.2546 |
| 2037/M              | 2/1             | 359.1                 | 530.6506     | 75.1201   | 33.0050 | 82.4861     | 81.9287      | 22.2324 |
| 2038/M              | 2/1             | 344.5                 | 626.6302     | 78.4654   | 32.6679 | 85.6550     | 85.1376      | 28.7144 |
| 2039/M              | 2/1             | 338.2                 | 548.1178     | 96.9352   | 43.1935 | 76.1302     | 78.8425      | 37.9221 |
| 2040/M              | 2/1             | 402.4                 | 648.3051     | 98.7126   | 34.9681 | 78.7163     | 80.0454      | 24.0622 |
| 2041/M              | 2/1             | 343.7                 | 543.3260     | 81.1894   | 32.0679 | 74.9596     | 72.3597      | 28.0139 |
| Mean:               |                 | 369.6                 | 574.6399     | 92.5803   | 35.7086 | 78.1924     | 78.5639      | 28.3305 |
| Standard deviation: |                 | 24.5                  | 50.9548      | 11.4837   | 4.1782  | 4.6403      | 3.8681       | 6.5882  |
| Number of observ. : |                 | (12)                  | (12)         | (11)      | (12)    | (12)        | (12)         | (12)    |
| -----               |                 |                       |              |           |         |             |              |         |
| 3030/M              | 3/1             | 378.8                 | 555.2155     | 90.5144   | 38.3920 | 70.2767     | 73.9388      | 21.3437 |
| 3031/M              | 3/1             | 385.0                 | 589.3541     | 87.1474   | 31.5598 | 82.1528     | 82.3087      | 26.3715 |
| 3032/M              | 3/1             | 379.0                 | 571.6463     | 92.1875   | 37.3588 | 88.5563     | 89.5103      | 26.5333 |
| 3033/M              | 3/1             | 361.0                 | 507.4183     | 87.5041   | 36.2195 | 74.5745     | 72.4763      | 24.6142 |
| 3034/M              | 3/1             | 415.5                 | 615.1092     | 96.0463   | 42.1947 | 73.3360     | 74.7027      | 43.1798 |
| 3035/M              | 3/1             | 351.2                 | 517.7272     | 98.2145   | 32.9733 | 88.0142     | 85.1633      | 27.3010 |
| 3036/M              | 3/1             | 402.8                 | 662.1291     | 81.9649   | 35.9599 | 85.4173     | 88.8265      | 28.7333 |
| 3037/M              | 3/1             | 425.2                 | 598.0434     | 103.7527  | 31.5879 | 71.5098     | 72.6291      | 26.7852 |
| 3038/M              | 3/1             | 389.0                 | 666.1196     | 97.1150   | 36.6776 | 78.8848     | 80.2164      | 32.4703 |
| 3039/M              | 3/1             | 365.4                 | 634.3762     | 79.4165   | 36.9755 | 78.0817     | 78.4142      | 27.1403 |
| 3040/M              | 3/1             | 400.5                 | 674.8087     | 84.3298   | 44.0586 | 72.8537     | 70.2646      | 36.7899 |
| 3041/M              | 3/1             | 411.0                 | 572.4545     | 89.6295   | 36.0167 | 72.8934     | 72.1364      | 32.2134 |
| Mean:               |                 | 388.7                 | 597.0335     | 90.6519   | 36.6645 | 78.0459     | 78.3823      | 29.4563 |

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Huntingdon Life Sciences  
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Main Study

Summary Statistics for % Organ to Brain Weight  
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| 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 |          |          |          |
| 1530/F              | 1/1             | 235.9                 | 3.5332         | 100.0000    | 44.2502       | 110.6665 | 430.8065 | 72.4491  |
| 1531/F              | 1/1             | 239.4                 | 2.8728         | 100.0000    | 52.3207       | 100.4202 | 350.3469 | 78.9281  |
| 1532/F              | 1/1             | 245.3                 | 3.9992         | 100.0000    | 45.6370       | 101.8112 | 395.6345 | 85.8042  |
| 1533/F              | 1/1             | 230.3                 | 3.4674         | 100.0000    | 44.5984       | 101.1169 | 387.0342 | 77.5256  |
| 1534/F              | 1/1             | 234.0                 | 4.5482         | 100.0000    | 48.7780       | 113.2830 | 441.8128 | 79.5954  |
| 1535/F              | 1/1             | 232.8                 | 3.5255         | 100.0000    | 44.9176       | 110.1396 | 425.0352 | 79.7811  |
| 1536/F              | 1/1             | 260.3                 | 3.8622         | 100.0000    | 52.3899       | 118.0703 | 497.2099 | 67.0193  |
| 1537/F              | 1/1             | 259.8                 | 3.4176         | 100.0000    | 48.3262       | 121.5638 | 426.4081 | 104.7604 |
| 1538/F              | 1/1             | 227.0                 | 4.0138         | 100.0000    | 47.5981       | 104.7939 | 403.1646 | 89.1879  |
| 1539/F              | 1/1             | 234.4                 | 4.0916         | 100.0000    | 41.1437       | 94.6301  | 374.2495 | 82.7329  |
| 1540/F              | 1/1             | 213.0                 | 3.7340         | 100.0000    | 42.5505       | 88.5713  | 353.1090 | 72.0795  |
| 1541/F              | 1/1             | 218.2                 | 3.4192         | 100.0000    | 38.8948       | 96.5372  | 390.3139 | 67.2995  |
| M e a n:            |                 | 235.9                 | 3.7070         | 100.0000    | 45.9504       | 105.1337 | 406.2604 | 79.7636  |
| Standard deviation: |                 | 14.2                  | 0.4309         | 0.0000      | 4.1421        | 9.8509   | 41.1419  | 10.4229  |
| Number of observ. : |                 | (12)                  | (12)           | (12)        | (12)          | (12)     | (12)     | (12)     |
| 2530/F              | 2/1             | 238.3                 | 3.7388         | 100.0000    | 46.0169       | 102.7368 | 451.6151 | 80.8674  |
| 2531/F              | 2/1             | 265.7                 | 3.0775         | 100.0000    | 51.3901       | 103.6127 | 411.0858 | 79.8454  |
| 2532/F              | 2/1             | 240.9                 | 5.1392         | 100.0000    | 47.9509       | 123.2139 | 459.7031 | 79.0818  |
| 2533/F              | 2/1             | 250.4                 | 4.5879         | 100.0000    | 42.9754       | 107.6514 | 400.0291 | 80.3175  |
| 2534/F              | 2/1             | 240.4                 | 4.2610         | 100.0000    | 55.9434       | 105.1887 | 451.6405 | 89.3973  |
| 2535/F              | 2/1             | 225.1                 | 3.6812         | 100.0000    | 41.5528       | 107.9871 | 382.7375 | 68.3697  |
| 2536/F              | 2/1             | 234.4                 | 3.6578         | 100.0000    | 56.5411       | 98.2691  | 392.2971 | 86.2198  |
| 2537/F              | 2/1             | 243.1                 | 3.0158         | 100.0000    | 49.7216       | 104.2576 | 416.9320 | 76.0804  |
| 2538/F              | 2/1             | 230.0                 | 4.6342         | 100.0000    | 45.6538       | 114.2748 | 465.5162 | 61.6722  |
| 2539/F              | 2/1             | 234.1                 | 4.5148         | 100.0000    | 43.1404       | 110.1683 | 427.2737 | 71.2631  |
| 2540/F              | 2/1             | 227.9                 | 4.5299         | 100.0000    | 47.6534       | 131.1825 | 507.1320 | 66.1838  |
| 2541/F              | 2/1             | 246.3                 | 4.0812         | 100.0000    | 48.9797       | 119.9146 | 452.4155 | 70.0859  |
| M e a n:            |                 | 239.7                 | 4.0766         | 100.0000    | 48.1266       | 110.7048 | 434.8648 | 75.7820  |
| Standard deviation: |                 | 11.1                  | 0.6538         | 0.0000      | 4.7793        | 9.6804   | 36.1015  | 8.3517   |
| Number of observ. : |                 | (12)                  | (12)           | (12)        | (12)          | (12)     | (12)     | (12)     |
| 3530/F              | 3/1             | 254.9                 | 3.7700         | 100.0000    | 47.2203       | 102.9441 | 375.8748 | 82.2469  |
| 3531/F              | 3/1             | 232.3                 | 3.0653         | 100.0000    | 41.5519       | 97.5715  | 372.9355 | 71.9828  |
| 3532/F              | 3/1             | 234.9                 | 3.5811         | 100.0000    | 47.6118       | 101.0581 | 420.1334 | 69.8357  |
| 3533/F              | 3/1             | 246.8                 | 4.1395         | 100.0000    | 50.7950       | 119.0374 | 442.9257 | 89.1069  |
| 3534/F              | 3/1             | 297.8                 | 3.8039         | 100.0000    | 54.3726       | 115.4353 | 479.6808 | 94.1795  |
| 3535/F              | 3/1             | 258.6                 | 4.1498         | 100.0000    | 47.5321       | 110.5112 | 465.8644 | 77.5375  |
| 3536/F              | 3/1             | 252.4                 | 4.2769         | 100.0000    | 49.7015       | 109.2898 | 460.1956 | 75.3474  |
| 3537/F              | 3/1             | 267.4                 | 3.6389         | 100.0000    | 53.9490       | 116.2092 | 450.2091 | 97.4138  |
| 3539/F              | 3/1             | 244.1                 | 3.9292         | 100.0000    | 46.4903       | 113.3992 | 429.6276 | 74.7672  |
| 3540/F              | 3/1             | 219.9                 | 3.8045         | 100.0000    | 42.5462       | 113.9434 | 340.9328 | 65.4112  |
| 3541/F              | 3/1             | 240.3                 | 3.4992         | 100.0000    | 47.1214       | 130.6738 | 437.7086 | 72.3352  |
| 3554/F              | 3/1             | 246.5                 | 3.6980         | 100.0000    | 46.7374       | 119.3659 | 469.9601 | 73.2586  |
| M e a n:            |                 | 249.7                 | 3.7797         | 100.0000    | 47.9691       | 112.4532 | 428.8374 | 78.6186  |

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

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

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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 |         |                 |
| 1530/F              | 1/1             | 235.9                 | 4.2430      | 3.6978      | 30.9864       | 25.6326 | 35.4968         |
| 1531/F              | 1/1             | 239.4                 | 3.7913      | 3.1366      | 22.9236       | 22.3813 | 40.4583         |
| 1532/F              | 1/1             | 245.3                 | 3.4728      | 3.7928      | 35.7707       | 24.2531 | 85.2057         |
| 1533/F              | 1/1             | 230.3                 | 3.7618      | 3.7567      | 24.0684       | 19.6974 | 36.2626         |
| 1534/F              | 1/1             | 234.0                 | 4.0734      | 3.8738      | 31.0440       | 20.1726 | 46.9436         |
| 1535/F              | 1/1             | 232.8                 | 3.7063      | 3.5054      | 26.8230       | 18.8429 | 68.9484         |
| 1536/F              | 1/1             | 260.3                 | 3.7498      | 4.5176      | 28.8236       | 33.1164 | 44.2816         |
| 1537/F              | 1/1             | 259.8                 | 4.2009      | 3.3243      | 31.8957       | 16.8314 | 37.8963         |
| 1538/F              | 1/1             | 227.0                 | 3.6929      | 3.4806      | 30.7233       | 31.0195 | 52.9943         |
| 1539/F              | 1/1             | 234.4                 | 2.3581      | 3.3411      | 25.1404       | 18.9279 | 59.7521         |
| 1540/F              | 1/1             | 213.0                 | 4.0715      | 3.0220      | 23.9755       | 21.0168 | 41.3217         |
| 1541/F              | 1/1             | 218.2                 | 4.0391      | 3.1480      | 23.9394       | 16.3406 | 37.8778         |
| M e a n:            |                 | 235.9                 | 3.7634      | 3.5497      | 28.0095       | 22.3527 | 48.9533         |
| Standard deviation: |                 | 14.2                  | 0.5006      | 0.4131      | 4.1045        | 5.3053  | 15.3454         |
| Number of observ. : |                 | (12)                  | (12)        | (12)        | (12)          | (12)    | (12)            |
| 2530/F              | 2/1             | 238.3                 | 2.6022      | 3.2253      | 30.4686       | 28.8285 | 40.5882         |
| 2531/F              | 2/1             | 265.7                 | 2.8941      | 3.4987      | 30.2840       | 20.4173 | 36.7511         |
| 2532/F              | 2/1             | 240.9                 | 3.8900      | 3.7914      | 29.4105       | 29.9748 | 64.4313         |
| 2533/F              | 2/1             | 250.4                 | 2.8650      | 3.7071      | 27.0919       | 20.9360 | 63.0402         |
| 2534/F              | 2/1             | 240.4                 | 3.6373      | 4.1719      | 29.9790       | 21.9759 | 33.9780         |
| 2535/F              | 2/1             | 225.1                 | 3.1569      | 2.8948      | 28.8862       | 23.2640 | 55.8871         |
| 2536/F              | 2/1             | 234.4                 | 3.7630      | 3.7248      | 31.2661       | 26.8863 | 48.5225         |
| 2537/F              | 2/1             | 243.1                 | 2.7004      | 3.2918      | 25.0234       | 29.9660 | 34.3320         |
| 2538/F              | 2/1             | 230.0                 | 5.6385      | 3.7267      | 28.9523       | 27.5045 | 43.6044         |
| 2539/F              | 2/1             | 234.1                 | 3.7607      | 3.5110      | 28.7819       | 16.7108 | 30.6498         |
| 2540/F              | 2/1             | 227.9                 | 4.4298      | 3.7293      | 24.5984       | 26.4525 | 84.1875         |
| 2541/F              | 2/1             | 246.3                 | 3.3216      | 2.2591      | 25.0633       | 18.7875 | 34.7500         |
| M e a n:            |                 | 239.7                 | 3.5550      | 3.4610      | 28.3171       | 24.3087 | 47.5602         |
| Standard deviation: |                 | 11.1                  | 0.8568      | 0.4991      | 2.3132        | 4.5453  | 16.3115         |
| Number of observ. : |                 | (12)                  | (12)        | (12)        | (12)          | (12)    | (12)            |
| 3530/F              | 3/1             | 254.9                 | 2.6110      | 2.9130      | 27.0293       | 26.3943 | 37.1270         |
| 3531/F              | 3/1             | 232.3                 | 3.9291      | 3.4947      | 25.4948       | 17.4787 | 42.1541         |
| 3532/F              | 3/1             | 234.9                 | 4.1101      | 3.6065      | 27.3564       | 18.2258 | 41.6603         |
| 3533/F              | 3/1             | 246.8                 | 4.7108      | 4.0209      | 28.5237       | 30.0760 | 53.7595         |
| 3534/F              | 3/1             | 297.8                 | 5.0129      | 5.1993      | 36.2468       | 31.1383 | 32.5146         |
| 3535/F              | 3/1             | 258.6                 | 3.3833      | 2.9195      | 25.9825       | 24.8841 | 37.9485         |
| 3536/F              | 3/1             | 252.4                 | 4.8070      | 3.8188      | 31.8734       | 31.4617 | 37.1899         |
| 3537/F              | 3/1             | 267.4                 | 3.3985      | 3.7302      | 29.9620       | 22.0882 | 38.5714         |
| 3539/F              | 3/1             | 244.1                 | 3.8371      | 3.3562      | 28.8601       | 21.0069 | 40.0133         |
| 3540/F              | 3/1             | 219.9                 | 3.0932      | 3.2030      | 21.5046       | 22.9176 | 53.2818         |
| 3541/F              | 3/1             | 240.3                 | 3.2332      | 3.1289      | 30.9658       | 21.5269 | 67.6836         |
| 3554/F              | 3/1             | 246.5                 | 3.6468      | 4.5636      | 30.9465       | 22.9769 | 54.9170         |
| M e a n:            |                 | 249.7                 | 3.8144      | 3.6629      | 28.7288       | 24.1813 | 44.7351         |

Huntingdon Life Sciences  
Princeton Research Center  
East Millstone, New Jersey

Summary Statistics for % Organ to Brain Weight  
Study number: 034242

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## Main Study

| Animal Group/<br>No/sex Subgroup | Terminal<br>Body wt. (g) | Ovary Left | Ovary Right | Spleen  | Thymus  | Uterus w/vagina |
|----------------------------------|--------------------------|------------|-------------|---------|---------|-----------------|
| Standard deviation:              | 19.7                     | 0.7397     | 0.6786      | 3.7279  | 4.7337  | 10.3195         |
| Number of observ. :              | (12)                     | (12)       | (12)        | (12)    | (12)    | (12)            |
| 4530/F 4/1                       | 247.1                    | 2.5664     | 2.9160      | 27.1295 | 25.8750 | 45.0419         |
| 4531/F 4/1                       | 236.6                    | 3.3318     | 3.7262      | 28.8387 | 19.6319 | 55.1747         |
| 4532/F 4/1                       | 241.9                    | 5.7022     | 5.2433      | 25.4125 | 30.1918 | 50.6342         |
| 4533/F 4/1                       | 222.8                    | 3.9392     | 3.6130      | 27.2983 | 18.4564 | 40.8872         |
| 4534/F 4/1                       | 269.8                    | 5.5281     | 4.3149      | 27.0926 | 25.5467 | 35.9523         |
| 4535/F 4/1                       | 203.0                    | 3.7703     | 3.0858      | 23.3661 | 15.7494 | 56.3427         |
| 4536/F 4/1                       | 222.9                    | 4.3378     | 3.7315      | 28.7278 | 26.5885 | 46.7541         |
| 4537/F 4/1                       | 235.5                    | 3.2688     | 3.2688      | 26.7489 | 24.9792 | 59.2286         |
| 4538/F 4/1                       | 244.8                    | 3.7925     | 3.4178      | 27.8619 | 26.9025 | 38.4550         |
| 4539/F 4/1                       | 250.1                    | 3.4554     | 3.2782      | 31.8567 | 25.9795 | 41.6667         |
| 4540/F 4/1                       | 237.4                    | 3.1651     | 3.0672      | 31.5480 | 23.7847 | 51.4666         |
| 4541/F 4/1                       | 224.8                    | 3.4884     | 3.7902      | 25.2448 | 22.4657 | 74.4058         |
| M e a n:                         | 236.4                    | 3.8622     | 3.6211      | 27.5938 | 23.8460 | 49.6675         |
| Standard deviation:              | 16.9                     | 0.9298     | 0.6423      | 2.4519  | 4.0926  | 10.7335         |
| Number of observ. :              | (12)                     | (12)       | (12)        | (12)    | (12)    | (12)            |