PDCN: 88940000357

8EHQ-94-13115
SP001 02/14/95

Shell Oil Company

8EHQ-0295-1315

One Shell Plaza
P.O. Box 4320
Houston, Texas 77210

ORIGINAL

89950000129

B

February 2, 1995

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Dear Sir:

SUBJECT: SUPPLEMENTAL INFORMATION TO 8EHQ-0794-13115

The following supplemental information is submitted under TSCA 8(e) in response to your request for additional information.

A copy of the final report of the original TSCA 8(e) filing (8EHQ-0794-13115) by Shell, which was also submitted to the EPA TSCA 4 office by the CMA Oxo Process Panel, to which Shell is a member, is attached. Final results of the study indicated that CNS effects seen in rats exposed to 6000 ppm isobutanol were considered residual anesthetic effects; no treatment-related effects were seen at 3000 ppm; and hypoactivity was seen in rats at 1500 ppm isobutanol during, but not after, the 6-hour exposure period.

Based on the final results of the study, Shell has taken the following voluntary actions in response to the findings. The material safety data sheet for isobutanol was reviewed to determine the adequacy of health effects warnings for CNS depression. In addition, the vapor concentration at which hypoactivity was observed was compared to the occupational exposure limit followed by Shell and the odor threshold for isobutanol. As a result, it was determined that 1) Shell already adequately warns for CNS depression on the MSDS, and 2) the mild hypoactivity effects in rats in the reported study were observed at a vapor concentration of 1500 ppm compared to an ACGIH 8-hr TWA of 50 ppm and an odor threshold of approximately 1.6 ppm. Thus, it was concluded that no additional changes were needed at this time either on the MSDS or in the handling of isobutanol in order to provide adequate worker protection.

RECEIVED 5/23/95

SH9503305.W60

This report is filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

This report has been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

This report contains no confidential business information.

The following person should be contacted if you have questions or a need for discussion.

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Very truly yours,

R. N. Shulman

R. N. Shulman, General Manager
Health, Safety, and Environment
Shell Oil Company

THG/sjh

Attachment

SH9503305.W60

CMA

CHEMICAL MANUFACTURERS ASSOCIATION

September 28 , 1994

VIA MESSENGER

ATTN: TSCA Section 4
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TSCA Public Information Office (MS - 7407)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Room N.E. Mall G102
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Washington, D.C. 20460

For Distribution by CMA
CHEMSTAR DIVISION
From: Barbara Francis
Ref. No. OxoPanel | Isobutanol
Date 9/28/94

RE: Multi-substance Final Rule for the Testing of Neurotoxicity for Isobutanol (40 CFR 799.5050). Submission of Final Report for Acute Neurotoxicity Study of Isobutanol in Sprague-Dawley Rats.

Dear Sir/Madam:

The Chemical Manufacturers Association Oxo Process Panel submits six copies of the final report entitled:

"Acute Neurotoxicity Study of Isobutanol in Sprague-Dawley Rats."

The study report is submitted on behalf of the test sponsors indicated on Attachment I, as part of the Multi-substance Final Rule.

Any questions regarding this submission should be directed to the Oxo Process Panel Manager, Barbara O. Francis, at (202) 887-1314.

Sincerely,

Langley Spurlock

Langley A. Spurlock, Ph.D.
Vice President, CHEMSTAR

Enclosures (6)

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OCT 03 1994
SE&T/HSE
BUSINESS SUPPORT

cc: Michael Stahl, Director, Office of Compliance Monitoring
Catherine Roman, EPA
Oxo Process Panel
Isobutantol Task Group

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Responsible Care
A Public Commitment

ATTACHMENT I

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STUDY TITLE

Acute Neurotoxicity Study of Isobutanol in Sprague-Dawley Rats

DATA REQUIREMENT

40 CFR Part 799 Multi-Substance Rule for the Testing of Neurotoxicity
40 CFR Part 798.1150 Inhalation Test Guidelines

Test Guidelines 798.6050 & 798.6200 updated by
Neurotoxicity Guideline 81-8, Subdivision F

AUTHORS

A. A. Li, T.A. Kaempfe, P.E. O'Donnell, D. Smolboski

STUDY COMPLETED ON

September 15, 1994

PERFORMING LABORATORIES

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Environmental Health Laboratory (EHL)
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St. Louis, Missouri 63110

Union Carbide Corporation
PO Box 8361
South Charleston, West Virginia 25303

PROJECT NUMBER

Monsanto Laboratory Project Numbers: EHL 94009 (94010)
Union Carbide Laboratory Project Number: #37-AEG-131

SPONSOR COMPANY

Chemical Manufacturers Association
2501 M Street, NW
Washington, DC 20037

GLP COMPLIANCE STATEMENT

This study EHL 94009 and the accompanying pilot study EHL 94010 (Appendix 7) were conducted in accordance with the principles of Good Laboratory Practice (GLP) Standards of the EPA (USA, FIFRA: 40 CFR, Part 160), MAFF (Japan, 1984), and the GLP Principles of the OECD (1981).

This compliance statement does not cover the Union Carbide study characterizing the neat test material in Appendix 6 or the positive control data in Appendix 12 which each have their own compliance statement.

Study Director	9/15/94 Date
R. M. Folk Director, Environmental Health Laboratory	9/15/94 Date
Barbara O. Dawes Sponsor/Submitter	9/16/94 Date

QUALITY ASSURANCE AUDIT STATEMENT

Study Numbers: 94009/94010

Protocol Amendments: 94009 - One - March 14, 1994
94010 - None

Study Title: Acute Neurotoxicity Study of Isobutanol by Whole-Body Inhalation to CD® Rats

#94009

Dates of Inspections and Audits:	Dates of Communication to Management:
February 24, 1994	February 25, 1994
March 01, 16, 24, 1994	March 02, 17, 25, 1994
May 04, 09, 10, 13, 16, 17, 19, 23, 24, 27, 1994	May 04, 09, 10, 13, 16, 17, 19, 23, 24, 27, 1994
June 06, 1994	June 06, 1994

#94010

January 31, 1994	February 04, 1994
May 09, 11, 24, 25, 27, 1994	May 09, 11, 24, 25, 27, 1994
June 02, 1994	June 02, 1994

Quality Assurance Review Conducted by:

#94009	#94010
S.M. Haag	S.M. Haag
N.K. Harakas	C.K. Russell
S.H. McClain	P.A. Winzenburger
C.K. Russell	
P.A. Winzenburger	

This signed statement indicates the ESH Quality and Compliance Assurance Unit has monitored this study and reviewed the data and final report. These reviews indicate the final report accurately presents the raw data as developed during the study.

John L. Henshaw
Director Quality & Compliance Assurance

Date June 10, 1994

REPORT SIGNATURE PAGE

This report (EHL 94009) and the accompanying report for the pilot study (EHL 94010; Appendix 7) is a true and accurate account of the work conducted in these studies.

Abby, A. Li, Ph.D, Study Director
Neurotoxicology Team Leader

9/15/94
Date

Terry A. Kaempfe, Principle Investigator

9/15/94
Date

Roger M. Folk, Ph.D.
Director, Environmental Health Laboratory

9/15/94
Date

SUMMARY

Four groups of 10 rats/sex were exposed by inhalation for 6 hours to a vapor of isobutanol at 0, 1500, 3000, and 6000 ppm. Neurobehavioral tests (functional observational battery and motor activity) were conducted prior to exposure (pretest), immediately after exposure (day 0), the day after exposure (day 1), and 7 and 14 days after dosing. Each animal was sacrificed 15 days after exposure to isobutanol. Five animals from each group were perfused, and the female reproductive tract and selected central and peripheral nervous tissues from these animals were retained but were not microscopically examined. The remaining animals from each group were given a complete gross necropsy and in females, the reproductive tracts were retained.

Isobutanol clearly causes a rapidly reversible general depression of the central nervous system at concentrations of 3000 and 6000 ppm during a 6 hour exposure period. The transient decrease in alertness in female rats, transient decrease in motor activity in male and female rats, and transient, slight, incoordinated gait observed in one male rat are considered residual effects of the anesthetic effects of 6000 ppm concentration of isobutanol. There were no treatment-related effects in rats at the 3000 ppm concentration following acute exposure. Minimal effects (hypoactivity) were seen in rats at the 1500 ppm concentration during, but not after, the 6-hour exposure period. No treatment-related findings were observed in any tissues or organs during gross necropsy 15 days after exposures were conducted. The 1500 ppm concentration is considered to be a Lowest-Observed-Effect-Level (LOEL) for the study.

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TRADEMARKS

The following registered trademarks were used in this report:

ITEM	REGISTERED TRADEMARK OF:
RODENT CHOW	Purina Mills, Inc., St. Louis, MO
CD	Charles River Laboratories, Inc., Wilmington, MA

NOTES TO READER

The following terms are used as column headings in some data tables:

PERIOD (PER) A number corresponding to a specified interval within the study; used to facilitate data reporting.

WINDOW A series of days within a study when data could have been collected for the corresponding period. Actual data collection occurred on one or more of the days within the window.

ANIMAL IDENTIFICATION SYSTEM

The current EHL animal number format is YYXXXSGGANNN where YYXXX is the study number, Y is the study year, and X is the sequence number within the year. The S represents the animal's sex, G is the primary group code, A represents the subgroup code (which is not used in acute studies and is left blank), and N is the animal's sequence number within the group, e.g., 99999M02 001. The animal designation may be further reduced by exclusion of the study number, e.g., M02 001.

INTRODUCTION

Purpose: To use a neurotoxicity screening battery to determine the potential for isobutanol to alter the function of the nervous system following a single acute whole-body inhalation exposure. Neurotoxicity is defined as any adverse effect on the structure or function of the nervous system related to exposure to a chemical substance. The neurotoxicity screening battery consists of a functional observational battery (FOB) and motor activity (MA).

Date Protocol Signed by Study Director:	February 28, 1994
Date of First Exposure (Day 0 of Study):	March 15, 1994
Date Last Animal Sacrificed:	April 2, 1994

Experimental Design: Four groups of 10 rats/sex were exposed by inhalation to isobutanol vapor at 0, 1500, 3000, and 6000 ppm. Neurobehavioral tests (functional observational battery and motor activity) were conducted prior to exposure (pretest), as soon as possible after exposure, the morning following exposure, and 7 and 14 days after dosing. Each animal was sacrificed 15 days after dosing. Five animals from each group were perfused, and the female reproductive tract and selected central and peripheral nervous tissues from these animals were retained. The remaining animals from each group were given a complete gross necropsy and female reproductive tracts were retained. The retained tissues were not microscopically examined.

MATERIALS AND METHODS

Test Material

Identification:	Isobutanol
EHL Substance Identification Code:	T940007
Lot Number:	EH 3639
Stated Purity:	>99.9%
Date Received:	December 27, 1993
Description at Receipt:	Clear liquid
Source:	Union Carbide Chemicals and Plastics Company, Inc. 10521 Sheldon Road Houston, Texas 77044

Group Designations/Exposure Concentrations:

Groups (Male,Female)	Target Exposure Concentration (ppm)
M00, F00	0
M01, F01	1500
M02, F02	3000
M03, F03	6000

Exposure System (See Inhalation Subreport in Appendix 5 for complete details)

Exposure Chambers:	Four 2000-liter stainless steel and glass Hazelton H-2000 chambers
Animal Housing during Exposure:	Individual stainless steel wire mesh cages, positioned in one tier in the chamber
Exposure Duration:	6 hours
Test Atmosphere Generation System:	Test material was fed into a Laskin-type nebulizer mounted in a filtered supply air inlet at top of the inhalation chamber. Exposure concentrations were controlled by using an adjustable-flow valveless pump to regulate the rate at which isobutanol was delivered to the nebulizer.
Test Atmosphere Sampling Method:	Six test atmosphere samples were drawn through a Miran 1A infrared detector calibrated for isobutanol.
Sampling Location:	In the animal breathing area from a port halfway down on the chamber door
Chamber Atmosphere Distributions:	Chamber atmospheres were sampled in 2 different locations for all 3 exposure concentrations.

Analysis of Test Material and Gas Chromatography Analysis of Pre-Test Samples (See Appendix 6 for complete details):

Stability of Neat Test Material:	Analyses were conducted using gas chromatography with a flame ionization detector. The material was assayed before and after the study by comparison with an independently obtained high purity standard.
Gas Chromatography Analysis:	Samples of the chamber atmospheres were collected in two impingers, in series, containing methanol. The solutions were analyzed for isobutanol content using gas chromatography with a flame ionization detector.

Animals

Note: Animal housing and husbandry were in accordance with the provisions of 'Guide to the Care and Use of Laboratory Animals', USPHS-NIH Publication No. 86-23.

Species:	Rat
Strain:	Sprague-Dawley (CD)
Source:	Charles River Raleigh, Raleigh, N.C.
Number Used in Study:	80 (40 males, 40 females) Unhealthy animals were excluded from assignment to the study as specified in the protocol.
Test Group Size:	10 animals/sex
Method of Assignment:	Randomization by ear-tag number
Method of Identification:	Individual ear-tag, bar-coded cage card
Acclimation Period:	Approximately 5 weeks (Including quarantine and pretest evaluation periods)
Age on Day of Exposure:	8 weeks old

Animals

Weight Range on Day of Exposure:	Males: 288-388 grams Females: 187-290 grams
Type of Housing:	Individual stainless steel cages with wire mesh bottoms suspended over paper bedding.
Water Availability:	*ad libitum* (St. Louis public water supply which is treated with sodium zeolite)
Food Availability:	*ad libitum* (Purina Mills Certified RODENT CHOW #5002)

Inlife Observations

Checks for mortality and moribundity and noteworthy signs of toxicity were made daily from the day of randomization until the day of sacrifice.

Clinical Observations During Exposure

Clinical signs of toxicity were recorded by exception once every hour during the 6 hour exposure period. The observer was aware of the exposure concentration for each animal.

Behavioral Tests

The behavioral tests consisted of a functional observational battery (FOB) and a test for motor activity (MA). Both tests were conducted at the following 5 time periods:

(1) before the start of the study (pretest)[1],
(2) as soon as possible after exposure (day 0)
(3) 1 day after exposure (day 1)
(4) 7 days after exposure (day 7)
(5) 14 days after exposure (day 14)

---

[1]Animals were tested twice prior to treatment (pretest); once when they were 6 weeks old and then again when they were 7 weeks old. This was done because it was discovered after the first pretest data were collected that the animals were one week younger than anticipated. The study director wanted the animals to be 8 weeks old when exposed since that was the age of the animals used to set exposure concentrations in the pilot study. Pretest FOB and MA were conducted again when the animals were 7 weeks old so that there would be pretest data one week prior to exposure. Only the later pretest data will be reported in the study. The first set of pretest data will be archived but not reported.

For each time period, behavioral tests were conducted over a 4-day period with 5 animals/group (2-3 animals/sex/group) tested each day. In other words, the time of testing for all periods was balanced across dose groups and sex. MA and FOB tests were conducted at approximately the same time of day throughout this study. On the day of exposure (day 0), animals were taken out of the inhalation chambers and were immediately put into motor activity chambers. After the motor activity session was completed, the animals were returned to their home cages where they remained undisturbed for about 30 minutes prior to recording home cage observations. This allowed for a more accurate assessment of home cage observations.

Motor Activity (MA): Motor activity was tested by placing individuals animals into an automated photobeam activity recording device (San Diego Instruments, Photobeam Activity System). Each monitoring session was 1 hour long. This length of time had been previously determined as being long enough for the activity of untreated rats to approach asymptotic concentrations for the last 20% of the session (see Appendix 12, Exhibit 3). Prior to each test session, a diagnostic test was performed to ensure proper photocell operation and equivalent functioning across devices. The 20 animals (2-3 animals/sex/group) tested each day were balanced across the 20 activity devices.

Functional Observational Battery (FOB): An FOB (see Appendix 3, Exhibit 1 for details) was performed to detect gross functional deficits and to quantify behavioral effects. A single trained observer was used to conduct the FOB on all animals. Previous to the study, the observer demonstrated proficiency in conducting the FOB (see Appendix 12, Exhibit 2). Precautions were taken to insure that the observer was unaware of each animal's treatment. In addition, the observer could not associate any particular animal with others from the same group. Finally, the order in which the animals were tested was such that there was no discernible pattern to the order in which animals from different exposure concentrations were tested. This also insured that the animals from different groups were balanced over the time of testing of approximately 2 hours for each set of 20 animals. This latter point is only relevant for day 0 when the animals were thought to be rapidly recovering from the effects of the chemical.

Ophthalmic Examination

Frequency:	Twice (pretest and following completions of all Day 7 behavioral testing).
Animals Examined:	All animals at both time points
Mydriatic:	1% atropine
Method of Examination:	Indirect ophthalmoscopy

Gross Necropsy and Perfusion of Animals Selected for *In-Situ* Perfusion

Occurrence: Fifteen days after acute exposure (day 15)

Method of Euthanasia: Halothane anesthesia followed by perfusion

Animals Examined: Five rats/sex/dose were randomly selected to be perfused.

Extent of Examination: These rats were not given a complete necropsy. However, abnormalities observed during perfusion or tissue collection were documented.

Perfusion and Fixation: Heparin sulfate was injected intraperitoneally approximately 10 minutes prior to necropsy. The rats were anesthetized with halothane after which the thoracic cavity was opened and whole body perfusion-fixation was accomplished by intracardial infusion of sodium nitrite followed by 4% formaldehyde/1.5% glutaraldehyde.

Organs Weighed: None

Tissues Retained: Female reproductive tract, brain, spinal cord (cervical, thoracic, and lumbar segments), dorsal and ventral spinal nerve roots with dorsal root ganglia (C3-C6, L1-L4), Gasserian ganglion, and sciatic, tibial, and sural nerves. Tissues were stored in perfusion fixative.

Gross Necropsy of Animals Not Selected for *In Situ* Perfusion

Occurrence: 15 days after acute exposure (day 15)

Method of Euthanasia: Halothane anesthesia followed by exsanguination

Animals Examined: Animals not assigned for *in situ* perfusion

Extent of Examination: External surface and internal cavities. Organs were examined in place and then removed. Hollow organs were opened and examined.

Organs Weighed: None

Tissues Retained: Female reproductive tract

Histopathology:

None of the retained tissues were examined microscopically.

Statistics for FOB and MA data

Summarized in Appendix 1, Exhibit 1.

Positive Control Data (See Appendix 12)

Positive control data for the MA, FOB, and Neuropathology tests were collected prior to this study in accordance with EPA guidelines on Neurotoxicity Testing (EPA, 1991). The FOB positive control data provided evidence of the ability of the observational methods used by this laboratory to detect major neurotoxic endpoints including limb weakness (repeated exposure to acrylamide), tremor (p,p'-DDT), and autonomic signs (carbaryl) (Appendix 12, Exhibit 2). The neuropathology positive control data demonstrated the sensitivity of the procedures used and ability of the pathologist to detect central nervous system pathology (trimethyltin) and peripheral nervous system pathology (acrylamide) (Appendix 12, Exhibit 2). The MA positive control data showed that the procedure for measuring motor activity is sensitive to chemically-induced increases (amphetamine) and decreases (chlorpromazine) in activity (Appendix 12, Exhibit 3).

RESULTS

Analysis of Test Material and Exposure Concentrations:

Appendix 5: Inhalation Subreport
Appendix 6: Analytical Chemistry Report

Stability: The neat test material was stable over a period greater than it was used for this study.

Exposure Concentrations: Analytical (Miran IR) and nominal concentration data are presented in the table below. The nominal values serve as a second confirmation of the analytical values that were obtained from on-line infrared spectroscopic measurement of the chamber atmospheres. The uniformity of chamber atmosphere distributions was acceptable at all concentrations.

Target Concentration	1500 ppm	3000 ppm	6000 ppm
Nominal ± S.D.	1474 ± 54	3488 ± 156	7029 ± 224
Analytical ± S.D. (Miran IR)	1555 ± 18	3003 ± 29	5961 ± 65
Nominal/Ratios	0.95	1.16	1.18

Gas Chromatography (GC) Values for Exposure Concentration: Mean GC values for 6 samples taken at each exposure concentration, over 3 days, were within 16% of concentrations determined by the Miran IR for the 1500 ppm concentration and within 10% for the 3000 and 6000 ppm concentration. The values obtained using the GC method were consistently lower than those from the Miran IR. This is explained by the loss of analyte inherent in the impinger method used to collect the sample for GC analysis. The GC values serve as a third confirmation of the exposure concentrations, the first and second confirmation being the nominal and IR values, respectively.

Mortality

All but one of the animals survived until scheduled sacrifice. One male (M03 007) exposed to the 6000 ppm concentration died the day after atropine drops were applied to its eyes for ophthalmic examination. This animal died 11 days after it was exposed to isobutanol. There were no unusual behavioral changes or obvious signs of toxicity noted that would indicate that this death was related to exposure to isobutanol. Since spontaneous deaths in control animals can occur as a result of application of atropine to the eyes of rats, the death of this male is considered to be unrelated to exposure to isobutanol.

Clinical Observations (made during exposure)

Appendix 5 : Inhalation Subreport

There was clear evidence of generalized depression of the central nervous system (animals were non-responsive to tapping on side of inhalation chambers) and labored respiration in rats during the 6 hours of exposure to 6000 and 3000 ppm of isobutanol. One male animal at the 6000 ppm concentration was prostrate at the end of his exposure, and another male animal at the same concentration level was lacrimating at the end of the exposure. The 6000 ppm concentration animals were affected to a greater extent than the 3000 ppm concentration rats. Minimal effects (hypoactivity) were seen in rats at the 1500 ppm level.

Behavioral Tests

Appendix 1: Condensed summary of statistically significant results
Occurrences of descriptive observations

Appendix 1 contains a condensed summary table of statistically significant results based on statistical analysis of the raw data. This table was intended only to serve as a quick reference for statistically significant effects. These effects may or may not be treatment-related as will be discussed in greater detail in the sections on Motor Activity and the FOB. In addition, this table does not contain effects that are not statistically significant but may be regarded as treatment-related.

Alertness (Appendix 3 ,Table 14):

Transient, statistically significant increases in alertness were detected in male rats immediately after exposure to 1500 and 3000 ppm of isobutanol. These increases are not regarded as treatment-related. These statistically significant increases were a result of lower control values in males (mean score was 1.2 on a scale of 0 - 4 where 2 is considered a normal level of alertness) rather than an increase in the treated animals. Indeed, the rats exposed to isobutanol had mean values of 1.8 and 1.9 which were essentially unchanged from pretest values of 2.0 (normal level of alertness). The only treatment-related effect in alertness appears to be a slight, non-significant, transient decrease in alertness in females at the 6000 ppm concentration.

Gait/Gait Score (Appendix 3, Tables 15,16):

One male rat at the 6000 ppm concentration had a gait abnormality characterized by waddling, rocking, or lurching. The severity of this gait abnormality was rated as slight and this animal's mobility score was normal. None of the other animals had abnormal gait at any of the time points when they were observed.

Body Weight (Appendix 3, Table 29A, Table 29B, Figure 1):

Body weights of male rats in the 3000 and 6000 ppm groups were significantly lower than the male controls throughout the study. These statistically significant results are due to pretest differences and not because of exposure to the chemical. This is clearly illustrated by Table 29B and the graph in Figure 1 which shows that there are no statistically significant treatment related effects at any time period when the data is normalized for pretest differences. This is further supported by the fact that the repeated measures analysis of covariance was not statistically significant at the p=0.05 level for the dose term and for the dose x time interaction term.

<u>Ophthalmic Examination</u>

Appendix 8: Ophthalmic Examination Report

One female at the 3000 ppm concentration (F02 009) was noted to have atrophy in a localized portion of the choroid during the post-exposure examination. This finding is considered to be incidental and not related to treatment with isobutanol. No other lesions were noted in the examined animals. There were no ocular abnormalities which can be attributed to exposure to the test material.

Motor Activity

Appendix 1, Table 1: Condensed summary of statistically significant results
Appendix 1, Exhibit 1: Explanation of summary tables and statistical analysis for FOB and MA
Appendix 2: Summary tables and figures for motor activity
Appendix 9: Individual Motor Activity Data

A statistically significant decrease in motor activity was measured in the 6000 ppm male rats immediately after exposure (day 0). This effect is regarded as a slight, transient treatment-related effect. Statistically significant increases in motor activity were detected in female rats in the 6000 ppm concentration group pretest and on day 1 and in the 1500 ppm concentration group on day 14. The increase at the 1500 ppm concentration on day 14 is not regarded as treatment-related because of the lack of a dose response for that day. The increases in activity on day 1 in females at the 6000 ppm concentration are due to pretest differences in motor activity and not to the chemical. However, a non-significant treatment-related decrease in activity immediately after exposure is believed to have occurred in female rats at the 6000 ppm concentration. The decreases in motor activity in both sexes at 6000 ppm is particularly noticable graphically for the first 30 minutes (see Appendix 2, Figure 2). Repeated measured analysis of covariance was positive (p= .01) for the dose term for female motor activity. The interaction term was negative for both sexes and the dose term was negative for the males. In summary, exposure concentrations of 6000 ppm of isobutanol caused a transient decrease in motor activity in male and female rats immediately after exposure.

Functional Observational Battery (FOB):

Appendix 1: Condensed summary of statistically significant results; Occurrences of descriptive observations;
Explanation of summary tables and statistical analysis for FOB and MA.
Appendix 3: Instructions for the FOB (contains definitions of terminology used and explanations of how tests were conducted)
Summary tables for each FOB category.
Appendix 10: Individual FOB data

Only those behavioral effects differing statistically significantly from control and/or considered treatment-related and will be discussed below:

Gross Necropsy

Appendix 4: Summary tables for gross necropsy
Appendix 11: Individual tables for gross necropsy findings

There were no treatment-related lesions or other gross changes in the tissues and organs examined during necropsy. Enlarged, dilated, distended uteri were observed at necropsy in the low, mid, and high groups at incidences of 3/10, 1/10, and 1/10, respectively. This finding was not observed in the control group. The severity was minimal in all instances. This is a common observation and usually reflects physiologic changes related to the estrus cycle. This is further substantiated by the inverse dose response. Therefore, although histologic examination was not conducted, it appears that these observations are unassociated with treatment and reflect the normal variation expected with different stages of the estrus cycle.

DISCUSSION

Isobutanol clearly causes a reversible, nonspecific depression of function of the central nervous system at concentrations of 3000 and 6000 ppm during a 6 hour exposure period. However, animals rapidly recover from most of these non-specific effects immediately after they are removed from the exposure chambers. The only possible treatment related effects (see results section for more explanation) were a transient decrease in alertness in female rats, transient decrease in motor activity in male and female rats, and transient, slight, incoordinated gait observed in one male rat. These effects are considered residual effects of the narcosis that the 6000 ppm concentration of isobutanol appeared to cause. There were no treatment-related effects in rats at the 1500 and 3000 ppm concentration after the animals were removed from exposure.

The large number of behavioral measures made in this study, many of which are very subjective, increases the opportunity for incidental, non-treatment related differences to occur. In order to minimize false positive conclusions, the Report of the Neurotoxicity Risk Assessment Guidelines Peer Review Workshop (Eastern Research Group, Inc., 1992) recommends that neurobehavioral data be grouped into functional domains in order to avoid placing too much emphasis on each of the FOB measures. The Peer Review Workshop concluded that the extent to which there is a cluster of effects in any one domain, as well as the severity and persistence of these effects, must be taken into account in assessing whether a particular domain has been affected. This approach aids in determining whether changes are part of a pattern of neurobehavioral toxicity. This concept of domains is more of a conceptual approach to be performed by inspection of the data. One suggested grouping of domains has been described as follows (Moser, 1991):

1. **Autonomic** (lacrimation, salivation, pupil response, palpebral closure, defecation, urination);
2. **CNS excitability** (ease of removal from cage, handling reactivity, clonic movements, tonic movements, alertness, vocalizations);
3. **CNS activity** (home cage posture, palpebral closure, rearing, motor activity);
4. **Neuromuscular** (gait score, mobility score, landing foot splay, forelimb grip strength, hindlimb grip strength, righting reflex);
5. **Sensorimotor** (tail pinch, click, and approach response); and
6. **Physiological** (body weight, piloerection).

Using this general approach, there was no consistent pattern of effects in any of the domains that indicates that isobutanol at exposure concentrations of up to 6000 ppm causes a specific effect on the nervous system once exposure to the chemical was terminated.

In order to establish a sense of proportion for the exposure concentrations used in this study, it is useful to note that the highest concentration used in this study (6000 ppm) is equivalent to 18 mg/liter[2] which is more than 3 times the limit dose of 5 mg/liter required by TSCA guidelines for acute inhalation studies (798.1150). The lowest exposure concentration used in this study (1500 ppm=4.5 mg/L) is only slightly below this limit dose.

CONCLUSION

Marked signs of narcosis were observed during exposure in the 3000 and 6000 ppm groups that rapidly disappeared after exposure to isobutanol was terminated. There were no treatment-related findings during gross necropsy. Minimal effects (hypoactivity) were seen in rats at the 1500 ppm concentration only during the 6 hour exposure period which is considered to be a Lowest-Observable-Effect-Level (LOEL) for the study.

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[2] air concentration (mg/l) = ppm * (M.W. of the compound / 24,450)

= 6000 * (74.12 / 24,450)

= 18 mg/l

REFERENCES

Eastern Research Group, Inc (EPA Contractor) (1992). Report of the Neurotoxicity Risk Assessment Guidelines Peer Review Workshop June 2-3, 1992, Washington, DC. Risk Assessment Forum, USEPA (P.5-20).

Environmental Protection Agency (1991). Neurotoxicity Guidelines. Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals Addendum 10.

Moser V.C. (1991). Applications of a neurobehavioral screening battery. J Am College of Tox. 10:661-669.

SUPPLEMENTARY STUDY INFORMATION

Study Performed at: Environmental Health Laboratory (EHL),
645 S. Newstead, St. Louis, MO 63110
Location of Study Protocol, Original Data, Retained Tissues, Final Report and Facilities Records: Environmental Health Laboratory Archives

Study Participants:

Functional Observational Battery	Denean Smolboski(observer) Pat O'Donnell (scribe) Frank Speck (scribe) Jim Warneke (scribe) Derek Branch (data analysis)
Motor Activity:	Terry Kaempfe (data analysis) Frank Speck (technician) Jim Warneke (technician)
Inlife:	Frank Speck (project coordinator)
Neuropathology:	Kim Shevlin (technician)
Inhalation:	Terry Kaempfe Steve Becktame Charles Bechtel Robert Quevreaux

Supervisory Personnel:

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R. M. Folk, Ph.D., Director, Environmental Health Laboratory

M. E. Holland, Ph.D., Manager, Analytical Services

M. V. Roloff, Ph.D., Senior Inhalation Toxicology Consultant

F. A. Ruecker, D.V.M., Pathology Technical Leader

M. A. Senne, A.H.T., B.S., Supervisor, Toxicology Services

L. D. Stout, D.V.M., M.S., Manager, Toxicology Studies

F. J. White, M.S., M.B.A, Pathology Supervisor

MONSANTO COMPANY
THE AGRICULTURAL GROUP
ENVIRONMENTAL HEALTH LABORATORY (EHL)
St. Louis, Missouri 63110

PROTOCOL AMENDMENT I

NOTE: Please discard previous version of the protocol and replace with this version.

SPONSOR:
Chemical Manufacturers Association
2501 M Street, NW
Washington D.C., 20037

TITLE:
Acute Neurotoxicity Study of Isobutanol Administered by Whole-Body Inhalation to CD® Rats

Monsanto EHL Study Number: 94009

Study Director: Signature _____
Date 3/14/94

Principal Investigator: Signature _____
Date 3/14/94

Director, EHL: Signature _____
Date 3/14/94

Sponsor, CMA: Signature Barbara Frances
Date 3/25/94

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1. INTRODUCTION

1.1 **Proposed Starting Date:** March, 1994

1.2 **Proposed Completion Dates:**
Terminal Sacrifice: April, 1994
Data Collection: April, 1994

1.3 **Purpose:** The purpose of this study is to use a neurotoxicity screening battery to determine the potential for isobutanol to alter the function of the nervous system following a single acute whole-body inhalation exposure. Neurotoxicity is defined as any adverse effect on the structure or function of the nervous system related to exposure to a chemical substance. The neurotoxicity screening battery consists of a functional observational battery (FOB) and motor activity (MA).

1.4 **Justification for Route of Administration:** Because there is a potential for human inhalation exposure, this is an appropriate route of administration. This route of administration has also been mandated by the USEPA in the Multisubstance Test Rule (40 CFR, Part 799).

1.5 **Justification for Selection of Test System:** Rats have been chosen for this study because they are susceptible to neurotoxicity, a large database exists for possible comparison, and rats are recommended by many regulatory authorities. The USEPA has mandated that adult rats be used for studies conducted as part of the Multisubstance Test Rule (40 CFR, Part 799).

1.6 **Good Laboratory Practices:** This study will be performed in compliance with the appropriate provisions of the USEPA, OECD, and EEC Good Laboratory Practice Standards/Principles. The study may be subjected to periodic inspections, and the final report will be reviewed by the Quality Assurance Unit.

1.7 **Test Guidelines/Regulations:** This study is being conducted in compliance with a Test Rule promulgated by the U. S. Environmental Protection Agency in accordance with the Toxic Substances Control Act. The work conducted in this study will generally conform to the EPA Test Guidelines for FOB, Sec. 798.6050 and motor activity, Sec. 798.6200. The proposed design, however, incorporates certain modifications to the guidelines as approved by authorized representatives of EPA, and also reflects advances in methodology as specified in the EPA's more recent neurotoxicity testing guidelines. The inhalation procedures followed will be in accordance with the U.S. EPA Health Effects Testing Guidelines, 40 CFR, Part 798.1150.

2. METHODS AND MATERIALS

2.1 **Duration:** A single exposure followed by a 14-day observation period for each animal.

2.2 **Test Material:**

2.2.1 **Name:** Isobutanol

(2.2.2) **Chemical Characterization:** The neat test material will be characterized by Union Carbide Corporation, PO Box 8361, South Charleston, West Virginia 25303.

2.2.3 **Test Material Information:**

CAS #:	78-83-1
Lot #:	EH 3639
EHL Substance Identification #	T940007
Supplier:	Union Carbide Chemicals and Plastics Co., Inc. 10521 Sheldon Road Houston, TX 77044
Expected Stability:	Approximately 1 year
% purity:	99.9%
Safety Precautions:	Flammable Liquid; vapors form from this product which may be moved by air currents and ignited by sparks or other ignition sources distant from this product handling point; causes severe irritation avoid ingestion, inhalation, skin contact and eye contact

2.2.4 **Exposure Concentrations and Duration:** Animals will be exposed to isobutanol at four different exposure levels (including control). The actual concentrations will be determined by the Study Director in consultation with the Sponsor based on the results of a rangefinding study. Exposures will be 6 hours long.

2.2.5 **Stability:** The stability of the neat test material will be determined by analyses prior to its first use in the study and after it is last used.

2.3 **Test Atmosphere Generation and Analyses:**

(2.3.1) **Exposure System:** The exposure system will consist of 2000-liter glass and stainless steel inhalation chambers and an atmosphere generation system. This is expected to maintain an animal loading factor below 5%. Inhalation chamber airflow will be maintained at or above 12 air changes per hour. Diluent air supplied to the chambers will be filtered. This is expected to maintain the oxygen level above 19%. The desired ranges for temperature and humidity will be 22±2 degrees C and 40 to 60%, respectively, dependent on the characteristics of the test material which may not allow maintenance of these ranges. The test atmosphere will be generated by an appropriate means, determined during the prestudy period, and will consist of isobutanol vapor.

Animals will be individually placed in wire mesh cages which will be placed inside the exposure chamber. Airflow in the system will be monitored throughout the exposure and held as constant as possible. The specific values for airflow, temperature and relative humidity will be recorded approximately every 30 minutes. In addition, chamber temperature and relative humidity will be monitored continuously. The oxygen level will be determined once for each exposure level with an electronic sensor or Draeger tube.

2.3.2 **Test Atmosphere Analyses:** The nominal concentration of each exposure level will be determined at least once per exposure. Samples of chamber atmosphere, including the control chamber, will be obtained from the breathing zone of the animals at least three times during each exposure and will be analyzed with an infrared analyzer. The infrared analytical method will be confirmed during pretest by gas chromatographic analysis. Uniformity of exposure atmosphere distribution within the chambers will be confirmed using

the infrared analyzer during the pretest period by sampling from various points within the breathing zone of the animals according to appropriate Standard Operating Procedures. The analytical method will be available prior to the first exposure.

2.4 **Animals:**

2.4.1 **Sex and Species:** Male and female outbred albino rats. Female rats should be nulliparous and nonpregnant.

2.4.2 **Strain:** Sprague-Dawley (CD)

2.4.3 **Source:** Charles River Laboratories

2.4.4 **Age on Test Day 1:** Approximately 8 weeks old.

2.4.5 **Number of Animals:** Ten rats per sex will be used for each exposure level. For four exposure levels, a total of 40 males and 40 females will be used.

(2.4.6) **Body Weight:** The weight of all animals shall be within 20% of the mean weight of their sex at the time that they are assigned to the study.

2.5 **Animal Husbandry:**

2.5.1 **Identification:** Individual ear tags or tail tattoo and bar coded cage cards.

2.5.2 **Housing:** Individual cages (suspended, stainless steel with wire-mesh bottoms).

2.5.3 **Food and Water:** Water and Certified Rodent Diet #5002 (PMI Feeds, Inc., St. Louis, MO) will be available *ad libitum* except during the exposures. Both food and water will be withheld during exposure. This diet has been assayed by the manufacturer for contaminants likely to interfere with this study. All laboratory water used is furnished by the City of St. Louis, meets human drinking water standards and is sodium zeolite-conditioned upon entering the laboratory. No contaminants are expected to be present which would interfere with the results or conclusions of this study.

2.5.4 **Environmental Conditions:** Animal housing and husbandry will be in accordance with the provisions of 'Guide to the Care and Use of Laboratory Animals', USPHS-NIH Publication No. 86-23. Animal room temperature and relative humidity are targeted at 70 - 74 degrees F. and 40 - 60%, respectively, which are within the USPHS-NIH guidelines of 64.4-78.8 degrees F. and 40-70%. There will be a 12 hour light/dark cycle.

2.5.5 **Pretest Examination and Acclimation:** After arrival, the animals will be examined for any gross signs of injury, disease or other abnormalities when they are transferred to their cages. Within the first week after arrival, the animals will be given a brief inspection to assess general health status. The animals will be examined for ectoparasites and treated, if necessary, at the discretion of the Animal Resources Veterinarian, in consultation with the Study Director. Animals will be quarantined for at least ten days and will be observed daily during this period. Only animals judged to be healthy will be included in the study. Animals will be housed in the same room during both the quarantine period and the study

period. Observations, data collected, treatments, if provided, and the final evaluation for all animals examined will become part of the quarantine record.

2.5.6 **Randomization and Bias Control:** Animals will be assigned to test groups using a computer-generated randomization scheme that assigns animals on a weight basis and produces groups of uniform body weight distribution.

2.6 **Absorption of Test Compound:** Determination of the degree of absorption of the test or control materials is not necessary to achieve the objectives of this study and will not be performed.

(3.) EXPERIMENTAL DESIGN:

This study consists of one control and three exposure groups of rats (10 animals/sex/group). Motor activity measurements and a functional observational battery (FOB) will be performed on the animals prior to exposure (pretest), as soon as possible after cessation of exposure, approximately 18 hours following the end of the exposure (Day 1), and seven and 14 days after exposure to the chemical. Each of the 80 animals will be exposed once, but exposures will occur over 4 days (20 animals exposed each day). In order for the time of testing to be balanced across groups, 5 animals (2 - 3 rats per sex per group) from each level will be exposed each day (i.e., all 4 exposure levels will be generated every day for 4 consecutive days). Ophthalmic examinations will be performed prestudy and during the post-exposure period. At the end of the study, five animals/sex/group will be perfused in preparation for possible neuropathologic examination. Nervous system and female reproductive tract tissues will be retained from perfused animals but will not be examined microscopically except at the discretion of the Study Director in consultation with the Sponsor. The remaining animals that survive until the end of the study will be given a gross necropsy, and their female reproductive tissues will be retained. All animals dying or sacrificed *in extremis* during the study, will undergo a complete necropsy, but no tissues will be retained except at the discretion of the necropsy team.

The following table illustrates the experimental design:

Group	Exposure Level (ppm)	FOB & MA (Pretest, Peak Effect, Day 1, Day 7, &14)	Perfused Day 15	Gross Necropsy Day 15
MN	0	10	5	5
FN	0	10	5	5
M1	1500	10	5	5
F1	1500	10	5	5
M2	3000	10	5	5
F2	3000	10	5	5
M3	6000	10	5	5
F3	6000	10	5	5

Historical positive control data for the FOB, and motor activity tests were collected prior to this study in accordance with USEPA guidelines on Neurotoxicity Testing. The FOB positive control data provides evidence of the ability of the observational methods used by this laboratory to detect major neurotoxic endpoints. Motor activity positive control data shows that the procedure for measuring motor activity is sensitive to chemically-induced increases and decreases in activity.

4. OBSERVATIONS AND NEUROBEHAVIORAL TESTS

(4.1) **Routine Inlife:** All animals will be observed at least twice daily (morning and afternoon) for mortality, moribundity, and noteworthy signs of toxicity which will be documented by exception. During the exposure, gross signs of toxicity will be recorded hourly. It will not be necessary to conduct weekly physical examinations of the rats since the FOB will be performed weekly in this acute study. Body weights will also be determined weekly as part of the FOB. Body weights will also be determined on the day of exposure, just prior to exposure.

4.2 **Motor Activity (MA):** Motor activity will be measured before the start of the study (pretest), as soon as possible after cessation of exposure, approximately 18 hours after the end of the exposure, and on post-exposure days seven and 14. Motor activity will be tested by placing individual animals into an automated photocell activity recording device (Photobeam Activity System, San Diego Instruments Inc., San Diego, CA) approximately 30 minutes after cessation of the exposure. The enclosure for the recording device is a rectangular polycarbonate cage with a raised stainless steel wire floor insert. The time of testing will be balanced across groups. In addition, treatment groups will be balanced, as best as possible, across the motor activity devices. The total number of photobeams broken (ambulatory and fine movements combined) will be measured over a 1 hour period. Sixty minutes has been demonstrated to be long enough for activity to reach asymptotic levels by the last 20% of the test session for non-treated control animals. White noise will be provided in the test room by the room's air handlers to keep external noises from affecting animal's activity.

(4.3) **Functional Observational Battery (FOB):** An FOB (see Appendix 1 for details), designed to measure various aspects of sensory and motor functioning and general level of excitability, will be performed (after the motor activity test session) before the start of the study (pretest), as soon as possible after cessation of exposure, approximately 18 hours after the end of the exposure, and seven and 14 days after exposure to the test chemical. The FOB will be performed approximately 30 minutes after the completion of motor activity testing. The time of testing will be balanced across groups, and the observer will be blind to the exposure level of each animal.

(4.4) **Ophthalmic Examination:** Ophthalmic examinations will be performed pretest and during the post-exposure period on all animals.

5. NECROPSY:

5.1 **Unscheduled Sacrifices and Deaths:** All animals found dead or sacrificed *in extremis* will be given a gross necropsy including an examination of the female reproductive tract. No tissues will be retained except at the discretion of the pathologist.

5.2 **Scheduled Sacrifices of Animals for Neuropathologic Examination:** Five rats/sex/group will be selected for neuropathology prior to the start of the study to be sacrificed on post-exposure Day 15. There will be no standardized attempt to distribute the animals with behavioral alterations between the neuropathology animals and the gross necropsy animals. However, consideration will be given to conducting a neuropathology evaluation for the rare animal with severe and unusual behavioral alterations if that animal was not originally scheduled for neuropathology examination. All animals scheduled to be perfused will be fasted overnight. Tissues retained will not be examined microscopically, except at the discretion of the study director in consultation with the sponsor.

5.2.1: **Perfusion and Fixation:** Each animal will be intraperitoneally administered heparin sulfate. Approximately 10-15 minutes later and following induction of deep anesthesia with halothane, the thorax will be opened, and intracardial perfusion will be performed with sodium nitrite flush until auricular effluent is free of blood. Immediately thereafter, the animal will be perfused with 4% formaldehyde/1.5% glutaraldehyde or other appropriate fixative. Retained tissues (see 5.2.3) will be placed in 10% neutral buffered formalin or other appropriate preservative.

5.2.2: **Necropsy:** Animals assigned for neuropathological examination will not undergo a complete necropsy. However, abnormalities observed during perfusion or tissue collection will be documented.

5.2.3: **Nervous Tissues to be Retained:** Brain, spinal cord (cervical, thoracic, and lumbar), Gasserian ganglia, dorsal root ganglia with dorsal root and ventral root fibers (C3-C6, L1-L4), sciatic nerves, tibial nerves, and sural nerves.

5.2.4 **Non-nervous Tissues to be Retained:** Female reproductive tract (uterus and ovaries)

5.3 **Scheduled Sacrifice of Remaining Animals:** On post-exposure Day 15, animals that were not assigned for neuropathological examination will be fasted overnight and euthanized by an overdose of halothane or other appropriate anesthetic.

5.3.1 **Necropsy:** These animals will be given a complete necropsy in which the external surface and internal cavities of each rat will be examined. In addition, organs will be examined *in situ*, and the hollow organs will be opened and examined. No organs will be weighed.

5.3.2 **Tissues to be Retained:** The female reproductive tract (uterus and ovaries) will be retained. No other tissues will be retained except at the discretion of the pathologist.

6. **STATISTICS:** The following statistical procedures will be used:

6.1 Body weights will be evaluated by Dunnett's Multiple Comparison Test (2-tailed, $p \leq 0.05$ and $p \leq 0.01$).

6.2 FOB and Motor Activity determinations will be evaluated by appropriate statistical procedures ($p \leq 0.05$ and $p \leq 0.01$) as described in Appendix 2. An appropriate method of correction for multiple comparisons may be conducted.

7. **RECORDS AND REPORT**

7.1 **Records:** All original records, raw data, retained tissues, protocol and final report will be maintained in the EHL archives.

7.2 **Report:** The report shall be prepared in general accordance will specifications in the EPA regulations. It will include a summary of results and conclusions, a brief description of the methods, summary and individual animal data tables, historical positive control data for motor activity and FOB (as appendices), Quality Assurance Statement and GLP Compliance Statement. The final report will be audited by the Quality Assurance Unit and will contain a signed quality assurance statement.

7.3 **Report Schedule:** Draft Report: Second Quarter, 1994
Final Report: Third Quarter, 1994

8. DISTRIBUTION

CMA	A. A. Li	K. M. Shevlin
D. K. Branch	J. G. Napier	D. Smolboski
R. M. Folk	P. E. O'Donnell	F. L. Speck
M. E. Holland	M. V. Roloff	L. D. Stout
W. E. Hopkins	F. A. Ruecker	Quality Assurance (2)
T. A. Kaempfe	B. J. Sauls	F. J. White
S. Kuhlman	M. A. Senne	T. V. Wilson

9. GENERAL INFORMATION

9.1 The testing facility is the Environmental Health Laboratory, Monsanto Company, 645 South Newstead, St. Louis, Missouri 63110.

9.2 Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. The EHL reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered to be in jeopardy. In this event, the Sponsor shall be notified of the alteration as soon as possible, and written verification of the change will be the responsibility of the Study Director. All protocol modifications will be signed by the Study Director and a representative of the Sponsor.

9.3 Reserved for amendments.

9.3.1 Amendment I

Section	Reason
2.2.2	Monsanto was incorrectly listed as the lab that would conduct the neat test material characterization. The correct lab is Union Carbide Corporation.
2.3.1	Typographical error; removed "a" and replaced "vapors" with "vapor".
2.4.6	Animals need to be assigned to the study using the stated weight requirement at least 1 1/2 weeks prior to first exposure (since pretest motor activity and FOB must be conducted) instead of at the commencement of the study (e.g. first exposure).
3	Clinical signs of toxicity at 18 hours after exposure were replaced with a complete FOB.
4.1	Hourly clinical observations during the exposure were added. Clinical signs of toxicity at 18 hours after exposure were removed and replaced with a full FOB. This section also added that body weights will be measured on the day of exposure just prior to exposure.

4.3 A complete FOB was added at 18 hours after exposure. This replaces clinical signs of toxicity at this timepoint.

4.4 The original protocol states that ophthalmic examinations will be performed on high dose and control animals, and that examinations will be performed on intermediate dose animals only if effects are seen at the high dose. This section was changed to indicate that ophthalmic examinations will be performed on ALL animals during the post exposure period.

Appendix 1 This section was corrected to state that evidence of exophthalmia will be recorded during handling instead of as part of the home cage observations.

(APPENDIX 1)

FUNCTIONAL OBSERVATIONAL BATTERY (FOB)

Four basic groups of observations and measurements will be conducted as part of the Functional Observational Battery:

I. **Home cage observations:** General posture/activity level, and any clonic or tonic movementswill be recorded while the animal is in its home cage; prior to any handling.

II. **Observation during handling:** The animal will then be removed from its home cage and ease of such removal, reactivity toward the investigator, degree of lacrimation, salivation, and palpebral opening, evidence of exophthalmia, presence or absence of piloerection, and any general descriptive clinical effects will be recorded.

III. **Observations in the open field:** The animal will then be placed on a table surrounded by a plexiglass wall and covered by an absorbent material for a two minute interval. Any evidence of clonic or tonic movements, abnormal gait, spontaneous vocalization (though this would also be recorded should it occur at other times), and stereotypic or unusual behavior will be recorded, as will degree of general alertness and impairment of gait and mobility. The number of times the animal rears (raises both forelimbs from the table), fecal boli, and urinary pools will be counted and recorded for the same interval. Following this period, the animal will be approached from the front with a blunt object and its reaction will be recorded. The animal's tail will be pinched near the tip of the tail and the response to this stimulus will be assessed and recorded. Finally, a small mechanism will be "clicked" behind its head for assessment of response to sound.

IV. **Reflexes and physiological measurements:** Pupillary reflex, righting reflex, fore and hind limb grip strength, and landing foot splay will be measured.

APPENDIX 2

Explanation of Statistical Analyses

V. Motor activity, FOB interval data, and rearing

VI. Data types

A. Motor activity (Total number of photocell interruptions resulting from both ambulatory and fine movements)
B. Number of rears in the open field
C. Body weight
D. Forelimb grip strength
E. Hindlimb grip strength
F. Landing foot splay

VII. Tests performed

A. Levene's Test for homogeneity of variance (two-tailed; considered positive only if the probability ≤ 0.01) (Snedecor and Cochran 1980)
B. Dunnett's Multiple Comparison Test (two-tailed) (Dunnett 1955; Dunnett 1964); an appropriate correction may be performed for multiple comparisons.
C. The parameters listed above will also be analyzed with repeated measures ANOVAs using baseline values as covariates (ANCOVAs).

VIII. FOB ordinal data (where values are assigned from a predetermined scale from 1 to n) and data with minimal numbers of counts

IX. Data types

A. Ease of removal from cage (a)
B. Reactivity to investigator (a)
C. Lacrimation (b)
D. Salivation (b)
E. Palpebral closure (b)
F. Alertness in the open field (a)
G. Gait score (b)
H. Mobility score (b)
I. Number of fecal boli in the open field (a)
J. Number of urine pools in the open field (a)
K. Approach response (a)
L. Tail pinch response (a)
M. Response to clicker (a)
N. Righting reflex (b)

X. Tests performed

A. Kruskal-Wallis analysis of variance by ranks (two-tailed for categories identified by "a" above, one-tailed for those identified by "b") (Breslow 1970)
B. Jonckheere's Test for non-parametric trend (one or two-tailed as in the Kruskal-Wallis test) (Hollander and Wolfe 1973)
C. If either of the above tests are positive, pairwise comparisons of each test group with the control group will be performed via the Mann-Whitney U Test (one or two-tailed as in the Kruskal-Wallis test) (Mann and Whitney 1947)

XI. FOB quantal data, which are graded as present or absent

XII. Data types

A. Pupillary reflex
B. Exophthalmia
C. Piloerection
D. Vocalization

XIII. FOB quantal data, which are graded as present or absent (cont.)

XIV. Tests performed

A. Overall chi-square test (one-tailed) (Snedecor and Cochran 1980)
B. Cochran-Armitage Test for linear trend in proportions (one-tailed) (Cochran 1954; Armitage 1955)
C. If either of the above tests are positive, pairwise comparisons of each test group will be made with the control group via Fisher's Exact Test (one-tailed) (Fisher 1946)

XV. FOB categorical data (descriptions of the animal's appearance, behavior, etc)

XVI. Data types

A. Activity/posture in home cage
B. Clonic movements in home cage
C. Tonic movements in home cage
D. Any general observations during handling
E. Clonic movements in the open field
F. Tonic movements in the open field
G. Description of gait
H. Stereotypic behavior
I. Unusual behavior

XVII. Data will be analyzed by inspection

REFERENCES

Armitage, P. Tests for linear trends in proportions and frequencies. Biometrics 11:375-386, 1955

Breslow, N. A generalized Kruskal-Wallis test for comparing K-Samples subject to unequal patterns of censorship. Biometrika 57: 579-594, 1970

Cochran, W. G. Some methods for strengthening the common x^2 test. Biometrics 10:417-451, 1954

Dunnett, C. W., Multiple comparison procedure for comparing several treatments with a control. Jour. Am. Stat. Assoc. 50:1096-1121, 1955

Dunnett, C. W., New tables for multiple comparisons with a control. Biometrics 20:482-491, 1964

Fisher, R. A., Statistical Methods for Research Workers. Oliver and Boyd, Edinburgh, U.K., 1946

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Mann, H. B. and Whitney, D. R. On a test of whether one of two variables is stochastically larger than the other. Ann. Math. Stat. 18: 50, 1947

Snedecor, G. W. and Cochran, W. G., Statistical Methods, 7th ed. Iowa State University Press, 1980

MONSANTO COMPANY
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ENVIRONMENTAL HEALTH LABORATORY (EHL)
St. Louis, Missouri 63110

SPONSOR:
Chemical Manufacturers Association
2501 M Street, NW
Washington D.C., 20037

TITLE:
Exposure Concentration Range-Finding Study for an Acute Neurotoxicity Study of Isobutanol Administered by Whole-Body Inhalation to CD® Rats

Sponsor's Study Number:
Monsanto EHL Study Number: 94010

Study Director: Signature _____
Date 1/27/94

Principal Investigator: Signature _____
Date 1/27/94

Director, EHL: Signature _____
Date 1/27/94

Sponsor, CMA: Signature _____
Date 2/1/94

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1. INTRODUCTION

1.1 **Proposed Starting Date:** January, 1994

1.2 **Proposed Completion Dates:**
Terminal Sacrifice: February, 1994
Data Collection: February, 1994

1.3 **Purpose:** The purpose of this study is to aid in the selection of exposure levels for a subsequent acute inhalation neurotoxicity study and to gather information regarding the time course for effect from the test material.

1.4 **Justification for Route of Administration:** Because there is a potential for human inhalation exposure, this an appropriate route of administration. This route of exposure has also been mandated by USEPA in the multisubstance test rule 40 CFR Part 799.

1.5 **Justification for Selection of Test System:** Rats have been chosen for this study because they are susceptible to neurotoxicity, a large database exists for possible comparison and are recommended by many regulatory authorities. USEPA has mandated that adult rats be used for studies conducted as part of the multisubstance test rule 40 CFR Part 799.

1.6 **Good Laboratory Practices:** This study will be performed in compliance with the appropriate provisions of USEPA, OECD, and EEC Good Laboratory Practice Standards/Principles. The study may be subjected to periodic inspections and the final report will be reviewed by the Quality Assurance Unit.

1.7 **Test Guidelines/Regulations:** While there is no guideline for this study, it is being conducted so as to conform with general principles outlined in the U.S. EPA Health Effects Testing Guidelines, 40 CFR Part 798.1150, for acute inhalation toxicity.

2. METHODS AND MATERIALS

2.1 **Duration:** A single six hour exposure followed by an approximately five-day observation period for each animal.

2.2 **Test Material:**

2.2.1 **Name:** Isobutanol

2.2.2 **Chemical Characterization:** The neat test material will be characterized the Monsanto Environmental Health Laboratory Analytical Chemistry Group using GC and/or LC methods.

2.2.3 **Test Material Information:**

CAS #:	78-83-1
Lot #:	EH 3639
EHL Substance Identification #	T940007
Supplier:	Union Carbide Chemicals and Plastics Co. Inc. 10521 Sheldon Road Houston, TX 77044
Expected Stability:	approximately 1 year
% purity:	99.9%
Safety Precautions:	Flammable Liquid; vapors form from this product which may be moved by air currents and ignited by sparks or other ignition sources distant from this product handling point; causes severe irritation avoid ingestion, inhalation, skin contact and eye contact

2.2.4 **Exposure Levels:** Animals will be exposed to isobutanol at four different exposure levels (including control). Exposures will be six hours long. The exposures will be conducted in pairs. The highest exposure level shall not exceed 50% of the lower explosion limit (approximately 8000 ppm). The first day exposure concentration will be selected, based on available toxicity data, to produce significant neurotoxic effects or other clearly toxic effects. If no pertinent data is available, the first exposure should be at, or near, the specified high limit (8000 ppm). At least two other exposure concentrations will be tested the following day, with the levels selected based on the first day's results. Data should support the establishment of a low exposure level that produces minimal or no effects and of a high exposure level that results in clearly toxic effects, but does not result in any fatalities. If necessary to fulfill the goal of the study, additional exposures will be made.

2.2.5 **Stability**: The stability of the neat test material will be determined by analysis prior to its first use in the study and after it is last used.

2.3 **Test Atmosphere Generation and Analyses:**

2.3.1 **Exposure System:** The exposure system will consist of 250 liter glass and stainless steel inhalation chambers and an atmosphere generation system. This is expected to maintain an animal loading factor below 5%. Inhalation chamber airflow will be maintained at or above 12 air changes per hour. This is expected to maintain the oxygen level above 19%. The desired ranges for temperature and humidity will be 22±2 degrees C and 40 to 60%, respectively, dependent on the characteristics of the test material. which may not allow maintenance of these ranges. The test atmosphere will be generated by an appropriate means and will consist of a vapor of isobutanol.

Animals will be individually placed in wire mesh cages which will be placed inside the exposure chamber. Airflow in the system will be monitored throughout the exposure and held as constant as possible. The specific values for airflow, temperature and relative humidity will be recorded approximately every 30 minutes. In addition, chamber temperature and relative humidity will be monitored continuously. The oxygen level will be determined once per exposure level with an electronic sensor or Draeger tube.

2.3.2 **Test Atmosphere Analyses:** The nominal concentration of each exposure level will be determined at least once per exposure. Samples of chamber atmosphere, including the control chamber, will be obtained from the breathing zone of the animals at least three times during each exposure and will be analytically determined with an infrared analyzer. The analytical method will be available prior to the first exposure.

2.4 **Animals:**

2.4.1 **Sex and Species:** Male and female outbred albino rats

2.4.2 **Strain:** Sprague-Dawley (CD)

2.4.3 **Source:** Charles River Breeding Laboratories

2.4.4 **Age on Test Day 1:** Approximately 8 weeks.

2.4.5 **Number of Animals:** Five rats per sex will be used for each exposure level. For four exposure levels, a total of 20 males and 20 females will be used.

2.4.6 **Body Weight:** On the day of exposure, the weight of all animals should be within 20% of the mean weight of their sex.

2.5 **Animal Husbandry:**

2.5.1 **Identification:** Individual ear tags or tail tattoo and bar coded cage cards.

2.5.2 **Housing:** Individual cages (suspended, stainless steel with wire mesh bottoms).

2.5.3 **Food and Water:** Water and Certified Rodent Diet 5002 (PMI Inc., St. Louis, MO) will be available *ad libitum* except during the exposures. Food and water will be withheld during exposures. This diet has been assayed by the manufacturer for contaminants likely to interfere with this study. All laboratory water used is furnished by the City of St. Louis, meets human drinking water standards, and is sodium zeolite-conditioned upon entering the laboratory. No contaminants are expected to be present which would interfere with the results or conclusions of this study.

2.5.4 **Environmental Conditions:** Animal housing and husbandry will be in accordance with the provisions of 'Guide to the Care and Use of Laboratory Animals', USPHS-NIH Publication No. 86-23. Animal room temperature and relative humidity are targeted at 70 - 74 degrees F. and 40 - 60%, respectively, which are within the USPHS-NIH guidelines of 64.4-78.8 degrees F. and 40-70%. There will be a 12 hour light/dark cycle.

2.5.5 **Pretest Examination and Acclimation:** After arrival, the animals will be examined for any gross signs of injury, disease or other abnormalities when they are transferred to their cages. Within the first week after arrival, the animals will be given a brief inspection to assess general health status. The animals will be examined for ectoparasites and treated, if necessary, at the discretion of the Animal Resources Veterinarian, in consultation with the Study Director. Animals will be quarantined for at least ten days and will be observed daily during this period. Only animals judged to be healthy will be included in the study. Animals will be housed in the same room during both the quarantine period and the study

period. Observations, data collected, treatments, if provided, and the final evaluation for all animals examined will become part of the quarantine record.

2.5.6 **Randomization and Bias Control:** Animals will be assigned to test groups using a computer-generated randomization scheme that assigns animals from a weight range.

2.6 **Absorption of Test Compound:** Determination of the degree of absorption of the test or control materials is not necessary to achieve the objectives of this study and will not be performed.

3. EXPERIMENTAL DESIGN:

The study will consist of one control and at least three exposure groups of rats (5 animals/sex/group). The exposures will be done in pairs for the first four groups with the control and highest exposure levels conducted the first day and two lower exposure levels run the second day. The concentrations used for the second set of exposures will be determined based on the results from the first set (see section 2.2.3). Animals will be observed for mortality and overt signs of toxicity every 30 minutes during the exposure. Detailed clinical signs of toxicity, including an open field assessment of gait, alertness, level of activity, and any other unusual signs of neurotoxicity, will be recorded pre-exposure, immediately following exposure and daily during approximately a five-day post-exposure observation period. Body weights will be recorded pre-exposure and on post-exposure Days 1, 2 and 3. All animals that die or are sacrificed *in extremis* during the study will be given a complete necropsy. No tissues will be weighed or retained except at the discretion of the pathologist. Survivors to the end of the exposure period will be sacrificed but will not be given a necropsy.

4. OBSERVATIONS

4.1 **Routine Inlife:** During the exposure, animals will be observed for mortality and overt signs of toxicity every 30 minutes. All animals will be observed at least twice daily (morning and afternoon) for mortality, moribundity, and overt signs of toxicity, which will be documented by exception. Clinical signs of toxicity, including an open field assessment of gait, alertness, level of activity, and any other unusual signs of neurotoxicity, will be recorded prior to exposure, immediately following exposure and once daily during the post-exposure period. Individual animal weights will be recorded on the day of exposure (prior to exposure), and on post-exposure Days 1, 2 and 3. Food and water consumption will not be measured.

4.2 **Necropsy**: All animals found dead or sacrificed *in extremis* will be given a gross necropsy. No tissues will be retained except at the discretion of the pathologist. Survivors will be not given a gross necropsy.

5. RECORDS AND REPORT

5.1 **Records:** All original records, raw data, retained tissues, protocol and final report will be maintained in the EHL archives.

5.2 **Report:** The report shall be prepared in general accordance will specifications in the EPA regulations. It will include a summary of results and conclusions, a brief description of the methods, summary and individual animal data tables, Quality Assurance Statement and GLP Compliance Statement.

5.3 **Report Schedule:** Draft Report: Second Quarter, 1994
Final Report: Third Quarter, 1994

6. DISTRIBUTION

CMA
C. L. Bechtel
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K. M. Shevlin
F. L. Speck
L. D. Stout
Quality Assurance (2)
F. J. White
T. V. Wilson

7. GENERAL INFORMATION

7.1 The testing facility is the Environmental Health Laboratory, Monsanto Company, 645 South Newstead, St. Louis, Missouri 63110.

7.2 Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. EHL reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered to be in jeopardy. In this event, the Sponsor shall be notified of the alteration as soon as possible, and written verification of the change will be the responsibility of the Study Director. All protocol modifications will be signed by the Study Director and a representative of the Sponsor.

7.3 Reserved for amendments.

Appendix 1: Condensed Summary of Behavioral Data

EHL 94009/CMA Isobutanol AC NT - Statistically Significant Results

	Dose		Male Rats					Female Rats			
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Alertness in open field	1500		↑★★								
	3000		↑★★								
	6000										
Body weight	1500										
	3000	↓★		↓★	↓★	↓★					
	6000	↓★	↓★	↓★★	↓★	↓★					
Motor activity	1500										↑★
	3000										
	6000		↓★				↑★		↑★		

Note: the arrows refer to the direction of difference from control
Stars indicate significant differences from control values at probability
levels of less than or equal to 0.05 (one star) or 0.01 (two stars)

EHL 94009/CMA Isobutanol AC NT - Occurrences of Descriptive Observations

Test Material: Isobutanol - Doses: 0, 1500, 3000, and 6000 ppm

Category	Dose ppm	Number of Male Rats Affected					Number of Female Rats Affected				
		Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Miscellaneous General Observations											
Alopecia (forelimb[s])											
	1500				1					1	1
One or both pupils would not dilate											
	0		1								
	1500						1				
Scab on neck, shoulder, or head											
	1500				1			1	1	1	
	6000		1	1							
Swollen digit on foot (in one case also noted to be red)											
	1500							1			
	6000							1	1		
Slight ocular opacity (unilateral)											
	6000		1								
Description of gait											
Waddles, rocks, or lurches											
	6000		1								
Unusual behavior											
Gait, gait score, and mobility score assessed after stimulation	0		4	1	1						
	1500			1	1			2			
	3000		1	1	1	3		1			
	6000		3	2	2	2		2	1		1

Explanation of Summary Tables and Statistical Analyses

I. Motor activity, FOB interval data, and rearing

A. Data types

1. Motor activity
2. Number of rears in the open field
3. Body weight
4. Forelimb grip strength
5. Hindlimb grip strength
6. Landing foot splay

B. Statistical analyses performed

1. Levene's Test for homogeneity of variance (two-tailed; considered positive only if the probability ≤ 0.01) (Snedecor and Cochran 1980)
2. Repeated measures ANOVAs using baseline values as covariates (ANCOVAs).
3. Dunnett's Multiple Comparison Test (two-tailed) (Dunnett 1955; Dunnett 1964)

C. Results reported in summary tables

1. Mean value in each group
2. Standard deviation in each group
3. Number of animals observed ("Count") in each group

II. FOB ordinal data (where values are assigned from a predetermined scale from 1 to n) and data with minimal numbers of counts

A. Data types[1]

1. Ease of removal from cage (a)
2. Reactivity to investigator (a)
3. Lacrimation (b)
4. Salivation (b)
5. Palpebral closure (b)
6. Alertness in the open field (a)
7. Gait score (b)
8. Mobility score (b)
9. Number of fecal boli in the open field (a)
10. Number of urine pools in the open field (a)
11. Approach response (a)
12. Tail pinch response (a)
13. Response to clicker (a)
14. Righting reflex (b)

---

1 Parameters identified by (a) were analyzed using two tailed tests and those identified by (b) were analyzed using one tailed tests.

B. **Statistical analyses performed**
1. Kruskal-Wallis analysis of variance by ranks (Breslow 1970)
2. Jonckheere's Test for non-parametric trend (Hollander and Wolfe 1973)
3. If either of the above tests are positive, pairwise comparisons of each test group with the control group are performed via the Mann-Whitney U Test (Mann and Whitney 1947)

C. **Results reported in summary tables**
1. Mean value in each group (The standard deviation will not be reported since it is not relevant to the statistical analysis of graded parameters.)
2. Number of animals observed ("Count") in each group

III. **FOB quantal data, which are graded as present or absent**

A. **Data types**
1. Pupillary reflex
2. Exophthalmia
3. Piloerection
4. Vocalization

B. **Statistical analyses performed**
1. Overall chi-square test (one-tailed) (Snedecor and Cochran 1980)
2. Cochran-Armitage Test for linear trend in proportions (one-tailed) (Cochran 1954; Armitage 1955)
3. If either of the above tests are positive, pairwise comparisons of each test group with the control group via Fisher's Exact Test (one-tailed) (Fisher 1946)

C. **Results reported in summary tables**
1. Mean value in each group (The standard deviation will not be reported since it is not relevant to the statistical analysis of quantal parameters.)
2. Number of animals observed ("Count") in each group

IV. **FOB categorical data (descriptions of the animal's appearance, behavior, etc)**

A. **Data types**
1. Activity/posture in home cage
2. Clonic movements in home cage
3. Tonic movements in home cage
4. Any general observations during handling
5. Clonic movements in the open field
6. Tonic movements in the open field
7. Description of gait
8. Stereotypic behavior
9. Unusual behavior

B. **Any occurrences of abnormalities in these categories will be counted and tabulated by group and time point**

V. **Gross necropsy data-** Inspection of frequency of abnormalities

REFERENCES

Armitage, P. Tests for linear trends in proportions and frequencies. Biometrics 11:375-386, 1955

Breslow, N. A generalized Kruskal-Wallis test for comparing K-Samples subject to unequal patterns of censorship. Biometrika 57: 579-594, 1970

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Snedecor, G. W. and Cochran, W. G., Statistical Methods, 7th ed. Iowa State University Press, 1980

Appendix 2: Summary Table and Figures for Motor Activity (MA)

EHL 94009/ML- - Motor Activity (counts/60 minutes)

Test Material: Isobutanol

Male Rats

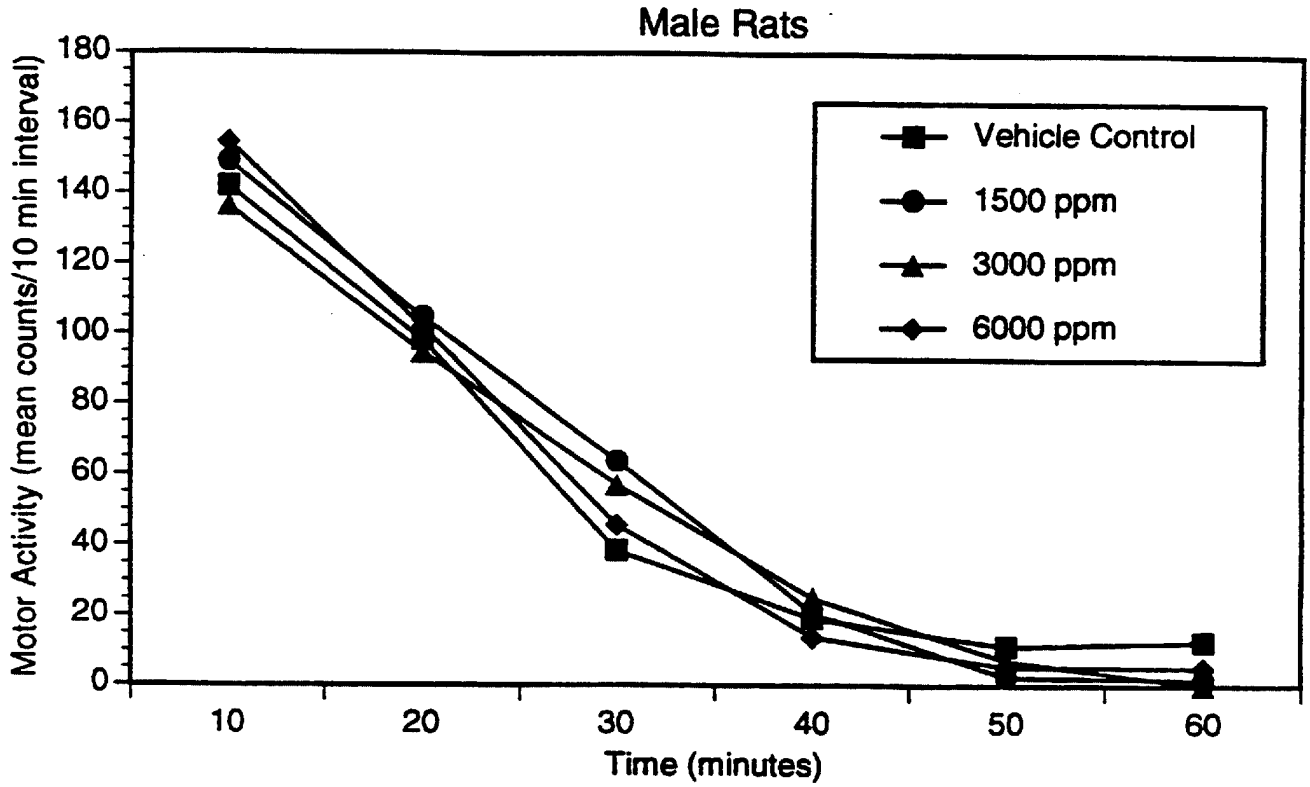
Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	321.2	188.0	322.0	379.9	416.6
	SD	114.0	94.0	157.2	141.0	118.3
	# Rats	10	10	10	10	10
1,500	Mean	341.7	195.8	298.8	466.0	427.3
	SD	107.5	69.8	140.1	200.7	173.1
	# Rats	10	10	10	10	10
3,000	Mean	320.0	151.9	276.3	450.1	452.4
	SD	82.4	63.9	115.3	200.0	192.6
	# Rats	10	10	10	10	10
6,000	Mean	325.8	101.0*	324.6	442.6	512.4
	SD	94.2	80.6	115.5	130.9	187.8
	# Rats	10	10	10	10	9

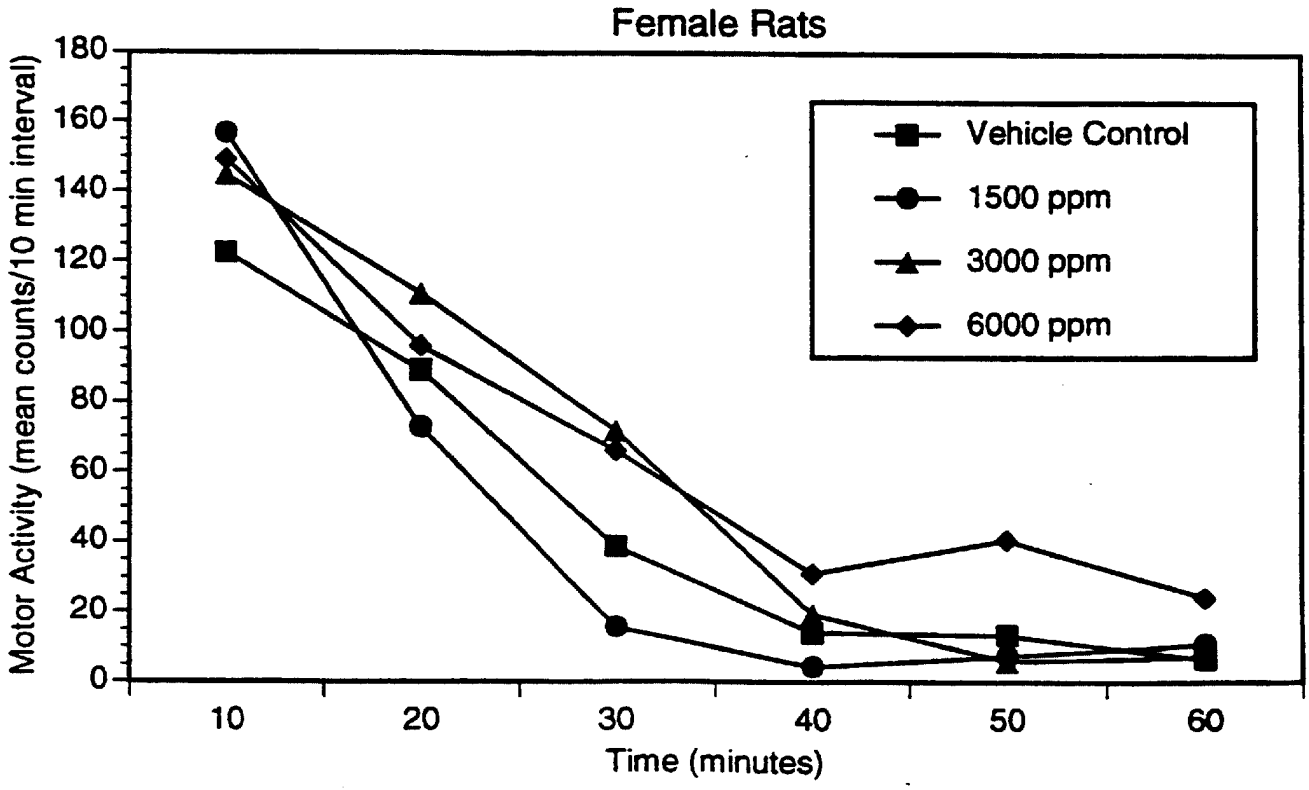
Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	284.2	154.8	203.1	369.8	348.6
	SD	88.0	72.2	101.2	151.2	83.8
	# Rats	10	10	10	10	10
1,500	Mean	267.4	210.2	283.5	459.3	494.1*
	SD	84.9	126.8	128.1	122.8	163.7
	# Rats	10	10	10	10	10
3,000	Mean	359.9	215.1	309.3	471.5	476.1
	SD	144.1	110.0	125.5	181.0	128.6
	# Rats	10	10	10	10	10
6,000	Mean	407.4*	103.7	398.5*	481.8	457.3
	SD	94.2	49.3	199.2	115.1	141.5
	# Rats	10	10	10	10	10

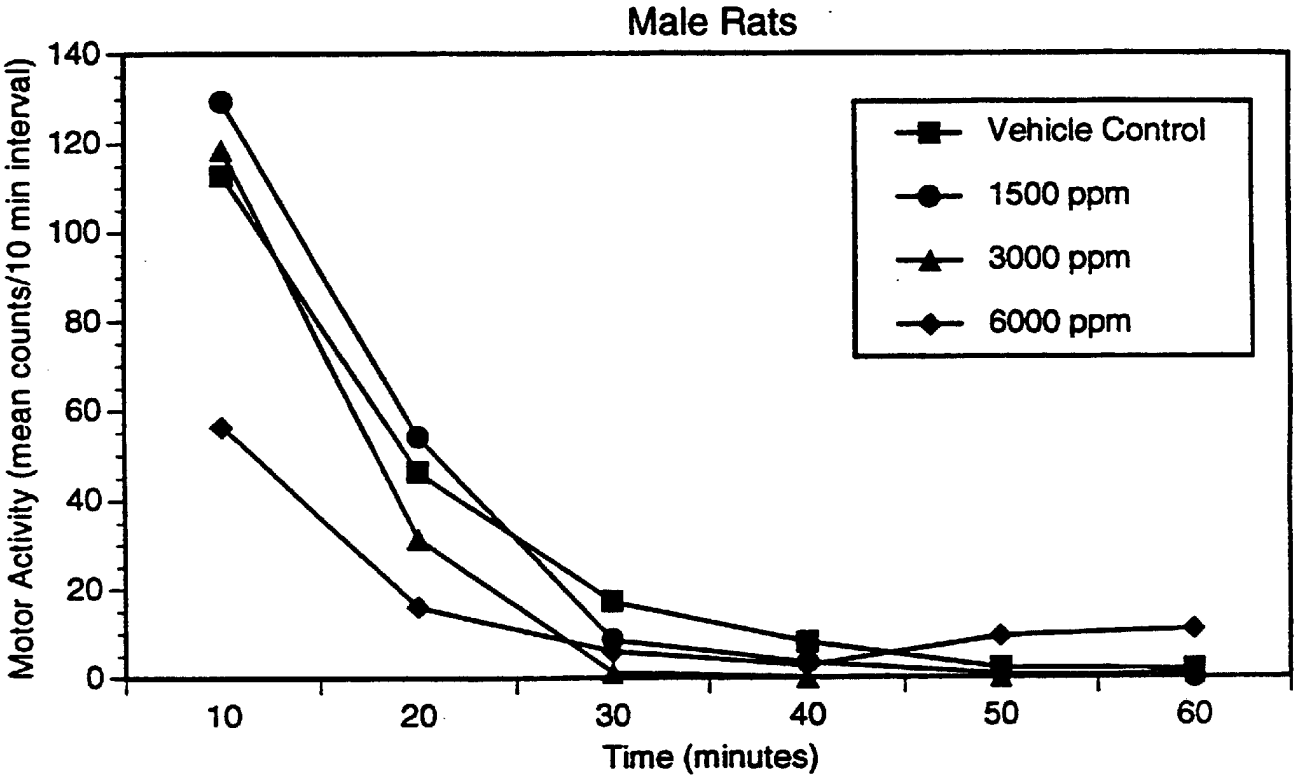
* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

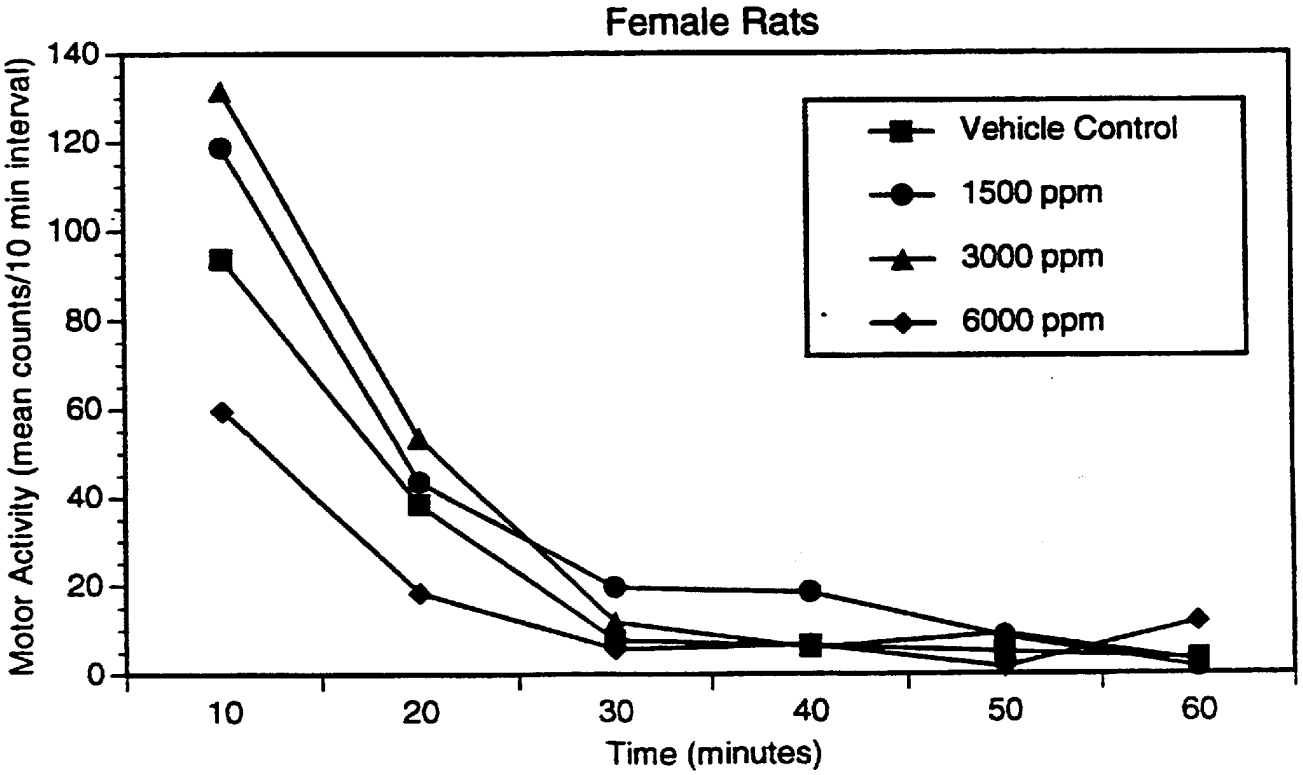
Effect of Isobutanol on Motor Activity
Pretest Baseline - EHL 94009



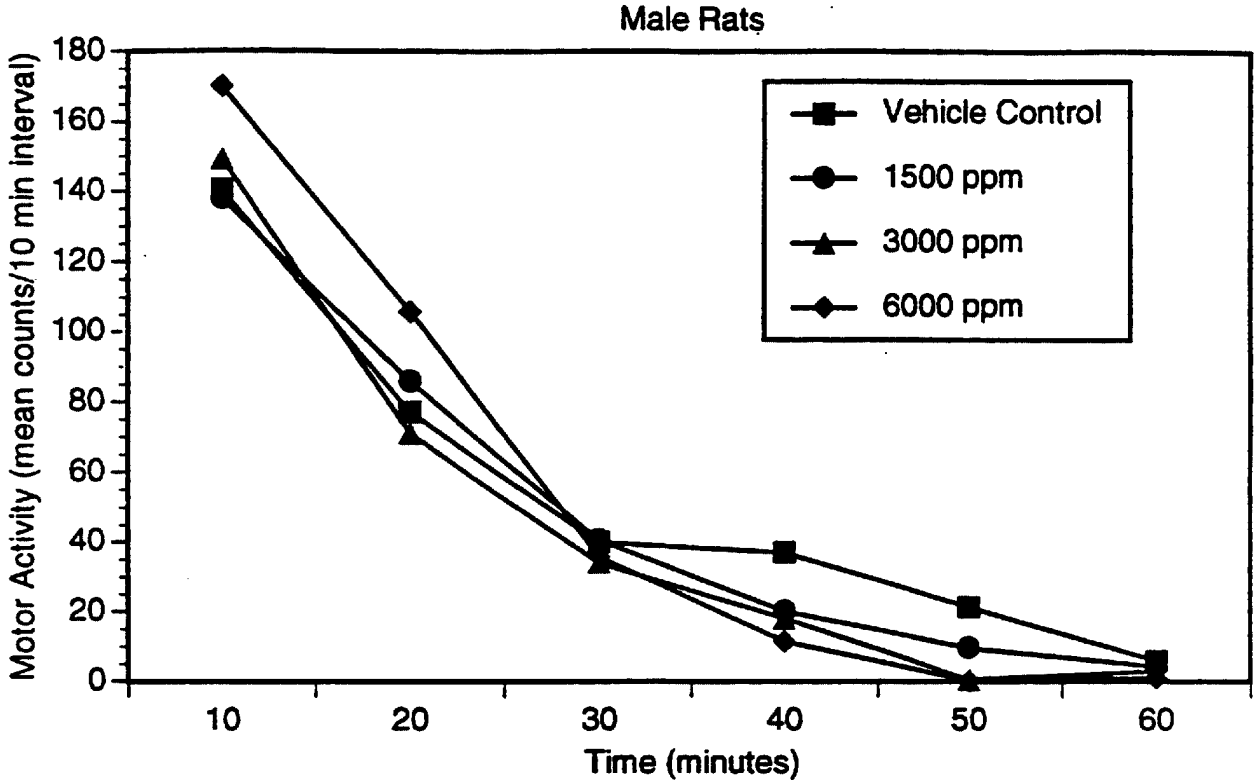


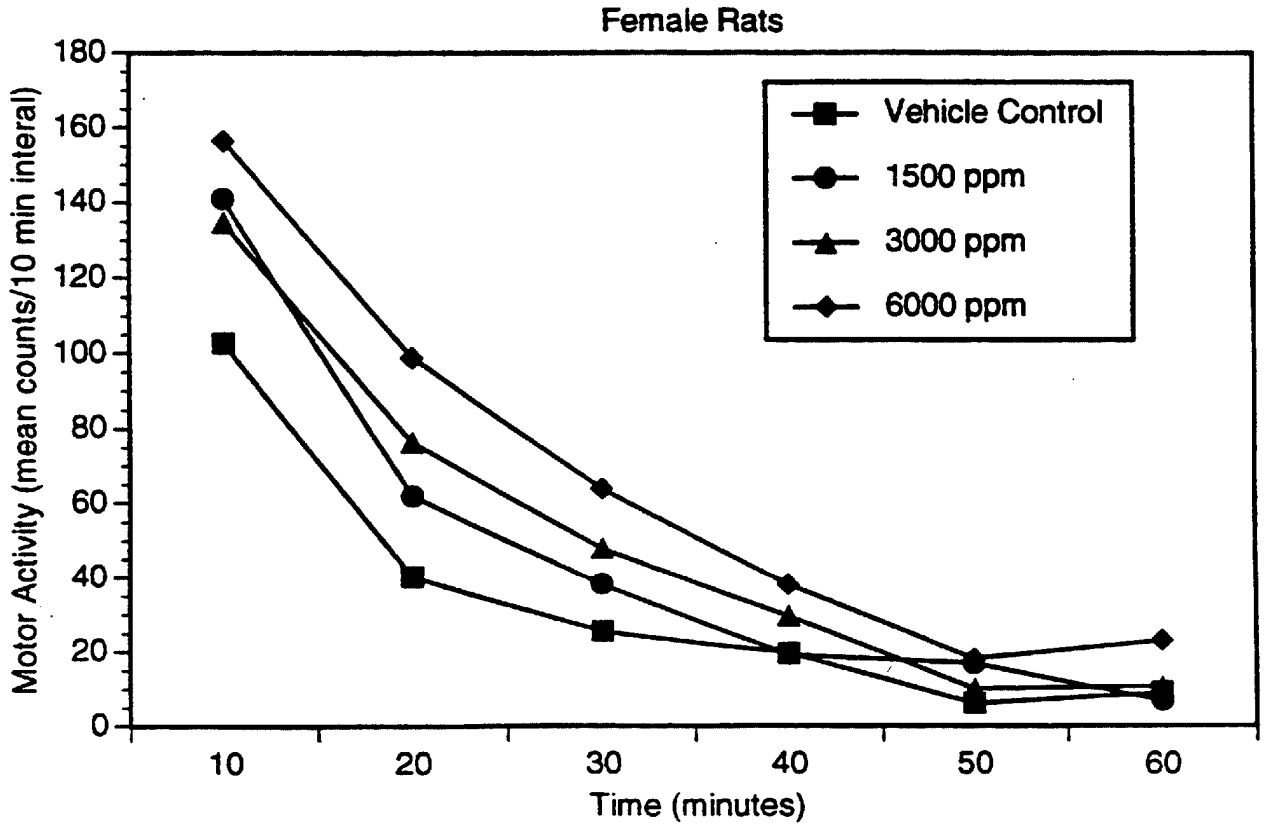
Effect of Isobutanol on Motor Activity
Day 0 - EHL 94009



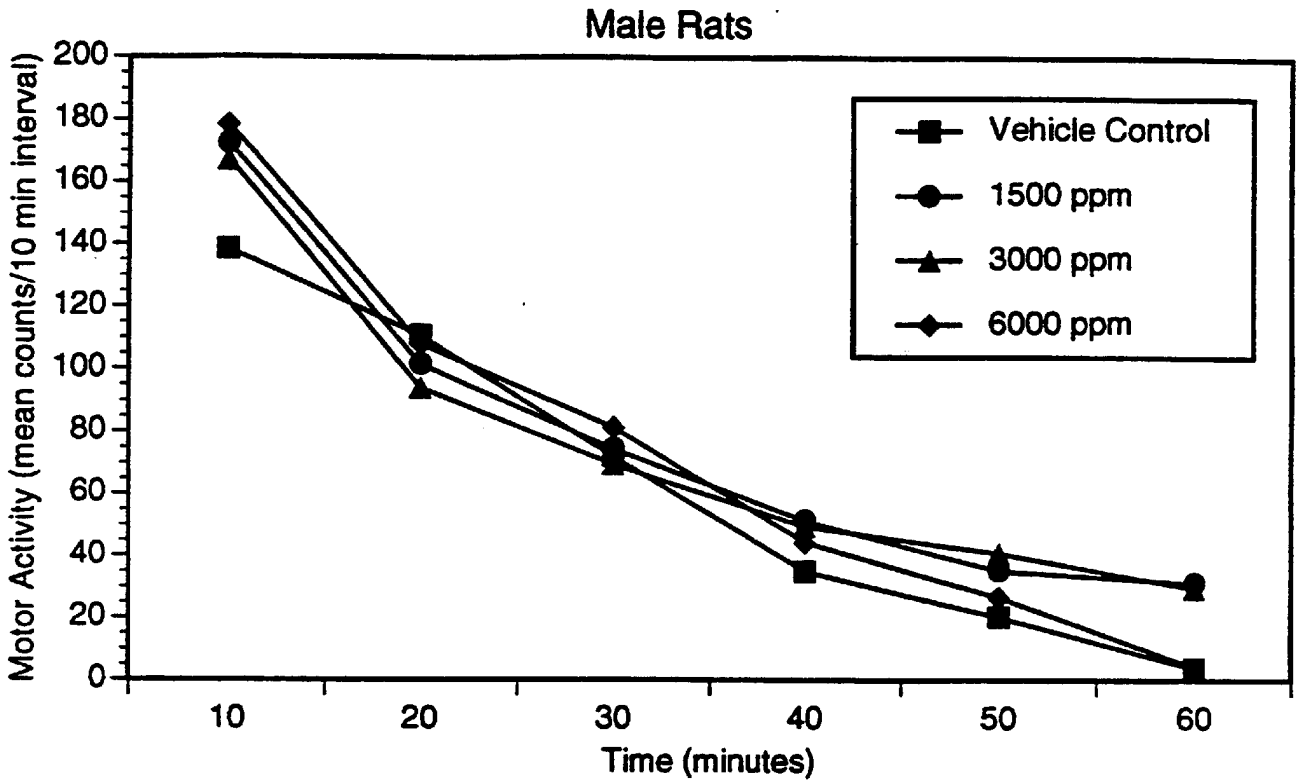


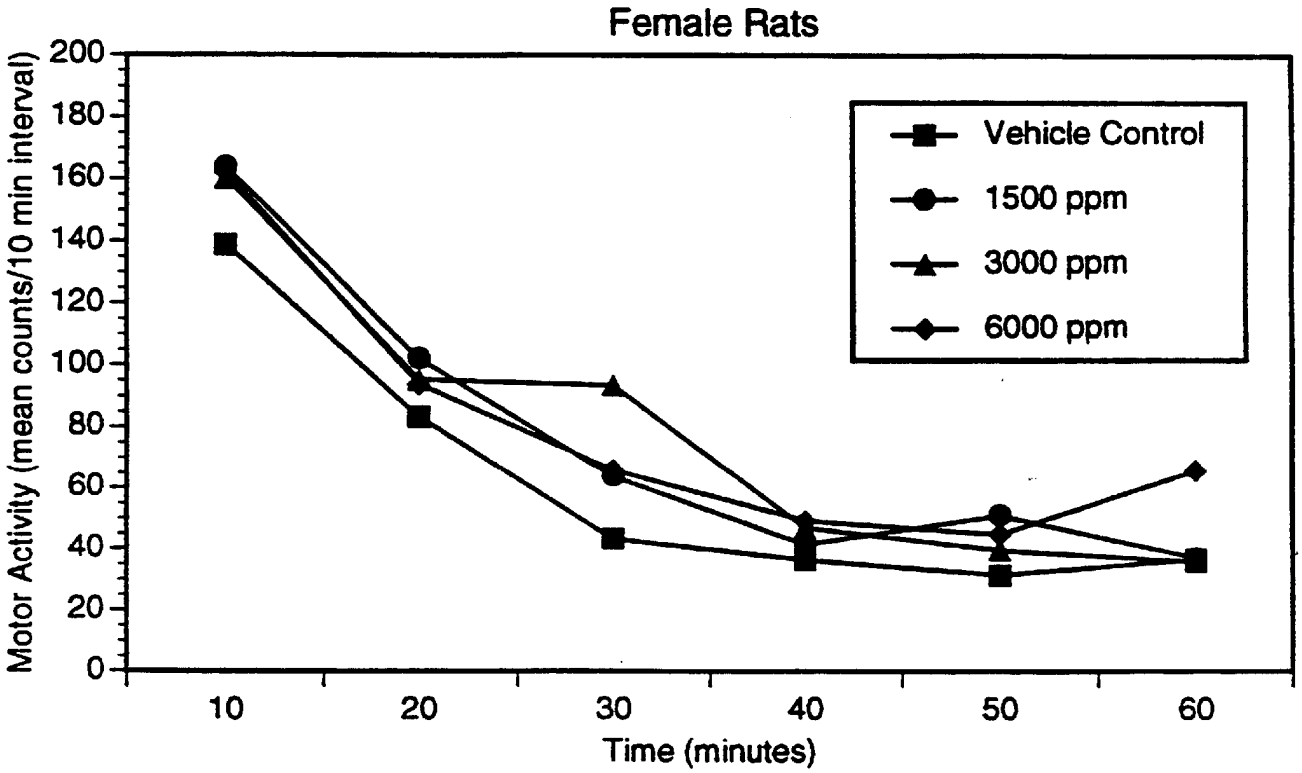
Effect of Isobutanol on Motor Activity
Day 1 - EHL 94009



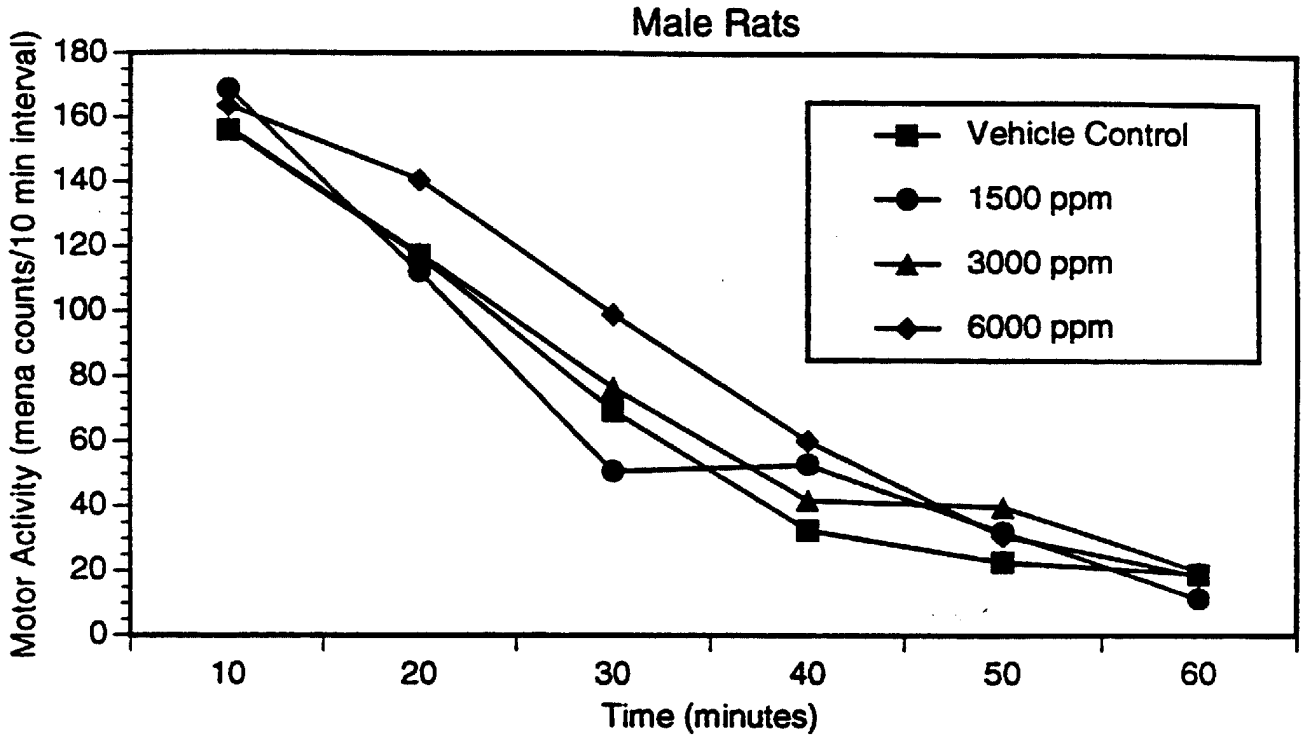


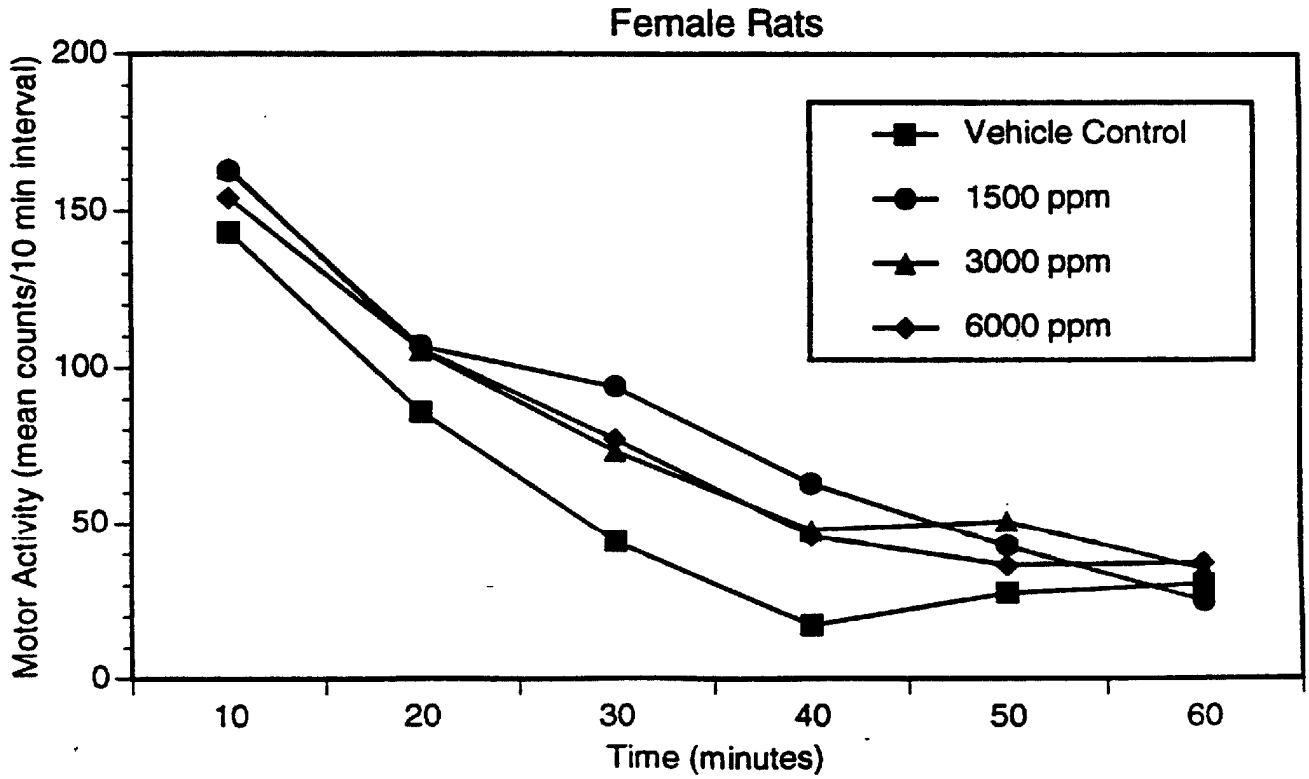
Effect of Isobutanol on Motor Activity
Day 7 - EHL 94009





Effect of Isobutanol on Motor Activity
Day 14 - EHL 94009





Appendix 3: Summary Tables for FOB

Instructions for the Functional Observational Battery (FOB)

Presented in the Order Tested

(Numbers refer to the scores used for that category)

I. **Home cage observations:** General posture/activity level, and any clonic or tonic movements will be recorded while the animal is in its home cage and prior to any handling. Values will be recorded as follows:

A. **Activity/posture**

0. Sniffing or walking around
0. Sitting or standing normally
0. Asleep, lying on side or curled up
1. Dead
2. Moribund
3. Flattened; limbs may be spread out
4. Hunched over
5. Lethargy
6. Abnormal head movements
7. Increased activity

B. **Clonic movements**

0. None
1. Repetitive movements of mouth and jaws
2. Twitches (arrhythmic)
3. Localized tremors
4. Whole body tremors
5. Myoclonic jerks
6. Clonic convulsions
7. Wet dog shakes
8. Sinuous muscle contractions

C. **Tonic movements**

0. None
1. Contraction of extensors - limbs rigid & extended
2. Opisthotonos - head & body arched backwards
3. Emprosthotonos - head & body extended forward
4. Explosive jumps - all four feet leave the ground
5. Convulsions resulting in dyspnea, depression or death

II. **Observations during handling:** The animal will then be removed from its home cage and ease of such removal, reactivity toward the investigator, degree of lacrimation, salivation, presence or absence of exophthalmia, degree of palpebral opening, presence or absence of piloerection, and any general descriptive clinical effects will be recorded.

A. **Cage removal ease**
   0. Very easy - absence of resistance
   1. Easy - slight resistance, some avoidance, may vocalize
   2. Moderately difficult - eg, running around the cage
   3. Very difficult - may include signs of aggression

B. **Reactivity to investigator**
   0. Limp/lack of resistance
   1. Moderately low (slight resistance +/- vocalization)
   2. Moderately high (freezing/tension/rigidity, may vocalize)
   3. High (squirming, tries to bite, +/- vocalization)

C. **Lacrimation**
   0. None
   1. Slight
   2. Severe

D. **Salivation**
   0. None
   1. Slight
   2. Excessive

E. **Exophthalmia**
   0. Absent
   1. Present

F. **Palpebral closure**
   0. Eyelids fully closed
   1. Eyelids partially closed
   2. Eyelids wide open

G. **Piloerection**
   0. None - normal
   1. Piloerected

H. **Miscellaneous observations**

0. None
1. Red nasal discharge/staining
2. Red ocular discharge
3. Perinasal encrustation
4. Dehydration
5. Emaciation
6. Diarrhea
7. Polyuria
8. Urogenital staining
9. Abnormal urine color
10. Pale color of extremities
11. Body cool to touch
12. Alopecia
13. Dyspnea
14. Rales
15. Head Tilt
16. Ocular Cloudiness/Opacity

III. **Observations in the open field:** The animal will then be placed on a table covered by an absorbent material for a two minute interval. Any evidence of clonic or tonic movements, abnormal gait, spontaneous vocalization (though this would also be recorded should it occur at other times), and stereotypic or unusual behavior will be recorded, as will the degree of general alertness and impairment of gait or mobility. The number of times the animal rears (raises both forelimbs from the table), fecal boli, and urinary pools will be counted and recorded for the same interval.

A. **Clonic movements**

0. None
1. Repetitive movements of mouth and jaws
2. Twitches (arrhythmic)
3. Localized tremors
4. Whole body tremors
5. Myoclonic jerks
6. Clonic convulsions
7. Wet dog shakes
8. Sinuous muscle contractions

B. **Tonic movements**

0. None
1. Contraction of extensors - limbs rigid & extended
2. Opisthotonos - head & body arched backwards
3. Emprosthotonos - head & body extended forward
4. Explosive jumps - all four feet leave the ground
5. Convulsions resulting in dyspnea, depression or death

C. Alertness

0. No movement
1. Low (some head or body movement)
2. Normal (alert, exploratory movements)
3. Somewhat high (slight excitement, tense, darting or freezing)
4. Very high (hyperalert, excited, sudden bouts of running)

D. Gait

0. Normal
1. Waddles, rocks or lurches
2. Misuse/disuse of hind limb(s)
3. Feet markedly point outwards from body
4. Misuse/disuse of forelimb(s)
5. Walks on tiptoes
6. Hunched or crouched body position
7. Moves with body flattened

E. Gait score

0. Severely abnormal
1. Moderately abnormal
2. Slightly abnormal
3. Normal - no abnormal gait

F. Mobility score

0. Totally impaired
1. Moderately impaired
2. Slightly impaired
3. Normal

G. Vocalization

0. Did not vocalize
1. Did vocalize

H. Stereotypy

0. None
1. Circling
2. Stereotypic grooming
3. Pacing
4. Head weaving

I. **Unusual behavior**
   0. None
   1. Self mutilation
   2. Straub tail
   3. Backing up
   4. Writhing
   5. Flopping
   6. Static flattened attitude
   7. Somersaulting
   8. Crossing of forelimbs
   9. Head shaking
   10. Lateral rolling motions
   11. Paws at air
   12. Static foot splay
   13. Gait, gait score, and mobility score assessed following stimulus
   14. Pupils would not dilate

J. **Rearing - The number of times both forelegs leave the table will be counted.**

K. **Excretion - Fecal boli will be counted.**

L. **Urination - Pools of urine will be counted.**

IV. **Reflexes and physiological measurements**

Following the 2-minute observation period, the animal will be approached from the front with a blunt object and its reaction will be recorded. The animal's tail will be pinched approximately five cm from the tip, and the response to this stimulus will be assessed and recorded. Finally, a small mechanism will be "clicked" behind its head for assessment of response to sound.

A. **Approach response**
   0. No reaction
   1. Slowly approaches and sniffs, turns away, or flinches
   2. Energetic response
   3. Exaggerated reaction - eg, jumps, bites, or attacks

B. **Tail pinch response**
   0. No reaction
   1. Turns or walks forward or vocalizes with little motion
   2. Energetic response
   3. Exaggerated reaction - eg, jumps, bites, or attacks

C. **Click response**
   0. No reaction
   1. Startle/slight reaction, evidence that noise was perceived
   2. Energetic response
   3. Exaggerated reaction - eg, jumps, bites, or attacks

D. **Pupillary reflex:** The animal will then be placed in a darkened environment such as a box for a short period following which pupillary response to light from a penlight or hand held ophthalmoscope will be determined. If, due to pupillary constriction, this assessment is not practical, it will be noted as such.
   0. One or both pupils do not contract
   1. Pupil contracts

E. **Righting reflex:** The animal will then be dropped in a supine position from a height of approximately 30 cm and the posture upon landing will be recorded. This will not be performed if it is deemed that the animal is incapacitated to such a degree that injury might result.
   0. Lands on back
   1. Lands on side
   2. Slightly uncoordinated landing
   3. Lands on feet

F. **Body weight:** The animal will then be weighed

G. **Fore and hind limb grip strength** will then be measured, generally following the procedure of Meyer, et al. (1979). However, the following modifications will be employed: (a) A wire mesh screen will be used as the gripping mechanism for both fore and hind limbs. (b) The gauge used for measurement of the forelimbs will be oriented in a manner so that the animal will fall toward a table when grip is released. (It will be caught.) Two trials will be recorded for each of the fore and hind limbs.

H. **Landing foot splay:** The animal's hind paws will be moistened with water, and the animal will then be dropped onto a chalkboard from a height of approximately 30 cm. Three trials will be performed, and the distance between the paw prints will be measured in mm for the latter two. This test will not be performed should it be felt that injury to the animal might result upon landing.

REFERENCE

Meyer, O. A., Tilson, H. A., Byrd, W. C., and Riley, M. T. (1979)
A Method for the Routine Assessment of Fore- and Hindlimb Grip Strength of Rats and Mice.
Neurobehavioral Toxicology 1:233-236

EHL 94009/CMA Isobutanol AC NT - Home Cage Activity/Posture

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Activity in home cage		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Clonic Movements in Home Cage

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Clonic movements in home cage		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Tonic Movements in Home Cage

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Tonic movements in home cage		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Cage Removal Ease

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

Very easy - absence of resistance - 0
Easy - slight resistance, some avoidance, may vocalize - 1
Moderately difficult - eg, running around the cage - 2
Very difficult - may include signs of aggression - 3

EHL 94009/CMA Isobutanol AC NT - Reactivity Toward Investigator

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

Limp/lack of resistance - 0
Moderately low (slight resistance with or without vocalization) - 1
Moderately high (freezing/tension/rigidity, may vocalize) - 2
High (squirming, tries to bite, with or without vocalization) - 3

EHL 94009/CMA Isobutanol AC NT - Lacrimation

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used
None - 0
Slight - 1
Severe - 2

EHL 94009/CMA Isobutanol AC NT - Salivation

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used
None - 0
Slight - 1
Excessive - 2

EHL 94009/CMA Isobutanol AC NT - Exophthalmia

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10

* Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.05
** Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.01

Scores used
Absent - 0
Present - 1

EHL 94009/CMA Isobutanol AC NT - Palpebral Closure

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
1500	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
3000	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
6000	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
1500	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
3000	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10
6000	Mean	2.0	2.0	2.0	2.0	2.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Eyelids wide open - 2
Eyelids partially closed - 1
Eyelids fully closed - 0

EHL 94009/CMA Isobutanol AC NT - Piloerection

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10

* Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.05
** Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Absent - 0
Present - 1

EHL 94009/CMA Isobutanol AC NT - Miscellaneous Observations

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Miscellaneous General Observations											
Alopecia (forelimb[s])											
	1500				1					1	1
One or both pupils would not dilate											
	0		1								
	1500						1				
Scab on neck, shoulder, or head											
	1500				1			1	1	1	
	6000		1	1							
Swollen digit on foot (in one case also											
noted to be red)	1500							1			
	6000							1	1		
Slight ocular opacity (unilateral)											
	6000		1								

EHL 94009/CMA Isobutanol AC NT - Clonic Movements in Open Field

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Clonic movements in open field		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Tonic Movements in Open Field

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Tonic movements in open field		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Alertness Level

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	2.0	1.2	1.5	1.5	1.8
	# Rats	10	10	10	10	10
1500	Mean	1.8	1.8**	1.8	1.9	1.8
	# Rats	10	10	10	10	10
3000	Mean	2.0	1.9**	1.7	1.6	1.7
	# Rats	10	10	10	10	10
6000	Mean	2.0	1.6	1.7	1.6	1.7
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	2.0	2.0	2.3	2.4	2.4
	# Rats	10	10	10	10	10
1500	Mean	1.9	2.0	2.3	2.4	2.2
	# Rats	10	10	10	10	10
3000	Mean	2.0	2.0	2.4	2.4	2.2
	# Rats	10	10	10	10	10
6000	Mean	2.0	1.5	2.1	2.3	2.2
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

No movement - 0
Low (some head or body movement) - 1
Normal (alert, exploratory movements) - 2
Somewhat high (slight excitement, tense, darting or freezing) - 3
Very high (hyperalert, excited, sudden bouts of running) - 4

EHL 94009/CMA Isobutanol AC NT - Description of Gait

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Description of Gait											
Waddles, rocks, or lurches	6000		1								

EHL 94009/CMA Isobutanol AC NT - Gait Score

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	2.9	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Normal - no abnormal gait - 3
Slightly abnormal - 2
Moderately abnormal - 1
Severely abnormal - 0

EHL 94009/CMA Isobutanol AC NT - Mobility Score

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used
Normal - 3
Slightly impaired - 2
Moderately impaired - 1
Totally impaired - 0

EHL 94009/CMA Isobutanol AC NT - Vocalization

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10

* Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.05

** Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Absent - 0

Present - 1

EHL 94009/CMA Isobutanol AC NT - Stereotypic Behavior

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Stereotypic Behavior		No abnormal observations					No abnormal observations				

EHL 94009/CMA Isobutanol AC NT - Unusual Behavior

Test Material: Isobutanol - Concentrations: 0, 1500, 3000, and 6000 ppm

	Conc	Number of Male Rats Affected					Number of Female Rats Affected				
Category	ppm	Pre	Day 0	Day 1	Day 7	Day 14	Pre	Day 0	Day 1	Day 7	Day 14
Unusual Behavior											
Gait, gait score, and mobility score											
assessed after stimulation	0		4	1	1						
	1500			1	1			2			
	3000		1	1	1	3		1			
	6000		3	2	2	2		2	1		1

EHL 94009/CMA Isobutanol AC NT - Rearing (occurrences/2 minutes)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	4.0	1.4	2.1	2.7	2.4
	SD	3.7	2.0	4.1	5.1	5.2
	# Rats	10	10	10	10	10
1500	Mean	3.5	2.8	2.6	4.2	3.7
	SD	3.4	2.5	2.8	4.4	2.9
	# Rats	10	10	10	10	10
3000	Mean	6.1	4.1	5.6	6.1	5.7
	SD	4.2	4.9	4.9	6.8	5.6
	# Rats	10	10	10	10	10
6000	Mean	5.7	3.0	3.8	5.3	5.3
	SD	5.5	5.8	5.3	5.8	6.7
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	8.8	7.1	14.5	16.4	16.7
	SD	5.3	4.7	8.4	7.3	8.9
	# Rats	10	10	10	10	10
1500	Mean	7.4	7.9	12.0	18.9	15.5
	SD	4.0	7.8	12.9	7.9	8.8
	# Rats	10	10	10	10	10
3000	Mean	8.0	7.3	12.7	18.4	17.9
	SD	4.6	6.5	8.4	5.6	4.6
	# Rats	10	10	10	10	10
6000	Mean	7.5	3.0	12.3	14.1	15.4
	SD	5.1	4.8	9.9	7.7	6.3
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Excretion (boli counted/2 min)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.7	0.6	0.9	0.4	0.5
	# Rats	10	10	10	10	10
1500	Mean	1.5	1.0	1.5	0.3	0.4
	# Rats	10	10	10	10	10
3000	Mean	0.6	0.8	0.4	0.3	0.2
	# Rats	10	10	10	10	10
6000	Mean	0.9	2.0	2.2	1.5	0.9
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.1	0.0	0.1	0.0
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.3	0.8	0.5	0.3	0.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Urination (pools counted/2 min)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.1	0.3	0.1	0.1
	# Rats	10	10	10	10	10
1500	Mean	0.4	0.0	0.0	0.1	0.8
	# Rats	10	10	10	10	10
3000	Mean	0.3	0.3	0.0	0.1	0.2
	# Rats	10	10	10	10	10
6000	Mean	0.5	0.2	0.5	0.6	0.7
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.0	0.1	0.0	0.0	0.0
	# Rats	10	10	10	10	10
1500	Mean	0.0	0.1	0.0	0.0	0.1
	# Rats	10	10	10	10	10
3000	Mean	0.0	0.0	0.0	0.0	0.0
	# Rats	10	10	10	10	10
6000	Mean	0.2	0.1	0.1	0.1	0.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Approach Response

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	0.9	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	0.9	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

No reaction - 0
Slowly approaches and sniffs, turns away, or flinches - 1
Energetic response - 2
Exaggerated reaction - eg, jumps, bites, or attacks - 3

EHL 94009/CMA Isobutanol AC NT - Tail Pinch Response

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.1	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.1	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.1
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.2	1.1	1.0	1.4
	# Rats	10	10	10	10	10
1500	Mean	1.1	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.1	1.0	1.1	1.2
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

No reaction - 0
Turns or walks forward or vocalizes with little motion - 1
Energetic response - 2
Exaggerated reaction - eg, jumps, bites, or attacks - 3

EHL 94009/CMA Isobutanol AC NT - Click Response

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (two-tailed) significant at p less than or equal to 0.01

Scores used

No reaction - 0
Startle/slight reaction, evidence that noise was perceived - 1
Energetic response - 2
Exaggerated reaction - eg, jumps, bites, or attacks - 3

EHL 94009/CMA Isobutanol AC NT - Pupillary Reflex

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	9	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
1500	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	9	10	10	10	10
3000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10
6000	Mean	1.0	1.0	1.0	1.0	1.0
	# Rats	10	10	10	10	10

* Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.05
** Fisher's Exact Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Pupil contracts - 1
One or both pupils do not contract - 0

EHL 94009/CMA Isobutanol AC NT - Righting Reflex

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
1500	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
3000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10
6000	Mean	3.0	3.0	3.0	3.0	3.0
	# Rats	10	10	10	10	10

* Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.05
** Mann-Whitney U Test (one-tailed) significant at p less than or equal to 0.01

Scores used

Lands on feet - 3
Slightly uncoordinated landing- 2
Lands on side - 1
Lands on back - 0

EHL 94009/CMA Isobutanol AC NT - Body Weights (grams)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	273.5	321.6	339.1	379.0	420.5
	SD	21.5	25.1	21.7	26.2	30.0
	# Rats	10	10	10	10	10
1500	Mean	268.6	316.6	336.1	370.0	411.5
	SD	17.2	20.7	18.6	20.6	25.5
	# Rats	10	10	10	10	10
3000	Mean	254.8*	302.9	317.1*	354.3*	392.4*
	SD	8.9	6.1	9.1	10.9	9.9
	# Rats	10	10	10	10	10
6000	Mean	254.8*	297.6*	311.3**	354.1*	391.0*
	SD	15.6	20.2	20.5	25.1	29.1
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	193.6	211.3	220.7	238.1	250.6
	SD	11.8	11.5	12.8	10.6	12.3
	# Rats	10	10	10	10	10
1500	Mean	192.0	208.1	220.5	231.9	249.3
	SD	17.7	19.6	24.2	26.1	27.4
	# Rats	10	10	10	10	10
3000	Mean	197.0	213.6	225.9	242.8	255.8
	SD	15.9	20.4	21.0	23.7	29.5
	# Rats	10	10	10	10	10
6000	Mean	199.1	214.0	227.6	246.3	260.9
	SD	16.3	19.5	23.2	28.2	23.4
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Pretest Body Weights and Subsequent Body Weights as a Percent of Pretest Values

Test Material: Isobutanol

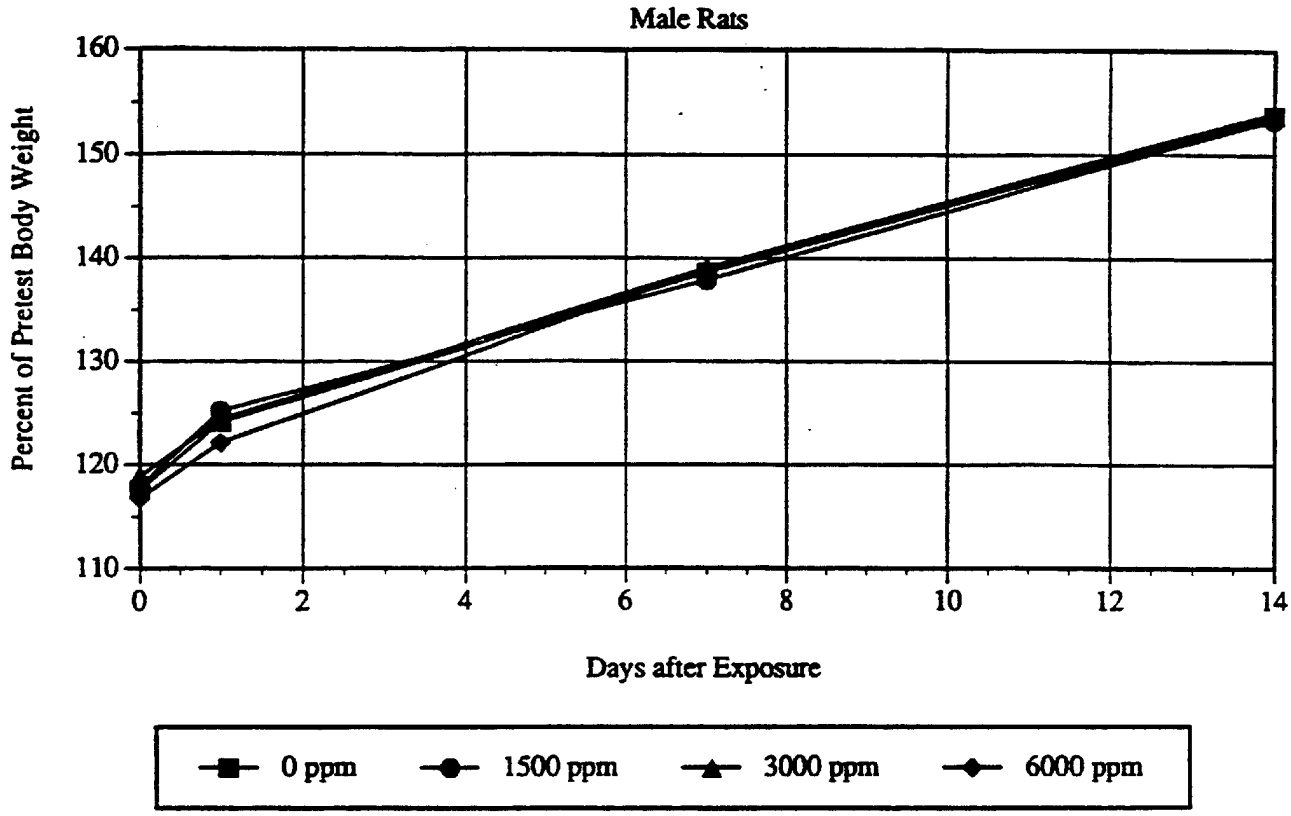
Male Rats

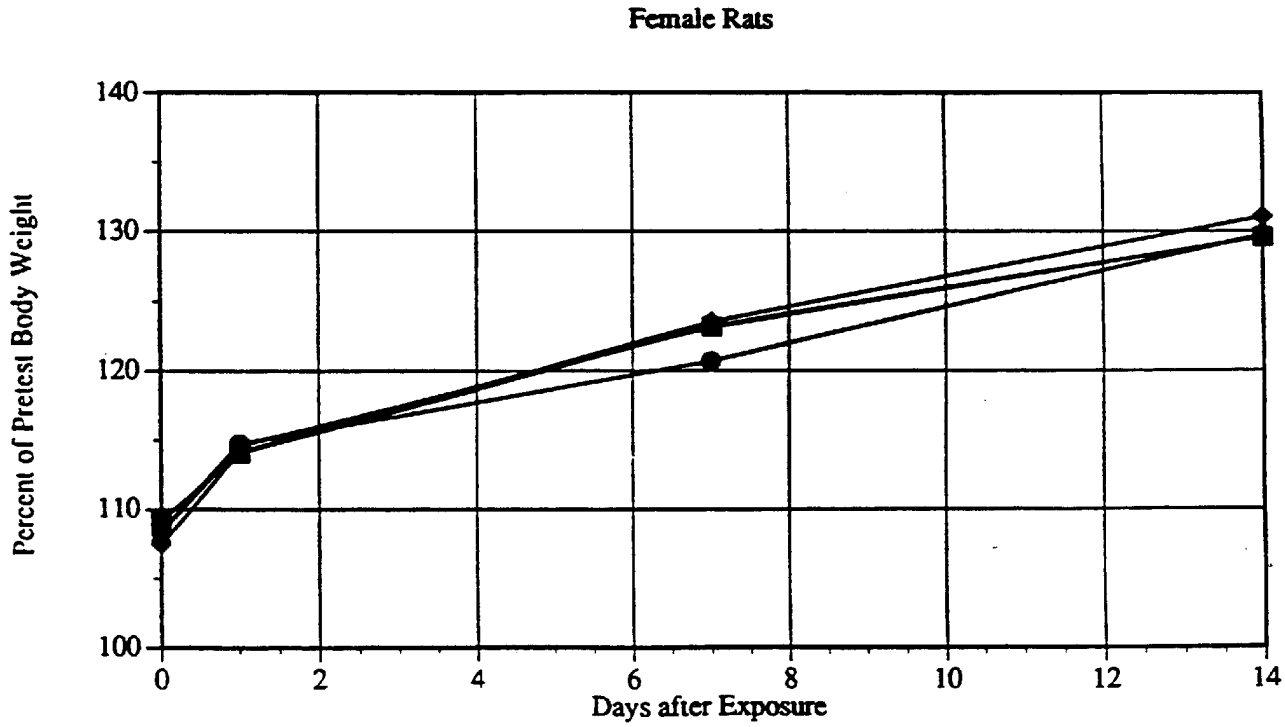
Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	273.5	117.6	124.1	138.6	153.8
	SD	21.5	2.3	2.2	2.0	2.0
	# Rats	10	10	10	10	10
1500	Mean	268.6	117.9	125.3	137.9	153.4
	SD	17.2	2.4	2.8	4.7	6.3
	# Rats	10	10	10	10	10
3000	Mean	254.8*	118.9	124.5	139.1	154.1
	SD	8.9	2.0	2.3	3.5	4.5
	# Rats	10	10	10	10	10
6000	Mean	254.8*	116.8	122.2	139.0	153.5
	SD	15.6	3.0	3.3	4.9	6.0
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	193.6	109.2	114.0	123.2	129.6
	SD	11.8	2.4	3.1	5.4	4.9
	# Rats	10	10	10	10	10
1500	Mean	192.0	108.4	114.7	120.7	129.8
	SD	17.7	2.8	2.7	4.0	4.7
	# Rats	10	10	10	10	10
3000	Mean	197.0	108.4	114.6	123.1	129.6
	SD	15.9	2.6	3.0	2.6	6.3
	# Rats	10	10	10	10	10
6000	Mean	199.1	107.4	114.2	123.5	131.1
	SD	16.3	3.0	2.8	7.9	5.1
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01


Male Rats
Percent of Pretest Body Weight
160
150
140
130
120
110
0
2
4
6
8
10
12
14
Days after Exposure
0 ppm
1500 ppm
3000 ppm
6000 ppm


Female Rats
Percent of Pretest Body Weight
140
130
120
110
100
0
2
4
6
8
10
12
14
Days after Exposure

EHL 94009/CMA Isobutanol AC NT - Forelimb Grip Strength (Kg)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.925	1.070	0.918	0.993	1.008
	SD	0.082	0.117	0.155	0.164	0.198
	# Rats	10	10	10	10	10
1500	Mean	0.904	1.037	1.015	0.987	1.123
	SD	0.101	0.177	0.196	0.196	0.231
	# Rats	10	10	10	10	10
3000	Mean	0.885	1.031	0.902	0.947	0.970
	SD	0.080	0.120	0.143	0.187	0.204
	# Rats	10	10	10	10	10
6000	Mean	0.928	1.034	0.941	0.964	1.033
	SD	0.125	0.166	0.220	0.200	0.259
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.893	0.999	0.841	0.873	0.905
	SD	0.162	0.167	0.191	0.126	0.255
	# Rats	10	10	10	10	10
1500	Mean	0.867	0.866	0.810	0.827	0.956
	SD	0.091	0.133	0.130	0.174	0.159
	# Rats	10	10	10	10	10
3000	Mean	0.876	0.995	0.903	0.884	0.953
	SD	0.094	0.160	0.159	0.179	0.182
	# Rats	10	10	10	10	10
6000	Mean	0.854	0.939	0.742	0.801	0.883
	SD	0.093	0.200	0.186	0.158	0.158
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Hindlimb Grip Strength (Kg)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.387	0.481	0.484	0.553	0.633
	SD	0.098	0.092	0.150	0.114	0.146
	# Rats	10	10	10	10	10
1500	Mean	0.377	0.479	0.537	0.555	0.646
	SD	0.100	0.133	0.127	0.113	0.148
	# Rats	10	10	10	10	10
3000	Mean	0.329	0.450	0.474	0.528	0.637
	SD	0.077	0.065	0.107	0.149	0.119
	# Rats	10	10	10	10	10
6000	Mean	0.390	0.498	0.478	0.553	0.606
	SD	0.049	0.115	0.133	0.114	0.143
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	0.381	0.443	0.447	0.448	0.445
	SD	0.078	0.089	0.078	0.074	0.090
	# Rats	10	10	10	10	10
1500	Mean	0.427	0.505	0.492	0.518	0.507
	SD	0.108	0.130	0.160	0.104	0.102
	# Rats	10	10	10	10	10
3000	Mean	0.398	0.529	0.461	0.534	0.479
	SD	0.057	0.100	0.091	0.098	0.127
	# Rats	10	10	10	10	10
6000	Mean	0.422	0.546	0.403	0.460	0.488
	SD	0.094	0.080	0.103	0.129	0.139
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

EHL 94009/CMA Isobutanol AC NT - Foot Splay (cm)

Test Material: Isobutanol

Male Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	6.5	5.9	5.6	5.2	5.7
	SD	1.2	1.0	1.4	0.7	1.4
	# Rats	10	10	10	10	10
1500	Mean	6.6	6.8	6.4	6.4	6.6
	SD	1.1	1.3	1.0	0.9	1.4
	# Rats	10	10	10	10	10
3000	Mean	7.4	7.0	6.7	6.3	6.7
	SD	1.8	1.7	1.8	1.6	2.2
	# Rats	10	10	10	10	10
6000	Mean	6.4	6.0	6.3	6.1	6.1
	SD	1.1	0.9	1.2	0.9	1.6
	# Rats	10	10	10	10	9

Female Rats

Dose Level (ppm)		Pretest	Day 0	Day 1	Day 7	Day 14
0	Mean	5.2	5.3	5.3	5.3LT	5.0
	SD	1.7	1.5	0.9	1.2	1.3
	# Rats	10	10	10	10	10
1500	Mean	5.2	5.0	5.0	5.5	5.5
	SD	0.8	0.8	0.8	0.7	1.1
	# Rats	10	10	10	10	10
3000	Mean	5.7	6.3	5.4	5.5	5.4
	SD	0.4	1.4	0.8	0.9	1.2
	# Rats	10	10	10	10	10
6000	Mean	5.0	4.9	5.3	5.3	5.3
	SD	1.1	0.8	1.2	1.6	0.9
	# Rats	10	10	10	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

Appendix 4: Summary Tables for Pathology

THIS REPORT WAS GENERATED FROM DATA LOCKED THROUGH 26-APR-94

STUDY NO: 94009 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 1

P A T H O L O G Y S E C T I O N

STUDY TYPE: AC SPECIES: RAT SUBSTANCE: PRINTED: 14-MAY-94

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

SELECTION CRITERIA: ALL DEATHS REPORTED

	---- M A L E ----			
	M00	M01	M02	M03
NO. IN GROUP AT RISK:	10	10	10	10
KIDNEY(S) -DILATED PELVIS	0	0	1	0
LY.NODE,SUBMAX. -ENLARGED/PROMINENT	0	0	0	0
SPLEEN -FOCUS, GRAY/WHITE	0	0	0	1
UTERUS -ENLARGED/DILATED/DISTENDED	0	0	0	0

STUDY NO: 94009

***** MONSANTO ENVIRONMENTAL HEALTH LAB *****
P A T H O L O G Y S E C T I O N

STUDY TYPE: AC SPECIES: RAT SUBSTANCE:

PRINTED: 14-MAY-94

SELECTION CRITERIA: ALL DEATHS REPORTED

** SUMMARY INCIDENCE OF INDIVIDUAL GROSS NECROPSY ALTERATIONS **

	---- F E M A L E ----			
	F00	F01	F02	F03
NO. IN GROUP AT RISK:	10	10	10	10
KIDNEY(S)				
-DILATED PELVIS	0	0	0	0
LY.NODE,SUBMAX.				
-ENLARGED/PROMINENT	0	1	0	0
SPLEEN				
-FOCUS, GRAY/WHITE	0	0	0	0
UTERUS				
-ENLARGED/DILATED/DISTENDED	0	3	1	1

Appendix 5: Inhalation Subreport

Inhalation Subreport for an Acute Inhalation Study of Isobutanol

Author: Terry A Kaempfe 9/15/94
T. A. Kaempfe, B.S. Date

SUMMARY

The inhalation exposure phase of an acute (single exposure/animal) neurotoxicity study of isobutanol was performed over four days. Four groups of 10 male and 10 female Sprague-Dawley rats were exposed to target isobutanol concentrations of 0 (control), 1500 (low), 3000 (mid) or 6000 ppm (high) for six hours. Five animals from each group were exposed each day, and each animal was exposed once for six hours. The mean analytical exposure concentrations were 1555, 3003 and 5961 ppm isobutanol for the low, mid and high exposure groups, respectively. Animals observed during exposure were hypoactive and/or nonresponsive, and had labored respiration at all three exposure concentrations.

INHALATION MATERIALS AND METHODS

Test Material

Name:	Isobutanol
Date Received:	December 27, 1993
Description:	Clear liquid
Lot Number:	EH 3639
Stated Purity:	>99.9%
EHL Test Substance Number:	T940007
Source:	Union Carbide Chemicals & Plastics Co. 10521 Sheldon Road Houston, Texas 77044

Exposure System

Exposure Chambers: Four 2000-liter Hazelton H-2000 stainless steel and glass chambers (Figure 1)

Animal Housing during Exposure: Individual stainless steel wire mesh cages, positioned in one tier in the chamber

Exposure Duration: 6 hours

Test Atmosphere Generation System: Test atmospheres were generated by feeding test isobutanol to a Laskin-type nebulizer (1) mounted in the supply air inlet at top of the chamber (Figure 1). The test atmosphere was mixed with the filtered supply air as it entered the chamber. The chamber exposure concentration was controlled by regulating the rate at which isobutanol was delivered to the nebulizer using an adjustable-flow valveless pump (Fluid Metering, Inc., Oyster Bay, NY).

Monitoring of Environmental Parameters: Chamber airflow, temperature and % relative humidity were monitored continuously and recorded approximately every 30 minutes.

Procedures for Monitoring the Amount of Test Material in the Chamber

Atmospheric Analytical Sampling: Six samples per exposure at approximately equal intervals

Sampling Method: Test atmosphere was drawn through a Miran 1A infrared detector (Foxboro Inc, Cambridge, MA) calibrated for isobutanol. The absorbance value was read and recorded, and the concentration was determined from the calibration curve (Exhibit 1).

Sampling Location: In the animal breathing area from a port halfway down on the chamber door

Analytical Method: Infrared absorption (Exhibit 1)

Nominal Concentration: Calculated once per exposure by determining the total amount (weight) of test material delivered to the chamber and

dividing this amount by the total air volume passing through the chamber during the exposure.

Uniformity of Chamber Distribution: Distribution of the test material throughout the chambers was determined, during the pretest period, by comparing the concentrations from two different points within the animal area of each chamber.

Observations

Pre-Exposure Body Weights: Each animal was weighed, prior to exposure, on the day it was exposed.

During Exposure Observations: Animals were observed for signs of toxicity once per hour during the exposures.

RESULTS

Exposure Concentrations

Mean nominal and analytical values for the three exposure levels of isobutanol were:

	Low	Mid	High
Target Level (ppm)	1500	3000	6000
Nominal ± S.D.	1474 ± 54	3488 ± 156	7029 ± 224
Analytical, IR ± S.D.	1555 ± 18	3003 ± 29	5961 ± 65
Nominal/Analytical, IR	0.95	1.16	1.18

Analytical and nominal concentration data for the exposures are presented in Tables 1 and 2. The nominal/analytical ratios indicate that very little test material was lost from impaction on the animals' cages and the chamber walls. This is consistent with the observation that little or no test material was present as an aerosol in the exposure chambers. This indicates that the test material was generated as a vapor. The uniformity of test material distribution within the chambers was acceptable at all levels (Table 3). Mean chamber environmental conditions are presented in Table 4.

Observations During Exposures

Signs of toxicity observed during the exposure periods are presented in Tables 5 and 6. Labored respiration was observed in most animals at

every exposure level. Hypoactivity and/or nonresponsiveness were also observed in most animals at every exposure level. One male animal at the 6000 ppm level was prostrate at the end of his exposure, and another male animal at the same level was lacrimating at the end of the exposure. However, both animals recovered by the next day.

Pre-Exposure Body Weights

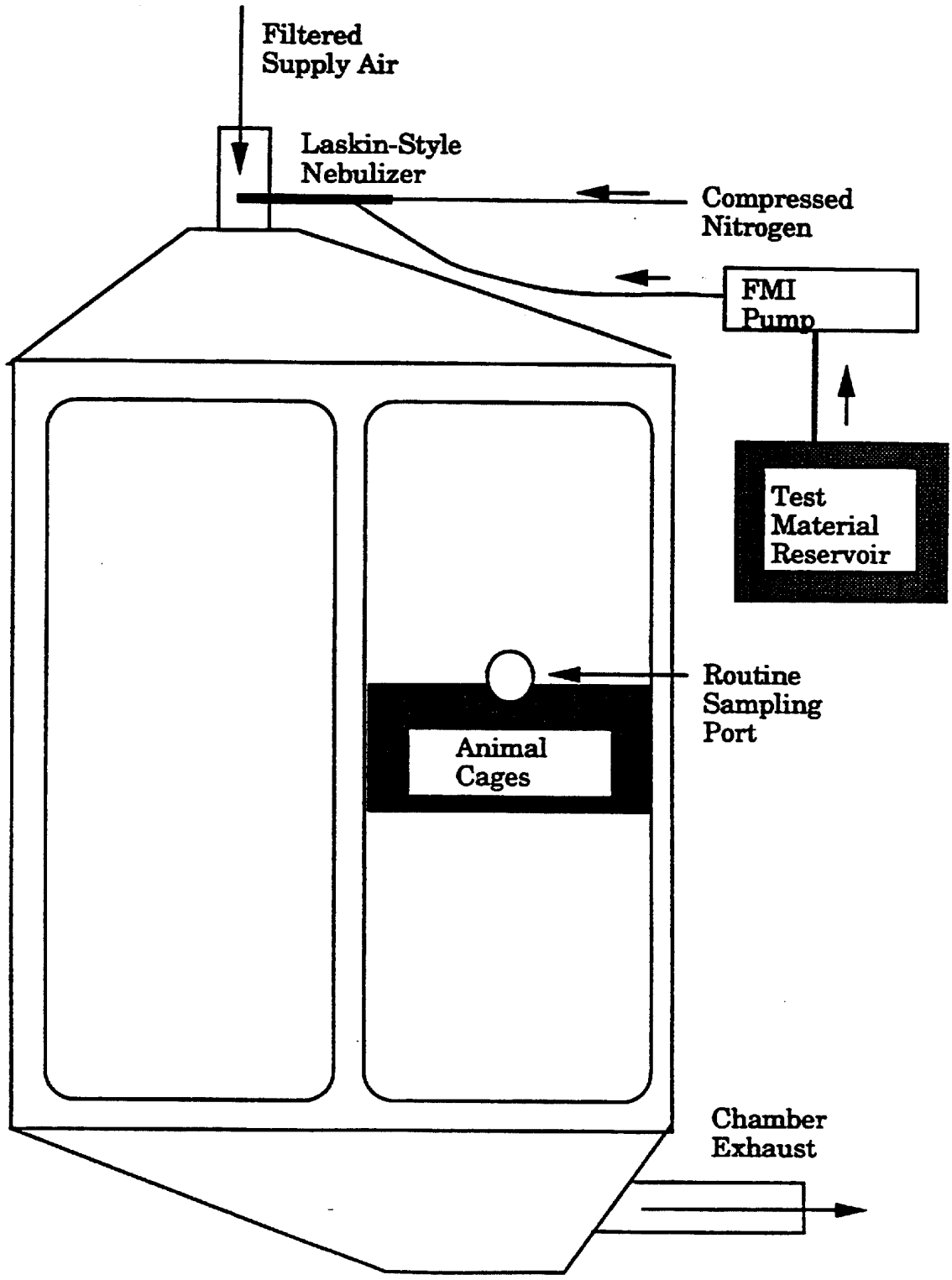
Pre-exposure body weights are presented in Table 7.

REFERENCES

1. Drew, R.T., Bernstein, D.M., and Laskin, S. The Laskin Generator. J. Tox. Environ. Health 4, 661-670 (1978).

2. Kennedy, G.L. Jr., Inhalation Toxicology. In: Principles and Methods in Toxicology, edited by A. W. Hayes, p. 373. Raven Press, New York (1989)

Figure 1
Inhalation Chamber And Generation System



Not to Scale
Arrows indicate direction of flow

EHL 94009 - Table 1
Daily Nominal and Mean Analytical Chamber Concentration Summary

	Run 1	Run 2	Run 3	Run 4	Overall	
					Mean	St. Dev.
Low Level (1500 ppm)						
Nominal	1485	1511	1394	1505	1474	54
Mean Analytical	1545	1577	1538	1561	1555	17
Nominal/Analyticial	0.96	0.96	0.91	0.96	0.95	0.03
Mid Level (3000 ppm)						
Nominal	3329	3581	3386	3657	3488	156
Mean Analytical	2963	3001	3028	3021	3003	29
Nominal/Analyticial	1.12	1.19	1.12	1.21	1.16	0.05
High Level (6000 ppm)						
Nominal	6844	7083	6865	7324	7029	224
Mean Analytical	5868	5996	6014	5966	5961	65
Nominal/Analyticial	1.17	1.18	1.14	1.23	1.18	0.04

EHL 94009 - Table 2

Analytical Chamber Concentrations of Isobutanol

Control Level (0 ppm)					
Hour of Exposure	Run 1	Run 2	Run 3	Run 4	Overall
1	0	0	0	0	
2	0	0	0	0	
3	0	0	0	0	
4	0	0	0	0	
5	0	0	0	0	
6	0	0	0	0	
Mean	0	0	0	0	0
St. Dev.	0	0	0	0	0

Low Exposure Level (1500 ppm)					
Hour of Exposure	Run 1	Run 2	Run 3	Run 4	Overall
1	1344	1576	1523	1568	
2	1409	1617	1580	1617	
3	1580	1587	1602	1568	
4	1757	1580	1512	1538	
5	1644	1538	1504	1546	
6	1538	1565	1504	1531	
Mean	1545	1577	1538	1561	1555
St. Dev.	152	26	43	31	18

Mid Exposure Level (3000 ppm)					
Hour of Exposure	Run 1	Run 2	Run 3	Run 4	Overall
1	2650	2963	3035	3050	
2	3071	2953	3098	2973	
3	3040	3035	3030	2928	
4	3040	2988	2999	2958	
5	2973	3025	3009	3146	
6	3004	3040	2999	3071	
Mean	2963	3001	3028	3021	3003
St. Dev.	157.0	37.9	37.4	82.3	29.3

High Exposure Level (6000 ppm)					
Hour of Exposure	Run 1	Run 2	Run 3	Run 4	Overall
1	5665	5890	6017	6049	
2	5665	5932	6114	6006	
3	5869	5974	6038	5964	
4	5995	5985	5974	5859	
5	6017	5985	5985	6038	
6	5995	6212	5953	5880	
Mean	5868	5996	6014	5966	5961
St. Dev.	165.5	112.0	57.9	80.6	65.2

Hour of Exposure refers to the time interval from the start of the exposure.

EHL 94009 - Table 3
Pretest Distribution of Isobutanol in Inhalation Chambers

Date:	3/9/94	3/9/94	3/9/94
Location	Low Level (ppm)	Mid Level (ppm)	High Level (ppm)
Front of Animal Area	1719	2999	5943
Back of Animal Area	1727	2907	5890
Mean	1723	2953	5917
% Range	0.5	3.1	0.9

% Range = [(High Value - Low Value)/Mean] X 100%

EHL 94009 - Table 4
Mean Chamber Environmental Measures

Level (Target)	Control	Low (1500 ppm)	Mid (3000 ppm)	High (6000 ppm)
Chamber Airflow (l/min)	513.0	441.9	426.5	434.1
St. Dev.	2.64	5.52	8.61	12.11
Airchanges/Hour	15	13	13	13
T99 (minutes)	18	21	22	21
Temperature (°C)	21.3	20.0	21.0	20.1
St. Dev.	0.13	0.57	0.46	0.43
% Relative Humidity	29.0	29.0	27.9	27.7
St. Dev.	9.32	7.66	8.09	9.08

Airchanges/Hour = Chamber Airflow (l/min) * 60 minutes/ Chamber Volume (2000 liters)

T99 = the time it takes for the concentration to reach 99% of equilibrium concentration.
= 4.6 * (Chamber Volume (2000 Liters)/Chamber Airflow)

Kennedy, G.L. Jr., (1989): Inhalation Toxicology. In: Principles and Methods in Toxicology edited by A.W. Hayes, p. 373. Raven Press , New York.

EHL 94009 - Table 5
Summary of Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Group	Approximate time of exposure (hours) 1:00	2:00	3:00	4:00	5:00	6:00
Labored Respiration	F00	0	0	0	0	0	0
	F01	0	5	7	8	8	8
	F02	7	7	7	7	7	7
	F03	8	8	8	10	10	10
	M00	0	0	0	0	0	0
	M01	0	6	7	7	7	7
	M02	8	8	8	8	8	8
	M03	7	7	7	10	10	10
Hypoactive	F00	0	0	0	0	0	0
	F01	0	0	2	7	8	10
	F02	4	6	10	5	5	6
	F03	10	10	7	4	1	0
	M00	0	0	0	0	0	0
	M01	0	0	2	7	9	10
	M02	6	8	10	3	5	5
	M03	10	9	6	2	1	1
Nonresponsive	F00	0	0	0	0	0	0
	F01	0	0	0	0	0	0
	F02	0	0	2	4	4	4
	F03	0	0	3	6	9	10
	M00	0	0	0	0	0	0
	M01	0	0	0	0	1	0
	M02	0	0	0	7	5	5
	M03	0	1	4	8	9	8
Prostrate	F00	0	0	0	0	0	0
	F01	0	0	0	0	0	0
	F02	0	0	0	0	0	0
	F03	0	0	0	0	0	0
	M00	0	0	0	0	0	0
	M01	0	0	0	0	0	0
	M02	0	0	0	0	0	0
	M03	0	0	0	0	0	1

Values represent the number of animals with the observation at each timepoint of ten total animals per group.

EHL 94009 - Table 5
Summary of Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Group	Approximate time of exposure (hours) 1:00	2:00	3:00	4:00	5:00	6:00
Lacrimation	F00	0	0	0	0	0	0
	F01	0	0	0	0	0	0
	F02	0	0	0	0	0	0
	F03	0	0	0	0	0	0
	M00	0	0	0	0	0	0
	M01	0	0	0	0	0	0
	M02	0	0	0	0	0	0
	M03	0	0	0	0	1	1
Normal	F00	10	10	10	10	10	10
	F01	10	5	3	2	2	0
	F02	3	3	0	0	0	0
	F03	0	0	0	0	0	0
	M00	10	10	10	10	10	10
	M01	10	4	3	3	0	0
	M02	2	2	0	0	0	0
	M03	0	0	0	0	0	0

Values represent the number of animals with the observation at each timepoint of ten total animals per group.

EHL 94009 - Table 6
Individual Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Number	Approximate time of exposure (hours)					
		1:00	2:00	3:00	4:00	5:00	6:00
Labored Respiration	F01 001			X	X	X	X
	F01 002		X	X	X	X	X
	F01 004		X	X	X	X	X
	F01 005		X	X	X	X	X
	F01 006			X	X	X	X
	F01 007		X	X	X	X	X
	F01 009		X	X	X	X	X
	F01 010				X	X	X
	M01 001			X	X	X	X
	M01 002		X	X	X	X	X
	M01 004		X	X	X	X	X
	M01 005		X	X	X	X	X
	M01 006		X	X	X	X	X
	M01 007		X	X	X	X	X
	M01 009		X	X	X	X	X
	F02 001	X	X	X	X	X	X
	F02 002	X	X	X	X	X	X
	F02 004	X	X	X	X	X	X
	F02 005	X	X	X	X	X	X
	F02 006	X	X	X	X	X	X
	F02 007	X	X	X	X	X	X
	F02 009	X	X	X	X	X	X
	M02 001	X	X	X	X	X	X
	M02 002	X	X	X	X	X	X
	M02 004	X	X	X	X	X	X
	M02 005	X	X	X	X	X	X
	M02 006	X	X	X	X	X	X
	M02 007	X	X	X	X	X	X
	M02 009	X	X	X	X	X	X
	M02 010	X	X	X	X	X	X
	F03 001	X	X	X	X	X	X
	F03 002	X	X	X	X	X	X
	F03 003				X	X	X
	F03 004	X	X	X	X	X	X
	F03 005	X	X	X	X	X	X
	F03 006	X	X	X	X	X	X
	F03 007	X	X	X	X	X	X
	F03 008				X	X	X
	F03 009	X	X	X	X	X	X
	F03 010	X	X	X	X	X	X
	M03 001	X	X	X	X	X	X

EHL 94009 - Table 6
Individual Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Number	Approximate time of exposure (hours)					
		1:00	2:00	3:00	4:00	5:00	6:00
Labored Respiration	M03 002	X	X	X	X	X	X
	M03 003				X	X	X
	M03 004	X	X	X	X	X	X
	M03 005				X	X	X
	M03 006	X	X	X	X	X	X
	M03 007	X	X	X	X	X	X
	M03 008				X	X	X
	M03 009	X	X	X	X	X	X
	M03 010	X	X	X	X	X	X
Hypoactive	F01 001			X	X	X	X
	F01 002				X	X	X
	F01 003						X
	F01 004				X	X	X
	F01 005				X	X	X
	F01 006			X	X	X	X
	F01 007				X	X	X
	F01 008						X
	F01 009				X	X	X
	F01 010					X	X
	M01 001			X	X		X
	M01 002				X	X	X
	M01 003					X	X
	M01 004				X	X	X
	M01 005				X	X	X
	M01 006			X	X	X	X
	M01 007				X	X	X
	M01 008					X	X
	M01 009				X	X	X
	M01 010					X	X
	F02 001	X	X	X	X		
	F02 002	X	X	X		X	X
	F02 003			X	X	X	
	F02 004			X	X	X	X
	F02 005		X	X		X	X
	F02 006	X	X	X	X		
	F02 007	X	X	X	X	X	X
	F02 008			X			X
	F02 009		X	X			X
	F02 010			X			
	M02 001	X	X	X			
	M02 002	X	X	X	X	X	X

EHL 94009 - Table 6
Individual Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Number	Approximate time of exposure (hours)					
		1:00	2:00	3:00	4:00	5:00	6:00
Hypoactive	M02 003			X			
	M02 004		X	X		X	X
	M02 005	X	X	X			
	M02 006	X	X	X	X		
	M02 007	X	X	X		X	X
	M02 008			X			
	M02 009		X	X	X	X	X
	M02 010	X	X	X		X	X
	F03 001	X	X		X		
	F03 002	X	X	X			
	F03 003	X	X	X		X	
	F03 004	X	X	X			
	F03 005	X	X		X		
	F03 006	X	X		X		
	F03 007	X	X	X	X		
	F03 008	X	X	X			
	F03 009	X	X	X			
	F03 010	X	X	X			
	M03 001	X	X				
	M03 002	X	X	X			
	M03 003	X	X	X			
	M03 004	X	X	X	X		
	M03 005	X	X	X		X	
	M03 006	X	X	X	X		
	M03 007	X	X				
	M03 008	X	X	X			
	M03 009	X	X				X
	M03 010	X					
Nonresponsive	M01 001					X	
	F02 001					X	X
	F02 002				X		
	F02 003						X
	F02 005			X			
	F02 006					X	X
	F02 008				X	X	
	F02 009			X	X		
	F02 010				X	X	X
	M02 001				X	X	X

EHL 94009 - Table 6
Individual Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Number	Approximate time of exposure (hours)					
		1:00	2:00	3:00	4:00	5:00	6:00
Nonresponsive	M02 003				X	X	X
	M02 004				X		
	M02 005				X	X	X
	M02 006					X	X
	M02 007				X		
	M02 008				X	X	X
	M02 010				X		
	F03 001			X		X	X
	F03 002				X	X	X
	F03 003				X		X
	F03 004				X	X	X
	F03 005			X		X	X
	F03 006			X		X	X
	F03 007					X	X
	F03 008				X	X	X
	F03 009				X	X	X
	F03 010				X	X	X
	M03 001			X	X	X	X
	M03 002				X	X	X
	M03 003				X	X	X
	M03 004					X	
	M03 005				X		X
	M03 006					X	X
	M03 007			X	X	X	X
	M03 008				X	X	X
	M03 009			X	X	X	
	M03 010		X	X	X	X	X
Prostrate	M03 004						X
Lacrimation	M03 006					X	X
Normal	F00 001	X	X	X	X	X	X
	F00 002	X	X	X	X	X	X
	F00 003	X	X	X	X	X	X
	F00 004	X	X	X	X	X	X
	F00 005	X	X	X	X	X	X
	F00 006	X	X	X	X	X	X
	F00 007	X	X	X	X	X	X
	F00 008	X	X	X	X	X	X
	F00 009	X	X	X	X	X	X
	F00 010	X	X	X	X	X	X

EHL 94009 - Table 6
Individual Occurences of Signs of Toxicity Observed During Exposure

Observation	Animal Number	Approximate time of exposure (hours)					
		1:00	2:00	3:00	4:00	5:00	6:00
Normal	M00 001	X	X	X	X	X	X
	M00 002	X	X	X	X	X	X
	M00 003	X	X	X	X	X	X
	M00 004	X	X	X	X	X	X
	M00 005	X	X	X	X	X	X
	M00 006	X	X	X	X	X	X
	M00 007	X	X	X	X	X	X
	M00 008	X	X	X	X	X	X
	M00 009	X	X	X	X	X	X
	M00 010	X	X	X	X	X	X
	F01 001	X	X				
	F01 002	X					
	F01 003	X	X	X	X	X	
	F01 004	X					
	F01 005	X					
	F01 006	X	X				
	F01 007	X					
	F01 008	X	X	X	X	X	
	F01 009	X					
	F01 010	X	X	X			
	M01 001	X	X				
	M01 002	X					
	M01 003	X	X	X	X		
	M01 004	X					
	M01 005	X					
	M01 006	X					
	M01 007	X					
	M01 008	X	X	X	X		
	M01 009	X					
	M01 010	X	X	X	X		
	M02 003	X	X				
	M02 008	X	X				
	F02 003	X	X				
	F02 008	X	X				
	F02 010	X	X				

EHL 94009 - Table 7 - Pre-Exposure Body Weights

Animal Number	Body Weight (grams)	Animal Number	Body Weight (grams)
M00 001	307.9	F00 001	200.7
M00 002	342.9	F00 002	244.5
M00 003	345.1	F00 003	230.7
M00 004	358.5	F00 004	230.7
M00 005	314.6	F00 005	225.1
M00 006	336.6	F00 006	217.3
M00 007	353.4	F00 007	223.4
M00 008	321.1	F00 008	228.9
M00 009	387.8	F00 009	215.6
M00 010	362.0	F00 010	206.6
M01 001	314.5	F01 001	208.7
M01 002	344.5	F01 002	251.4
M01 003	323.2	F01 003	266.4
M01 004	372.8	F01 004	217.1
M01 005	361.8	F01 005	219.6
M01 006	342.3	F01 006	211.5
M01 007	360.8	F01 007	186.8
M01 008	307.7	F01 008	219.6
M01 009	334.7	F01 009	209.2
M01 010	327.6	F01 010	202.6
M02 001	327.9	F02 001	235.9
M02 002	315.9	F02 002	263.7
M02 003	333.3	F02 003	215.9
M02 004	331.5	F02 004	244.1
M02 005	328.6	F02 005	215.7
M02 006	320.5	F02 006	201.9
M02 007	317.6	F02 007	214.0
M02 008	322.9	F02 008	225.7
M02 009	320.9	F02 009	264.1
M02 010	308.9	F02 010	194.0
M03 001	302.9	F03 001	212.8
M03 002	317.4	F03 002	225.1
M03 003	330.4	F03 003	220.5
M03 004	344.6	F03 004	227.6
M03 005	307.3	F03 005	234.4
M03 006	322.9	F03 006	230.7
M03 007	334.9	F03 007	230.2
M03 008	360.6	F03 008	206.8
M03 009	321.4	F03 009	289.6
M03 010	288.3	F03 010	237.2

Analytical Procedure for the Determination of Isobutanol in Air

Study Number: 94009

Description:

This is an infrared analyzer method designed to measure the concentration of an atmosphere containing isobutanol vapor. Concentration calibrations range from 230 to 9300 ppm. Samples of test atmosphere will be drawn directly through an infrared analyzer; light of the desired wavelength is absorbed by the test chemical, detected by the instrument and output through a gauge. This value is recorded.

Instrumentation:

Wilks Miran® General Purpose Gas Analyzer with ambient air pump

Analyzer (#1A-1815)

Wavelength:	9.6 µm
Pathlength:	0.75 meters (0.05 dial reading)
Slit Width:	2 mm
Range:	1A
Course Zero:	X10
Meter Response:	1 sec

Analyzer (#1A-2918)

Wavelength:	9.6 µm
Pathlength:	0.75 meters (14.97 dial reading)
Slit Width:	2 mm
Range:	1A
Course Zero:	X1
Meter Response:	1 sec

Analyzer (#1A-2264)

Wavelength:	9.6 µm
Pathlength:	0.75 meters (14.86 dial reading)
Slit Width:	2 mm
Range:	1A
Course Zero:	X10
Meter Response:	1 sec

Materials:

Isobutanol, Lot #EH 3639, stated purity > 99.9%, EHL Test Substance Number is T940007

Calculations

1. Standard Concentration for all Calibration Loops:

$$C\ (ppm) = \frac{0.8030\ (g/ml) * \text{Injection Volume}\ (\mu l) * 24.4\ (\text{liters/mole}) * 10^6}{74.12\ (g/mole) * 5.64\ (\text{liters}) * (1000\ \mu l/ml)}$$

Where: C = Standard Concentration (ppm)
5.64 = volume of the closed loop (Liters)
0.8030 = the density of isobutanol (g/ml)
24.4 = molar volume of a vapor at 25° C at 1 atm. (liters/mole)
74.12 = molecular weight of isobutanol (g/mole)
10^6 = conversion factor for ppm units

2. Calibration Curve:

The standards listed in Tables 1, 2 and 3 are used to graph the calibration curve (Figures 1, 2 and 3) and fit a curve using the Fit Function procedure in the software application DeltaGraph Pro (Delta Point Inc., Monterey, CA).

3. Concentration of Test Material in Air

The concentration of test material in the test atmosphere is obtained by converting the absorbance measured by the Miran IR Analyzer to ppm using the appropriate calibration curve.

Comments

Samples are drawn through the analyzer using the system pump. The inlet and outlet tubes of the analyzer are connected to the exposure chamber creating a closed-loop system. Readings are taken approximately every 30 minutes.

The development of the method is found in the study record.

A check of the calibration should be performed on each study day. The check is performed by injecting a volume of the test material to achieve a desired concentration. The expected absorbance is compared to the absorbance measured by the instrument. The calibration checks should be within 10% of the standard. If repeated checks do not fall within 10% of the standard the instrument should be recalibrated. The calibration checks should be performed so that the exposure level concentrations fall within the calibration range of the instrument.

The following personnel are trained in the use of this method and are capable of performing these analyses:

Name	Date Training Completed
Bob Quevreaux	1/28/94
Terry Kaempfe	1/28/94
Steve Becktame	2/22/94
Myron Lewis	3/10/94

Prepared by: _____ Date: 3-14-94

Reviewed by: _____ Date: 3-14-94

Table 1

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-1815

Volume of Test Material (µl)	Concentration (ppm)	A, Mean Absorbance
5	234	0.066
10	469	0.132
25	1172	0.313
50	2343	0.583
75	3515	0.806
100	4687	0.985
125	5859	1.122
150	7030	1.227
175	8202	1.310
200	9374	1.375

Least Squares Fit: $Conc = 4430.382*A^3 - 5455.854*A^2 + 6006.315*A - 207.0674$

$R^2 = 0.99936$

where A = absorbance reading and

Conc = concentration in ppm of isobutanol

Calibration Date: 26 January 1994
Calibration Check: 22 February 1994

Table 2

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-2264

Volume of Test Material (µl)	Concentration (ppm)	A, Mean Absorbance
5	234	.055
10	469	.108
25	1172	.255
50	2343	.453
75	3515	.604
100	4687	.715
125	5859	.798
150	7030	.863
175	8202	.918
200	9374	.965

Least Squares Fit: $Conc = 13359.49*A^3 - 10384.63*A^2 + 7437.031*A - 195.8215$
$R^2 = 0.99973$
where A = absorbance reading and
Conc = concentration in ppm of isobutanol

Calibration Date: 26 January 1994
Calibration Check: 23 February 1994

Table 3

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-2918

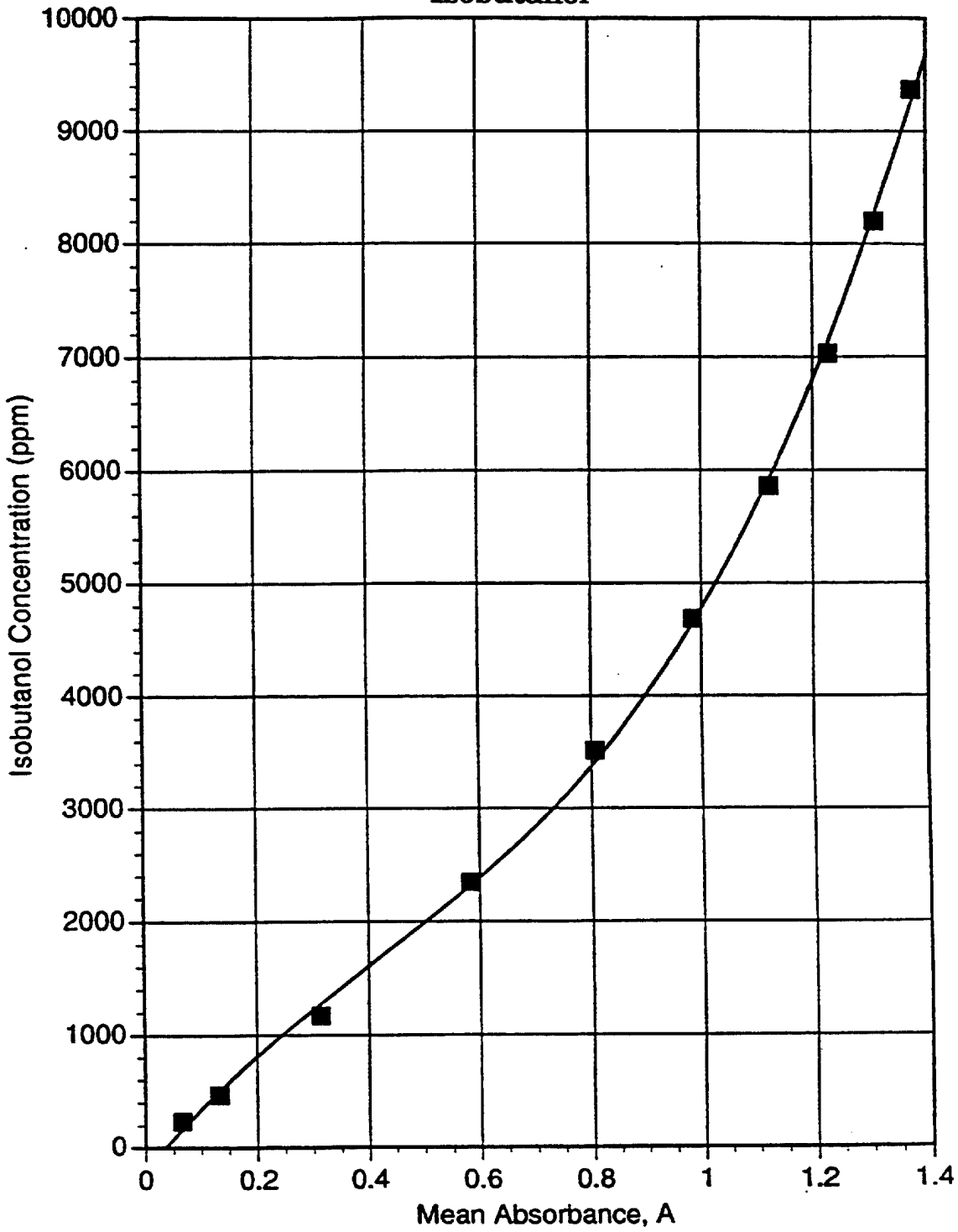
Volume of Test Material (µl)	Concentration (ppm)	A, Mean Absorbance
5	234	.047
10	469	.090
25	1172	.211
50	2343	.384
75	3515	.531
100	4687	.656
125	5859	.766
150	7030	.864
175	8202	.955
200	9374	1.033

Least Squares Fit: $Conc = 2033.326*A^3 + 1640.051*A^2 + 5212.372*A - 15.93514$
$R^2 = 0.99999$

where A = absorbance reading and
Conc = concentration in ppm of isobutanol

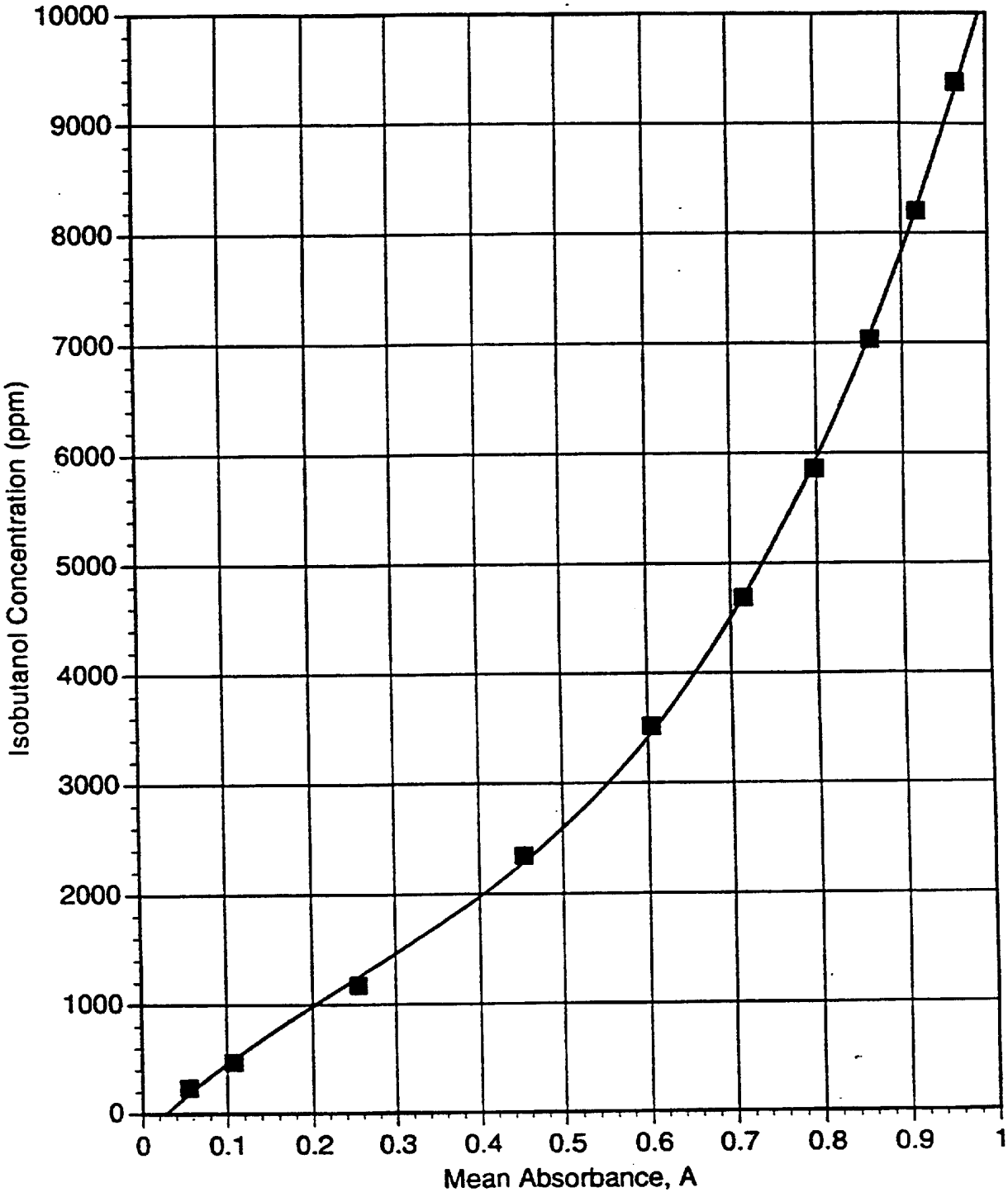
Calibration Date: 23 February 1994

Figure 1
EHL 94009 -- Miran 1A-1815 Calibration Curve for Isobutanol



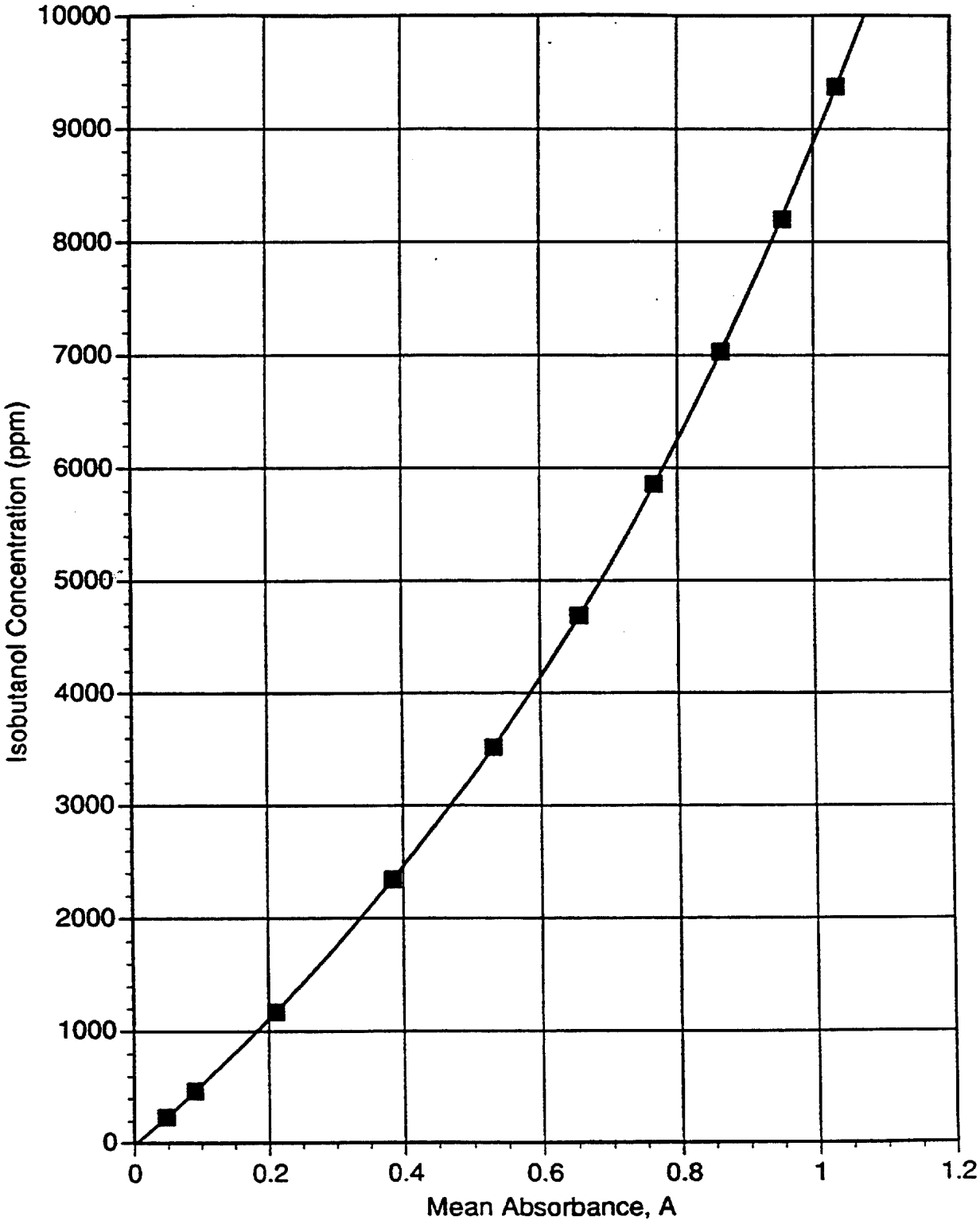
Conc (ppm) = 4430.382*A^3 - 5455.854*A^2 + 6006.315*A -207.0671
R0^2 = 9.993647E-1

Figure 2
EHL 94009 - Miran 1A-2264 Calibration Curve for Isobutanol



Conc (ppm) = 13359.49*A^3 -10384.63*A^2 + 7437.031*A -195.8215
R0^2 = 9.997337E-1

Figure 3
EHL 94009 - Miran 1A-2918 Calibration Curve for Isobutanol



Conc (ppm) = 2033.326*A^3 + 1640.051*A^2 + 5212.372*A -15.93514
R0^2 = 9.999892E-1

Appendix 6: Analytical Chemistry Reports

BUSINESS CONFIDENTIAL PROJECT REPORT

ISOBUTANOL

GLP ANALYSIS - FINAL REPORT

AUTHORS: N. A. Broyles (2)
R. A. McDonie (2)

SUPERVISORS: T. L. Dawson (2)

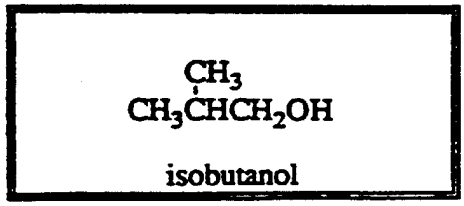
DATE:

STUDY #: 37-AEG-131

FILE NO:

SUMMARY Isobutanol was analyzed to provide analytical data to Chemical Manufacturers Association (CMA) for toxicity testing at Monsanto Company. The analyses were performed in compliance with Good Laboratory Practice standards (GLP) to meet EPA Section 4 Test Rule requirements and FDA, 21 CFR 58. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the sample's identity. Purity, measured by capillary GC, is ≈99.9%. The sample was received from Union Carbide Corporation Technical Center, South Charleston, WV. All raw data, documentation, records, protocols, final reports, and the sample are being retained.

Shown at right is the structure of isobutanol; its Chemical Abstracts Service Registry number (CAS #) is 78-83-1.



Nancy A. Broyles

Richard A. McDonie

NAB/RAM
Date Study initiated: 2/14/94
Manuscript date (Date Study completed): 4/20/94
Attachments: 1 GLP Report

KEY WORDS: RN=00078-83-1.

RESEARCH AND DEVELOPMENT
UNION CARBIDE CORPORATION. (UCC)
SOUTH CHARLESTON, WEST VIRGINIA

UNION CARBIDE

Union Carbide Corporation

STUDY TITLE

GLP Analysis-Final Report

TEST SUBSTANCE

Isobutanol

DATA REQUIREMENT

U.S. FDA, 21 CFR 58
U.S. EPA TSCA, 40 CFR 792
U.S. EPA FIFRA 40 CFR 160

STUDY DIRECTOR

Nancy A. Broyles

STUDY COMPLETED ON

April 20, 1994

PERFORMING LABORATORY

Union Carbide Corporation
PO Box 8361
South Charleston, West Virginia 25303

UCC R/D LABORATORY PROJECT ID

Study # 37-AEG-131

SPONSOR COMPANY

Chemical Manufacturers Association
2501 M Street, NW
Washington, DC 20037

STUDY COMPLIANCE STATEMENT

Study Compliance Statement for Union Carbide Corporation (UCC) Study # 37-AEG-131, isobutanol study for Chemical Manufacturers Association (CMA), Washington, D.C.

To the best of the signers knowledge and belief, the study described by this report was conducted in compliance with the U.S. EPA Good Laboratory Practice standards; TSCA 40 CFR 792 (revision effective as of September 18, 1989); FIFRA 40 CFR 160 (revision effective as of October 16, 1989) and FDA, 21 CFR 58 (revision effective as of October 5, 1987). All original raw data, records, protocols, final reports, and the sample are being retained at UCC's South Charleston, WV, Technical Center.

Nancy A. Broyles 4/20/94

Nancy A. Broyles Date
Study Director
Union Carbide Corporation

Barbara Francis 4/25/94

Barbara Francis Date
Associate Director, Oxo Process Panel
Chemical Manufacturers Association

PROTOCOL DEVIATION STATEMENT

Protocol Deviation Statement for Union Carbide Corporation (UCC) Study # 37-AEG-131, isobutanol study for Chemical Manufacturers Association, Washington, DC.

In accordance with UCC's intent that all tests conducted by our facility follow good laboratory practices, UCC's study director for the above test confirms that there were no protocol deviations taken during the study. The study was conducted in compliance with the protocol established and signed on 2/14/94 by Alexander E. Gabany, GLP Study Director. A protocol amendment was signed on April 15, 1994 indicating a change in Study Director effective April 1, 1994.

Nancy A. Broyles 4/20/94
Nancy A. Broyles Date
Study Director

SIGNATURE PAGE

Submitted by: Union Carbide Corporation
P.O. Box 8361
South Charleston, West Virginia 25303

Prepared by:

Nancy A. Broyles 4/20/94
Nancy A. Broyles
Study Director
Date

Richard A. McDonie 4-28-94
Richard A. McDonie
GC/MS Skill Area Specialist
Date

Quality Assurance Review by:

Denise L. Johnson 4-21-94
Denise L. Johnson
GLP Quality Assurance Unit
(QAU) Representative
Date

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Isobutanol

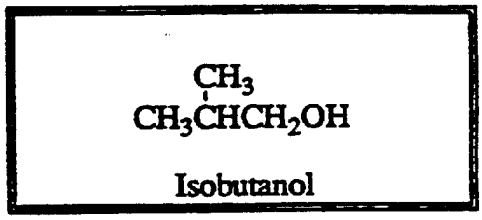
Isobutanol
Study # 37-AEG-131

ABSTRACT Isobutanol was analyzed to provide analytical data to Chemical Manufacturers Association (CMA) for toxicity testing at Monsanto Company. The analyses were performed in compliance with Good Laboratory Practice standards (GLP) to meet EPA Section 4 Test Rule requirements and FDA, 21 CFR 58. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the sample's identity. Purity, measured by capillary GC, is ≈99.9%. The sample was received from Union Carbide Corporation Technical Center, South Charleston, WV. All raw data, documentation, records, protocols, final reports, and the sample are being retained.

INTRODUCTION Barbara Francis, Associate Director, Oxo Process Panel, Chemical Manufacturers Association (CMA), this study's sponsor, requested that Union Carbide Corporation (UCC) provide analytical data for toxicity testing at Monsanto Company. Such studies must follow GLP standards established by the EPA that require they be conducted with a material whose identity and purity are verified analytically.

An ≈ 40 gram sample of isobutanol (37-AEG-134) was received 1/3/94 in a clear glass bottle for analytical characterization. This sample is a subsample of a larger quantity of isobutanol from UCC's Texas City facility (Analysis # EH 3639) tested at Monsanto Company. A GLP protocol describing the analytical characterization of the sample was prepared (Appendix I). The protocol called for structural identification by NMR and GC/MS and for the capillary GC measurement of any impurities identified by GC/MS. Subsequently, the protocol was amended (Appendix II) to include only a change in Study Director.

Shown at right is the structure of Isobutanol; its Chemical Abstracts Service Registry number (CAS #) is 78-83-1.



DISCUSSION The data from the analyses are summarized below.

NMR Analyses Proton and carbon NMR data were collected in the UCC NMR Skill Center using a General Electric GN-300NB spectrometer. The acquisition parameters are shown in the figures; for the ^1H NMR spectrum, the pulses used correspond to <3° flip angles; the ^{13}C flip angles were 30°; the $^{13}C\{^1H\}$ (proton decoupled ^{13}C) spectrum used Waltz 16 modulation for ^1H decoupling. The spectra were not acquired under quantitative conditions; the acquisition conditions were established to identify the major component and to look for any substantial impurities. The sample was dissolved in deuterochloroform for analysis; tetramethylsilane (TMS) was added to provide an internal chemical shift reference. The TMS and deuterochloroform were used as received.

Figure 1 shows the ^1H NMR spectrum obtained from the sample 37-AEG-134. The observed chemical shifts, spin-spin coupling patterns, and relative intensities are appropriate for isobutanol: the rapidly exchanging hydroxyl proton is seen as a singlet at 4.00 ppm; the methylene protons are seen as a doublet at 3.35 ppm; the methine proton is seen as a nine-line pattern centered at 1.74 ppm; the methyl protons are seen as a doublet at 0.91 ppm. ^{13}C-satellites are seen as small lines around the methyl and methylene doublets. Minor peaks for residual $CHCl_3$ in the $CDCl_3$ and for TMS are seen at 7.38 ppm and 0 ppm, respectively.

Figure 2 shows the $^{13}C\{^1H\}$ spectrum for the same sample. No unusual or unexpected resonances are seen; the three types of carbons present in isobutanol are seen: the methylene carbon is at 69.3 ppm; the methine carbon is at 30.8 ppm; the methyl carbons are at 19.0 ppm. The 1:1:1 triplet at 77.3 ppm is from the deuterochloroform, and TMS is at 0 ppm.

The NMR spectra are totally consistent with the sample being pure isobutanol.

GC/MS Analysis Electron ionization (EI) mass spectral data were collected in the UCC MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard (HP) 5890 gas chromatograph. The sample, 37-AEG-134, was analyzed by injecting 0.1 µL aliquots onto a CP-Sil-5-CB capillary column held at 30°C for 4 minutes, and then programmed to 250°C at 8°/minute. Figure 3 shows the EI total ion current chromatogram for the

sample (scanned from m/z 10 to m/z 310 EI mode). This chromatogram is annotated with identifications based on the components' EI mass spectrum.

Capillary GC A HP 5890 gas chromatograph equipped with a flame ionization detector was used to analyze the sample. Aliquots (1 µL) were injected via autoinjector with a 100:1 split ratio onto a DB-1 capillary column started at 60°C and held for 4 minutes, then programmed to 250°C at 12°/minute (see Figure 4). The averages of triplicate analysis are given below (normalized chromatogram area percent).

Component name	Retention time, min.	37-AEG-134
n-propanol	3.8	0.02
butyraldehyde	4.2	0.01
Isobutanol	5.1	99.9
n-butanol	5.5	0.03
methyl butyrate	6.8	0.006
isobutyl ether	9.7	0.007
C_8-aldehyde	10.6	0.003
all other impurities		0.02

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC Skill Centers show that this sample is isobutanol. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purity, measured by capillary GC, is ≈ 99.9%.

ARCHIVES All raw data, records, protocols, samples, and final reports are being retained at UCC's South Charleston, WV, Technical Center as follows:

- raw data from GC, NMR, and GC/MS studies are in 770-361, 770-127, and 770-123, respectively;
- protocols, notebook and other records are to be kept in the GLP archives;
- the remainder of each sample is being kept in a locked GLP sample box in 770-361.

ACKNOWLEDGMENTS We would like to thank Trudy Barker for sample handling, collecting the GC data, and preparing the bulk of the report, and Kathy Canterbury for collecting the NMR data.

NOTEBOOK REFERENCE: 37-AEG-131 and related pages

Confidentiality No claim of confidentiality is made for any information contained in this study as it pertains to use by any government agency to which it is submitted. This document, however, is proprietary to UCC and is confidential and trade secret information in all other countries and for all purposes other than those directly related to the purposes of the reviewing agency. Information contained in these studies should not be reviewed, abstracted or used by persons other than the agency without the expressed written consent of UCC except as required to carry out statutory requirements.

Figure 1 — ^{1}H NMR Spectrum of 37-AEG-134 (Isobutanol)

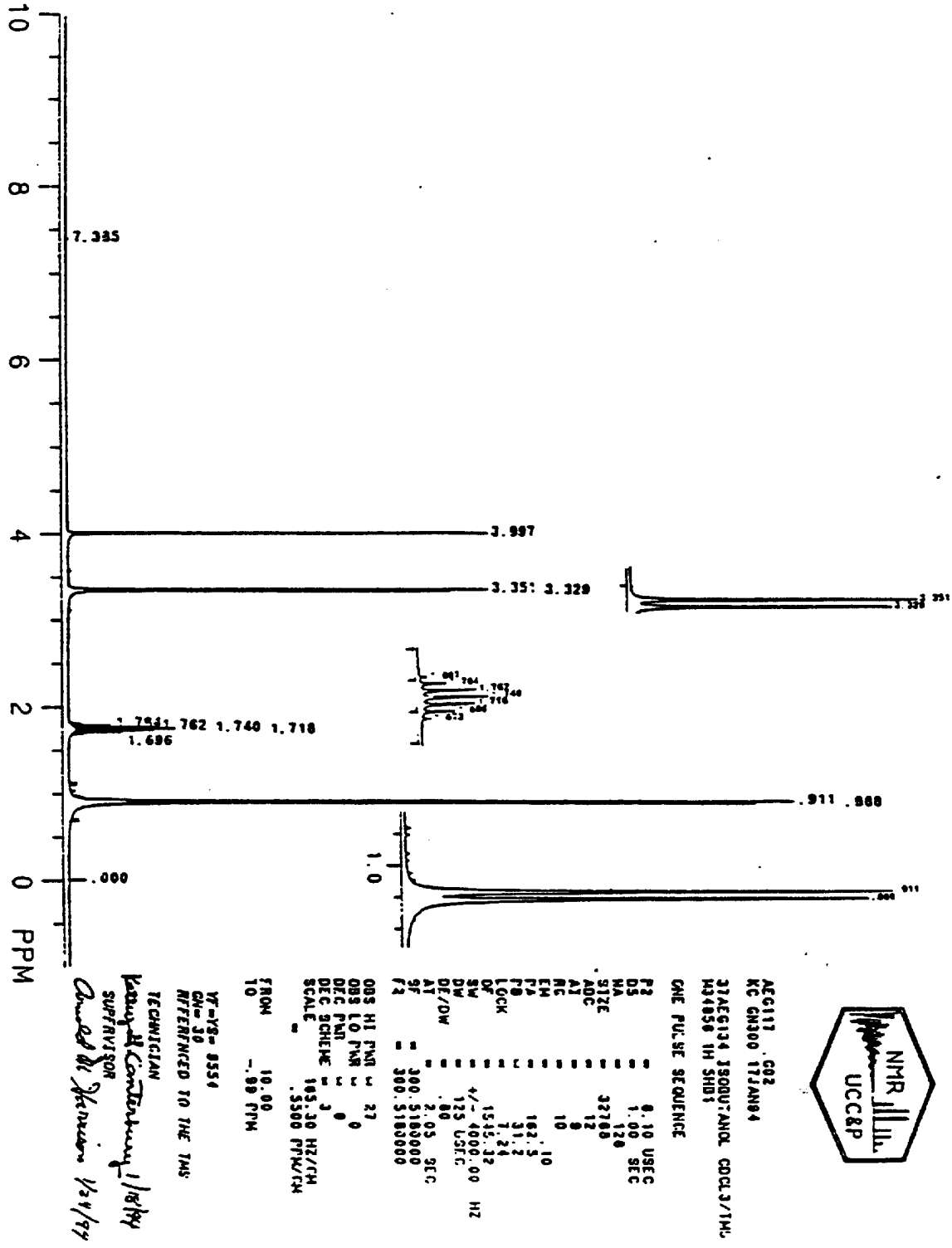


Figure 2 — ^{13}C NMR Spectrum of 37-AEG-134 (Isobutanol)

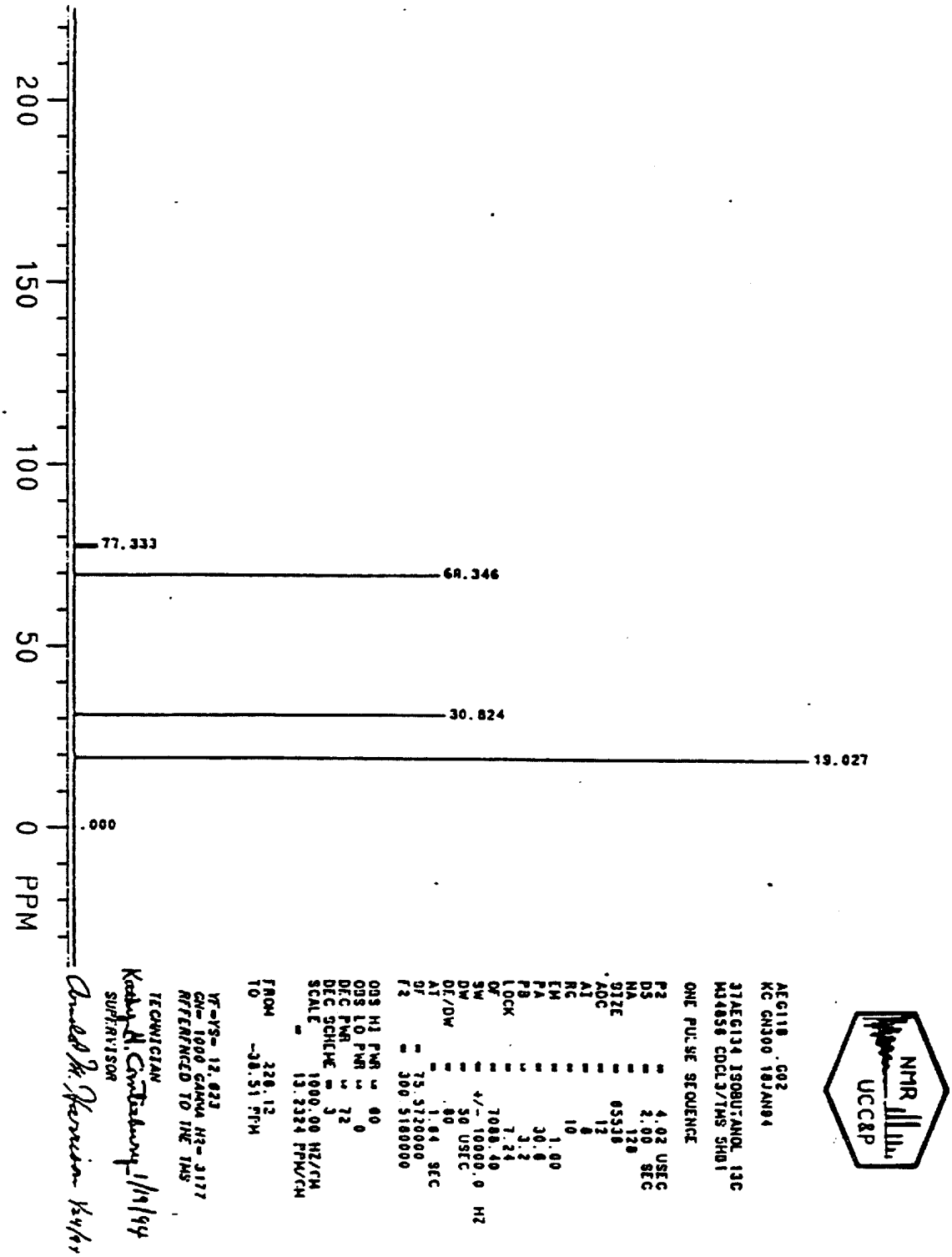


Figure 3 — Capillary GC/MS RIC of 37-AEG-134 (Isobutanol)

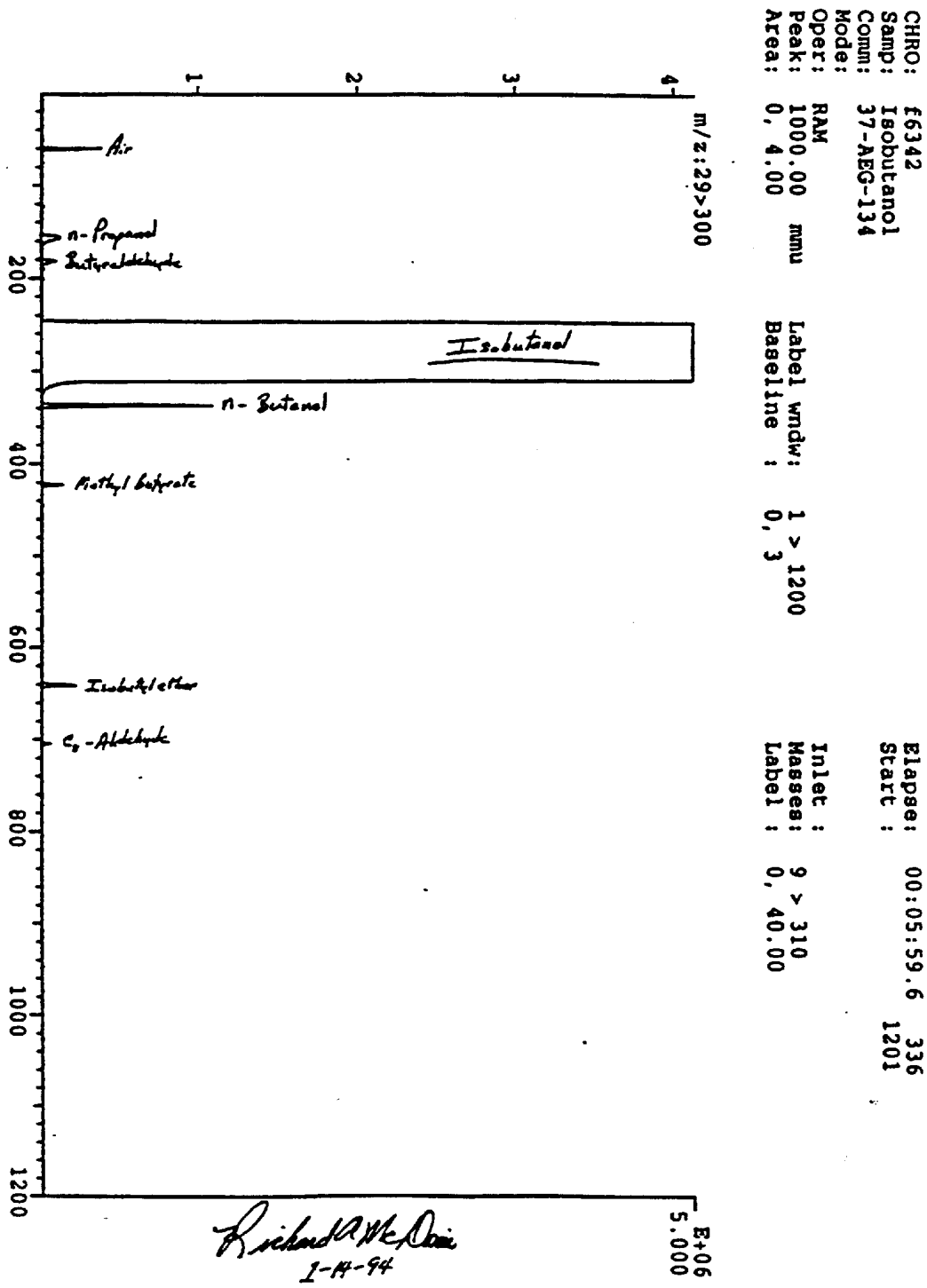
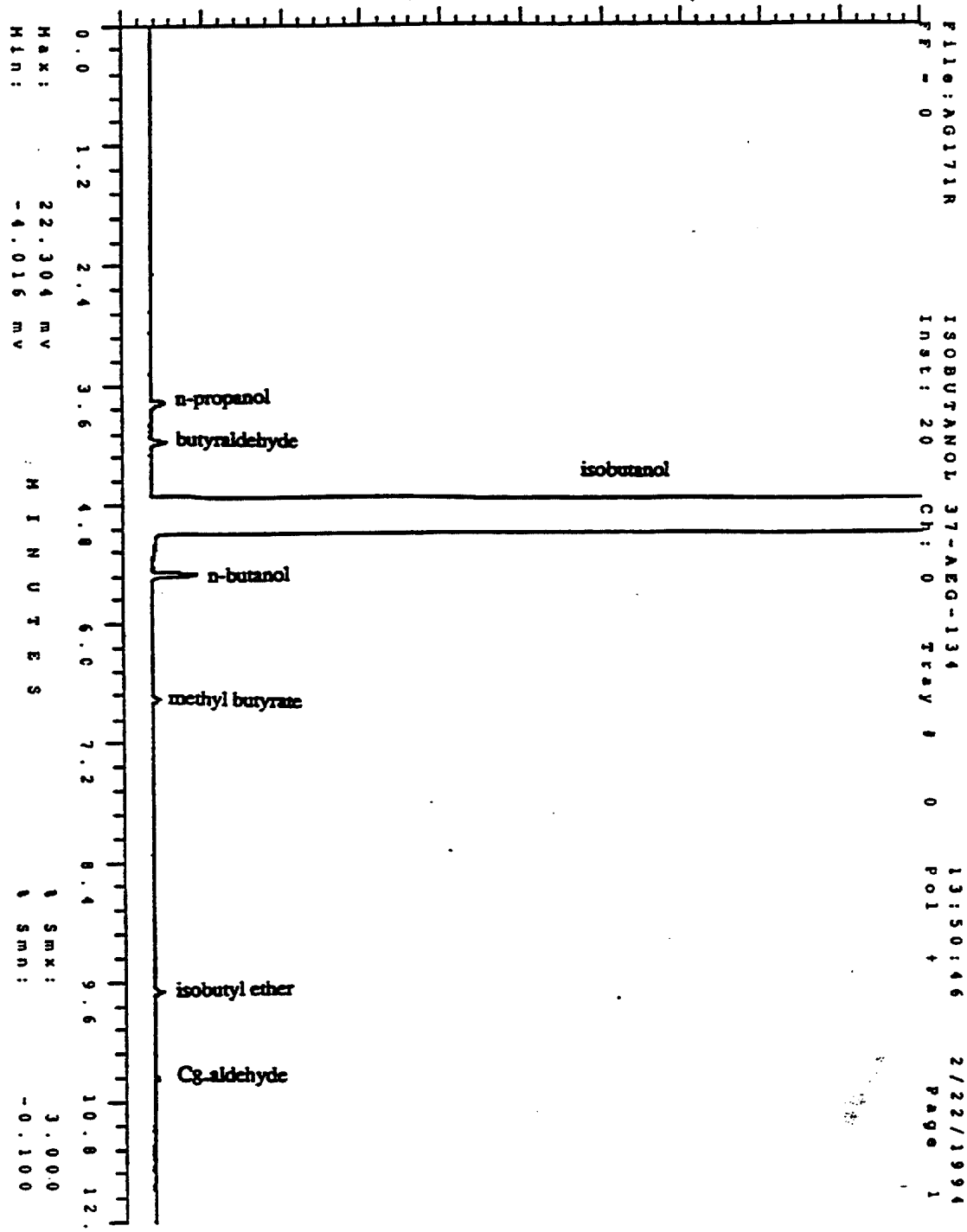


Figure 4 — Capillary Gas Chromatogram of 37-AEG-134 (Isobutanol)

Trudy C Barker 2/23/94



APPENDIX I **Protocol**

PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

title	Isobutanol
purpose	Analytical Characterization of Sample(s) for neurotoxicity testing at Monsanto Company
study number	37-AEG-131
sponsor	CMA Oxo Process Panel Chemical Manufacturers Association 2501 M Street, NW Washington, DC 20037
testing facility	UCC Technical Center, South Charleston, WV 25303 (Location 511)

Proposed Starting Date: Monday, February 14, 1994
Proposed Completion Date: April 1, 1994
Estimated Date of Final Report: May 1, 1994

Test Substance(s) 37-AEG-70

Name	isobutanol; isobutyl alcohol
Source	Analysis # EH 3639; UCC, Houston, TX
CAS Registry No.	78-83-1
Description	colorless, non-viscous liquid
Purity	≈ 99.9%
Health/Safety	moderately toxic; stable. MSDS available upon request
Storage Conditions	room temperature

Study Design

The test substance(s) will be characterized by:

- Verification of identity by proton- and carbon-NMR.
- Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥0.1 wt. %.
- Quantitation of the identified impurities by capillary GC.

Reviewed and Approved by:

3/14/94	2/17/94	Barbara Francis 2/25/94
Alexander E. Gábany date GLP Study Director	Denise L. Johnson date GLP Quality Assurance Unit (QAU) Representative	Barbara Francis date CMA Oxo Process Panel, Associate Director, Sponsor's Representative

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

APPENDIX II **Protocol Amendment**

AMENDED 4/15/94

PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

title	Isobutanol
purpose	Analytical Characterization of Sample(s) for neurotoxicity testing at Monsanto Company
study number	37-AEG-131
sponsor	CMA Oxo Process Panel Chemical Manufacturers Association 2501 M Street, NW Washington, DC 20037
testing facility	UCC Technical Center, South Charleston, WV 25303 (Location 511)

Proposed Starting Date:	Monday, February 14, 1994
Proposed Completion Date:	April 1, 1994
Estimated Date of Final Report:	May 1, 1994

Test Substance(s) 37-AEG-70

Name	isobutanol; isobutyl alcohol
Source	Analysis # EH 3639; UCC, Houston, TX
CAS Registry No.	78-83-1
Description	colorless, non-viscous liquid
Purity	≈ 99.9%
Health/Safety	moderately toxic; stable. MSDS available upon request
Storage Conditions	room temperature

Study Design

The test substance(s) will be characterized by:

- Verification of identity by proton- and carbon-NMR.
- Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥0.1 wt. %.
- Quantitation of the identified impurities by capillary GC.

This Protocol amendment includes only a change in Study Director as of April 1, 1994.

Reviewed and Approved by:

Nancy A. Broyles 4/15/94	Denise L. Johnson 4/15/94	Barbara Francis 4/19/94
Nancy A. Broyles Date	Denise L. Johnson Date	Barbara Francis Date
GLP Study Director	GLP Quality Assurance Unit (QAU) Representative	CMA Oxo Process Panel, Associate Director, Sponsor's Representative

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

UCC BUSINESS CONFIDENTIAL
QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: ISOBUTANOL

Study No.: 37-AEG-131

Study Director: N.A. Broyles

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

Inspection Date	Inspection Type	Date QAU Report Issued To Study Director	Date QAU Report Issued To Management
Feb. 10, 1992	Laboratory Compliance Review*	Feb. 10, 1992	May, 1992
Feb. 17, 1994	Protocol Compliance Review	Feb. 17, 1994	Feb. 17, 1994
April 15, 1994	Protocol Amendment #1 Compliance Review	April 15, 1994	April 15, 1994
Apr. 21, 1994	Final Report Compliance Review	Apr. 21, 1994	Apr. 21, 1994

*The process of doing the GLP characterization studies is audited periodically to assure these studies comply with GLP requirements. The QA unit is exempted from performing in-life study inspections for studies designed to determine physical and chemical characteristics of a test substance as described in 40 CFR 792.135.

Denise L. Johnson 4/21/94

Denise L. Johnson, QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Results of the Analysis of Isobutanol for an Acute Inhalation Neurotoxicity Study

Authors: W. E. Hopkins, II — 5/31/94 Date

D. L. Maher — 5/31/94 Date

J. E. Mueller — 5-31-94 Date

S. Schermes — 5-31-94 Date

Approved by: M. E. Holland, Ph.D. — 5/31/94 Date
Manager, Analytical Services Group

SUMMARY

Samples were collected during a pretest period for an acute inhalation study by the inhalation toxicology group. The isobutanol was collected in impingers containing ice-cold methanol and the solutions were analyzed for isobutanol content using gas chromatography with a flame ionization detector with integration of the chromatographic peak due to isobutanol. Chamber air concentrations of isobutanol were calculated in ppm by using the formula weight of the compound multiplied by the air concentrations. Air concentrations for the three exposures are shown in Table 1 in ppm.

Results of the quality control samples are given in Table 2. All samples are within 10% of the target values.

Mean quality control data are given in Table 3. The largest percent difference from the expected value was 2.2%. This quality control data indicated the analytical method used was capable of giving precise and accurate data.

Stability of the neat test substance before and after the study was verified by assays against a refrigerated analytical standard of isobutanol and was determined to be acceptable. Stability results are shown in Table 4.

Mean analytical concentrations of isobutanol measured by gas chromatography (GC) were within 16% at the low level, 10% at the mid level and 9% at the high level of concentrations measured by infrared spectroscopy.

The difference between the results obtained using gas chromatography and the Miran Infrared spectrometer is believed due to the impinger method of collection used for the GC analyses. The Miran values were measured on line. In contrast, the GC values required that the isobutanol be collected in methanol-containing impingers and subsequently analyzed by GC.

Table 1

Isobutanol Acute Inhalation Study Results
Low Level Chamber

Pretest Exposure	Sample I.D.	GC Determined Concentration (ppm isobutanol in air)	Miran Determined Concentration (ppm isobutanol in air)	Percent diff.*
6 *	L-1	1420	1650	-14
*	L-2	1420	1690	-16
7 *	L-1	1220	1440	-15
*	L-2	1190	1430	-17
8 *	L-1	1450	1680	-14
*	L-2	1350	1680	-20
			Mean ± S.D. = -16 ± 2.3	

Samples were collected in ice-cold methanol.

$$* \frac{\text{Miran concentration} - \text{GC concentration}}{\text{Miran concentration}} \times 100$$

Table 1

Isobutanol Acute Inhalation Study Results
Mid Level Chamber

Pretest Exposure	Sample I.D.	GC Determined Concentration (ppm isobutanol in air)	Miran Determined Concentration (ppm isobutanol in air)	Percent diff.*
6 *	M-1	2630	2790	-5.7
*	M-2	2700	2850	-5.3
7 *	M-1	2630	3000	-12
*	M-2	2930	3010	- 2.7
8 *	M-1	2900	3020	-4.0
*	M-2	2210	3020	-27
			Mean ± S.D. =	-9.5 ± 9.2

Samples were collected in ice-cold methanol.

$$* \frac{\text{Miran concentration} - \text{GC concentration}}{\text{Miran concentration}} \times 100$$

Table 1

Isobutanol Acute Inhalation Study Results
High Level Chamber

Pretest Exposure	Sample I.D.	GC Determined Concentration (ppm isobutanol in air)	Miran Determined Concentration (ppm isobutanol in air)	Percent diff.*
6 *	H-1	5600	5990	-6.5
*	H-2	4940	5770	-14
7 *	H-1	5600	6070	-7.7
*	H-2	5270	6010	-12
8 *	H-1	5930	5930	0.0
*	H-2	5270	5900	-11

Mean ± S.D. = -8.5 ± 5.0

Samples were collected in ice-cold methanol.

$$* \frac{\text{Miran concentration} - \text{GC concentration}}{\text{Miran concentration}} \times 100$$

Table 2

Quality Control Data for Isobutanol
Air Samples in (mg/L)

Exposure Day	QC-L Target	QC-L Found	QC-L %Diff*	QC-M Target	QC-M Found	QC-M %Diff*
6	506	522	3.2	1010	1010	0.0
7	506	517	2.2	1010	1010	0.0
8	506	511	1.0	1010	1010	0.0

$$* \% \text{ Difference} = \frac{(\text{Found} - \text{Target})\ (100)}{\text{Target}}$$

All analytical results are reported to 3 significant figures as per SOP.

All samples are means of duplicate analyses.

Table 2

Quality Control Data for Isobutanol
Air Samples in (mg/L)

Exposure	QC-H		
Day	Target	Found	%Diff*
6	2020	2020	0.0
7	2020	2000	-1.0
8	2020	2060	2.0

$$* \ \% \text{ Difference} = \frac{(\text{Found} - \text{Target})\ (100)}{\text{Target}}$$

All analytical results are reported to 3 significant figures as per SOP.

All samples are means of duplicate analyses.

Table 3

Quality Control Mean (ppm)

	Concentrations (ppm)		
	QC-L	QC-M	QC-H
Mean Target	506	1010	2020
Mean Found	517	1010	2030
% Difference from target	2.2	0.0	0.50

$$* \text{ \% Difference from target} = \frac{(\text{Mean Found} - \text{Mean Target}) * (100)}{\text{Mean Target}}$$

Table 4

Stability of Test Substance Isobutanol

Analysis Date	% Isobutanol*
2/1/94	101 ± 2.2% **
4/12/94	101 ± 1.4% **

* Assay against analytical standard (AS-127). Lot #: 07573CF provided by Aldrich Chemical Co., Purity = 99.94%.

** Average assay of ten analyses.

Reported purity value on test material sample submission form = 99.9% (Lot #: EH 3639).

Analytical Procedure for Determination of Isobutanol in Air

Study Number: 94009 & 94010 Page Number: 1

Description

This GC method is designed to measure isobutanol in air. It is based on trapping isobutanol from about 2.5-20 liters of air in an impinger containing methanol. Quantitation is achieved using a gas chromatograph with a flame ionization detector and integration of the chromatographic peaks due to isobutanol.

Instrumentation:

Typical GC Operating Conditions and Parameters:

Detector: flame ionization, range 10^{-11}, attenuation = 64.

Column: Glass; 6 foot x 4 mm ID 5% Carbowax 20M on 80/120 mesh Supelcoport

Gas Flows: He - 20 mL/minute
H_2 - 35 mL/minute
Air - 350 mL/minute

Temperatures: Detector - 270°C
Injector - 250°C
Initial Column Temperature - 40°C isothermal for 10 minutes.

Injection Volume: 1 microliter

Chromatograph: Varian 3700 GC with autosampler; integration by Spectra-Physics 4270 integrator.

Materials

isobutanol: EHL Test Substance control Number T940007, Lot number EH 3639.
Methanol: Optima grade, Fisher Scientific Co.

Required Standard Solutions

Study Number: 94009 & 94010 Page Number: 2

Stock Standards

Identification	Approximate Sample Weight (g)[b]	Volume of Stock Standard (mL)	Approximate Stock Standard Concentration (mg/mL)
A	0.2500	50	5000
B	0.5000	50	10000
Stock QC	0.2500	50	5000

Working Standards

Identification	Stock Standard	Volume of Stock Standard (mL)	Volume of Working Standard (mL)	Approximate Concentration of Working Standard (mg/L)
WS-1	A	1.0	50	100
WS-2	B	1.25	50	250
WS-3	A	5.0	50	500
WS-4	B	5.0	50	1000
WS-5	A	25.0	50	2500
WS-6	B	25.0	50	5000
QC-L	QC	5.0	50	500
QC-M	QC	10.0	50	1000
QC-H	QC	20.0	50	2000

(a) Prepared using EHL Test Substance Number T940007.
(b) To the nearest 0.1 mg.

Comments: Fresh stock and working standards will be prepared in methanol every two weeks. Additional standards, fewer standards and/or alternate concentrations of standards may be used for the calculation of the linear regression coefficients at the discretion of a professional of the chemistry group.

Calculations

Study Number: 94009 & 94010 Page Number: 3

1.) Working Standard Concentrations

$C_w = (C_s * V_s) / V_w$

where: C_w = concentration of working standard (mg/L)

C_s = concentration of stock standard (mg/L)

V_s = volume of stock standard (mL)

V_w = volume of working standard (mL)

Values are reported to three significant figures.

2.) Regression Coefficients

Linear regression lines will be calculated from the standard concentrations C_w (in mg/L) and the corresponding areas A. The A and C_w will be treated as X and Y, respectively. The expression $C_w = a+b*A$ will be used to calculate the concentration of the test material in the impinger solutions. Standards 1-4 will be used to calculate the regression coefficients for any solution having a peak area less than or equal to the front WS-4. Standards 1-6 will be used to calculate regression coefficients for samples with areas greater than the front WS-4.

3.) Net Peak Area

If the blank sample exhibits a peak interfering with the test material with an area exceeding 10% of the area of the lowest working standard, then a net peak will be calculated:

$A_N = A_T - A_b$

where: A_N = net area of test material

A_b = area of blank peak at test material retention time

A_T = apparent area of test material

4.) Solution Concentrations

The solution concentration C_x will be calculated directly from the regression coefficient equation by the labnet computer. Solution concentrations will be reported to three significant figures. Solution concentrations less than the lowest working standard concentration will be reported as not measurable (N.M.).

Calculations (cont'd.)

Study Number: 94009 & 94010 Page Number: 4

5.) Air Concentrations (in mg/L)

$C_{air} = C_x * V_{sol} * 10^{-3}$ liter/mL $* 1/V_{air} *$ D.F.

where: C_{air} = Air concentration of isobutanol (mg/L)

C_x = Solution concentration (mg/L)

V_{sol} = Solvent volume (mL)

V_{air} = Volume of air sampled (l)

D.F. = dilution factor (if neeeded)

Air concentrations in mg/L will be reported to three significant figures.

6.) Air Concentrations (in ppm)

$C = C_{air} * FACT_{con}$

where: C = Air concentration of isobutanol (ppm)
C_{air} = Air concentration of isobutanol (mg/L)
$FACT_{con}$ = Conversion factor to convert mg/L to ppm. See factor note below.

Air concentrations in ppm will be reported to three significant figures.

Factor note: The air concentrations (in mg/mL) obtained from the labnet computer must be converted to parts per million (ppm) where: ppm = mg/kg

1 kg of isobutanol in air volume $= \frac{1 \text{ mole}}{0.07412 \text{ kg}} \times \frac{24.4 \text{ L}}{1 \text{ mole}}$

$= 329.20$ L/kg

* = molecular weight of isobutanol in kg.

Procedure

The samples are diluted in methanol (prior to being analyzed) if the expected solution concentration will fall outside the 100-5000 mg/L range of the working standards.

Transfer solution into autosampler vial and analyze.

Comments

Study Number: 94009 & 94010 Page Number: 5

A typical chromatogram of a working standard of isobutanol is attached.

It is necessary to re-analyze the sample and/or the QC sample if the sample differs from the expected value by greater than 20%.

Two sets of standards will be run with each set of samples. One set will be run at the start of the analytical run and the other set will be run at the end of the analytical run. Unless otherwise directed by a professional of the chemistry group, all peak areas will be used to calculate the correlation coefficients and the linear regression lines and all sample concentrations. QC samples will be run in duplicate both near the beginning and near the end of each analytical run (thus bracketing all samples for that day). Unless a professional of the chemistry group determines that analytical, sampling or instrumental conditions dictate otherwise, all peak areas for QC samples will be used for concentration calculations. QC sample concentrations may vary during the course of the study to approximately match impinger sample concentrations.

Different weights and volumes of stock standards and working standards may be used at the discretion of the analyst as long as the samples and QC samples are still within the range of the working standard concentrations.

Computer-generated "interim" data may contain more significant figures than is specified in this analytical method. The final analytical data (in the analytical report) will, however, be rounded to the number of significant figures indicated.

This method was developed by James E. Mueller and written on 2/23/94. The following technician is judged capable of performing this analysis:

Technician	Date Training Completed
Susan Schermes	2/23/94

Prepared by: James E. Mueller Date: 5-31-94

Reviewed by: Mark E. [illegible] Date: 5/31/94

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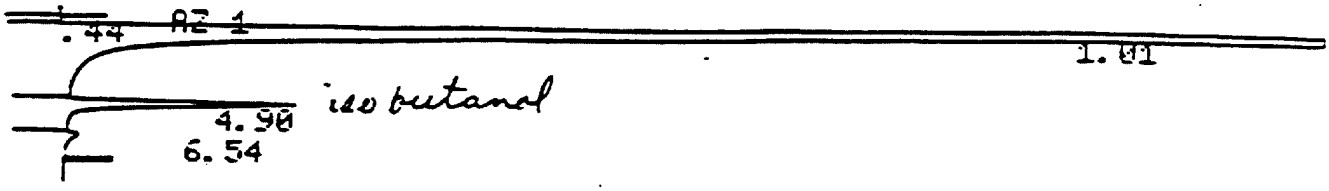


34010ISOBUTANOL PRE-STAB 01/30/94 13:10:35 CH= "A" PS= 1.

FILE 1. METHOD 5. RUN 2 INDEX 2

ANALYST: James E Mueller

SAMPLE 2 WS-2

SA	IS	XF
0.	0.	1.

NAME	RT	AREA	BC	RF
1	0.44	4221	02	
2	1.01	33004747	02	
TANOL	4.9	206284	08	1.
4	6.54	12510	05	
TOTALS		33227762		

Analytical Procedure for Assay of Isobutanol

Study Number: 94009 & 94010 Page Number: 1

Description:

Appropriate dilutions (in acetone) of isobutanol are analyzed by gas chromatography using a flame ionization detector. The material is assayed by comparison of peak areas obtained using a set of standards prepared with HPLC grade isobutanol. Assay values determined before and after the study are used as a measure of stability of the test material.

Instrumentation:

Typical GC Operating Conditions and Parameters:

Detector: flame ionization, range 10^{-11}, attenuation = 32.

Column: Glass; 6 foot x 4 mm ID 5% Carbowax 20M on 80/120 mesh Supelcoport

Gas Flows: He - 20 mL/minute
H_2 - 35 mL/minute
Air - 350 mL/minute

Temperatures: Detector - 270°C
Injector - 250°C
Initial Column Temperature - 40°C for 10 minutes. Temperature program at 30°C per minute to 100°C and hold for 2 minutes.

Injection Volume: 1 microliter

Chromatograph: Varian 3700 GC with autosampler; integration by Spectra-Physics 4270 integrator.

Materials

Volumetric Pipets
Volumetric Flasks
2-Methyl-1-propanol : HPLC grade (99.94%); Sigma-Aldrich Lot No. 07573CF; AS-127
Acetone: Optima grade, Fisher Scientific Co.
Isobutanol : EHL Test Substance control number T940007, Lot No. EH 3639

Required Standard Solutions

Study Number: 94009 & 94010 Page Number: 2

Stock Standards [a]

Identification	Approximate Sample Weight (g) [c]	Volume of Stock Standard (mL)	Approximate Stock Standard Concentration (mg/L)
A [b]	0.100	100	1000
TEST [d]	0.100	100	1000

Working Standards

Identification	Stock Standard	Volume of Stock Standard (mL)	Volume of Working Standard (mL)	Approximate Concentration of Working Standard (mg/L)
WS-1	A	10.0	50	200
WS-2	A	20.0	50	400
WS-3	A	30.0	50	600
WS-4	A	20.0	25	800
WS-5	A	---	---	1000
Assay	TEST	30.0	50	[e] 600

[a] All working standards and stock standards will be freshly prepared in acetone for each stability analysis.

[b] Stock solution A will be prepared using HPLC grade 2-Methyl-1-propanol; AS-127

[c] Record weight to ± 0.1 mg.

[d] Stock solution "Test" will be prepared using EHL Test Substance control number T940007.

[e] Actual concentration = C_{Theo} (see calculation on Page 5).

Test Procedure

Study Number: 94009 & 94010 Page Number: 3

Directions for Sample Analysis

Before the study, chromatograph the assay solution ten times to obtain ten assay values at time zero for isobutanol. After the study, prepare a fresh assay solution and chromatograph ten times to again obtain ten assay values for isobutanol.

Reporting Data

Compare the mean assay values obtained after the study with the mean assay value obtained before the study. Solution concentrations are reported to three significant figures. Assay values are reported in percents to three significant figures.

Storage of Test Substance and Analytical Standard

The analytical standard will be stored at room temperature, in a closed container. The test substance will also be stored in a closed container at room temperature.

Calculations

Study Number: 94009 & 94010 Page Number: 4

1. Working Standard Concentrations

$C_w = (C_s * V_s)/V_w$

where: C_w = concentration of working standard (mg/L)
C_s = concentration of stock standard (mg/L)
V_s = volume of stock standard (mL)
V_w = volume of working standard (mL)

Values are reported to three significant figures.

2. Regression Coefficients

A low linear regression will be calculated from the working standards 1 through 5 conforming to the equation:

$C_w = a + b * A$

Where A is the mean peak area of the working standards. The A and C_w will be treated as X and Y, respectively.

3. Assay Solution Concentration

The concentration of isobutanol in the assay solution is obtained from the peak area and the regression coefficients a and b.

$C = a + b * A_{assay\ Solution}$

where: C = solution concentration of isobutanol in mg/L.

Report assay solution concentrations to three significant figures. Solution concentrations less than the concentration of the lowest standard will be reported as N.M. (not measurable).

Calculations (cont.)

Study Number: 94009 & 94010 Page Number: 5

4. Assay Value

The assay value will be obtained from the measured assay sample concentration and the theoretical assay sample concentration as determined using the actual sample weight from page 2.

$A.V. = (C/C_{Theo}) * 100 * \text{Purity of Analytical Standard}$

where: A.V. = Assay Value (%)

C_{Theo} = Theoretical assay value of isobutanol concentration (mg/L) (as prepared on page 2)

C = Concentration of isobutanol in assay sample (mg/L)

Purity of analytical standard (0.9994 for #AS-127) (ie., 99.94% pure)

Comments

Study Number: 94009 & 94010 Page Number: 6

A typical chromatogram of a working standard of isobutanol is attached.

Different standard weights and volumes of stocks and volumetric flasks may be used as long as the approximate concentrations of the stocks and working standards will correspond to those given on page 2.

The analyst may, at his discretion, use either integrator determined peak heights or peak areas to calculate the regression lines and all the test substance assay values.

Computer generated "interim" data may contain more significant figures than is specified in this analytical method. The final analytical data (in the analytical report) will, however, be rounded to the number of significant figures indicated.

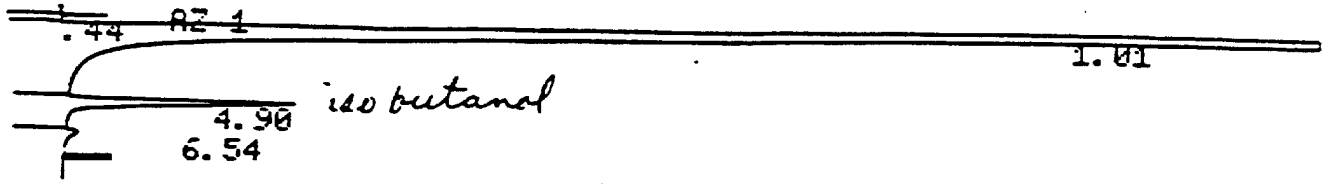
This method was developed by James E. Mueller and written on 1/30/94. The following technicians are trained in performing this analysis.

Technician	Date Training Completed
James E. Mueller	1/30/94
Susan Schermes	1/30/94

Prepared by: James E. Mueller Date: 4-26-94

Reviewed by: Diane L. Maher Date: 4/26/94

'ANNEL A INJECT 01/30/94 13:10:35



94010ISOBUTANOL PRE-STAB 01/30/94 13:10:35 CH= "A" PS= 1.

FILE 1. METHOD 5. RUN 2 INDEX 2

ANALYST: James E Mueller

SAMPLE . 2 WS-2

SA	IS	XF
0.	0.	1.

NAME	RT	AREA	BC	RF
1	0.44	4221	02	
2	1.01	33004747	02	
TANOL	4.9	206284	08	1.
4	6.54	12510	05	
TOTALS		33227762		

Appendix 7: Pilot Acute Neurotoxicity Study

Pilot Range-Finding Study for an Acute Neurotoxicity Study of Isobutanol

Study Number: 94010

INTRODUCTION

Purpose: The main purpose of this range-finding acute study was to determine exposure levels for a subsequent acute inhalation neurotoxicity study.

Date Protocol Signed by Study Director: January 27, 1994

Date First Animal Dosed: January 31, 1994

Date Last Animal Sacrificed: February 8, 1994

Applicable Testing Guidelines/Regulation:

While there was no guideline for this study, it was conducted to conform with general principles outlined in the U.S. EPA Health Effects Testing Guidelines, 40 CFR Part 798.1150, for acute inhalation toxicity.

Experimental Design:

Four groups of 5 male and 5 female Charles River Sprague-Dawley rats were exposed to atmospheres containing either filtered conditioned air or isobutanol for 6 hours. Exposure levels were 0, 2000, 6000, and 8000 ppm. The 0 and 8000 ppm level animals were exposed the first day. The 2000 and 6000 ppm level animals were exposed the following day. Animals were observed for mortality and overt signs of toxicity every 30 minutes during exposure. Detailed clinical signs of toxicity, including an open field assessment of gait, alertness, level of activity, and any other unusual signs of neurotoxicity were recorded pre-exposure, immediately following exposure and on post-exposure days 1, 2, and 3. An ophthalmic examination was conducted approximately one week following exposure.

MATERIALS AND METHODS

Test Material:

Name:	Isobutanol
Lot Number:	EH 3639
EHL Substance Identification #:	T940007
Stated Purity:	99.9%

Test Material (cont.):

Date Received:	December 27, 1993
Description:	Clear Liquid
Source:	Union Carbide Chemicals and Plastics Co. Inc., Houston, Texas

Exposure System:

Exposure Chamber:	250 liter glass and stainless steel inhalation chambers and an atmosphere generation system
Animal Housing During Exposure:	Individual wire mesh cages
Exposure Duration:	6 hours
Test Atmosphere Generation System:	Modified Laskin-type nebulizer fed by an adjustable-flow valveless pump
Monitoring of Environmental Parameters:	Chamber airflow, temperature and % relative humidity were monitored continuously and recorded every 30 minutes. Oxygen level was determined once per exposure level with an electronic sensor.

Procedure for Monitoring Test Material in the Chamber:

Atmospheric Analytical Sampling:	Twelve samples per exposure level at approximately equal intervals
Sampling Method:	Test atmosphere was drawn through a Miran 1A infrared detector

Procedure for Monitoring Test Material in the Chamber (cont'd):

Sampling Location: In the animal breathing area

Analytical Method: Infrared spectroscopy

Nominal Concentration: Calculated once per exposure by determining the total weight of test material delivered to the chamber and dividing this amount by the total air volume passing through the chamber during the exposure

Group Designations/ Exposure Levels:

Groups (Male, Female)	Exposure Level (ppm)
M00, F00	0
M01, F01	2000
M02, F02	6000
M03, F03	8000

Animals

Note: Animal housing and husbandry were in accordance with the provisions of 'Guide to the Care and Use of Laboratory Animals', USPHS-NIH Publication No. 86-23.

Species: Rat

Strain: Sprague-Dawley (CD)

Source: Charles River Breeding Laboratory, Raleigh, NC

Acclimation Period: 13 days

Animals (cont'd):

Number Used in Study:	40 (20 males, 20 females), Any unhealthy animals were excluded from assignment from the study.
Test Group Size:	5 males and 5 females
Method of Assignment:	Randomization by body weight
Method of Identification:	Individual ear-tag; bar-coded cage card
Age at Study Start:	Approximately 8 weeks old
Weight Range at Study Start:	254-301 grams (males); 190-227 grams (females)
Type of Housing:	Individual stainless steel cages with wire mesh bottoms suspended over paper bedding.
Water Availability:	*ad libitum* (St. Louis public water supply)
Food Availability:	*ad libitum*

Behavioral Observations:

Animals were observed for mortality and overt signs of toxicity every 30 minutes during the exposure. Detailed clinical signs of toxicity, including an open field assessment of gait, alertness, level of activity, and any other unusual signs of neurotoxicity were recorded pre-exposure, immediately following exposure and for the three days following exposure. The observer was blind to the treatment each animal was given. The overt and detailed clinical signs of toxicity including level of activity were listed by exception. An assessment of alertness and gait were recorded for each animal according to the following scores:

A. Alertness

0. No movement
1. Low (some head or body movement)
2. Normal (alert, exploratory movements)
3. Somewhat high (slight excitement, tense, darting or freezing)
4. Very high (hyperalert, excited, sudden bouts of running)

B. Gait score

0. Severely abnormal
1. Moderately abnormal
2. Slightly abnormal
3. Normal - no abnormal gait

Ophthalmic Examination (Exhibit 2):

Ophthalmic examinations were performed on all the rats approximately one week after exposure using an indirect ophthalmoscope. The eyes were examined with and without dilation with 1% atropine. The examinations were performed without knowledge of the treatment group of the animal.

Inlife Observations:

Check for Mortality, Moribundity, and Noteworthy Signs of Toxicity:	Twice daily (AM and PM) from the day of pretest until the day of sacrifice (9 days after test material administration); every 30 minutes during exposures
Detailed Observations for Signs of Toxicity:	Pre-exposure, immediately following exposure and post-exposure days 1,2,3
Ophthalmic examinations:	Approximately one week after exposure
Body Weight Measurement:	Animals were weighed twice on day of exposure and post-exposure days 1, 2, and 3

Data analysis

The effects of the test material were determined by inspection of the data.

RESULTS

Test Exposure Concentrations (Table 1):

Mean nominal and analytical values for the three exposure levels of isobutanol were:

	Low	Mid	High
Target Level (ppm)	2000	6000	8000
Nominal Conc. (ppm)	1843	7176	8262
Mean Analytical Conc. (ppm) (Std. Dev)	2007 (11.4)	6000 (47.6)	7991 (32.4)
Nominal/Analytical Ratio	0.9	1.2	1.0

The nominal/analytical ratios indicate that little test material was lost as a result of adsorption on the animals' cages and the chamber walls. This is consistent with observations made during pretest that the test material was generated solely as a vapor. The control chamber was checked every 30 minutes during exposure and test material was not detected.

Mean Exposure Atmosphere Conditions:

Exposure Level	Control	2000 ppm	6000 ppm	8000 ppm
Airflow (L/min) (St. Dev)	63.1 3.0	64.9 1.1	65.8 1.6	68.8 2.3
Air changes/hour	15	16	16	17
Equilibration Period (T99, minutes)	18	18	17	17

Exposure Level	Control	2000 ppm	6000 ppm	8000 ppm
Temperature (°C) St. Dev.	23.4 0.2	23.1 0.2	23.2 0.2	23.3 0.2
%Relative Humidity St. Dev.	33.3 2.5	37.2 5.4	41.6 5.8	36.4 3.7

Air changes/Hour = Chamber Airflow (l/min) * 60 minutes/Chamber Volume (250 liters)
T99 = the time it takes for the concentration to reach 99% of equilibrium concentration.

Clinical Observations During Exposure (Table 2, 3):

All rats exposed to isobutanol at 8000 and 6000 ppm exhibited clear signs of lacrimation and were non-responsive to external stimuli for most of the exposure period of 6 hours. All the rats at 8000 ppm also breathed rapidly. In contrast, only a few rats at 6000 ppm had rapid or labored breathing patterns. Based on these observations, the chemical had an anesthetic effect on the rats at both 8000 and 6000 ppm during exposure.

Clinical Observations After Exposure (Table 4)

Males and females exposed to atmospheres of 8000 ppm exhibited severe signs of toxicity immediately after exposure (Day 0). A large percentage of these animals were hypoactive, had urine-stained hair, had moderate to severely abnormal gait (moves with flattened body, waddles-rocks-or lurches, disuse of limbs), and had signs of lacrimation. One female was unresponsive and prostrate and another female's eyes were opaque. The observer also noted that most of the high dose animals that were hypoactive in the open field were prostrate in their home cages and had no resistance to handling. These severe signs of toxicity were transient and were not evident the day after exposure. On the second day after exposure (Day 2), the eyes of 3 females and 2 males were opaque. The incidence of this eye opacity remained the same for the females and increased to 4 males on the third day after exposure. Aside from the eye opacity, there were no other abnormal clinical signs two and three days after exposure.

Rats exposed to atmospheres of 6000 ppm also exhibited clear signs of toxicity that were not as severe as those observed in the 8000 ppm level rats. A few animals had signs of lacrimation and urine-stained hair. Three of the females were hypoactive, one of which was prostrate. All 5 males and 2 females had slight to moderately abnormal gait (waddled, rocked, or lurched). None of these signs of toxicity were evident the day after exposure

Clinical Observations After Exposure (Table 4) (cont'd)

or the following 2 days. The transient hypoactivity and uncoordinated gait isconsistent with what one would expect of an animal that was recovering from narcotic effects. Eye opacity developed in one male and one female rat two days after exposure. An additional female rat had opaque eyes three days after exposure.
There were no treatment-related signs of toxicity in any of the rats exposed to atmospheres of 0 or 2000 ppm of isobutanol.

Body Weights (Table 5)

The average body weights for all groups of rats decreased as expected after they were in the inhalation chambers without food for 6 hours. There was a dose dependent effect in how quickly the animals recovered from this body weight decrease, particularly for males at the 8000 ppm level.

Ophthalmic Examinations (Exhibit 2, Table 6)

The evidence of eye opacity that developed 2 days after exposure prompted a more thorough ophthalmic examination by the laboratory's veterinarian approximately 1 week after exposure. Treatment-related lesions described as unilateral or bilateral corneal opacity localized to the anterior surface of the cornea were noted in 6000 and 8000 ppm level rats. The lesions were generally more severe in the 8000 ppm group with other inflammatory changes often developing. These inflammatory changes included unilateral or bilateral iritis, as evidenced by vascular congestion, and anterior synechia, where the iris adheres to the posterior surface of the cornea. No lesions related to the compound were noted in the 2000 ppm and control level animals.

DISCUSSION/CONCLUSIONS

Severe signs of toxicity were evident at 6000 and 8000 ppm levels during exposure. The 8000 ppm level was regarded to be excessively toxic and therefore too high for an acute study. Therefore, it was determined that 6000 ppm should be the highest exposure level for the acute study.

TECHNICAL ASSISTANCE

Inhalation exposure: Steve Becktame, Bob Quevreaux, Terry Kaempfe, Charles Bechtel
Detailed clinical observations: Pat O'Donnell.
Exposure observations: Terry Kaempfe and Bob Quevreaux.

REPORT PREPARED BY: Pat O'Donnell and Terry Kaempfe

EHL 94010 - Table 1
Analytical Chamber Concentration of Isobutanol

Approximate Sample Time	Run 1 (Target: Control)	Run 1 (Target: 8000 ppm)
0:30	0.0	7967
1:00	0.0	8046
1:30	0.0	8006
2:00	0.0	7980
2:30	0.0	8019
3:00	0.0	8006
3:30	0.0	8019
4:00	0.0	7928
4:30	0.0	7980
5:00	0.0	7954
5:30	0.0	8006
6:00	0.0	7980
Mean	0.0	7991
St. Dev.	0.0	32.4
Nominal	0.0	8262
Nominal to Analytical Ratio		1.0
Approximate Sample Time	**Run 2 (Target: 2000 ppm)**	**Run 2 (Target: 6000 ppm)**
0:30	2010	5869
1:00	2005	6028
1:30	2023	6039
2:00	1988	5996
2:30	2010	6007
3:00	2023	6007
3:30	1988	5996
4:00	2014	5953
4:30	2001	6007
5:00	2014	6039
5:30	2010	6028
6:00	2001	6028
Mean	2007	6000
St. Dev.	11.4	47.6
Nominal	1843	7176
Nominal to Analytical Ratio	0.9	1.2

Table 2
EHL 94010 - Summary of Clinical Observations During Exposure

Observation	Animal Group	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Hypoactive	M00	0	0	0	0	0	0	0	0	0	0	0	0
	M01	0	0	0	0	0	0	0	0	0	0	0	0
	M02	1	5	5	5	4	2	1	0	0	0	0	0
	M03	5	5	5	5	5	5	5	0	0	0	0	0
	F00	0	0	0	0	0	0	0	0	0	0	0	0
	F01	0	0	0	0	0	0	0	0	0	0	0	0
	F02	0	5	5	4	2	0	0	0	0	0	0	0
	F03	5	5	5	5	5	5	5	0	0	0	0	0
Nonresponsive	M00	0	0	0	0	0	0	0	0	0	0	0	0
	M01	0	0	0	0	0	0	0	0	0	0	0	0
	M02	0	0	0	0	0	0	4	5	5	5	5	5
	M03	0	0	0	0	0	0	0	5	5	5	5	5
	F00	0	0	0	0	0	0	0	0	0	0	0	0
	F01	0	0	0	0	0	0	0	0	0	0	0	0
	F02	0	0	0	0	0	0	4	4	4	5	5	5
	F03	0	0	0	0	0	0	0	5	5	5	5	5

Hypoactivity and nonresponsiveness were determined by observing the animals while physical stimuli of rapid hand movements were applied to the chamber wall.

Values represent the number of animals within each group of five with the stated observation.

Table 2
EHL 94010 - Summary of Clinical Observations During Exposure

Observation	Animal Group	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Lacrimation	M00	0	0	0	0	0	0	0	0	0	0	0	0
	M01	0	0	0	0	0	0	0	0	0	0	0	0
	M02	5	5	5	5	5	5	5	5	5	3	3	4
	M03	5	5	5	5	5	5	5	5	5	5	5	5
	F00	0	0	0	0	0	0	0	0	0	0	0	0
	F01	0	0	0	0	0	0	0	0	0	0	0	0
	F02	5	5	5	5	5	5	5	5	5	5	5	5
	F03	5	5	5	5	5	5	5	5	5	5	5	5
Rapid Respiration	M00	0	0	0	0	0	0	0	0	0	0	0	0
	M01	0	0	0	0	0	0	0	0	0	0	0	0
	M02	0	0	0	0	0	0	2	0	0	0	0	0
	M03	5	5	5	5	5	5	5	5	5	5	5	5
	F00	0	0	0	0	0	0	0	0	0	0	0	0
	F01	0	0	0	0	0	0	0	0	0	0	0	0
	F02	0	0	0	0	0	0	1	2	0	0	0	0
	F03	5	5	5	5	5	5	5	5	5	5	5	5

Values represent the number of animals within each group of five with the stated observation.

Table 2
EHL 94010 - Summary of Clinical Observations During Exposure

Observation	Animal Group	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Labored Respiration	M00	0	0	0	0	0	0	0	0	0	0	0	0
	M01	0	0	0	0	0	0	0	0	0	0	0	0
	M02	0	0	0	0	0	1	1	1	0	1	1	1
	M03	0	0	0	0	0	0	0	0	0	0	0	0
	F00	0	0	0	0	0	0	0	0	0	0	0	0
	F01	0	0	0	0	0	0	0	0	0	0	0	0
	F02	0	0	0	0	0	0	0	0	0	0	0	1
	F03	0	0	0	0	0	0	0	0	0	0	0	0

Values represent the number of animals within each group of five with the stated observation.

EHL 94010 - Table 3
Individual Clinical Observations During Exposure

Observation	Animal Number	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Hypoactive	F02 001		X	X	X								
	F02 002		X	X	X	X							
	F02 003		X	X									
	F02 004		X	X	X	X							
	F02 005		X	X	X								
	M02 001	X	X	X	X	X	X						
	M02 002		X	X	X								
	M02 003		X	X	X	X							
	M02 004		X	X	X	X	X	X					
	M02 005		X	X	X	X							
	F03 001	X	X	X	X	X	X	X					
	F03 002	X	X	X	X	X	X	X					
	F03 003	X	X	X	X	X	X	X					
	F03 004	X	X	X	X	X	X	X					
	F03 005	X	X	X	X	X	X	X					
	M03 001	X	X	X	X	X	X	X					
	M03 002	X	X	X	X	X	X	X					
	M03 003	X	X	X	X	X	X	X					
	M03 004	X	X	X	X	X	X	X					
	M03 005	X	X	X	X	X	X	X					
Nonresponsive	F02 001							X	X	X	X	X	X
	F02 002							X	X	X	X	X	X
	F02 003										X	X	X
	F02 004							X	X	X	X	X	X
	F02 005							X	X	X	X	X	X
	M02 001							X	X	X	X	X	X
	M02 002							X	X	X	X	X	X
	M02 003							X	X	X	X	X	X
	M02 004								X	X	X	X	X
	M02 005							X	X	X	X	X	X
	F03 001								X	X	X	X	X
	F03 002								X	X	X	X	X
	F03 003								X	X	X	X	X
	F03 004								X	X	X	X	X
	F03 005								X	X	X	X	X
	M03 001								X	X	X	X	X
	M03 002								X	X	X	X	X
	M03 003								X	X	X	X	X
	M03 004								X	X	X	X	X
	M03 005								X	X	X	X	X

EHL 94010 - Table 3
Individual Clinical Observations During Exposure

Observation	Animal Number	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Lacrimation	F02 001	X	X	X	X	X	X	X	X	X	X	X	X
	F02 002	X	X	X	X	X	X	X	X	X	X	X	X
	F02 003	X	X	X	X	X	X	X	X	X	X	X	X
	F02 004	X	X	X	X	X	X	X	X	X	X	X	X
	F02 005	X	X	X	X	X	X	X	X	X	X	X	X
	M02 001	X	X	X	X	X	X	X	X	X	X	X	X
	M02 002	X	X	X	X	X	X	X	X	X	X	X	X
	M02 003	X	X	X	X	X	X	X	X	X	X	X	X
	M02 004	X	X	X	X	X	X	X	X	X			X
	M02 005	X	X	X	X	X	X	X	X	X			
	F03 001	X	X	X	X	X	X	X	X	X	X	X	X
	F03 002	X	X	X	X	X	X	X	X	X	X	X	X
	F03 003	X	X	X	X	X	X	X	X	X	X	X	X
	F03 004	X	X	X	X	X	X	X	X	X	X	X	X
	F03 005	X	X	X	X	X	X	X	X	X	X	X	X
	M03 001	X	X	X	X	X	X	X	X	X	X	X	X
	M03 002	X	X	X	X	X	X	X	X	X	X	X	X
	M03 003	X	X	X	X	X	X	X	X	X	X	X	X
	M03 004	X	X	X	X	X	X	X	X	X	X	X	X
	M03 005	X	X	X	X	X	X	X	X	X	X	X	X
Rapid Respiration	F02 001							X	X				
	F02 002								X				
	F02 003												
	F02 004												
	F02 005												
	M02 001												
	M02 002							X					
	M02 003												
	M02 004							X					
	M02 005												
	F03 001	X	X	X	X	X	X	X	X	X	X	X	X
	F03 002	X	X	X	X	X	X	X	X	X	X	X	X
	F03 003	X	X	X	X	X	X	X	X	X	X	X	X
	F03 004	X	X	X	X	X	X	X	X	X	X	X	X
	F03 005	X	X	X	X	X	X	X	X	X	X	X	X
	M03 001	X	X	X	X	X	X	X	X	X	X	X	X
	M03 002	X	X	X	X	X	X	X	X	X	X	X	X
	M03 003	X	X	X	X	X	X	X	X	X	X	X	X
	M03 004	X	X	X	X	X	X	X	X	X	X	X	X
	M03 005	X	X	X	X	X	X	X	X	X	X	X	X

EHL 94010 - Table 3
Individual Clinical Observations During Exposure

Observation	Animal Number	Approximate time of exposure (hours)											
		0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00
Labored Respiration	F02 001												X
	F02 002												
	F02 003												
	F02 004												
	F02 005												
	M02 001						X	X	X		X	X	X
	M02 002												
	M02 003												
	M02 004												
	M02 005												
	F03 001												
	F03 002												
	F03 003												
	F03 004												
	F03 005												
	M03 001												
	M03 002												
	M03 003												
	M03 004												
	M03 005												

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 0 - Males

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
M00 001	X														2	3
M00 002	X														2	3
M00 003	X														2	3
M00 004	X														2	3
M00 005	X														2	3
M01 001	X														2	3
M01 002	X														2	3
M01 003	X														2	3
M01 004	X														2	3
M01 005	X														2	3
M02 001												X			2	1
M02 002					X				X			X			2	1
M02 003												X			2	2
M02 004												X			2	1
M02 005									X			X			2	1
M03 001		X	X		X		X			X					0	1
M03 002		X			X					X					1	1
M03 003		X					X			X					1	1
M03 004					X				X		X				2	0
M03 005		X			X					X					1	1

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 0 - Females

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
F00 001	X														2	3
F00 002	X														2	3
F00 003	X														2	3
F00 004	X														2	3
F00 005													X	X	2	2
F01 001	X														2	3
F01 002	X														2	3
F01 003	X														2	3
F01 004	X														2	3
F01 005	X														2	3
F02 001		X										X			1	2
F02 002		X	X	X	X										0	*
F02 003	X														2	3
F02 004	X														2	3
F02 005		X			X							X			1	2
F03 001		X			X				X			X			1	2
F03 002									X						1	3
F03 003		X			X	X			X	X					1	1
F03 004			X	X	X		X	X							0	*
F03 005		X			X				X		X				1	0

* Unable to assess, animal would not move

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 1 - Males

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Diause of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
M00 001	X														2	3
M00 002	X														2	3
M00 003	X														2	3
M00 004	X														2	3
M00 005	X														2	3
M01 001	X														2	3
M01 002	X														2	3
M01 003	X														2	3
M01 004	X														2	3
M01 005	X														1	3
M02 001	X														2	3
M02 002	X														2	3
M02 003	X														2	3
M02 004	X														2	3
M02 005	X														2	3
M03 001	X														2	3
M03 002	X														2	3
M03 003	X														2	3
M03 004	X														2	3
M03 005	X														2	3

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 1 - Females

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
F00 001	X														2	3
F00 002	X														2	3
F00 003	X														2	3
F00 004	X														2	3
F00 005													X	X	2	3
F01 001	X														2	3
F01 002	X														2	3
F01 003	X														2	3
F01 004	X														2	3
F01 005	X														2	3
F02 001	X														2	3
F02 002	X														2	3
F02 003	X														2	3
F02 004	X														2	3
F02 005	X														2	3
F03 001	X														2	3
F03 002	X														2	3
F03 003	X														2	3
F03 004	X														2	3
F03 005	X														2	3

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 2 - Males

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
M00 001	X														2	3
M00 002	X														2	3
M00 003	X														2	3
M00 004	X														2	3
M00 005	X														2	3
M01 001	X														2	3
M01 002	X														2	3
M01 003	X														2	3
M01 004	X														2	3
M01 005	X														1	3
M02 001	X														2	3
M02 002	X														2	3
M02 003	X														2	3
M02 004						X									2	3
M02 005	X														2	3
M03 001	X														2	3
M03 002	X														2	3
M03 003						X									2	3
M03 004	X														2	3
M03 005						X									2	3

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 2 - Females

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
F00 001	X														2	3
F00 002	X														2	3
F00 003	X														2	3
F00 004	X														2	3
F00 005														X	2	3
F01 001	X														2	3
F01 002	X														2	3
F01 003	X														2	3
F01 004	X														2	3
F01 005	X														2	3
F02 001	X														2	3
F02 002	X														2	3
F02 003	X														2	3
F02 004	X														2	3
F02 005						X									2	3
F03 001	X														2	3
F03 002	X														2	3
F03 003						X									2	3
F03 004						X									2	3
F03 005						X									2	3

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 3 - Males

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
M00 001	X														2	3
M00 002	X														2	3
M00 003	X														2	3
M00 004	X														2	3
M00 005	X														2	3
M01 001	X														2	3
M01 002	X														2	3
M01 003	X														2	3
M01 004	X														2	3
M01 005	X														2	3
M02 001	X														2	3
M02 002	X														2	3
M02 003	X														2	3
M02 004						X									2	3
M02 005	X														2	3
M03 001						X									1	3
M03 002	X														2	3
M03 003						X									2	3
M03 004						X									2	3
M03 005						X									2	3

Table 4
EHL 94010 - Individual Clinical Observations After Exposure
Day 3 - Females

Animal Number	Normal	Hypo-active	Non-responsive	Prostrate	Lacri-mation	Eye Opacity	Eyelid partially\ completely closed	Pilo-erection	Urine-Stained Hair	Moves with body flattened	Disuse of limbs	Waddles-Rocks Lurches	Feet and Limbs Swollen	Loss of Limb (toe)	Alert-ness	Gait Score
F00 001	X														2	3
F00 002	X														2	3
F00 003	X														2	3
F00 004	X														2	3
F00 005														X	2	3
F01 001	X														2	3
F01 002	X														2	3
F01 003	X														2	3
F01 004	X														2	3
F01 005	X														2	3
F02 001	X														2	3
F02 002	X														2	3
F02 003	X														2	3
F02 004						X									2	3
F02 005						X									2	3
F03 001	X														2	3
F03 002	X														2	3
F03 003						X									2	3
F03 004						X									2	3
F03 005						X									2	3

Table 5
EHL 94010 - Body Weights

Animal Number	Pre-exposure Day 0	Post-exposure Day 0	Day 1	Day 2	Day 3
M00 001	262.5	248.8	255.2	264	270
M00 002	254.3	242.2	252.2	257.8	262
M00 003	272.8	260.5	270.8	276.3	282.6
M00 004	281.8	268.7	275.6	282	289.1
M00 005	276.8	266	271.1	282.2	288.6
Mean	269.6	257.2	265.0	272.5	278.5
Std Dev	11.1	11.4	10.5	11.0	12.0
Mean Change from Pre-exposure		-12.4	-4.6	2.9	8.9
M01 001	291.2	268.6	285.9	300.4	308
M01 002	275	258.2	267.2	280.6	285.8
M01 003	301.2	283.5	293.9	303.8	314.4
M01 004	276.3	256.2	267.7	278	284.3
M01 005	272.9	253.6	264.6	271.2	281.4
Mean	283.3	264.0	275.9	286.8	294.8
Std Dev	12.3	12.3	13.2	14.4	15.2
Mean Change from Pre-exposure		-19.3	-7.4	3.5	11.5
M02 001	294.7	271.9	273.2	289.2	295.6
M02 002	297.3	271.3	270.5	285.4	292.1
M02 003	281.2	258.9	265.1	280.3	286.8
M02 004	272.4	253.3	258.2	268.7	276.6
M02 005	291.2	272.3	273.7	290.2	298.7
Mean	287.4	265.5	268.1	282.8	290.0
Std Dev	10.4	8.8	6.5	8.8	8.7
Mean Change from Pre-exposure		-21.9	-19.3	-4.6	2.6
M03 001	261.5	244	243.2	257.5	265.5
M03 002	262.8	244.8	240	253.9	265.3
M03 003	275.8	256.6	255	267.8	280.1
M03 004	289.4	268.1	266.6	284.7	293.3
M03 005	270.8	249	243.8	261.6	267.7
Mean	272.1	252.5	249.7	265.1	274.4
Std Dev	11.3	10.0	11.0	12.1	12.2
Mean Change from Pre-exposure		-19.6	-22.4	-7.0	2.3

Table 5
EHL 94010 - Body Weights

Animal Number	Pre-exposure Day 0	Post-exposure Day 0	Day 1	Day 2	Day 3
F00 001	203.1	192.4	195.3	200.6	203.2
F00 002	199.9	193.5	200.2	203.5	205.6
F00 003	203.9	192.6	199.5	203	200.3
F00 004	214.8	204.6	214.6	214.9	217.8
F00 005	210.6	199.6	196.4	204.6	202.4
Mean	206.5	196.5	201.2	205.3	205.9
Std Dev	6.1	5.4	7.8	5.6	6.9
Mean Change from Pre-exposure		-10.0	-5.3	-1.2	-0.6
F01 001	221.6	205.4	215.8	218.5	218.8
F01 002	226.6	209.9	213.5	221.9	223.4
F01 003	205.7	194.6	198.7	203.7	211.9
F01 004	197	183.9	190.8	195.6	197.5
F01 005	213.6	199.7	206	205.8	213.5
Mean	212.9	198.7	205.0	209.1	213.0
Std Dev	11.9	10.1	10.4	10.9	9.8
Mean Change from Pre-exposure		-14.2	-7.9	-3.8	0.1
F02 001	218.1	198.8	203.2	211.2	212.6
F02 002	190.5	178.1	177.1	185.4	185.1
F02 003	217.9	202.5	204.9	209.9	210.4
F02 004	213.4	197.1	201.1	209.5	209.5
F02 005	213.6	190.9	198.3	206.9	214
Mean	210.7	193.5	196.9	204.6	206.3
Std Dev	11.5	9.6	11.4	10.8	12.0
Mean Change from Pretest		-17.2	-13.8	-6.1	-4.4
F03 001	207.8	188.5	189	197.3	198.7
F03 002	221.4	206.7	210.5	217.6	219.3
F03 003	206.5	189.6	188.1	199.8	205.6
F03 004	220.1	208	203.5	211	216.2
F03 005	200.3	190.1	189.3	197	200.2
Mean	211.2	196.6	196.1	204.5	208.0
Std Dev	9.2	9.9	10.3	9.3	9.3
Mean Change from Pre-exposure		-14.6	-15.1	-6.7	-3.2

Ophthalmoscopic Examination of Sprague-Dawley Rats on Study 94010
Pilot Acute Neurotoxicity Study - Isobutanol

A terminal examination was performed February 7, 1994 (approximately one week following acute inhalation exposure to isobutanol) on all 40 animals (5 animals/sex/dose) using an indirect ophthalmoscope. An ophthalmoscopic examination was not performed prior to the initiation of this study. The first part of the examination was performed without dilating the eyes so that only the cornea was examined. The second part of the examination included the entire eye after dilation with 1% atropine. These examinations were performed without knowledge of the treatment group for the animal.

At the termination of this study, there appeared to be a compound effect that was related to the treatment group. The lesion appeared as some degree of unilateral or bilateral corneal opacity that was centrally located on the anterior surface of the cornea. The lesions were generally more severe in the high dose group with other inflammatory changes often developing. These inflammatory changes included unilateral or bilateral iritis, as evidenced by vascular congestion, and anterior synechia, where the iris adheres to the posterior surface of the cornea. Corneal opacities were graded as slight (similar to a dehydration effect), mild (similar to mild corneal dystrophy), moderate (small, well-defined opacity), or severe (more extensive opacity with the corneal surface appearing ulcerated). No lesions related to the compound were noted in the low dose group animals.

The unilateral lens vacuole (Low dose group animal M0029) and the bilateral, slight corneal opacity (Control group animal M0024) are considered to be incidental findings.

Table 6
EHL 94010 - Individual Animal Ophthalmic Findings

Animal Number	Normal	Corneal Opacity	Iritis	Anterior Synechia	Lens Vacuole
M00 001	X				
M00 002	X				
M00 003		B-slight			
M00 004	X				
M00 005	X				
M01 001	X				
M01 002	X				
M01 003					R
M01 004	X				
M01 005	X				
M02 001		B-slight			
M02 002		L-slight			
M02 003		B-mild			
M02 004		B-moderate			
M02 005		L-slight			
M03 001		R-mild;L-moderate	L	L	
M03 002		B-slight			
M03 003		R-severe;L-moderate	R		
M03 004		B-severe	B		
M03 005		R-moderate			

R- Right Eye
L- Left Eye
B- Both Eyes

Table 6
EHL 94010 - Individual Animal Ophthalmic Findings

Animal Number	Normal	Corneal Opacity	Iritis	Anterior Synechia	Lens Vacuole
F00 001	X				
F00 002	X				
F00 003	X				
F00 004	X				
F00 005	X				
F01 001	X				
F01 002	X				
F01 003	X				
F01 004	X				
F01 005	X				
F02 001		B-slight			
F02 002	X				
F02 003		B-slight			
F02 004		R-slight;L-severe			
F02 005		B-severe			
F03 001	X				
F03 002		R-slight			
F03 003		R-severe;L-moderate	R	R	
F03 004		R-severe;L-moderate	R	R	
F03 005		R-moderate;L-severe			

R- Right Eye
L- Left Eye
B- Both Eyes

Analytical Procedure for the Determination of Isobutanol in Air

Study Number: 94010

Description:

This is an infrared analyzer method designed to measure the concentration of an atmosphere containing isobutanol vapor. Concentration calibrations range from 1200 to 9300 ppm. Samples of test atmosphere will be drawn directly through an infrared analyzer; light of the desired wavelength is absorbed by the test chemical, detected by the instrument and output through a gauge. This value is recorded.

Instrumentation:

Three Wilks Miran® General Purpose Gas Analyzers with ambient air pumps

Analyzer (#1A-2264)

Detector:	Wavelength:	9.6 µm
	Pathlength:	0.75 meters (14.86 dial reading)
	Slit Width:	2 mm
	Range:	1A
	Course Zero:	X10
	Meter Response:	1 sec

Analyzer (#1A-1815)

Detector:	Wavelength:	9.6 µm
	Pathlength:	0.75 meters (0.05 dial reading)
	Slit Width:	2 mm
	Range:	1A
	Course Zero:	X10
	Meter Response:	1 sec

Analyzer (#1A-2918)

Detector:	Wavelength:	9.6 µm
	Pathlength:	0.75 meters (14.86 dial reading)
	Slit Width:	2 mm
	Range:	1A
	Course Zero:	X10
	Meter Response:	1 sec

Materials:

Isobutanol, Lot #EH 3639, stated purity > 99.9%, EHL Test Substance Number is T940007

Table 1

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-1815

Volume of Test Material (µl)	Concentration (ppm)	Mean Absorbance (St Dev)
25	1172	0.313 (.000)
50	2343	0.583 (.001)
75	3515	0.806 (.002)
100	4687	0.985 (.001)
125	5859	1.122 (.001)
150	7030	1.227 (.001)
175	8202	1.310 (.001)
200	9374	1.375 (.003)

Least Squares Fit: $Conc = 6{,}470.384*A^3 - 10{,}886.51*A^2 + 10{,}400.33*A - 1{,}233.567$
$R^2 = 0.99962$
where A = absorbance reading and
Conc = concentration in ppm

Calibration Date: 26 January 1994

Table 2

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-2918

Volume of Test Material (µl)	Concentration (ppm)	Mean Absorbance (St Dev)
25	1172	0.234 (.003)
50	2343	0.428 (.003)
75	3515	0.590 (.003)
100	4687	0.731 (.001)
125	5859	0.848 (.001)
150	7030	0.954 (.003)
175	8202	1.047 (.001)
200	9374	1.131 (.001)

Least Squares Fit: $Conc = 2{,}400.892*A^3 - 808.5719*A^2 + 5{,}194.727*A - 79.51709$
$R^2 = 0.99999$
where A = absorbance reading and
Conc = concentration in ppm

Calibration Date: 26 January 1994

Table 3

Isobutanol Miran 1A Standard Concentration Absorbance Readings

Miran #1A-2264

Volume of Test Material (µl)	Concentration (ppm)	Mean Absorbance (St Dev)
25	1172	0.255 (.003)
50	2343	0.453 (.003)
75	3515	0.604 (.003)
100	4687	0.715 (.004)
125	5859	0.798 (.004)
150	7030	0.863 (.004)
175	8202	0.918 (.004)
200	9374	0.965 (.004)

Least Squares Fit: $Conc = 1{,}883.872*A^3 - 20{,}818.52*A^2 + 13{,}533.90*A - 1{,}242.967$
$R^2 = 0.99996$
where A = absorbance reading and
Conc = concentration in ppm

Calibration Date: 26 January 1994

Calculations

1. Standard Concentration for all Calibration Loops:

$$C\ (ppm) = \frac{\text{Density (mg/µl)} * \text{Injection Volume (µl)} * 24.4\ \text{(liters/mole)} * 1000}{\text{Molecular Weight (g/mole) Closed Loop Volume (liters)}}$$

Where:
C = Standard Concentration (ppm)
5.64 = volume of the closed loop
0.8030 = the density of the test material
24.4 = molar volume of a vapor at STP
74.12 = molecular weight of test material
1000 = liters/cubic meter

2. Calibration Curve:

The standards listed in Tables 1, 2 and 3 are used to graph each calibration curve (Figures 1, 2 and 3) and fit a curve using the Fit Function procedure in the software application DeltaGraph Pro (Delta Point Inc., Monterey, CA).

3. Concentration of Test Material in Air

The concentration of test material in the test atmosphere is obtained by converting the absorbance measured by the Miran IR Analyzer to ppm using the appropriate calibration curve.

Comments

Samples are drawn through the analyzer using the system pump. The inlet and outlet tubes of the analyzer are connected to the exposure chamber creating a closed-loop system. Readings are taken approximately every 30 minutes.

The development of the method is found in the study record.

A check of the calibration should be performed on each study day. The check is performed by injecting a volume of the test material to achieve a desired concentration. The expected absorbance is compared to the absorbance measured by the instrument. The calibration checks should be within 10% of the standard. If repeated checks do not fall within 10 % of the standard the instrument should be recalibrated. The calibration checks should be performed so that the exposure level concentrations fall within the calibration range of the instrument.

The following personnel are trained in the use of this method and are capable of performing these analyses:

Name	Date Training Completed
Bob Quevreaux	1/28/94
Terry Kaempfe	1/28/94

Prepared by: _____ Date: 1/31/94

Reviewed by: _____ Date: 1/31/94

Figure 1
EHL 94010
Miran 1A 1815 Calibration Curve for Isobutanol

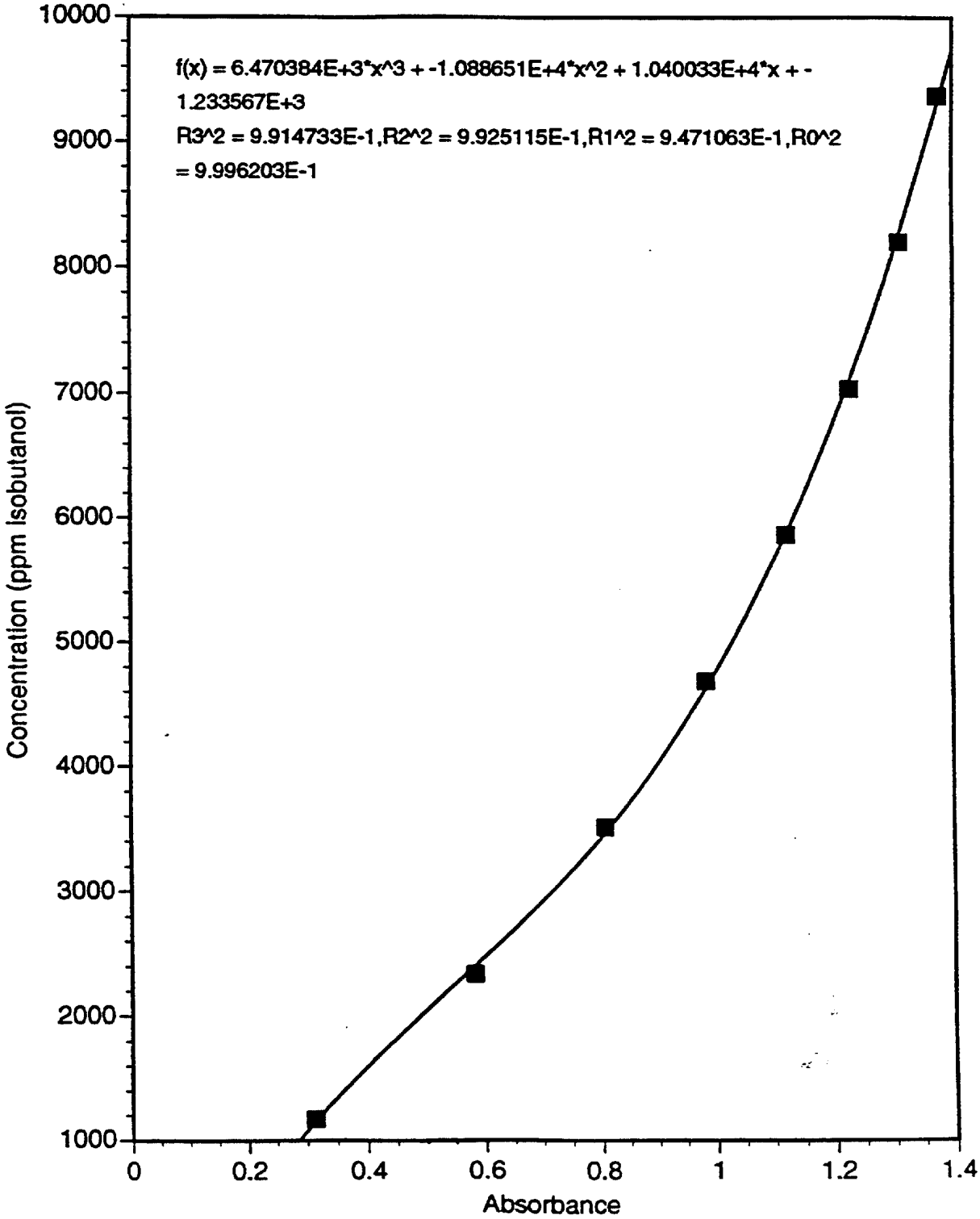


Figure 2
EHL 94010
Miran 1A 2918 Calibration Curve for Isobutanol

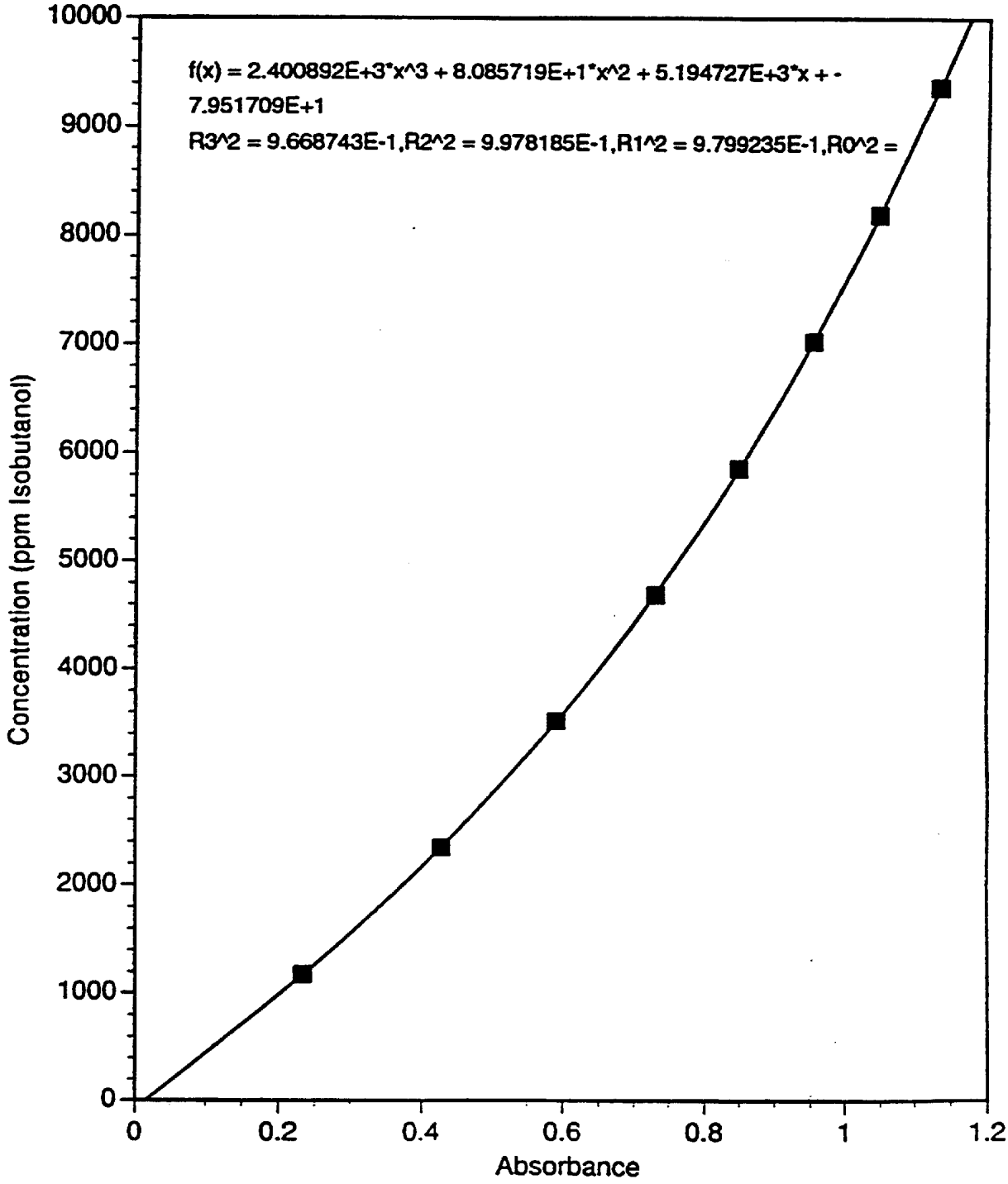
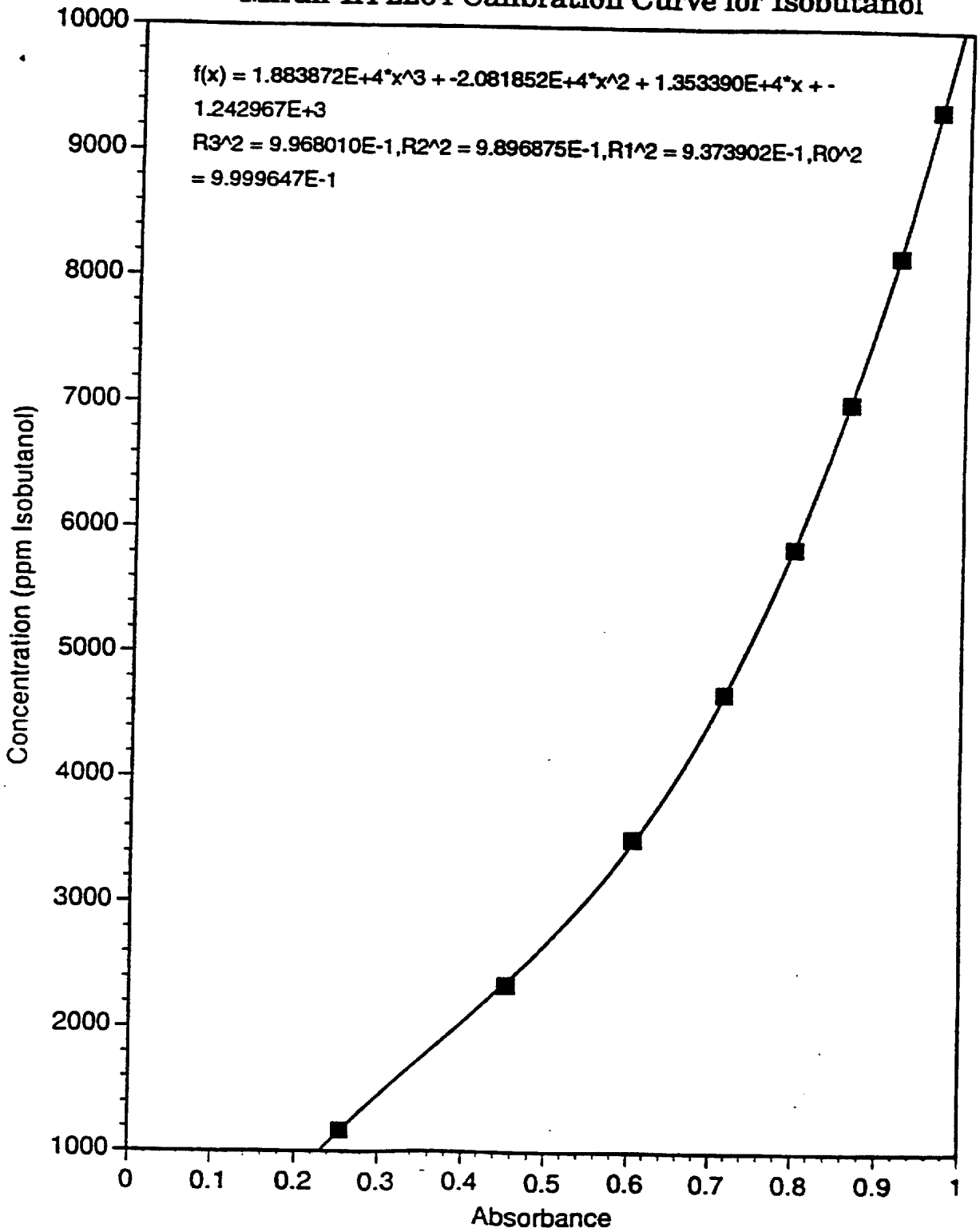


Figure 3
EHL 94010
Miran 1A 2264 Calibration Curve for Isobutanol



Appendix 8: Ophthalmic Examination Report

R # 1 Box 368
13820 N. Level Rd.
Hallsville, MO 65255
May 25, 1994

Abby Li
Environmental Health Labs
Monsanto Co
645 S. Newstead Ave
St. Louis, MO 63110

Dear Abby:

This report describes ophthalmic examination findings of laboratory rats on EHL study No. 94009. Pretest examinations were performed on 2-24-94 and post exposure examinations were conducted on 3-26-94. Prior to each examination, eyes of all animals were dilated with 1% ophthalmic atropine solution. Examinations were performed with a Keeler binocular indirect ophthalmoscope and a 28 diopter Nikon condensing lens.

One hundred nine animals (54 males and 55 females) were examined prior to initiation of the study and at the end of the study 80 animals (40 males and 40 females) including controls and treated rats were examined. Pretest examinations revealed one male with an ocular lesion (M0021). It was advised that this animal be excluded from the study.

At the post-exposure examination a lesion was noted in one female animal (F0030). No other ocular lesions were noted in the remaining animals. Therefore, using the ophthalmic examination procedures employed for this study, I conclude that no ocular abnormalities occurred related to the test compound. If I can be of further assistance, please feel free to contact me.

Sincerely,

Cecil P. Moore, DVM, MS
Diplomate ACVO

Appendix 9: Individual Motor Activity Data

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Male Rats					
94009M00001	1	155	94009M00006	1	135
94009M00001	2	77	94009M00006	2	82
94009M00001	3	6	94009M00006	3	44
94009M00001	4	0	94009M00006	4	40
94009M00001	5	26	94009M00006	5	5
94009M00001	6	0	94009M00006	6	8
94009M00002	1	88	94009M00007	1	118
94009M00002	2	72	94009M00007	2	99
94009M00002	3	33	94009M00007	3	34
94009M00002	4	0	94009M00007	4	37
94009M00002	5	0	94009M00007	5	0
94009M00002	6	0	94009M00007	6	0
94009M00003	1	173	94009M00008	1	195
94009M00003	2	141	94009M00008	2	90
94009M00003	3	20	94009M00008	3	56
94009M00003	4	0	94009M00008	4	9
94009M00003	5	0	94009M00008	5	0
94009M00003	6	0	94009M00008	6	0
94009M00004	1	114	94009M00009	1	159
94009M00004	2	110	94009M00009	2	133
94009M00004	3	0	94009M00009	3	102
94009M00004	4	0	94009M00009	4	68
94009M00004	5	20	94009M00009	5	48
94009M00004	6	3	94009M00009	6	108
94009M00005	1	127	94009M00010	1	156
94009M00005	2	68	94009M00010	2	109
94009M00005	3	88	94009M00010	3	0
94009M00005	4	37	94009M00010	4	0
94009M00005	5	2	94009M00010	5	10
94009M00005	6	0	94009M00010	6	7

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Male Rats					
94009M01001	1	137	94009M01006	1	106
94009M01001	2	95	94009M01006	2	99
94009M01001	3	32	94009M01006	3	99
94009M01001	4	0	94009M01006	4	8
94009M01001	5	0	94009M01006	5	6
94009M01001	6	0	94009M01006	6	0
94009M01002	1	131	94009M01007	1	189
94009M01002	2	136	94009M01007	2	126
94009M01002	3	117	94009M01007	3	52
94009M01002	4	20	94009M01007	4	11
94009M01002	5	0	94009M01007	5	0
94009M01002	6	0	94009M01007	6	0
94009M01003	1	124	94009M01008	1	189
94009M01003	2	32	94009M01008	2	140
94009M01003	3	0	94009M01008	3	147
94009M01003	4	0	94009M01008	4	78
94009M01003	5	0	94009M01008	5	0
94009M01003	6	11	94009M01008	6	0
94009M01004	1	156	94009M01009	1	140
94009M01004	2	84	94009M01009	2	91
94009M01004	3	59	94009M01009	3	16
94009M01004	4	0	94009M01009	4	0
94009M01004	5	0	94009M01009	5	0
94009M01004	6	2	94009M01009	6	0
94009M01005	1	197	94009M01010	1	120
94009M01005	2	146	94009M01010	2	97
94009M01005	3	62	94009M01010	3	53
94009M01005	4	8	94009M01010	4	82
94009M01005	5	0	94009M01010	5	17
94009M01005	6	0	94009M01010	6	2

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Level (3,000 ppm), Male Rats					
94009M02001	1	161	94009M02006	1	123
94009M02001	2	84	94009M02006	2	33
94009M02001	3	74	94009M02006	3	1
94009M02001	4	19	94009M02006	4	5
94009M02001	5	1	94009M02006	5	59
94009M02001	6	0	94009M02006	6	0
94009M02002	1	83	94009M02007	1	112
94009M02002	2	54	94009M02007	2	86
94009M02002	3	13	94009M02007	3	115
94009M02002	4	17	94009M02007	4	119
94009M02002	5	0	94009M02007	5	11
94009M02002	6	0	94009M02007	6	0
94009M02003	1	135	94009M02008	1	160
94009M02003	2	81	94009M02008	2	87
94009M02003	3	61	94009M02008	3	51
94009M02003	4	7	94009M02008	4	59
94009M02003	5	0	94009M02008	5	0
94009M02003	6	0	94009M02008	6	0
94009M02004	1	151	94009M02009	1	166
94009M02004	2	126	94009M02009	2	129
94009M02004	3	111	94009M02009	3	72
94009M02004	4	8	94009M02009	4	1
94009M02004	5	0	94009M02009	5	0
94009M02004	6	0	94009M02009	6	0
94009M02005	1	147	94009M02010	1	126
94009M02005	2	157	94009M02010	2	108
94009M02005	3	33	94009M02010	3	39
94009M02005	4	3	94009M02010	4	12
94009M02005	5	0	94009M02010	5	0
94009M02005	6	0	94009M02010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Male Rats					
94009M03001	1	127	94009M03006	1	126
94009M03001	2	99	94009M03006	2	85
94009M03001	3	98	94009M03006	3	33
94009M03001	4	68	94009M03006	4	1
94009M03001	5	46	94009M03006	5	7
94009M03001	6	47	94009M03006	6	3
94009M03002	1	122	94009M03007	1	106
94009M03002	2	84	94009M03007	2	130
94009M03002	3	33	94009M03007	3	73
94009M03002	4	20	94009M03007	4	27
94009M03002	5	0	94009M03007	5	0
94009M03002	6	0	94009M03007	6	0
94009M03003	1	223	94009M03008	1	175
94009M03003	2	168	94009M03008	2	94
94009M03003	3	42	94009M03008	3	27
94009M03003	4	12	94009M03008	4	0
94009M03003	5	0	94009M03008	5	0
94009M03003	6	0	94009M03008	6	0
94009M03004	1	183	94009M03009	1	178
94009M03004	2	126	94009M03009	2	97
94009M03004	3	44	94009M03009	3	96
94009M03004	4	8	94009M03009	4	0
94009M03004	5	0	94009M03009	5	0
94009M03004	6	0	94009M03009	6	0
94009M03005	1	96	94009M03010	1	209
94009M03005	2	63	94009M03010	2	72
94009M03005	3	9	94009M03010	3	0
94009M03005	4	1	94009M03010	4	0
94009M03005	5	0	94009M03010	5	0
94009M03005	6	0	94009M03010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Male Rats					
94009M00001	1	137	94009M00006	1	107
94009M00001	2	0	94009M00006	2	50
94009M00001	3	0	94009M00006	3	0
94009M00001	4	30	94009M00006	4	0
94009M00001	5	0	94009M00006	5	0
94009M00001	6	0	94009M00006	6	0
94009M00002	1	75	94009M00007	1	72
94009M00002	2	24	94009M00007	2	56
94009M00002	3	0	94009M00007	3	32
94009M00002	4	0	94009M00007	4	33
94009M00002	5	0	94009M00007	5	0
94009M00002	6	0	94009M00007	6	0
94009M00003	1	98	94009M00008	1	195
94009M00003	2	39	94009M00008	2	74
94009M00003	3	0	94009M00008	3	113
94009M00003	4	0	94009M00008	4	16
94009M00003	5	0	94009M00008	5	3
94009M00003	6	0	94009M00008	6	6
94009M00004	1	131	94009M00009	1	140
94009M00004	2	31	94009M00009	2	83
94009M00004	3	0	94009M00009	3	27
94009M00004	4	0	94009M00009	4	0
94009M00004	5	0	94009M00009	5	18
94009M00004	6	0	94009M00009	6	13
94009M00005	1	55	94009M00010	1	117
94009M00005	2	32	94009M00010	2	73
94009M00005	3	0	94009M00010	3	0
94009M00005	4	0	94009M00010	4	0
94009M00005	5	0	94009M00010	5	0
94009M00005	6	0	94009M00010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Male Rats					
94009M01001	1	91	94009M01006	1	158
94009M01001	2	1	94009M01006	2	25
94009M01001	3	0	94009M01006	3	0
94009M01001	4	0	94009M01006	4	0
94009M01001	5	0	94009M01006	5	0
94009M01001	6	0	94009M01006	6	0
94009M01002	1	88	94009M01007	1	127
94009M01002	2	65	94009M01007	2	20
94009M01002	3	2	94009M01007	3	0
94009M01002	4	1	94009M01007	4	0
94009M01002	5	6	94009M01007	5	0
94009M01002	6	0	94009M01007	6	0
94009M01003	1	82	94009M01008	1	147
94009M01003	2	44	94009M01008	2	126
94009M01003	3	0	94009M01008	3	22
94009M01003	4	16	94009M01008	4	0
94009M01003	5	0	94009M01008	5	0
94009M01003	6	0	94009M01008	6	0
94009M01004	1	147	94009M01009	1	144
94009M01004	2	47	94009M01009	2	118
94009M01004	3	2	94009M01009	3	55
94009M01004	4	0	94009M01009	4	6
94009M01004	5	0	94009M01009	5	0
94009M01004	6	0	94009M01009	6	0
94009M01005	1	170	94009M01010	1	138
94009M01005	2	32	94009M01010	2	62
94009M01005	3	0	94009M01010	3	4
94009M01005	4	0	94009M01010	4	10
94009M01005	5	0	94009M01010	5	2
94009M01005	6	0	94009M01010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Level (3,000 ppm), Male Rats					
94009M02001	1	84	94009M02006	1	79
94009M02001	2	0	94009M02006	2	0
94009M02001	3	0	94009M02006	3	0
94009M02001	4	0	94009M02006	4	0
94009M02001	5	0	94009M02006	5	0
94009M02001	6	0	94009M02006	6	0
94009M02002	1	100	94009M02007	1	186
94009M02002	2	12	94009M02007	2	77
94009M02002	3	0	94009M02007	3	0
94009M02002	4	0	94009M02007	4	0
94009M02002	5	0	94009M02007	5	0
94009M02002	6	0	94009M02007	6	0
94009M02003	1	120	94009M02008	1	170
94009M02003	2	7	94009M02008	2	79
94009M02003	3	0	94009M02008	3	0
94009M02003	4	0	94009M02008	4	0
94009M02003	5	0	94009M02008	5	0
94009M02003	6	0	94009M02008	6	5
94009M02004	1	160	94009M02009	1	71
94009M02004	2	3	94009M02009	2	71
94009M02004	3	3	94009M02009	3	9
94009M02004	4	0	94009M02009	4	0
94009M02004	5	0	94009M02009	5	0
94009M02004	6	5	94009M02009	6	0
94009M02005	1	83	94009M02010	1	131
94009M02005	2	32	94009M02010	2	32
94009M02005	3	0	94009M02010	3	0
94009M02005	4	0	94009M02010	4	0
94009M02005	5	0	94009M02010	5	0
94009M02005	6	0	94009M02010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Male Rats					
94009M03001	1	41	94009M03006	1	52
94009M03001	2	0	94009M03006	2	0
94009M03001	3	0	94009M03006	3	0
94009M03001	4	10	94009M03006	4	0
94009M03001	5	84	94009M03006	5	0
94009M03001	6	17	94009M03006	6	43
94009M03002	1	68	94009M03007	1	61
94009M03002	2	23	94009M03007	2	0
94009M03002	3	0	94009M03007	3	0
94009M03002	4	0	94009M03007	4	0
94009M03002	5	0	94009M03007	5	7
94009M03002	6	0	94009M03007	6	0
94009M03003	1	155	94009M03008	1	17
94009M03003	2	60	94009M03008	2	0
94009M03003	3	7	94009M03008	3	0
94009M03003	4	0	94009M03008	4	17
94009M03003	5	2	94009M03008	5	0
94009M03003	6	11	94009M03008	6	23
94009M03004	1	5	94009M03009	1	18
94009M03004	2	1	94009M03009	2	0
94009M03004	3	0	94009M03009	3	0
94009M03004	4	0	94009M03009	4	0
94009M03004	5	0	94009M03009	5	0
94009M03004	6	0	94009M03009	6	0
94009M03005	1	130	94009M03010	1	16
94009M03005	2	61	94009M03010	2	15
94009M03005	3	40	94009M03010	3	12
94009M03005	4	0	94009M03010	4	0
94009M03005	5	0	94009M03010	5	0
94009M03005	6	0	94009M03010	6	14

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Male Rats					
94009M00001	1	123	94009M00006	1	130
94009M00001	2	99	94009M00006	2	76
94009M00001	3	103	94009M00006	3	60
94009M00001	4	76	94009M00006	4	3
94009M00001	5	79	94009M00006	5	0
94009M00001	6	0	94009M00006	6	0
94009M00002	1	61	94009M00007	1	125
94009M00002	2	8	94009M00007	2	101
94009M00002	3	0	94009M00007	3	79
94009M00002	4	2	94009M00007	4	24
94009M00002	5	0	94009M00007	5	0
94009M00002	6	4	94009M00007	6	1
94009M00003	1	201	94009M00008	1	205
94009M00003	2	93	94009M00008	2	78
94009M00003	3	0	94009M00008	3	27
94009M00003	4	20	94009M00008	4	9
94009M00003	5	0	94009M00008	5	0
94009M00003	6	0	94009M00008	6	0
94009M00004	1	126	94009M00009	1	186
94009M00004	2	55	94009M00009	2	114
94009M00004	3	24	94009M00009	3	87
94009M00004	4	15	94009M00009	4	127
94009M00004	5	0	94009M00009	5	112
94009M00004	6	0	94009M00009	6	37
94009M00005	1	87	94009M00010	1	162
94009M00005	2	67	94009M00010	2	80
94009M00005	3	15	94009M00010	3	5
94009M00005	4	63	94009M00010	4	31
94009M00005	5	8	94009M00010	5	15
94009M00005	6	0	94009M00010	6	17

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Male Rats					
94009M01001	1	68	94009M01006	1	147
94009M01001	2	55	94009M01006	2	97
94009M01001	3	3	94009M01006	3	62
94009M01001	4	1	94009M01006	4	28
94009M01001	5	0	94009M01006	5	36
94009M01001	6	0	94009M01006	6	1
94009M01002	1	160	94009M01007	1	213
94009M01002	2	80	94009M01007	2	132
94009M01002	3	51	94009M01007	3	72
94009M01002	4	28	94009M01007	4	82
94009M01002	5	4	94009M01007	5	31
94009M01002	6	4	94009M01007	6	14
94009M01003	1	93	94009M01008	1	222
94009M01003	2	43	94009M01008	2	159
94009M01003	3	14	94009M01008	3	97
94009M01003	4	0	94009M01008	4	24
94009M01003	5	0	94009M01008	5	0
94009M01003	6	0	94009M01008	6	0
94009M01004	1	118	94009M01009	1	131
94009M01004	2	77	94009M01009	2	77
94009M01004	3	0	94009M01009	3	43
94009M01004	4	0	94009M01009	4	17
94009M01004	5	0	94009M01009	5	6
94009M01004	6	0	94009M01009	6	15
94009M01005	1	134	94009M01010	1	95
94009M01005	2	95	94009M01010	2	43
94009M01005	3	1	94009M01010	3	64
94009M01005	4	19	94009M01010	4	3
94009M01005	5	0	94009M01010	5	20
94009M01005	6	0	94009M01010	6	9

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Level (3,000 ppm), Male Rats					
94009M02001	1	159	94009M02006	1	136
94009M02001	2	102	94009M02006	2	85
94009M02001	3	89	94009M02006	3	53
94009M02001	4	43	94009M02006	4	7
94009M02001	5	0	94009M02006	5	1
94009M02001	6	0	94009M02006	6	0
94009M02002	1	87	94009M02007	1	169
94009M02002	2	62	94009M02007	2	150
94009M02002	3	2	94009M02007	3	80
94009M02002	4	0	94009M02007	4	97
94009M02002	5	0	94009M02007	5	4
94009M02002	6	0	94009M02007	6	11
94009M02003	1	194	94009M02008	1	163
94009M02003	2	6	94009M02008	2	9
94009M02003	3	11	94009M02008	3	0
94009M02003	4	12	94009M02008	4	1
94009M02003	5	0	94009M02008	5	0
94009M02003	6	0	94009M02008	6	0
94009M02004	1	193	94009M02009	1	135
94009M02004	2	102	94009M02009	2	9
94009M02004	3	34	94009M02009	3	0
94009M02004	4	19	94009M02009	4	0
94009M02004	5	0	94009M02009	5	0
94009M02004	6	0	94009M02009	6	19
94009M02005	1	115	94009M02010	1	143
94009M02005	2	103	94009M02010	2	82
94009M02005	3	0	94009M02010	3	72
94009M02005	4	2	94009M02010	4	0
94009M02005	5	0	94009M02010	5	1
94009M02005	6	0	94009M02010	6	1

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Male Rats					
94009M03001	1	163	94009M03006	1	209
94009M03001	2	115	94009M03006	2	43
94009M03001	3	32	94009M03006	3	1
94009M03001	4	16	94009M03006	4	0
94009M03001	5	0	94009M03006	5	0
94009M03001	6	0	94009M03006	6	0
94009M03002	1	191	94009M03007	1	208
94009M03002	2	137	94009M03007	2	101
94009M03002	3	78	94009M03007	3	66
94009M03002	4	15	94009M03007	4	0
94009M03002	5	0	94009M03007	5	0
94009M03002	6	1	94009M03007	6	8
94009M03003	1	139	94009M03008	1	212
94009M03003	2	180	94009M03008	2	159
94009M03003	3	23	94009M03008	3	84
94009M03003	4	0	94009M03008	4	78
94009M03003	5	2	94009M03008	5	0
94009M03003	6	0	94009M03008	6	1
94009M03004	1	154	94009M03009	1	167
94009M03004	2	74	94009M03009	2	65
94009M03004	3	17	94009M03009	3	48
94009M03004	4	0	94009M03009	4	1
94009M03004	5	0	94009M03009	5	0
94009M03004	6	0	94009M03009	6	0
94009M03005	1	64	94009M03010	1	194
94009M03005	2	33	94009M03010	2	150
94009M03005	3	0	94009M03010	3	10
94009M03005	4	6	94009M03010	4	0
94009M03005	5	0	94009M03010	5	0
94009M03005	6	1	94009M03010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Male Rats					
94009M00001	1	139	94009M00006	1	120
94009M00001	2	175	94009M00006	2	132
94009M00001	3	142	94009M00006	3	106
94009M00001	4	57	94009M00006	4	56
94009M00001	5	13	94009M00006	5	48
94009M00001	6	0	94009M00006	6	6
94009M00002	1	112	94009M00007	1	153
94009M00002	2	33	94009M00007	2	112
94009M00002	3	5	94009M00007	3	72
94009M00002	4	0	94009M00007	4	37
94009M00002	5	0	94009M00007	5	30
94009M00002	6	0	94009M00007	6	0
94009M00003	1	187	94009M00008	1	192
94009M00003	2	169	94009M00008	2	155
94009M00003	3	81	94009M00008	3	66
94009M00003	4	28	94009M00008	4	11
94009M00003	5	14	94009M00008	5	6
94009M00003	6	3	94009M00008	6	0
94009M00004	1	79	94009M00009	1	177
94009M00004	2	62	94009M00009	2	115
94009M00004	3	16	94009M00009	3	140
94009M00004	4	10	94009M00009	4	78
94009M00004	5	3	94009M00009	5	40
94009M00004	6	16	94009M00009	6	1
94009M00005	1	144	94009M00010	1	81
94009M00005	2	77	94009M00010	2	75
94009M00005	3	48	94009M00010	3	43
94009M00005	4	48	94009M00010	4	25
94009M00005	5	30	94009M00010	5	19
94009M00005	6	0	94009M00010	6	12

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Male Rats					
94009M01001	1	162	94009M01006	1	164
94009M01001	2	88	94009M01006	2	120
94009M01001	3	8	94009M01006	3	128
94009M01001	4	0	94009M01006	4	100
94009M01001	5	0	94009M01006	5	97
94009M01001	6	4	94009M01006	6	51
94009M01002	1	177	94009M01007	1	175
94009M01002	2	99	94009M01007	2	114
94009M01002	3	28	94009M01007	3	81
94009M01002	4	0	94009M01007	4	33
94009M01002	5	6	94009M01007	5	0
94009M01002	6	0	94009M01007	6	0
94009M01003	1	159	94009M01008	1	264
94009M01003	2	45	94009M01008	2	122
94009M01003	3	4	94009M01008	3	133
94009M01003	4	1	94009M01008	4	132
94009M01003	5	7	94009M01008	5	122
94009M01003	6	72	94009M01008	6	77
94009M01004	1	144	94009M01009	1	151
94009M01004	2	111	94009M01009	2	121
94009M01004	3	24	94009M01009	3	87
94009M01004	4	0	94009M01009	4	79
94009M01004	5	8	94009M01009	5	10
94009M01004	6	1	94009M01009	6	0
94009M01005	1	187	94009M01010	1	140
94009M01005	2	66	94009M01010	2	128
94009M01005	3	109	94009M01010	3	142
94009M01005	4	68	94009M01010	4	100
94009M01005	5	25	94009M01010	5	78
94009M01005	6	21	94009M01010	6	87

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Level (3,000 ppm), Male Rats					
94009M02001	1	197	94009M02006	1	132
94009M02001	2	105	94009M02006	2	116
94009M02001	3	149	94009M02006	3	26
94009M02001	4	32	94009M02006	4	0
94009M02001	5	7	94009M02006	5	0
94009M02001	6	0	94009M02006	6	0
94009M02002	1	128	94009M02007	1	205
94009M02002	2	80	94009M02007	2	154
94009M02002	3	19	94009M02007	3	78
94009M02002	4	0	94009M02007	4	105
94009M02002	5	0	94009M02007	5	106
94009M02002	6	0	94009M02007	6	123
94009M02003	1	120	94009M02008	1	216
94009M02003	2	20	94009M02008	2	67
94009M02003	3	2	94009M02008	3	21
94009M02003	4	62	94009M02008	4	0
94009M02003	5	74	94009M02008	5	0
94009M02003	6	91	94009M02008	6	0
94009M02004	1	185	94009M02009	1	112
94009M02004	2	29	94009M02009	2	162
94009M02004	3	10	94009M02009	3	199
94009M02004	4	0	94009M02009	4	109
94009M02004	5	0	94009M02009	5	19
94009M02004	6	0	94009M02009	6	2
94009M02005	1	199	94009M02010	1	176
94009M02005	2	120	94009M02010	2	85
94009M02005	3	91	94009M02010	3	99
94009M02005	4	113	94009M02010	4	73
94009M02005	5	124	94009M02010	5	78
94009M02005	6	59	94009M02010	6	22

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Male Rats					
94009M03001	1	167	94009M03006	1	180
94009M03001	2	106	94009M03006	2	136
94009M03001	3	129	94009M03006	3	81
94009M03001	4	77	94009M03006	4	75
94009M03001	5	48	94009M03006	5	22
94009M03001	6	13	94009M03006	6	0
94009M03002	1	200	94009M03007	1	209
94009M03002	2	133	94009M03007	2	133
94009M03002	3	104	94009M03007	3	50
94009M03002	4	76	94009M03007	4	30
94009M03002	5	57	94009M03007	5	0
94009M03002	6	9	94009M03007	6	0
94009M03003	1	253	94009M03008	1	179
94009M03003	2	120	94009M03008	2	71
94009M03003	3	102	94009M03008	3	59
94009M03003	4	53	94009M03008	4	70
94009M03003	5	128	94009M03008	5	6
94009M03003	6	16	94009M03008	6	0
94009M03004	1	132	94009M03009	1	254
94009M03004	2	148	94009M03009	2	91
94009M03004	3	90	94009M03009	3	64
94009M03004	4	20	94009M03009	4	0
94009M03004	5	3	94009M03009	5	0
94009M03004	6	2	94009M03009	6	0
94009M03005	1	86	94009M03010	1	123
94009M03005	2	30	94009M03010	2	110
94009M03005	3	83	94009M03010	3	50
94009M03005	4	41	94009M03010	4	1
94009M03005	5	4	94009M03010	5	0
94009M03005	6	2	94009M03010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Male Rats					
94009M00001	1	110	94009M00006	1	168
94009M00001	2	78	94009M00006	2	126
94009M00001	3	67	94009M00006	3	72
94009M00001	4	53	94009M00006	4	0
94009M00001	5	0	94009M00006	5	0
94009M00001	6	0	94009M00006	6	0
94009M00002	1	132	94009M00007	1	148
94009M00002	2	111	94009M00007	2	74
94009M00002	3	85	94009M00007	3	120
94009M00002	4	11	94009M00007	4	80
94009M00002	5	2	94009M00007	5	57
94009M00002	6	1	94009M00007	6	25
94009M00003	1	199	94009M00008	1	165
94009M00003	2	213	94009M00008	2	134
94009M00003	3	33	94009M00008	3	31
94009M00003	4	0	94009M00008	4	0
94009M00003	5	16	94009M00008	5	0
94009M00003	6	19	94009M00008	6	4
94009M00004	1	129	94009M00009	1	148
94009M00004	2	82	94009M00009	2	164
94009M00004	3	25	94009M00009	3	102
94009M00004	4	0	94009M00009	4	84
94009M00004	5	2	94009M00009	5	43
94009M00004	6	0	94009M00009	6	14
94009M00005	1	185	94009M00010	1	176
94009M00005	2	70	94009M00010	2	119
94009M00005	3	53	94009M00010	3	106
94009M00005	4	46	94009M00010	4	50
94009M00005	5	53	94009M00010	5	54
94009M00005	6	25	94009M00010	6	102

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Male Rats					
94009M01001	1	187	94009M01006	1	149
94009M01001	2	60	94009M01006	2	157
94009M01001	3	41	94009M01006	3	71
94009M01001	4	4	94009M01006	4	85
94009M01001	5	3	94009M01006	5	69
94009M01001	6	2	94009M01006	6	3
94009M01002	1	142	94009M01007	1	165
94009M01002	2	103	94009M01007	2	124
94009M01002	3	35	94009M01007	3	3
94009M01002	4	25	94009M01007	4	0
94009M01002	5	78	94009M01007	5	26
94009M01002	6	0	94009M01007	6	3
94009M01003	1	95	94009M01008	1	194
94009M01003	2	94	94009M01008	2	129
94009M01003	3	21	94009M01008	3	91
94009M01003	4	0	94009M01008	4	221
94009M01003	5	9	94009M01008	5	33
94009M01003	6	2	94009M01008	6	1
94009M01004	1	173	94009M01009	1	139
94009M01004	2	116	94009M01009	2	87
94009M01004	3	3	94009M01009	3	48
94009M01004	4	12	94009M01009	4	25
94009M01004	5	10	94009M01009	5	0
94009M01004	6	1	94009M01009	6	0
94009M01005	1	228	94009M01010	1	214
94009M01005	2	119	94009M01010	2	132
94009M01005	3	81	94009M01010	3	112
94009M01005	4	37	94009M01010	4	118
94009M01005	5	6	94009M01010	5	86
94009M01005	6	32	94009M01010	6	69

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Level (3,000 ppm), Male Rats					
94009M02001	1	172	94009M02006	1	146
94009M02001	2	142	94009M02006	2	87
94009M02001	3	111	94009M02006	3	41
94009M02001	4	81	94009M02006	4	0
94009M02001	5	96	94009M02006	5	0
94009M02001	6	40	94009M02006	6	0
94009M02002	1	90	94009M02007	1	206
94009M02002	2	50	94009M02007	2	161
94009M02002	3	0	94009M02007	3	179
94009M02002	4	0	94009M02007	4	100
94009M02002	5	0	94009M02007	5	128
94009M02002	6	0	94009M02007	6	28
94009M02003	1	173	94009M02008	1	180
94009M02003	2	94	94009M02008	2	119
94009M02003	3	15	94009M02008	3	55
94009M02003	4	2	94009M02008	4	4
94009M02003	5	0	94009M02008	5	19
94009M02003	6	0	94009M02008	6	109
94009M02004	1	187	94009M02009	1	107
94009M02004	2	128	94009M02009	2	167
94009M02004	3	45	94009M02009	3	102
94009M02004	4	17	94009M02009	4	52
94009M02004	5	4	94009M02009	5	30
94009M02004	6	0	94009M02009	6	0
94009M02005	1	151	94009M02010	1	156
94009M02005	2	115	94009M02010	2	115
94009M02005	3	102	94009M02010	3	115
94009M02005	4	89	94009M02010	4	72
94009M02005	5	70	94009M02010	5	51
94009M02005	6	2	94009M02010	6	19

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Male Rats					
94009M03001	1	151	94009M03006	1	180
94009M03001	2	98	94009M03006	2	141
94009M03001	3	153	94009M03006	3	116
94009M03001	4	168	94009M03006	4	33
94009M03001	5	124	94009M03006	5	4
94009M03001	6	50	94009M03006	6	1
94009M03002	1	190	94009M03007	1	Missing
94009M03002	2	130	94009M03007	2	Data (c)
94009M03002	3	69	94009M03007	3	
94009M03002	4	49	94009M03007	4	
94009M03002	5	6	94009M03007	5	
94009M03002	6	3	94009M03007	6	
94009M03003	1	221	94009M03008	1	242
94009M03003	2	188	94009M03008	2	216
94009M03003	3	33	94009M03008	3	173
94009M03003	4	10	94009M03008	4	168
94009M03003	5	9	94009M03008	5	63
94009M03003	6	74	94009M03008	6	18
94009M03004	1	121	94009M03009	1	154
94009M03004	2	125	94009M03009	2	151
94009M03004	3	102	94009M03009	3	72
94009M03004	4	8	94009M03009	4	9
94009M03004	5	2	94009M03009	5	0
94009M03004	6	0	94009M03009	6	0
94009M03005	1	38	94009M03010	1	175
94009M03005	2	64	94009M03010	2	152
94009M03005	3	63	94009M03010	3	110
94009M03005	4	43	94009M03010	4	53
94009M03005	5	69	94009M03010	5	0
94009M03005	6	19	94009M03010	6	1

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.
(c) Animal died prior to Day 14 session.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Female Rats					
94009F00001	1	134	94009F00006	1	152
94009F00001	2	137	94009F00006	2	44
94009F00001	3	77	94009F00006	3	0
94009F00001	4	28	94009F00006	4	0
94009F00001	5	0	94009F00006	5	30
94009F00001	6	0	94009F00006	6	0
94009F00002	1	115	94009F00007	1	125
94009F00002	2	32	94009F00007	2	71
94009F00002	3	0	94009F00007	3	14
94009F00002	4	0	94009F00007	4	48
94009F00002	5	1	94009F00007	5	37
94009F00002	6	0	94009F00007	6	0
94009F00003	1	117	94009F00008	1	127
94009F00003	2	85	94009F00008	2	110
94009F00003	3	30	94009F00008	3	45
94009F00003	4	0	94009F00008	4	29
94009F00003	5	0	94009F00008	5	2
94009F00003	6	0	94009F00008	6	0
94009F00004	1	132	94009F00009	1	106
94009F00004	2	130	94009F00009	2	108
94009F00004	3	94	94009F00009	3	67
94009F00004	4	34	94009F00009	4	0
94009F00004	5	59	94009F00009	5	0
94009F00004	6	0	94009F00009	6	0
94009F00005	1	110	94009F00010	1	108
94009F00005	2	106	94009F00010	2	68
94009F00005	3	36	94009F00010	3	24
94009F00005	4	1	94009F00010	4	0
94009F00005	5	5	94009F00010	5	0
94009F00005	6	64	94009F00010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Female Rats					
94009F01001	1	147	94009F01006	1	193
94009F01001	2	107	94009F01006	2	118
94009F01001	3	42	94009F01006	3	60
94009F01001	4	0	94009F01006	4	26
94009F01001	5	0	94009F01006	5	29
94009F01001	6	0	94009F01006	6	0
94009F01002	1	157	94009F01007	1	124
94009F01002	2	67	94009F01007	2	41
94009F01002	3	1	94009F01007	3	0
94009F01002	4	0	94009F01007	4	16
94009F01002	5	0	94009F01007	5	33
94009F01002	6	0	94009F01007	6	0
94009F01003	1	109	94009F01008	1	107
94009F01003	2	27	94009F01008	2	62
94009F01003	3	3	94009F01008	3	27
94009F01003	4	0	94009F01008	4	0
94009F01003	5	0	94009F01008	5	0
94009F01003	6	0	94009F01008	6	0
94009F01004	1	140	94009F01009	1	247
94009F01004	2	21	94009F01009	2	109
94009F01004	3	0	94009F01009	3	18
94009F01004	4	0	94009F01009	4	0
94009F01004	5	3	94009F01009	5	0
94009F01004	6	101	94009F01009	6	5
94009F01005	1	164	94009F01010	1	179
94009F01005	2	106	94009F01010	2	70
94009F01005	3	0	94009F01010	3	5
94009F01005	4	0	94009F01010	4	0
94009F01005	5	7	94009F01010	5	1
94009F01005	6	0	94009F01010	6	2

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Dose (3,000 ppm), Female Rats					
94009F02001	1	165	94009F02006	1	172
94009F02001	2	121	94009F02006	2	151
94009F02001	3	57	94009F02006	3	147
94009F02001	4	15	94009F02006	4	74
94009F02001	5	0	94009F02006	5	11
94009F02001	6	0	94009F02006	6	0
94009F02002	1	82	94009F02007	1	129
94009F02002	2	60	94009F02007	2	178
94009F02002	3	24	94009F02007	3	96
94009F02002	4	0	94009F02007	4	4
94009F02002	5	0	94009F02007	5	0
94009F02002	6	13	94009F02007	6	0
94009F02003	1	138	94009F02008	1	69
94009F02003	2	92	94009F02008	2	8
94009F02003	3	51	94009F02008	3	34
94009F02003	4	0	94009F02008	4	2
94009F02003	5	0	94009F02008	5	0
94009F02003	6	0	94009F02008	6	46
94009F02004	1	107	94009F02009	1	176
94009F02004	2	84	94009F02009	2	127
94009F02004	3	151	94009F02009	3	8
94009F02004	4	9	94009F02009	4	1
94009F02004	5	15	94009F02009	5	0
94009F02004	6	12	94009F02009	6	0
94009F02005	1	184	94009F02010	1	226
94009F02005	2	179	94009F02010	2	109
94009F02005	3	130	94009F02010	3	21
94009F02005	4	89	94009F02010	4	0
94009F02005	5	32	94009F02010	5	0
94009F02005	6	0	94009F02010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Pretest Baseline Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Female Rats					
94009F03001	1	117	94009F03006	1	127
94009F03001	2	71	94009F03006	2	115
94009F03001	3	65	94009F03006	3	100
94009F03001	4	49	94009F03006	4	45
94009F03001	5	72	94009F03006	5	0
94009F03001	6	24	94009F03006	6	0
94009F03002	1	109	94009F03007	1	251
94009F03002	2	81	94009F03007	2	84
94009F03002	3	32	94009F03007	3	1
94009F03002	4	0	94009F03007	4	0
94009F03002	5	0	94009F03007	5	0
94009F03002	6	0	94009F03007	6	0
94009F03003	1	143	94009F03008	1	140
94009F03003	2	49	94009F03008	2	128
94009F03003	3	20	94009F03008	3	53
94009F03003	4	56	94009F03008	4	0
94009F03003	5	147	94009F03008	5	0
94009F03003	6	111	94009F03008	6	0
94009F03004	1	148	94009F03009	1	119
94009F03004	2	121	94009F03009	2	150
94009F03004	3	113	94009F03009	3	172
94009F03004	4	85	94009F03009	4	18
94009F03004	5	26	94009F03009	5	0
94009F03004	6	1	94009F03009	6	0
94009F03005	1	176	94009F03010	1	162
94009F03005	2	125	94009F03010	2	36
94009F03005	3	107	94009F03010	3	0
94009F03005	4	57	94009F03010	4	0
94009F03005	5	18	94009F03010	5	144
94009F03005	6	10	94009F03010	6	96

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Female Rats					
94009F00001	1	108	94009F00006	1	105
94009F00001	2	13	94009F00006	2	0
94009F00001	3	0	94009F00006	3	0
94009F00001	4	0	94009F00006	4	30
94009F00001	5	0	94009F00006	5	0
94009F00001	6	0	94009F00006	6	28
94009F00002	1	106	94009F00007	1	35
94009F00002	2	19	94009F00007	2	25
94009F00002	3	1	94009F00007	3	1
94009F00002	4	0	94009F00007	4	0
94009F00002	5	0	94009F00007	5	0
94009F00002	6	0	94009F00007	6	0
94009F00003	1	64	94009F00008	1	99
94009F00003	2	60	94009F00008	2	64
94009F00003	3	2	94009F00008	3	8
94009F00003	4	13	94009F00008	4	0
94009F00003	5	0	94009F00008	5	0
94009F00003	6	0	94009F00008	6	0
94009F00004	1	113	94009F00009	1	137
94009F00004	2	19	94009F00009	2	111
94009F00004	3	0	94009F00009	3	0
94009F00004	4	0	94009F00009	4	0
94009F00004	5	21	94009F00009	5	28
94009F00004	6	7	94009F00009	6	0
94009F00005	1	107	94009F00010	1	64
94009F00005	2	73	94009F00010	2	0
94009F00005	3	65	94009F00010	3	0
94009F00005	4	22	94009F00010	4	0
94009F00005	5	0	94009F00010	5	0
94009F00005	6	0	94009F00010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Female Rats					
94009F01001	1	75	94009F01006	1	136
94009F01001	2	0	94009F01006	2	36
94009F01001	3	0	94009F01006	3	0
94009F01001	4	15	94009F01006	4	0
94009F01001	5	0	94009F01006	5	1
94009F01001	6	0	94009F01006	6	0
94009F01002	1	145	94009F01007	1	42
94009F01002	2	23	94009F01007	2	8
94009F01002	3	0	94009F01007	3	0
94009F01002	4	0	94009F01007	4	1
94009F01002	5	0	94009F01007	5	0
94009F01002	6	0	94009F01007	6	0
94009F01003	1	117	94009F01008	1	82
94009F01003	2	147	94009F01008	2	58
94009F01003	3	68	94009F01008	3	46
94009F01003	4	94	94009F01008	4	57
94009F01003	5	68	94009F01008	5	14
94009F01003	6	5	94009F01008	6	0
94009F01004	1	195	94009F01009	1	129
94009F01004	2	67	94009F01009	2	5
94009F01004	3	0	94009F01009	3	50
94009F01004	4	0	94009F01009	4	18
94009F01004	5	0	94009F01009	5	0
94009F01004	6	3	94009F01009	6	6
94009F01005	1	114	94009F01010	1	152
94009F01005	2	0	94009F01010	2	91
94009F01005	3	0	94009F01010	3	32
94009F01005	4	0	94009F01010	4	0
94009F01005	5	1	94009F01010	5	0
94009F01005	6	1	94009F01010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Dose (3,000 ppm), Female Rats					
94009F02001	1	125	94009F02006	1	69
94009F02001	2	4	94009F02006	2	4
94009F02001	3	0	94009F02006	3	17
94009F02001	4	0	94009F02006	4	0
94009F02001	5	0	94009F02006	5	57
94009F02001	6	0	94009F02006	6	30
94009F02002	1	176	94009F02007	1	74
94009F02002	2	130	94009F02007	2	0
94009F02002	3	0	94009F02007	3	0
94009F02002	4	0	94009F02007	4	0
94009F02002	5	1	94009F02007	5	0
94009F02002	6	0	94009F02007	6	0
94009F02003	1	127	94009F02008	1	72
94009F02003	2	133	94009F02008	2	0
94009F02003	3	75	94009F02008	3	0
94009F02003	4	39	94009F02008	4	21
94009F02003	5	0	94009F02008	5	0
94009F02003	6	0	94009F02008	6	0
94009F02004	1	182	94009F02009	1	122
94009F02004	2	108	94009F02009	2	0
94009F02004	3	0	94009F02009	3	1
94009F02004	4	0	94009F02009	4	0
94009F02004	5	0	94009F02009	5	0
94009F02004	6	0	94009F02009	6	0
94009F02005	1	230	94009F02010	1	139
94009F02005	2	105	94009F02010	2	51
94009F02005	3	10	94009F02010	3	16
94009F02005	4	0	94009F02010	4	0
94009F02005	5	0	94009F02010	5	33
94009F02005	6	0	94009F02010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 0 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Female Rats					
94009F03001	1	28	94009F03006	1	47
94009F03001	2	7	94009F03006	2	2
94009F03001	3	0	94009F03006	3	0
94009F03001	4	0	94009F03006	4	0
94009F03001	5	0	94009F03006	5	0
94009F03001	6	41	94009F03006	6	0
94009F03002	1	1	94009F03007	1	56
94009F03002	2	5	94009F03007	2	19
94009F03002	3	2	94009F03007	3	48
94009F03002	4	18	94009F03007	4	0
94009F03002	5	9	94009F03007	5	0
94009F03002	6	12	94009F03007	6	0
94009F03003	1	61	94009F03008	1	42
94009F03003	2	59	94009F03008	2	0
94009F03003	3	4	94009F03008	3	2
94009F03003	4	49	94009F03008	4	0
94009F03003	5	0	94009F03008	5	0
94009F03003	6	0	94009F03008	6	0
94009F03004	1	95	94009F03009	1	89
94009F03004	2	4	94009F03009	2	0
94009F03004	3	0	94009F03009	3	0
94009F03004	4	0	94009F03009	4	0
94009F03004	5	4	94009F03009	5	1
94009F03004	6	66	94009F03009	6	0
94009F03005	1	84	94009F03010	1	93
94009F03005	2	51	94009F03010	2	37
94009F03005	3	0	94009F03010	3	0
94009F03005	4	0	94009F03010	4	0
94009F03005	5	1	94009F03010	5	0
94009F03005	6	0	94009F03010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Female Rats					
94009F00001	1	135	94009F00006	1	114
94009F00001	2	0	94009F00006	2	1
94009F00001	3	0	94009F00006	3	0
94009F00001	4	1	94009F00006	4	14
94009F00001	5	3	94009F00006	5	0
94009F00001	6	15	94009F00006	6	0
94009F00002	1	63	94009F00007	1	114
94009F00002	2	17	94009F00007	2	86
94009F00002	3	34	94009F00007	3	41
94009F00002	4	2	94009F00007	4	50
94009F00002	5	2	94009F00007	5	52
94009F00002	6	0	94009F00007	6	29
94009F00003	1	42	94009F00008	1	114
94009F00003	2	0	94009F00008	2	70
94009F00003	3	0	94009F00008	3	0
94009F00003	4	0	94009F00008	4	0
94009F00003	5	0	94009F00008	5	0
94009F00003	6	23	94009F00008	6	0
94009F00004	1	95	94009F00009	1	115
94009F00004	2	30	94009F00009	2	125
94009F00004	3	35	94009F00009	3	18
94009F00004	4	6	94009F00009	4	0
94009F00004	5	0	94009F00009	5	0
94009F00004	6	14	94009F00009	6	0
94009F00005	1	134	94009F00010	1	101
94009F00005	2	59	94009F00010	2	14
94009F00005	3	2	94009F00010	3	125
94009F00005	4	8	94009F00010	4	115
94009F00005	5	3	94009F00010	5	1
94009F00005	6	2	94009F00010	6	7

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Female Rats					
94009F01001	1	159	94009F01006	1	159
94009F01001	2	125	94009F01006	2	67
94009F01001	3	48	94009F01006	3	0
94009F01001	4	3	94009F01006	4	0
94009F01001	5	0	94009F01006	5	0
94009F01001	6	0	94009F01006	6	0
94009F01002	1	114	94009F01007	1	159
94009F01002	2	51	94009F01007	2	122
94009F01002	3	100	94009F01007	3	69
94009F01002	4	97	94009F01007	4	69
94009F01002	5	12	94009F01007	5	91
94009F01002	6	0	94009F01007	6	41
94009F01003	1	144	94009F01008	1	117
94009F01003	2	0	94009F01008	2	49
94009F01003	3	20	94009F01008	3	31
94009F01003	4	1	94009F01008	4	16
94009F01003	5	0	94009F01008	5	3
94009F01003	6	0	94009F01008	6	0
94009F01004	1	147	94009F01009	1	186
94009F01004	2	60	94009F01009	2	89
94009F01004	3	71	94009F01009	3	0
94009F01004	4	5	94009F01009	4	0
94009F01004	5	62	94009F01009	5	0
94009F01004	6	12	94009F01009	6	0
94009F01005	1	130	94009F01010	1	93
94009F01005	2	56	94009F01010	2	0
94009F01005	3	42	94009F01010	3	0
94009F01005	4	0	94009F01010	4	0
94009F01005	5	0	94009F01010	5	0
94009F01005	6	15	94009F01010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Dose (3,000 ppm), Female Rats					
94009F02001	1	215	94009F02006	1	194
94009F02001	2	86	94009F02006	2	54
94009F02001	3	56	94009F02006	3	84
94009F02001	4	64	94009F02006	4	2
94009F02001	5	20	94009F02006	5	0
94009F02001	6	0	94009F02006	6	0
94009F02002	1	91	94009F02007	1	105
94009F02002	2	84	94009F02007	2	68
94009F02002	3	48	94009F02007	3	51
94009F02002	4	11	94009F02007	4	9
94009F02002	5	0	94009F02007	5	0
94009F02002	6	1	94009F02007	6	0
94009F02003	1	132	94009F02008	1	100
94009F02003	2	71	94009F02008	2	101
94009F02003	3	24	94009F02008	3	112
94009F02003	4	0	94009F02008	4	85
94009F02003	5	0	94009F02008	5	0
94009F02003	6	0	94009F02008	6	0
94009F02004	1	132	94009F02009	1	120
94009F02004	2	47	94009F02009	2	129
94009F02004	3	4	94009F02009	3	83
94009F02004	4	0	94009F02009	4	114
94009F02004	5	0	94009F02009	5	80
94009F02004	6	13	94009F02009	6	42
94009F02005	1	185	94009F02010	1	73
94009F02005	2	97	94009F02010	2	27
94009F02005	3	2	94009F02010	3	15
94009F02005	4	0	94009F02010	4	11
94009F02005	5	0	94009F02010	5	0
94009F02005	6	0	94009F02010	6	51

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 1 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Female Rats					
94009F03001	1	119	94009F03006	1	142
94009F03001	2	92	94009F03006	2	70
94009F03001	3	40	94009F03006	3	17
94009F03001	4	21	94009F03006	4	13
94009F03001	5	0	94009F03006	5	0
94009F03001	6	2	94009F03006	6	68
94009F03002	1	162	94009F03007	1	182
94009F03002	2	148	94009F03007	2	109
94009F03002	3	125	94009F03007	3	132
94009F03002	4	59	94009F03007	4	162
94009F03002	5	46	94009F03007	5	98
94009F03002	6	5	94009F03007	6	147
94009F03003	1	248	94009F03008	1	103
94009F03003	2	146	94009F03008	2	47
94009F03003	3	102	94009F03008	3	4
94009F03003	4	15	94009F03008	4	0
94009F03003	5	0	94009F03008	5	11
94009F03003	6	0	94009F03008	6	8
94009F03004	1	133	94009F03009	1	238
94009F03004	2	91	94009F03009	2	154
94009F03004	3	47	94009F03009	3	20
94009F03004	4	0	94009F03009	4	0
94009F03004	5	0	94009F03009	5	0
94009F03004	6	0	94009F03009	6	0
94009F03005	1	160	94009F03010	1	78
94009F03005	2	127	94009F03010	2	5
94009F03005	3	117	94009F03010	3	36
94009F03005	4	61	94009F03010	4	50
94009F03005	5	0	94009F03010	5	25
94009F03005	6	0	94009F03010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Female Rats					
94009F00001	1	171	94009F00006	1	146
94009F00001	2	93	94009F00006	2	65
94009F00001	3	18	94009F00006	3	99
94009F00001	4	18	94009F00006	4	48
94009F00001	5	0	94009F00006	5	4
94009F00001	6	0	94009F00006	6	0
94009F00002	1	120	94009F00007	1	152
94009F00002	2	80	94009F00007	2	91
94009F00002	3	17	94009F00007	3	60
94009F00002	4	13	94009F00007	4	63
94009F00002	5	0	94009F00007	5	46
94009F00002	6	0	94009F00007	6	92
94009F00003	1	116	94009F00008	1	150
94009F00003	2	16	94009F00008	2	106
94009F00003	3	0	94009F00008	3	76
94009F00003	4	2	94009F00008	4	35
94009F00003	5	84	94009F00008	5	31
94009F00003	6	91	94009F00008	6	0
94009F00004	1	142	94009F00009	1	142
94009F00004	2	147	94009F00009	2	105
94009F00004	3	10	94009F00009	3	70
94009F00004	4	30	94009F00009	4	64
94009F00004	5	0	94009F00009	5	76
94009F00004	6	0	94009F00009	6	91
94009F00005	1	149	94009F00010	1	99
94009F00005	2	119	94009F00010	2	10
94009F00005	3	84	94009F00010	3	0
94009F00005	4	92	94009F00010	4	0
94009F00005	5	73	94009F00010	5	0
94009F00005	6	92	94009F00010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Female Rats					
94009F01001	1	142	94009F01006	1	165
94009F01001	2	120	94009F01006	2	130
94009F01001	3	95	94009F01006	3	15
94009F01001	4	100	94009F01006	4	12
94009F01001	5	70	94009F01006	5	122
94009F01001	6	88	94009F01006	6	74
94009F01002	1	172	94009F01007	1	203
94009F01002	2	83	94009F01007	2	118
94009F01002	3	3	94009F01007	3	100
94009F01002	4	0	94009F01007	4	41
94009F01002	5	0	94009F01007	5	0
94009F01002	6	0	94009F01007	6	0
94009F01003	1	172	94009F01008	1	144
94009F01003	2	111	94009F01008	2	65
94009F01003	3	157	94009F01008	3	77
94009F01003	4	91	94009F01008	4	88
94009F01003	5	86	94009F01008	5	93
94009F01003	6	52	94009F01008	6	46
94009F01004	1	169	94009F01009	1	190
94009F01004	2	84	94009F01009	2	103
94009F01004	3	24	94009F01009	3	72
94009F01004	4	4	94009F01009	4	26
94009F01004	5	73	94009F01009	5	0
94009F01004	6	63	94009F01009	6	0
94009F01005	1	88	94009F01010	1	193
94009F01005	2	86	94009F01010	2	120
94009F01005	3	29	94009F01010	3	68
94009F01005	4	52	94009F01010	4	0
94009F01005	5	67	94009F01010	5	0
94009F01005	6	47	94009F01010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Dose (3,000 ppm), Female Rats					
94009F02001	1	165	94009F02006	1	216
94009F02001	2	116	94009F02006	2	88
94009F02001	3	90	94009F02006	3	70
94009F02001	4	40	94009F02006	4	178
94009F02001	5	51	94009F02006	5	150
94009F02001	6	111	94009F02006	6	22
94009F02002	1	130	94009F02007	1	167
94009F02002	2	41	94009F02007	2	98
94009F02002	3	59	94009F02007	3	98
94009F02002	4	0	94009F02007	4	4
94009F02002	5	0	94009F02007	5	0
94009F02002	6	1	94009F02007	6	0
94009F02003	1	141	94009F02008	1	109
94009F02003	2	78	94009F02008	2	53
94009F02003	3	97	94009F02008	3	55
94009F02003	4	93	94009F02008	4	0
94009F02003	5	99	94009F02008	5	0
94009F02003	6	107	94009F02008	6	0
94009F02004	1	179	94009F02009	1	121
94009F02004	2	115	94009F02009	2	101
94009F02004	3	95	94009F02009	3	95
94009F02004	4	34	94009F02009	4	21
94009F02004	5	8	94009F02009	5	3
94009F02004	6	30	94009F02009	6	3
94009F02005	1	166	94009F02010	1	207
94009F02005	2	157	94009F02010	2	106
94009F02005	3	104	94009F02010	3	172
94009F02005	4	97	94009F02010	4	3
94009F02005	5	86	94009F02010	5	0
94009F02005	6	85	94009F02010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 7 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Female Rats					
94009F03001	1	146	94009F03006	1	146
94009F03001	2	111	94009F03006	2	124
94009F03001	3	111	94009F03006	3	95
94009F03001	4	90	94009F03006	4	73
94009F03001	5	95	94009F03006	5	3
94009F03001	6	89	94009F03006	6	68
94009F03002	1	148	94009F03007	1	157
94009F03002	2	47	94009F03007	2	79
94009F03002	3	8	94009F03007	3	101
94009F03002	4	88	94009F03007	4	56
94009F03002	5	87	94009F03007	5	53
94009F03002	6	0	94009F03007	6	164
94009F03003	1	217	94009F03008	1	132
94009F03003	2	103	94009F03008	2	43
94009F03003	3	34	94009F03008	3	0
94009F03003	4	31	94009F03008	4	0
94009F03003	5	32	94009F03008	5	10
94009F03003	6	0	94009F03008	6	112
94009F03004	1	151	94009F03009	1	145
94009F03004	2	102	94009F03009	2	149
94009F03004	3	67	94009F03009	3	123
94009F03004	4	0	94009F03009	4	74
94009F03004	5	34	94009F03009	5	78
94009F03004	6	75	94009F03009	6	29
94009F03005	1	180	94009F03010	1	199
94009F03005	2	106	94009F03010	2	74
94009F03005	3	118	94009F03010	3	3
94009F03005	4	81	94009F03010	4	0
94009F03005	5	43	94009F03010	5	13
94009F03005	6	14	94009F03010	6	107

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Vehicle Control, Female Rats					
94009F00001	1	128	94009F00006	1	120
94009F00001	2	44	94009F00006	2	75
94009F00001	3	0	94009F00006	3	0
94009F00001	4	3	94009F00006	4	1
94009F00001	5	115	94009F00006	5	53
94009F00001	6	47	94009F00006	6	1
94009F00002	1	130	94009F00007	1	150
94009F00002	2	107	94009F00007	2	49
94009F00002	3	5	94009F00007	3	77
94009F00002	4	0	94009F00007	4	26
94009F00002	5	0	94009F00007	5	2
94009F00002	6	0	94009F00007	6	89
94009F00003	1	103	94009F00008	1	148
94009F00003	2	72	94009F00008	2	101
94009F00003	3	39	94009F00008	3	63
94009F00003	4	0	94009F00008	4	40
94009F00003	5	13	94009F00008	5	58
94009F00003	6	68	94009F00008	6	53
94009F00004	1	186	94009F00009	1	151
94009F00004	2	113	94009F00009	2	95
94009F00004	3	94	94009F00009	3	86
94009F00004	4	61	94009F00009	4	41
94009F00004	5	16	94009F00009	5	0
94009F00004	6	0	94009F00009	6	17
94009F00005	1	158	94009F00010	1	158
94009F00005	2	125	94009F00010	2	79
94009F00005	3	48	94009F00010	3	30
94009F00005	4	0	94009F00010	4	0
94009F00005	5	19	94009F00010	5	0
94009F00005	6	29	94009F00010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Low Level (1,500 ppm), Female Rats					
94009F01001	1	128	94009F01006	1	217
94009F01001	2	87	94009F01006	2	139
94009F01001	3	19	94009F01006	3	133
94009F01001	4	0	94009F01006	4	115
94009F01001	5	0	94009F01006	5	67
94009F01001	6	0	94009F01006	6	23
94009F01002	1	184	94009F01007	1	142
94009F01002	2	139	94009F01007	2	122
94009F01002	3	91	94009F01007	3	70
94009F01002	4	112	94009F01007	4	60
94009F01002	5	116	94009F01007	5	31
94009F01002	6	62	94009F01007	6	3
94009F01003	1	126	94009F01008	1	180
94009F01003	2	69	94009F01008	2	86
94009F01003	3	112	94009F01008	3	129
94009F01003	4	2	94009F01008	4	80
94009F01003	5	0	94009F01008	5	79
94009F01003	6	0	94009F01008	6	48
94009F01004	1	113	94009F01009	1	176
94009F01004	2	109	94009F01009	2	95
94009F01004	3	117	94009F01009	3	131
94009F01004	4	112	94009F01009	4	31
94009F01004	5	98	94009F01009	5	0
94009F01004	6	112	94009F01009	6	0
94009F01005	1	169	94009F01010	1	192
94009F01005	2	88	94009F01010	2	136
94009F01005	3	31	94009F01010	3	108
94009F01005	4	87	94009F01010	4	29
94009F01005	5	36	94009F01010	5	0
94009F01005	6	0	94009F01010	6	0

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
Mid Dose (3,000 ppm), Female Rats					
94009F02001	1	194	94009F02006	1	172
94009F02001	2	126	94009F02006	2	103
94009F02001	3	105	94009F02006	3	87
94009F02001	4	53	94009F02006	4	26
94009F02001	5	118	94009F02006	5	115
94009F02001	6	70	94009F02006	6	92
94009F02002	1	176	94009F02007	1	121
94009F02002	2	128	94009F02007	2	108
94009F02002	3	18	94009F02007	3	136
94009F02002	4	0	94009F02007	4	117
94009F02002	5	36	94009F02007	5	9
94009F02002	6	71	94009F02007	6	0
94009F02003	1	141	94009F02008	1	131
94009F02003	2	80	94009F02008	2	82
94009F02003	3	73	94009F02008	3	205
94009F02003	4	74	94009F02008	4	124
94009F02003	5	106	94009F02008	5	3
94009F02003	6	115	94009F02008	6	0
94009F02004	1	189	94009F02009	1	180
94009F02004	2	88	94009F02009	2	52
94009F02004	3	0	94009F02009	3	0
94009F02004	4	53	94009F02009	4	0
94009F02004	5	29	94009F02009	5	0
94009F02004	6	1	94009F02009	6	0
94009F02005	1	170	94009F02010	1	162
94009F02005	2	160	94009F02010	2	129
94009F02005	3	110	94009F02010	3	0
94009F02005	4	6	94009F02010	4	25
94009F02005	5	0	94009F02010	5	90
94009F02005	6	0	94009F02010	6	2

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

EHL 94009 - Day 14 Motor Activity

Animal No.	Interval (a)	Activity (b)	Animal No.	Interval (a)	Activity (b)
High Level (6,000 ppm), Female Rats					
94009F03001	1	148	94009F03006	1	171
94009F03001	2	88	94009F03006	2	126
94009F03001	3	60	94009F03006	3	84
94009F03001	4	66	94009F03006	4	29
94009F03001	5	73	94009F03006	5	107
94009F03001	6	62	94009F03006	6	0
94009F03002	1	154	94009F03007	1	102
94009F03002	2	122	94009F03007	2	88
94009F03002	3	59	94009F03007	3	66
94009F03002	4	33	94009F03007	4	49
94009F03002	5	17	94009F03007	5	9
94009F03002	6	74	94009F03007	6	0
94009F03003	1	207	94009F03008	1	170
94009F03003	2	113	94009F03008	2	131
94009F03003	3	135	94009F03008	3	99
94009F03003	4	141	94009F03008	4	2
94009F03003	5	67	94009F03008	5	9
94009F03003	6	0	94009F03008	6	99
94009F03004	1	143	94009F03009	1	150
94009F03004	2	150	94009F03009	2	96
94009F03004	3	99	94009F03009	3	140
94009F03004	4	3	94009F03009	4	121
94009F03004	5	0	94009F03009	5	76
94009F03004	6	94	94009F03009	6	33
94009F03005	1	140	94009F03010	1	157
94009F03005	2	73	94009F03010	2	74
94009F03005	3	23	94009F03010	3	7
94009F03005	4	0	94009F03010	4	17
94009F03005	5	0	94009F03010	5	7
94009F03005	6	0	94009F03010	6	10

(a) Intervals are 10 minutes long.
(b) Activity is measured in units of counts per 10 minute interval.

Appendix 10: Individual FOB Data

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	Vehicle Control (Males)									
Animal Number	M00 001	M00 002	M00 003	M00 004	M00 005	M00 006	M00 007	M00 008	M00 009	M00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	9	1	4	0	1	8	1	10	4	2
Excretion	3	0	0	0	1	0	0	0	0	3
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	236.2	267.2	280.6	283.2	249.1	268.1	276.5	267.6	311	295.7
Foreleg Grip Strength 1 (Kg)	1.055	0.965	0.83	0.91	1.05	0.885	1.02	0.965	0.915	1.04
Foreleg Grip Strength 2 (Kg)	0.78	1.035	0.795	0.945	0.795	0.93	0.945	0.9	0.655	1.08
Hindleg Grip Strength 1 (Kg)	0.295	0.44	0.36	0.48	0.495	0.245	0.46	0.29	0.335	0.53
Hindleg Grip Strength 2 (Kg)	0.31	0.395	0.29	0.46	0.425	0.2	0.395	0.32	0.445	0.57
Foot Splay 1 (cm)	5.5	7.8	7.1	7	7.6	6.1	7.3	6.1	4.7	6.3
Foot Splay 2 (cm)	5.3	8.4	8.3	6.9	5.5	5	9	5.5	4.3	5.9

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

			1500 ppm Isobutanol (MALES)							
Animal Number	M01 001	M01 002	M01 003	M01 004	M01 005	M01 006	M01 007	M01 008	M01 009	M01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	1	2	2	2	1	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	0	10	0	4	0	6	6	2	1	6
Excretion	0	0	4	5	3	0	3	0	0	0
Urination	1	0	1	1	0	1	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	239	274.3	260.7	297.5	287.7	264.9	280.1	250.8	267.8	262.7
Foreleg Grip Strength 1 (Kg)	0.675	0.795	1.075	1	1.025	1.025	0.87	0.78	0.745	0.855
Foreleg Grip Strength 2 (Kg)	0.78	0.945	1.045	1.045	0.81	0.87	1.045	0.795	1.015	0.88
Hindleg Grip Strength 1 (Kg)	0.27	0.49	0.435	0.49	0.38	0.245	0.385	0.27	0.58	0.375
Hindleg Grip Strength 2 (Kg)	0.28	0.46	0.425	0.345	0.425	0.34	0.34	0.2	0.54	0.265
Foot Splay 1 (cm)	7.3	6.1	7.8	6.3	8	8.3	4.3	5.5	5.5	6.9
Foot Splay 2 (cm)	7	6.9	7.7	6	7.5	7	4.3	5.3	6.7	7

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	3000 ppm Isobutanol (MALES)									
Animal Number	M02 001	M02 002	M02 003	M02 004	M02 005	M02 006	M02 007	M02 008	M02 009	M02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	9	8	14	3	6	3	2	2	3	11
Excretion	0	2	1	0	0	2	0	0	1	0
Urination	0	0	1	0	1	0	1	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	249.2	255.5	266.9	268.9	263.3	250	247.5	252.3	253.3	241.4
Foreleg Grip Strength 1 (Kg)	0.915	0.92	0.965	0.56	0.8	0.965	0.96	0.895	0.795	0.89
Foreleg Grip Strength 2 (Kg)	0.825	0.975	0.93	0.885	0.955	1	0.93	0.88	0.98	0.675
Hindleg Grip Strength 1 (Kg)	0.42	0.225	0.335	0.405	0.2	0.36	0.29	0.275	0.505	0.285
Hindleg Grip Strength 2 (Kg)	0.41	0.21	0.29	0.345	0.275	0.385	0.295	0.305	0.42	0.355
Foot Splay 1 (cm)	5.6	6.4	4.3	4.6	8.3	7.6	9.1	8	9.7	10.1
Foot Splay 2 (cm)	5.5	7.4	4.9	5.5	7.5	8.4	8.8	6.8	9.4	9.4

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	6000 ppm Isobutanol (MALES)									
Animal Number	M03 001	M03 002	M03 003	M03 004	M03 005	M03 006	M03 007	M03 008	M03 009	M03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	13	0	12	2	5	4	2	15	3	1
Excretion	0	0	1	2	0	1	0	0	1	4
Urination	1	3	1	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	231.7	248.8	265.6	265	258.5	248	254.5	283	260.4	232.2
Foreleg Grip Strength 1 (Kg)	0.99	1.03	0.745	0.855	1.145	0.945	0.93	0.88	0.68	1.02
Foreleg Grip Strength 2 (Kg)	1.06	1.085	0.92	0.62	1.05	1.135	0.875	0.855	0.875	0.86
Hindleg Grip Strength 1 (Kg)	0.285	0.445	0.405	0.46	0.38	0.38	0.405	0.395	0.45	0.39
Hindleg Grip Strength 2 (Kg)	0.265	0.44	0.34	0.36	0.41	0.4	0.365	0.48	0.41	0.34
Foot Splay 1 (cm)	5.7	5.1	5.9	5.5	7.9	6.7	6.1	4.7	8.9	5
Foot Splay 2 (cm)	6.6	7.6	6.3	6	7.9	6.9	6.8	4.4	8.2	6.1

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	Vehicle Control (Males)									
Animal Number	M00 001	M00 002	M00 003	M00 004	M00 005	M00 006	M00 007	M00 008	M00 009	M00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	1	1	1	1	1	2	1	1	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	0	13	0	13	0	13	0
Rearing	1	0	1	0	0	5	0	2	0	5
Excretion	4	0	0	0	0	0	0	0	2	0
Urination	0	0	0	0	1	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1		1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	284.1	317.3	326.2	338.5	291	314.8	333	302	366.4	342.6
Foreleg Grip Strength 1 (Kg)	0.93	1.325	0.99	1.16	0.78	1.025	1.06	1.115	1.03	1.285
Foreleg Grip Strength 2 (Kg)	0.975	1.19	1.015	1.18	1.065	0.98	0.99	1.17	0.99	1.15
Hindleg Grip Strength 1 (Kg)	0.355	0.495	0.38	0.575	0.285	0.405	0.495	0.49	0.45	0.595
Hindleg Grip Strength 2 (Kg)	0.305	0.595	0.435	0.53	0.49	0.44	0.62	0.485	0.55	0.655
Foot Splay 1 (cm)	4.3	6.7	4.9	5.1	6	5.8	6.8	5.9	5.4	6.6
Foot Splay 2 (cm)	4.4	6.9	4.9	5.5	5.5	5.2	7.8	7.3	5.4	7.5

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	1500 ppm Isobutanol (MALES)									
Animal Number	M01 001	M01 002	M01 003	M01 004	M01 005	M01 006	M01 007	M01 008	M01 009	M01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	1	2	2	1	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	2	2	2	5	0	8	4	0	4	1
Excretion	0	0	0	3	1	2	0	4	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	291	320.2	304.7	347.4	340.4	313.5	341.4	287.9	309.2	310
Foreleg Grip Strength 1 (Kg)	0.605	1.27	1.12	1.06	1.025	0.985	0.76	0.955	1.18	1.135
Foreleg Grip Strength 2 (Kg)	0.835	1.2	1.185	1.175	1.045	0.805	0.88	1.03	1.28	1.2
Hindleg Grip Strength 1 (Kg)	0.41	0.49	0.43	0.535	0.67	0.55	0.425	0.32	0.635	0.3
Hindleg Grip Strength 2 (Kg)	0.355	0.655	0.31	0.6	0.57	0.465	0.38	0.265	0.77	0.45
Foot Splay 1 (cm)	7	5	7.7	7.5	7.5	8.1	5.5	4.1	7.9	7.4
Foot Splay 2 (cm)	7.4	5.1	7.8	7.9	6.8	7.8	5.9	4.6	8.2	6.7

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

			3000 ppm Isobutanol (MALES)							
Animal Number	M02 001	M02 002	M02 003	M02 004	M02 005	M02 006	M02 007	M02 008	M02 009	M02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	13	0	0	0
Rearing	12	1	2	9	3	0	0	2	0	12
Excretion	0	1	2	0	2	2	0	0	1	0
Urination	0	1	0	0	1	1	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	302.3	305.4	310.4	312.7	306	300.1	294.5	301	303.2	293.6
Foreleg Grip Strength 1 (Kg)	0.99	0.95	1.065	1.075	1.225	0.73	1.125	0.93	1.08	1.125
Foreleg Grip Strength 2 (Kg)	0.95	1.09	0.93	1.16	1.125	0.79	1.005	0.995	1.155	1.13
Hindleg Grip Strength 1 (Kg)	0.49	0.3	0.335	0.35	0.485	0.6	0.495	0.565	0.535	0.59
Hindleg Grip Strength 2 (Kg)	0.52	0.5	0.34	0.365	0.47	0.345	0.4	0.45	0.535	0.325
Foot Splay 1 (cm)	7.3	7	5.5	5.4	6.8	5.1	7.9	7.2	9.5	8
Foot Splay 2 (cm)	9.4	6.1	4.6	4.4	7.9	4.8	8.6	7.1	10.3	7.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	6000 ppm Isobutanol (MALES)									
Animal Number	M03 001	M03 002	M03 003	M03 004	M03 005	M03 006	M03 007	M03 008	M03 009	M03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	1	2	1	2	2	2	1
Gait	1	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	13	0	13	0	0	0	0
Rearing	4	0	19	0	3	0	0	3	1	0
Excretion	0	2	0	0	0	1	5	3	3	6
Urination	0	1	1	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	272.2	294.3	306.3	315.6	291.2	298.5	307.7	332.2	296.3	261.9
Foreleg Grip Strength 1 (Kg)	0.78	1.155	1.11	1.05	1.23	0.925	1.27	0.735	1.135	1.075
Foreleg Grip Strength 2 (Kg)	0.83	1.115	0.95	1.075	1.245	1.025	1.225	0.755	1.105	0.895
Hindleg Grip Strength 1 (Kg)	0.39	0.635	0.525	0.5	0.595	0.715	0.41	0.74	0.625	0.29
Hindleg Grip Strength 2 (Kg)	0.34	0.675	0.395	0.505	0.515	0.43	0.355	0.55	0.42	0.355
Foot Splay 1 (cm)	5.4	5.6	5.5	5.9	8	7.3	6.5	4.9	5.4	7.9
Foot Splay 2 (cm)	4.8	5	6.1	6	6	6.8	5.8	4.5	5.6	6.4

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

				Vehicle Control (Males)						
Animal Number	M00 001	M00 002	M00 003	M00 004	M00 005	M00 006	M00 007	M00 008	M00 009	M00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	1	1	1	2	1	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	13	0	0	0	0	0	0	0
Rearing	1	0	0	0	0	1	0	12	0	7
Excretion	3	1	1	0	0	0	2	0	1	1
Urination	0	0	0	0	0	0	0	0	0	3
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	303.9	333.6	349.1	348.7	315.2	333.6	339.7	328.8	380	358.7
Foreleg Grip Strength 1 (Kg)	0.755	0.885	0.72	1.13	0.995	0.775	1.235	0.95	0.735	0.845
Foreleg Grip Strength 2 (Kg)	1.03	1.13	0.765	0.96	0.97	0.635	1.11	0.915	0.69	1.13
Hindleg Grip Strength 1 (Kg)	0.335	0.54	0.335	0.59	0.33	0.535	0.49	0.38	0.985	0.42
Hindleg Grip Strength 2 (Kg)	0.525	0.64	0.175	0.49	0.305	0.62	0.53	0.505	0.575	0.385
Foot Splay 1 (cm)	4	7.1	4.2	5.6	4.4	4.8	5	4.6	6.9	7.4
Foot Splay 2 (cm)	4.6	7.9	4.4	6.8	4.9	4.1	5.9	4.9	6.5	8.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

			1500 ppm Isobutanol (MALES)							
Animal Number	M01 001	M01 002	M01 003	M01 004	M01 005	M01 006	M01 007	M01 008	M01 009	M01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	1	1	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	13	0	0	0	0	0
Rearing	1	7	0	0	0	5	7	2	2	2
Excretion	0	0	4	0	3	5	3	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	311.7	334.2	329.9	369.2	351.4	338.3	356.3	310.7	329.2	330.4
Foreleg Grip Strength 1 (Kg)	0.7	1.23	0.965	1.095	0.775	0.86	1.005	0.74	1.43	1.135
Foreleg Grip Strength 2 (Kg)	0.7	1.305	1.215	1.08	0.78	1.005	1.235	0.945	1.115	0.98
Hindleg Grip Strength 1 (Kg)	0.53	0.73	0.41	0.64	0.51	0.395	0.39	0.31	0.63	0.565
Hindleg Grip Strength 2 (Kg)	0.445	0.74	0.585	0.645	0.655	0.535	0.425	0.33	0.72	0.55
Foot Splay 1 (cm)	4.9	7.8	7.5	6.5	5.5	6.1	7	4.9	7.1	7.5
Foot Splay 2 (cm)	4.7	7	6.5	5.9	5.5	7.9	6.4	5.5	8	6.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

	3000 ppm Isobutanol (MALES)									
Animal Number	M02 001	M02 002	M02 003	M02 004	M02 005	M02 006	M02 007	M02 008	M02 009	M02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	2	2	2	2	1	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	0	0	0	0	0	0	0
Rearing	14	0	7	6	7	7	1	2	0	12
Excretion	0	4	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	0	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	316.8	311.2	329.3	331.6	321.7	318.9	303.1	318.9	312.5	306.9
Foreleg Grip Strength 1 (Kg)	0.915	0.905	0.97	0.825	0.78	0.77	1.24	0.69	0.745	1.125
Foreleg Grip Strength 2 (Kg)	0.965	1.02	0.82	0.8	1.015	0.91	1.08	0.95	0.53	0.985
Hindleg Grip Strength 1 (Kg)	0.45	0.38	0.395	0.485	0.495	0.445	0.61	0.375	0.475	0.715
Hindleg Grip Strength 2 (Kg)	0.485	0.35	0.49	0.205	0.535	0.46	0.585	0.4	0.48	0.67
Foot Splay 1 (cm)	8.8	6.3	4.4	4.3	6.5	5.3	7.9	6.4	7.6	9.6
Foot Splay 2 (cm)	8.4	5.8	5.3	4.1	5.5	5.9	8.1	5.4	7.5	10.2

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

			6000 ppm Isobutanol (MALES)							
Animal Number	M03 001	M03 002	M03 003	M03 004	M03 005	M03 006	M03 007	M03 008	M03 009	M03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	1	2	2	2	2	2	1
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	13	0	0	0	0	0	0
Rearing	12	0	8	0	1	0	0	13	4	0
Excretion	1	6	0	4	0	3	4	2	0	2
Urination	1	1	0	0	1	1	0	1	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	287.2	308	325.9	319.4	315	316.6	318.3	346	305	271.5
Foreleg Grip Strength 1 (Kg)	0.72	0.87	1.175	0.77	1.375	1.165	0.79	0.935	0.78	0.84
Foreleg Grip Strength 2 (Kg)	0.6	0.7	0.865	0.855	1.33	1.315	1.1	0.885	0.66	1.1
Hindleg Grip Strength 1 (Kg)	0.28	0.67	0.43	0.55	0.55	0.515	0.485	0.44	0.285	0.525
Hindleg Grip Strength 2 (Kg)	0.245	0.78	0.36	0.535	0.62	0.605	0.38	0.56	0.39	0.36
Foot Splay 1 (cm)	5.6	7	6.8	6.4	8.9	7.3	5.7	5.1	6.4	5.4
Foot Splay 2 (cm)	6.5	4.9	7.2	4.8	9.3	6.9	5	4.8	5	6.3

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

				Vehicle Control (Males)						
Animal Number	M00 001	M00 002	M00 003	M00 004	M00 005	M00 006	M00 007	M00 008	M00 009	M00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	1	2	1	1	1	2	2	2	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	13	0	0	0	0	0	0	0
Rearing	0	0	0	0	0	3	1	16	1	6
Excretion	3	0	0	0	1	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	1
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	2	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	330.2	378.7	388.6	390.5	351.3	375.4	382.5	365.9	424.5	401.9
Foreleg Grip Strength 1 (Kg)	0.93	1.24	0.855	1.04	1.08	0.82	1.35	0.91	1.085	1.205
Foreleg Grip Strength 2 (Kg)	1.005	1.185	0.635	1.125	0.86	0.785	1.04	0.77	0.86	1.08
Hindleg Grip Strength 1 (Kg)	0.415	0.46	0.54	0.655	0.72	0.44	0.62	0.465	0.535	0.71
Hindleg Grip Strength 2 (Kg)	0.425	0.52	0.375	0.785	0.645	0.52	0.58	0.495	0.445	0.715
Foot Splay 1 (cm)	4.3	5.1	5.4	5.4	5.1	5.4	3.9	4.6	6.1	5.6
Foot Splay 2 (cm)	4	4.4	7.1	5.1	5	5.1	4.4	6.3	5.8	6.4

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

			1500 ppm Isobutanol (MALES)							
Animal Number	M01 001	M01 002	M01 003	M01 004	M01 005	M01 006	M01 007	M01 008	M01 009	M01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	12	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	1	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	13	0	0	0
Rearing	0	9	7	0	0	4	0	2	10	10
Excretion	0	0	3	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	1	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	2	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	347.7	363.2	362.6	404.9	387.4	379.3	392.4	344.5	348.9	369
Foreleg Grip Strength 1 (Kg)	0.83	1.225	1.32	1.095	0.87	0.785	0.67	0.785	1.3	1.06
Foreleg Grip Strength 2 (Kg)	0.545	1.185	1.05	1.025	0.84	0.93	1.025	0.885	1.235	1.085
Hindleg Grip Strength 1 (Kg)	0.575	0.55	0.575	0.58	0.62	0.57	0.39	0.35	0.865	0.55
Hindleg Grip Strength 2 (Kg)	0.515	0.715	0.525	0.605	0.49	0.515	0.41	0.465	0.74	0.495
Foot Splay 1 (cm)	5	6.4	6.1	6.9	6.3	6.7	6.3	4.5	7.8	6.9
Foot Splay 2 (cm)	5.6	5.8	5.3	7.3	7.8	9.1	5.6	5.6	6.6	6.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

			3000 ppm Isobutanol (MALES)							
Animal Number	M02 001	M02 002	M02 003	M02 004	M02 005	M02 006	M02 007	M02 008	M02 009	M02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	2	2	2	1	1	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	0	0	0	0	0	0	0
Rearing	13	0	15	3	7	1	3	1	0	18
Excretion	0	3	0	0	0	0	0	0	0	0
Urination	0	1	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	354.3	344.8	373	369.8	353.2	357.1	338.1	358.4	347.3	346.8
Foreleg Grip Strength 1 (Kg)	0.865	1.04	1.185	0.78	0.915	0.88	1.305	0.8	0.57	1.185
Foreleg Grip Strength 2 (Kg)	1.015	1.005	1.035	0.925	0.915	0.995	1.12	0.855	0.515	1.025
Hindleg Grip Strength 1 (Kg)	0.455	0.79	0.47	0.36	0.475	0.62	0.64	0.515	0.49	0.785
Hindleg Grip Strength 2 (Kg)	0.445	0.645	0.565	0.295	0.24	0.59	0.62	0.29	0.535	0.745
Foot Splay 1 (cm)	6.4	5.9	5.5	3.8	8.5	5.6	6.4	5.4	9.1	8.3
Foot Splay 2 (cm)	5.9	6.4	4.1	4.3	8.9	5.2	7	4.3	7.4	8.5

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

			6000 ppm Isobutanol (MALES)							
Animal Number	M03 001	M03 002	M03 003	M03 004	M03 005	M03 006	M03 007	M03 008	M03 009	M03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	1	2	1	1	3	2	1
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	0	13	0	0	0	0	0	0
Rearing	15	1	10	0	10	0	0	12	4	1
Excretion	0	4	1	6	0	2	0	2	0	0
Urination	0	2	2	0	2	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	328.9	347.3	371.4	372.6	348	364.3	365.2	392.9	346	304
Foreleg Grip Strength 1 (Kg)	0.92	0.86	1.26	0.74	1.41	0.915	1.125	0.85	0.98	0.675
Foreleg Grip Strength 2 (Kg)	0.855	0.92	1.11	0.95	1.45	0.87	0.93	0.725	0.77	0.975
Hindleg Grip Strength 1 (Kg)	0.455	0.66	0.58	0.425	0.635	0.805	0.46	0.56	0.43	0.43
Hindleg Grip Strength 2 (Kg)	0.485	0.785	0.54	0.565	0.58	0.685	0.4	0.625	0.535	0.42
Foot Splay 1 (cm)	7.4	6.9	6.9	6.5	7.4	5.3	5.4	4.5	6.3	5.5
Foot Splay 2 (cm)	7	6.1	6.1	4.5	7.5	5	5.9	4.6	6.1	6.1

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

				Vehicle Control (Males)						
Animal Number	M00 001	M00 002	M00 003	M00 004	M00 005	M00 006	M00 007	M00 008	M00 009	M00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	1	2	2	2	2	1	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	0	0	1	0	1	1	2	17	0	2
Excretion	4	0	0	0	0	0	0	0	1	0
Urination	0	0	0	0	0	0	0	0	0	1
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	364.8	421.2	429.6	431.2	389.2	416.3	422	407.9	474.3	448.1
Foreleg Grip Strength 1 (Kg)	1.01	0.975	0.755	0.915	1.02	0.83	1.365	1.115	0.67	1.205
Foreleg Grip Strength 2 (Kg)	1.01	1.32	0.88	1.085	1.235	0.91	1.345	0.76	0.66	1.105
Hindleg Grip Strength 1 (Kg)	0.365	0.895	0.47	0.78	0.875	0.45	0.57	0.625	0.585	0.91
Hindleg Grip Strength 2 (Kg)	0.53	0.65	0.465	0.61	0.765	0.53	0.655	0.585	0.55	0.785
Foot Splay 1 (cm)	3.8	6.6	6.5	6.6	4.3	4.4	5.3	5.1	5.1	6.5
Foot Splay 2 (cm)	3.9	8.7	8	8.1	4.8	4.6	4.6	4.5	5.8	7.5

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

			1500 ppm Isobutanol (MALES)							
Animal Number	M01 001	M01 002	M01 003	M01 004	M01 005	M01 006	M01 007	M01 008	M01 009	M01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	1	2	2	2	1	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	2	10	0	4	0	4	4	3	4	6
Excretion	0	0	4	0	0	0	0	0	0	0
Urination	0	0	1	0	0	0	0	3	4	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	388.9	406.6	403.3	448.3	439.3	418.1	437.7	378.4	376.4	418.4
Foreleg Grip Strength 1 (Kg)	0.845	1.195	1.305	0.79	0.85	1.235	0.965	0.985	1.37	1.44
Foreleg Grip Strength 2 (Kg)	0.855	1.14	1.11	0.99	0.985	1.105	0.9	1.27	1.67	1.455
Hindleg Grip Strength 1 (Kg)	0.55	0.705	0.645	0.805	0.64	0.665	0.605	0.44	0.905	0.59
Hindleg Grip Strength 2 (Kg)	0.45	0.895	0.705	0.67	0.685	0.575	0.51	0.51	0.965	0.415
Foot Splay 1 (cm)	6.1	5	9.5	5.9	7.2	5.1	5.3	5.4	7.2	7.4
Foot Splay 2 (cm)	6.4	5.4	8.4	6.8	7.9	4.3	5.9	5.9	9.1	7.9

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

			3000 ppm Isobutanol (MALES)							
Animal Number	M02 001	M02 002	M02 003	M02 004	M02 005	M02 006	M02 007	M02 008	M02 009	M02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	1	1	1	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	13	13	13	0	0
Rearing	9	7	14	3	6	0	0	0	3	15
Excretion	0	0	0	0	0	2	0	0	0	0
Urination	0	0	0	0	2	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	400.3	381.7	403	404.1	390.1	393.3	375.9	400.7	392.9	382.2
Foreleg Grip Strength 1 (Kg)	0.955	1.16	1.075	1.15	0.535	0.845	0.925	0.57	1.195	1.27
Foreleg Grip Strength 2 (Kg)	0.97	1.325	1.085	0.955	0.86	0.72	1.245	0.68	0.82	1.055
Hindleg Grip Strength 1 (Kg)	0.52	0.735	0.68	0.585	0.4	0.54	0.785	0.535	0.68	0.74
Hindleg Grip Strength 2 (Kg)	0.55	0.82	0.54	0.585	0.495	0.78	0.735	0.535	0.6	0.89
Foot Splay 1 (cm)	11	5.9	4.7	4.5	4.5	5.1	7.1	7.1	8.1	9
Foot Splay 2 (cm)	10.8	6.3	5.2	3.9	4.6	4.9	8	5.7	8.4	8.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

			6000 ppm Isobutanol (MALES)							
Animal Number	M03 001	M03 002	M03 003	M03 004	M03 005	M03 006	M03 007	M03 008	M03 009	M03 010
Activity	0	0	0	0	0	0		0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0		0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0		0	0	0
Exophthalmia	0	0	0	0	0	0		0	0	0
Cage Removal Ease	1	1	1	1	1	1		1	1	1
Reactivity	1	1	1	1	1	1		1	1	1
Lacrimation	0	0	0	0	0	0		0	0	0
Salivation	0	0	0	0	0	0		0	0	0
Palpebral Closure	2	2	2	2	2	2		2	2	2
Piloerection	0	0	0	0	0	0		0	0	0
Miscellaneous Observations	0	0	0	0	0	0		0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0		0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0		0	0	0
Alertness	2	1	2	1	2	1		3	2	1
Gait	0	0	0	0	0	0		0	0	0
Gait Score	3	3	3	3	3	3		3	3	3
Mobility Score	3	3	3	3	3	3		3	3	3
Vocalization	0	0	0	0	0	0		0	0	0
Stereotypy	0	0	0	0	0	0		0	0	0
Unusual Behavior	0	13	0	13	0	0		0	0	0
Rearing	10	0	18	0	8	0		11	1	0
Excretion	0	1	0	1	0	3		0	0	3
Urination	0	1	2	1	1	1		0	0	0
Approach Response	1	1	1	1	1	1		1	1	1
Tail Pinch Response	1	1	1	2	1	1		1	1	1
Click Response	1	1	1	1	1	1		1	1	1
Pupillary Reflex	1	1	1	1	1	1		1	1	1
Righting Reflex	3	3	3	3	3	3		3	3	3
Weight (gm)	365.4	384.7	413.1	412.6	387.5	406.9		434	377.1	338.1
Foreleg Grip Strength 1 (Kg)	0.865	1.175	1.085	0.67	1.575	1.015		0.725	0.62	1.075
Foreleg Grip Strength 2 (Kg)	0.99	1.215	1.16	0.95	1.63	1.135		0.81	1.04	0.86
Hindleg Grip Strength 1 (Kg)	0.435	0.73	0.635	0.695	0.76	0.695		0.795	0.44	0.46
Hindleg Grip Strength 2 (Kg)	0.44	0.81	0.615	0.735	0.605	0.605		0.675	0.425	0.345
Foot Splay 1 (cm)	5.5	6.6	7.3	5.5	8.3	5.6		4.3	4.9	5
Foot Splay 2 (cm)	5.9	7	6.9	6	10.4	6.8		3.4	5	4.8

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	Vehicle Control (Females)									
Animal Number	F00 001	F00 002	F00 003	F00 004	F00 005	F00 006	F00 007	F00 008	F00 009	F00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	9	0	8	14	7	8	2	9	14	17
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	172.7	202.2	209	199.5	194.2	194	192.7	203.8	193.4	174.6
Foreleg Grip Strength 1 (Kg)	1.02	0.88	0.835	0.46	1.165	0.925	0.74	1.125	0.9	0.775
Foreleg Grip Strength 2 (Kg)	1.095	0.835	1.07	0.655	0.99	1.02	0.83	0.98	0.76	0.805
Hindleg Grip Strength 1 (Kg)	0.385	0.355	0.4	0.605	0.495	0.41	0.275	0.29	0.42	0.335
Hindleg Grip Strength 2 (Kg)	0.45	0.22	0.36	0.435	0.47	0.38	0.29	0.42	0.33	0.295
Foot Splay 1 (cm)	4.5	5.9	5.5	2.6	5.4	9	5.9	6.4	3.5	4.6
Foot Splay 2 (cm)	4.5	5.9	6.3	2.5	7.1	8.3	4	5.4	3.4	4.1

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	1500 ppm Isobutanol (FEMALES)									
Animal Number	F01 001	F01 002	F01 003	F01 004	F01 005	F01 006	F01 007	F01 008	F01 009	F01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	10	7	4	13	8	5	9	4	1	13
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	2	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1		1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	177.3	214.5	230.3	188.4	190.4	187.4	182.2	195.3	174.2	179.5
Foreleg Grip Strength 1 (Kg)	0.93	0.685	1.075	0.715	0.875	0.91	0.845	1.035	0.85	0.985
Foreleg Grip Strength 2 (Kg)	0.875	0.955	1.045	0.89	0.865	0.935	0.585	0.765	0.855	0.66
Hindleg Grip Strength 1 (Kg)	0.455	0.395	0.605	0.56	0.46	0.35	0.295	0.57	0.405	0.395
Hindleg Grip Strength 2 (Kg)	0.3	0.4	0.625	0.47	0.245	0.315	0.355	0.605	0.455	0.275
Foot Splay 1 (cm)	4.4	4.9	6	4.4	6.3	4.3	3.5	5.5	6	5.3
Foot Splay 2 (cm)	4.1	6	5.8	4.3	6.5	6.7	4.6	5	4.9	5

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	3000 ppm Isobutanol (FEMALES)									
Animal Number	F02 001	F02 002	F02 003	F02 004	F02 005	F02 006	F02 007	F02 008	F02 009	F02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	9	9	12	4	16	13	4	2	4	7
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	198	215.9	192.7	203.2	189.3	175.5	192.6	201.2	226.1	175.4
Foreleg Grip Strength 1 (Kg)	1.11	1.025	0.83	0.945	0.855	0.77	0.84	0.98	0.915	0.69
Foreleg Grip Strength 2 (Kg)	0.93	0.97	0.95	0.595	1.015	0.84	0.93	0.68	0.885	0.765
Hindleg Grip Strength 1 (Kg)	0.455	0.545	0.47	0.4	0.395	0.315	0.505	0.385	0.26	0.435
Hindleg Grip Strength 2 (Kg)	0.38	0.385	0.49	0.32	0.335	0.315	0.435	0.355	0.44	0.34
Foot Splay 1 (cm)	5.4	5.1	6.8	6.5	5.8	5.6	5.3	4.8	5.6	5.7
Foot Splay 2 (cm)	5.6	6.9	5.3	5.8	4.7	6	4.8	5.4	6.6	6.4

EHL 94009/CMA Isobutanol AC NT - Individual Pretest FOB Observations

	6000 ppm Isobutanol (FEMALES)									
Animal Number	F03 001	F03 002	F03 003	F03 004	F03 005	F03 006	F03 007	F03 008	F03 009	F03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	8	11	18	11	0	5	2	7	8	5
Excretion	0	0	0	0	0	0	0	0	3	0
Urination	1	0	0	0	0	0	0	0	1	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	187.8	194.1	206.4	204.7	195.7	200.9	197.4	172.3	236.5	195.6
Foreleg Grip Strength 1 (Kg)	0.635	0.93	1.07	0.94	0.935	1.005	0.91	0.945	0.795	0.97
Foreleg Grip Strength 2 (Kg)	0.625	0.65	0.905	0.845	0.805	0.74	0.815	0.835	0.88	0.84
Hindleg Grip Strength 1 (Kg)	0.42	0.43	0.21	0.485	0.445	0.585	0.265	0.585	0.46	0.34
Hindleg Grip Strength 2 (Kg)	0.41	0.39	0.285	0.5	0.42	0.57	0.385	0.435	0.405	0.41
Foot Splay 1 (cm)	3.2	6.3	5.5	4.4	5.9	3.5	4.4	6.5	5	4.4
Foot Splay 2 (cm)	4.4	6.5	5.4	4.7	7	4	2.8	6.4	4.2	5

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	Vehicle Control (Females)									
Animal Number	F00 001	F00 002	F00 003	F00 004	F00 005	F00 006	F00 007	F00 008	F00 009	F00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	2	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	9	0	9	10	8	5	2	2	12	14
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	1	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	2	1	1	1	2
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	189.4	229.4	219.5	214	212.8	210.7	211.2	218.2	212.7	195.2
Foreleg Grip Strength 1 (Kg)	0.83	1.06	1.09	0.69	1.21	1.125	1.07	1.21	1.105	0.905
Foreleg Grip Strength 2 (Kg)	0.86	1.13	0.88	0.615	1.135	1.01	0.8	1.25	1.005	0.99
Hindleg Grip Strength 1 (Kg)	0.365	0.44	0.345	0.61	0.53	0.295	0.37	0.625	0.325	0.385
Hindleg Grip Strength 2 (Kg)	0.44	0.455	0.44	0.455	0.55	0.445	0.425	0.585	0.31	0.465
Foot Splay 1 (cm)	3.4	5.1	6	4.6	7.4	7.8	4	4.3	4.3	6.4
Foot Splay 2 (cm)	3.7	4.6	6.6	3.4	6.6	7.8	5.5	4.1	3.6	6.4

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	1500 ppm Isobutanol (FEMALES)									
Animal Number	F01 001	F01 002	F01 003	F01 004	F01 005	F01 006	F01 007	F01 008	F01 009	F01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements In Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements In Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements In Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	3	1	1	2	2	2	2	2	2	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	2	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	13	13	0	0	0	0	0	0	0
Rearing	21	0	1	6	7	10	12	1	1	20
Excretion	0	0	1	0	0	0	0	0	0	0
Urination	0	0	1	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	193.2	233.5	249.3	201.5	207.3	206.1	184.7	213.1	195.3	197.4
Foreleg Grip Strength 1 (Kg)	1.025	1.055	0.89	0.95	0.815	1.02	0.69	0.775	1.05	0.635
Foreleg Grip Strength 2 (Kg)	0.985	0.9	0.705	0.95	1.105	0.955	0.65	0.61	0.77	0.795
Hindleg Grip Strength 1 (Kg)	0.535	0.645	0.61	0.34	0.55	0.58	0.43	0.8	0.675	0.42
Hindleg Grip Strength 2 (Kg)	0.565	0.54	0.655	0.205	0.635	0.275	0.39	0.51	0.45	0.29
Foot Splay 1 (cm)	5	5.6	5.8	3.9	5.6	4.9	4.4	5.6	5.5	4.1
Foot Splay 2 (cm)	3.8	5.3	5.6	4.1	5	6.6	3.9	5.9	5.3	3.9

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	3000 ppm Isobutanol (FEMALES)									
Animal Number	F02 001	F02 002	F02 003	F02 004	F02 005	F02 006	F02 007	F02 008	F02 009	F02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	3	2	2	1	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	13	0	0
Rearing	11	5	11	1	21	8	4	1	0	11
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	2	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	218.8	243.1	199.1	223	206.5	189.5	202.6	216.5	248	189.2
Foreleg Grip Strength 1 (Kg)	0.88	1.22	1.03	0.59	1.2	1.03	1.28	0.885	1.125	1.14
Foreleg Grip Strength 2 (Kg)	0.925	1.1	0.93	0.79	1.16	0.875	1.045	0.755	0.975	0.965
Hindleg Grip Strength 1 (Kg)	0.5	0.725	0.57	0.54	0.36	0.535	0.515	0.425	0.58	0.485
Hindleg Grip Strength 2 (Kg)	0.655	0.66	0.73	0.405	0.395	0.34	0.595	0.485	0.39	0.68
Foot Splay 1 (cm)	4.6	6.5	5	6.6	7.5	7.4	4.3	8.4	5.9	6.6
Foot Splay 2 (cm)	4.5	7.3	6.1	5.6	6.4	9.4	4.2	8.5	6.5	4.9

EHL 94009/CMA Isobutanol AC NT - Individual Day 0 FOB Observations

	6000 ppm Isobutanol (FEMALES)									
Animal Number	F03 001	F03 002	F03 003	F03 004	F03 005	F03 006	F03 007	F03 008	F03 009	F03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	1	2	1	1	1	1
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	13	0	13	0	0	0
Rearing	7	0	15	3	0	2	0	0	3	0
Excretion	0	0	0	0	4	0	0	0	4	0
Urination	0	0	0	0	0	0	0	0	1	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	197.6	207.7	209.1	218.3	214.7	214.5	210.9	186.2	261.5	219.7
Foreleg Grip Strength 1 (Kg)	0.945	0.85	1.19	1.145	0.965	0.93	0.84	1.125	0.555	1.285
Foreleg Grip Strength 2 (Kg)	0.745	0.96	1.095	0.985	0.735	0.715	0.905	0.96	0.57	1.27
Hindleg Grip Strength 1 (Kg)	0.655	0.67	0.515	0.49	0.545	0.47	0.53	0.62	0.745	0.68
Hindleg Grip Strength 2 (Kg)	0.425	0.56	0.725	0.505	0.385	0.335	0.505	0.675	0.515	0.38
Foot Splay 1 (cm)	4.1	5.2	5.5	5.2	6	4	6.5	5.4	5.9	4.4
Foot Splay 2 (cm)	3.8	4.5	4.4	4.8	5	3.5	5.7	5.1	5.6	3.8

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

	Vehicle Control (Females)									
Animal Number	F00 001	F00 002	F00 003	F00 004	F00 005	F00 006	F00 007	F00 008	F00 009	F00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	3	2	2	2	2	2	2	2	3	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	19	3	7	17	23	20	2	9	22	23
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	0	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	2
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	198.2	235.5	240.3	218.1	217.7	218.7	226.5	230.4	213.4	207.9
Foreleg Grip Strength 1 (Kg)	0.84	1.025	0.845	0.825	1.025	0.72	0.605	1.18	0.645	1.085
Foreleg Grip Strength 2 (Kg)	0.8	0.65	0.81	0.725	1.255	0.715	0.6	0.92	0.51	1.035
Hindleg Grip Strength 1 (Kg)	0.47	0.52	0.425	0.52	0.575	0.33	0.445	0.635	0.365	0.55
Hindleg Grip Strength 2 (Kg)	0.23	0.425	0.335	0.48	0.535	0.42	0.305	0.445	0.44	0.49
Foot Splay 1 (cm)	3.7	5.4	5.9	4.8	5.6	6.4	6	5.5	4.8	5.5
Foot Splay 2 (cm)	3.4	5.6	5.8	3.8	5.4	6.6	6.3	4.6	5	5.5

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

	1500 ppm Isobutanol (FEMALES)									
Animal Number	F01 001	F01 002	F01 003	F01 004	F01 005	F01 006	F01 007	F01 008	F01 009	F01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	4	2	2	2	2	2	2	2	2	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	41	2	2	14	7	4	4	21	2	23
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	196.9	250	274.6	212.3	221.3	216.5	202.1	220	202.1	208.8
Foreleg Grip Strength 1 (Kg)	0.86	0.925	0.795	1	0.975	1.1	0.615	0.71	0.54	0.77
Foreleg Grip Strength 2 (Kg)	0.735	0.77	0.705	0.905	0.805	1.035	0.74	0.68	0.95	0.58
Hindleg Grip Strength 1 (Kg)	0.58	0.645	0.61	0.225	0.745	0.4	0.465	0.535	0.54	0.27
Hindleg Grip Strength 2 (Kg)	0.395	0.545	0.75	0.34	0.66	0.33	0.46	0.69	0.44	0.21
Foot Splay 1 (cm)	4.1	4.9	6.5	4.8	4.8	4.8	4.9	6.1	4.6	5.4
Foot Splay 2 (cm)	3.8	4.7	6.9	5.8	4.9	5.1	4.1	6.3	4.4	4

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

			3000 ppm Isobutanol (FEMALES)							
Animal Number	F02 001	F02 002	F02 003	F02 004	F02 005	F02 006	F02 007	F02 008	F02 009	F02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	3	3	3	3	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	16	11	7	1	17	27	15	22	1	10
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	228.1	253.1	217.5	244	219.2	193.2	214.7	226	259.2	203.8
Foreleg Grip Strength 1 (Kg)	0.835	1.19	0.61	0.685	1.07	0.89	1.06	0.735	0.96	1.015
Foreleg Grip Strength 2 (Kg)	0.745	1.18	0.835	0.88	0.895	0.675	1.12	0.83	1.11	0.735
Hindleg Grip Strength 1 (Kg)	0.31	0.56	0.44	0.545	0.355	0.685	0.39	0.455	0.635	0.51
Hindleg Grip Strength 2 (Kg)	0.485	0.56	0.455	0.325	0.27	0.46	0.325	0.445	0.495	0.52
Foot Splay 1 (cm)	4.9	5.7	5.6	6.1	6.5	5.9	4.6	4.8	5.3	6.1
Foot Splay 2 (cm)	4.9	6.6	5.4	4.9	6.1	7.3	4.4	3.6	5.2	4.9

EHL 94009/CMA Isobutanol AC NT - Individual Day 1 FOB Observations

	6000 ppm Isobutanol (FEMALES)									
Animal Number	F03 001	F03 002	F03 003	F03 004	F03 005	F03 006	F03 007	F03 008	F03 009	F03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	3	2	1	3	2	3	1	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	13	0	0	0	0	0
Rearing	8	19	19	7	0	25	2	24	0	19
Excretion	0	0	0	0	3	0	0	0	2	0
Urination	0	0	0	0	0	0	0	0	1	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	212.5	215.5	235	228.7	230.2	229.6	223.6	192.6	283.6	224.8
Foreleg Grip Strength 1 (Kg)	0.625	0.93	0.77	1.095	0.74	0.685	0.455	0.865	0.57	1.055
Foreleg Grip Strength 2 (Kg)	0.55	0.89	0.815	0.775	0.63	0.57	0.325	0.735	0.8	0.97
Hindleg Grip Strength 1 (Kg)	0.385	0.425	0.32	0.52	0.32	0.605	0.32	0.41	0.45	0.28
Hindleg Grip Strength 2 (Kg)	0.565	0.645	0.285	0.44	0.26	0.42	0.26	0.495	0.395	0.27
Foot Splay 1 (cm)	3.4	6.5	4.8	4.5	6.5	5.7	5.4	5.5	4.7	4.9
Foot Splay 2 (cm)	2.5	7.6	4.9	5.7	6.2	6.4	5.5	6.2	4.8	3.9

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

	Vehicle Control (Females)									
Animal Number	F00 001	F00 002	F00 003	F00 004	F00 005	F00 006	F00 007	F00 008	F00 009	F00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	3	2	2	3	4
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	16	10	12	20	14	19	8	11	21	33
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	215.7	254.9	246.4	231.3	238.4	236.2	244.3	244.6	233.2	236
Foreleg Grip Strength 1 (Kg)	0.725	1.09	0.965	0.585	0.98	0.825	0.82	0.92	0.73	0.685
Foreleg Grip Strength 2 (Kg)	0.985	0.86	0.88	0.87	1.17	0.825	0.855	1.15	0.725	0.805
Hindleg Grip Strength 1 (Kg)	0.295	0.37	0.43	0.465	0.685	0.315	0.385	0.45	0.375	0.515
Hindleg Grip Strength 2 (Kg)	0.425	0.44	0.435	0.505	0.445	0.34	0.69	0.495	0.47	0.425
Foot Splay 1 (cm)	3.9	6.3	5.4	3.9	5.1	5.9	5.1	4.6	4.4	7.2
Foot Splay 2 (cm)	4.4	6.9	7.1	4.3	5	5.9	5.8	3.5	4.5	7.4

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

			1500 ppm Isobutanol (FEMALES)							
Animal Number	F01 001	F01 002	F01 003	F01 004	F01 005	F01 006	F01 007	F01 008	F01 009	F01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	12	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	3	2	2	3	2	3	2	2	2	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	23	4	15	25	19	30	14	13	18	28
Excretion	0	0	0	0	0	1	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	219.2	260.6	291.2	214.7	228.2	225	210.4	239.5	205.7	224.5
Foreleg Grip Strength 1 (Kg)	0.835	1.165	0.865	0.925	0.86	1.17	0.645	0.575	0.565	0.525
Foreleg Grip Strength 2 (Kg)	0.735	0.75	0.815	1.1	1.045	1.01	0.77	0.635	0.93	0.625
Hindleg Grip Strength 1 (Kg)	0.65	0.46	0.705	0.225	0.54	0.725	0.555	0.58	0.46	0.425
Hindleg Grip Strength 2 (Kg)	0.545	0.495	0.44	0.375	0.55	0.565	0.47	0.67	0.4	0.515
Foot Splay 1 (cm)	5.8	5.8	5.7	5.1	7.7	5.6	4.4	5	5.5	5.7
Foot Splay 2 (cm)	5.2	6	4.6	4.4	6.5	5.2	4.9	5.1	6.3	6

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

	3000 ppm Isobutanol (FEMALES)									
Animal Number	F02 001	F02 002	F02 003	F02 004	F02 005	F02 006	F02 007	F02 008	F02 009	F02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	3	2	3	2	3	2	2	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	19	12	19	19	24	20	20	20	6	25
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	2	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	249.7	270.9	233.2	250.1	233.2	209.2	233.6	243.7	288.2	216.2
Foreleg Grip Strength 1 (Kg)	0.545	1.095	0.49	0.81	1.05	1.01	1.14	0.72	1	0.96
Foreleg Grip Strength 2 (Kg)	0.65	1.115	0.83	0.91	0.82	0.945	0.98	0.635	0.88	1.085
Hindleg Grip Strength 1 (Kg)	0.52	0.765	0.73	0.605	0.26	0.53	0.43	0.78	0.63	0.41
Hindleg Grip Strength 2 (Kg)	0.49	0.58	0.38	0.4	0.335	0.56	0.595	0.44	0.53	0.71
Foot Splay 1 (cm)	5.5	5	6.8	6	6.4	6	4.5	4.1	5.3	4.5
Foot Splay 2 (cm)	5.5	5.5	7.6	6.6	5.9	5	3.5	5.1	5.9	5.1

EHL 94009/CMA Isobutanol AC NT - Individual Day 7 FOB Observations

			6000 ppm Isobutanol (FEMALES)							
Animal Number	F03 001	F03 002	F03 003	F03 004	F03 005	F03 006	F03 007	F03 008	F03 009	F03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	3	2	2	4	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	15	19	18	10	3	31	7	15	12	11
Excretion	0	0	0	0	2	0	0	0	0	1
Urination	0	0	0	0	0	0	0	0	1	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	228.5	229.1	243.2	241.2	248.3	234.7	281.4	206.3	305.7	244.1
Foreleg Grip Strength 1 (Kg)	0.795	0.66	1.16	0.685	1.085	0.635	0.605	0.59	0.59	0.935
Foreleg Grip Strength 2 (Kg)	0.66	0.7	1.025	0.68	0.855	0.535	1.075	0.955	0.835	0.95
Hindleg Grip Strength 1 (Kg)	0.34	0.43	0.305	0.525	0.4	0.685	0.585	0.825	0.525	0.385
Hindleg Grip Strength 2 (Kg)	0.43	0.365	0.415	0.515	0.4	0.575	0.305	0.63	0.33	0.24
Foot Splay 1 (cm)	4.1	5.5	4.1	3	7.5	6.4	6.5	6.1	4.3	3.7
Foot Splay 2 (cm)	3.2	6.4	4	4.4	8.6	5.5	7.1	7.5	4.4	3.8

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

	Vehicle Control (Females)									
Animal Number	F00 001	F00 002	F00 003	F00 004	F00 005	F00 006	F00 007	F00 008	F00 009	F00 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	2	3	2	2	3	4
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	17	12	13	15	15	21	14	3	19	38
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	2	1	1	2	1	1	3
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	227.6	268.2	264.8	241.7	248.6	256.4	255	257.9	243.4	242.2
Foreleg Grip Strength 1 (Kg)	0.685	0.88	1.21	0.71	1.345	0.65	1.05	1.23	0.555	0.535
Foreleg Grip Strength 2 (Kg)	0.845	1.025	1.11	0.705	1.215	0.81	1.02	1.165	0.83	0.53
Hindleg Grip Strength 1 (Kg)	0.365	0.445	0.33	0.44	0.595	0.2	0.5	0.37	0.405	0.425
Hindleg Grip Strength 2 (Kg)	0.38	0.415	0.545	0.49	0.61	0.34	0.44	0.45	0.495	0.655
Foot Splay 1 (cm)	3.3	5.4	3.6	3.7	5.4	6.1	4.3	3	7.3	3.6
Foot Splay 2 (cm)	4.1	6.3	4.4	3.7	5.8	7	5.3	3.6	6.8	6.3

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

	1500 ppm Isobutanol (FEMALES)									
Animal Number	F01 001	F01 002	F01 003	F01 004	F01 005	F01 006	F01 007	F01 008	F01 009	F01 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	12	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	3	2	2	2	2	2	3
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	23	8	10	22	22	21	13	7	1	28
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	1	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	225.5	278.9	310.5	229.4	242.2	255.9	229	252.9	224.8	243.7
Foreleg Grip Strength 1 (Kg)	0.865	1.195	1.255	1.21	0.795	0.905	0.995	1.17	0.985	0.485
Foreleg Grip Strength 2 (Kg)	0.81	0.77	0.965	1.07	1.105	1.055	1.065	0.995	0.685	0.735
Hindleg Grip Strength 1 (Kg)	0.665	0.52	0.53	0.595	0.55	0.365	0.555	0.635	0.51	0.32
Hindleg Grip Strength 2 (Kg)	0.625	0.455	0.64	0.42	0.565	0.325	0.495	0.495	0.545	0.32
Foot Splay 1 (cm)	5.4	5.6	6.5	3.6	5.1	6.9	3.2	5.6	6.4	5.8
Foot Splay 2 (cm)	5.6	7.2	7.1	3.4	4.6	5.6	4.5	5.9	6.2	5.6

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

			3000 ppm Isobutanol (FEMALES)							
Animal Number	F02 001	F02 002	F02 003	F02 004	F02 005	F02 006	F02 007	F02 008	F02 009	F02 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	2	2	2	3	3	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	0	0	0	0	0	0
Rearing	12	14	21	17	24	24	18	18	11	20
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	3	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	278	296.1	244.9	257.4	248	206.2	248.5	257	299.3	222.6
Foreleg Grip Strength 1 (Kg)	0.585	1.305	0.75	0.675	1.11	1.03	1.045	0.61	0.865	1.12
Foreleg Grip Strength 2 (Kg)	0.96	1.25	0.87	1.07	1.045	0.955	1.055	0.73	0.93	1.095
Hindleg Grip Strength 1 (Kg)	0.38	0.745	0.45	0.6	0.325	0.44	0.42	0.465	0.345	0.715
Hindleg Grip Strength 2 (Kg)	0.635	0.65	0.535	0.555	0.26	0.42	0.41	0.43	0.29	0.515
Foot Splay 1 (cm)	5.5	6.9	6.4	4.6	4	4.5	5.4	3.1	5.9	4.5
Foot Splay 2 (cm)	6	5.4	8.5	5	3.5	5.4	5.5	5.1	8.1	5.1

EHL 94009/CMA Isobutanol AC NT - Individual Day 14 FOB Observations

			6000 ppm Isobutanol (FEMALES)							
Animal Number	F03 001	F03 002	F03 003	F03 004	F03 005	F03 006	F03 007	F03 008	F03 009	F03 010
Activity	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Home Cage	0	0	0	0	0	0	0	0	0	0
Exophthalmia	0	0	0	0	0	0	0	0	0	0
Cage Removal Ease	1	1	1	1	1	1	1	1	1	1
Reactivity	1	1	1	1	1	1	1	1	1	1
Lacrimation	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0
Palpebral Closure	2	2	2	2	2	2	2	2	2	2
Piloerection	0	0	0	0	0	0	0	0	0	0
Miscellaneous Observations	0	0	0	0	0	0	0	0	0	0
Clonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Tonic Movements in Open Field	0	0	0	0	0	0	0	0	0	0
Alertness	2	3	3	2	1	3	2	2	2	2
Gait	0	0	0	0	0	0	0	0	0	0
Gait Score	3	3	3	3	3	3	3	3	3	3
Mobility Score	3	3	3	3	3	3	3	3	3	3
Vocalization	0	0	0	0	0	0	0	0	0	0
Stereotypy	0	0	0	0	0	0	0	0	0	0
Unusual Behavior	0	0	0	0	13	0	0	0	0	0
Rearing	17	20	20	19	1	16	20	11	10	20
Excretion	0	0	0	0	0	0	0	0	0	0
Urination	0	0	0	0	0	0	0	0	0	0
Approach Response	1	1	1	1	1	1	1	1	1	1
Tail Pinch Response	1	1	1	1	1	1	1	1	1	1
Click Response	1	1	1	1	1	1	1	1	1	1
Pupillary Reflex	1	1	1	1	1	1	1	1	1	1
Righting Reflex	3	3	3	3	3	3	3	3	3	3
Weight (gm)	244.7	249.7	259.4	249.4	262.6	257.2	273	233.2	319.9	260.2
Foreleg Grip Strength 1 (Kg)	0.775	1.025	1.03	0.86	1.05	0.7	0.63	1.01	0.845	1.14
Foreleg Grip Strength 2 (Kg)	0.935	0.665	0.925	1.015	0.59	0.78	0.515	0.935	1.035	1.19
Hindleg Grip Strength 1 (Kg)	0.355	0.465	0.285	0.8	0.415	0.685	0.405	0.625	0.595	0.375
Hindleg Grip Strength 2 (Kg)	0.42	0.54	0.34	0.695	0.445	0.64	0.37	0.535	0.385	0.38
Foot Splay 1 (cm)	3.1	5.4	6.2	6.5	5.4	5.3	5.1	6	6.1	4.1
Foot Splay 2 (cm)	4.6	5.6	6.1	5.5	5.6	5.8	4.1	5.4	6.4	3.2

Appendix 11: Individual Gross and Histopathology Data

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 001 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 002 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 003 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 004 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 005 SEX: MALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 006 SEX: MALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 007 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 008 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 009 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M00 010 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (FLSPEC)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 001 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 002 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 003 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 004 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 005 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (FLSPEC)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 006 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS	DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 007 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 008 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 009 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M01 010 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 001 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 002 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 003 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 004 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== ORGAN WEIGHTS (GM) and % BODY WEIGHT ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== GROSS OBSERVATIONS ===

NO GROSS ABNORMALITIES.

=== MICROSCOPIC TISSUE OBSERVATIONS ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 005 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 006 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

KIDNEY(S)
DILATED PELVIS -- RIGHT, MILD.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 007 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 008 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== ORGAN WEIGHTS (GM) and % BODY WEIGHT ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== GROSS OBSERVATIONS ===

NO GROSS ABNORMALITIES.

=== MICROSCOPIC TISSUE OBSERVATIONS ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 009 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M02 010 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d \ B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 001 SEX: MALE PROSECTOR : (FLSPEC)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 002 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (FLSPEC)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d \ B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 003 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 004 SEX: MALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 005 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 006 SEX: MALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d \ B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 007 SEX: MALE PROSECTOR : (JACROS)
ANIMAL STATUS CODE: D HOURS POST MORTEM = 12 DATE OF NECROPSY: 28-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (TVWILS)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

SPLEEN
FOCUS, GRAY/WHITE -- SEROSA - MULTIPLE, 0.1 - 0.3 CM, ROUND
TO IRREGULAR, DISCRETE TO CONFLUENT, WHITE, FLAT FOCI.
NOTE: LESION WAS NOT SAVED.

GROSS CONDITION
NOTE: ANIMAL DIED ON SUNDAY MARCH 27, 1994 AND WAS NOT
NECROPSIED UNTIL MONDAY MARCH 28, 1994.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 008 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (FLSPEC)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 009 SEX: MALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009M03 010 SEX: MALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS	DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 001 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 002 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 003 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 004 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== ORGAN WEIGHTS (GM) and % BODY WEIGHT ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== GROSS OBSERVATIONS ===

NO GROSS ABNORMALITIES.

=== MICROSCOPIC TISSUE OBSERVATIONS ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 005 SEX: FEMALE PROSECTOR : (FLSPEC)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 006 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 007 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 008 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 009 SEX: FEMALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F00 010 SEX: FEMALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 001 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 002 SEX: FEMALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

UTERUS
ENLARGED/DILATED/DISTENDED -- BILATERAL HORNS, MINIMALLY
DILATED AS COMPARED TO CONTROLS.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 003 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (FLSPEC)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== ORGAN WEIGHTS (GM) and % BODY WEIGHT ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== GROSS OBSERVATIONS ===

NO GROSS ABNORMALITIES.

=== MICROSCOPIC TISSUE OBSERVATIONS ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 004 SEX: FEMALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

UTERUS
ENLARGED/DILATED/DISTENDED -- BILATERAL HORNS, MINIMALLY
DILATED AS COMPARED TO CONTROLS.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 005 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 006 SEX: FEMALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS	DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 007 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

LY.NODE,SUBMAX.
ENLARGED/PROMINENT -- LEFT, 1.0 X 0.9 CM.

UTERUS
ENLARGED/DILATED/DISTENDED -- BILATERAL HORNS, MINIMALLY
DILATED AS COMPARED TO CONTROLS.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 008 SEX: FEMALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 009 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F01 010 SEX: FEMALE PROSECTOR : (FLSPEC)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 001 SEX: FEMALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 002 SEX: FEMALE PROSECTOR : (FLSPEC)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 003 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 004 SEX: FEMALE PROSECTOR : (PEODON)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 005 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d \ B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 006 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 007 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 31-MAR-94

PROSECTOR : (KMSHEV)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

UTERUS
ENLARGED/DILATED/DISTENDED -- BILATERAL HORNS, MINIMALLY
DILATED AS COMPARED TO CONTROLS.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 008 SEX: FEMALE PROSECTOR : (FLSPEC)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 009 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 2-APR-94

PROSECTOR : (DMSMOL)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== ORGAN WEIGHTS (GM) and % BODY WEIGHT ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== GROSS OBSERVATIONS ===

NO GROSS ABNORMALITIES.

=== MICROSCOPIC TISSUE OBSERVATIONS ===

TISSUE / HISTOPATHOLOGICAL FINDINGS	DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F02 010 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 001 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 002 SEX: FEMALE PROSECTOR : (DMSMOL)
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 003 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 004 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009
RTE OF ADMIN: INHALATION
STUDY START DATE: 15-MAR-1994

INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA

REPORT PRINT DATE: 14-MAY-1994
SPECIES: RAT
STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 005 SEX: FEMALE
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94

PROSECTOR : (PEODON)
ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 006 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 30-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (JGNAPI)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 007 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM - 0 DATE OF NECROPSY: 31-MAR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d \ B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

UTERUS
ENLARGED/DILATED/DISTENDED -- BILATERAL HORNS, MINIMALLY
DILATED AS COMPARED TO CONTROLS.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 008 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 1-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- G R O S S O B S E R V A T I O N S ---

N O G R O S S A B N O R M A L I T I E S.

--- M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 009 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

--- ORGAN WEIGHTS (GM) and % BODY WEIGHT ---

TERMINAL BODY WEIGHT -- NOT RECORDED

--- GROSS OBSERVATIONS ---

NO GROSS ABNORMALITIES.

--- MICROSCOPIC TISSUE OBSERVATIONS ---

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

NO TISSUES EXAMINED.

STUDY NUMBER: 94009 INDIVIDUAL GROSS AND HISTOPATHOLOGY DATA REPORT PRINT DATE: 14-MAY-1994
RTE OF ADMIN: INHALATION SPECIES: RAT
STUDY START DATE: 15-MAR-1994 STRAIN/BREED: SPRAGUE-DAWLEY

ANIMAL NO: 94009F03 010 SEX: FEMALE PROSECTOR : (KMSHEV)
ANIMAL STATUS CODE: S HOURS POST MORTEM = 0 DATE OF NECROPSY: 2-APR-94 ORGAN WTS. BY: ( )
PATHOLOGIST : (KMSHEV)

=== O R G A N W E I G H T S (G M) a n d % B O D Y W E I G H T ===

TERMINAL BODY WEIGHT -- NOT RECORDED

=== G R O S S O B S E R V A T I O N S ===

N O G R O S S A B N O R M A L I T I E S.

=== M I C R O S C O P I C T I S S U E O B S E R V A T I O N S ===

TISSUE / HISTOPATHOLOGICAL FINDINGS DISTRIBUTION (SEVERITY)

N O T I S S U E S E X A M I N E D.

Appendix 12: Positive Control Data

Appendix 12, Exhibit 1
Explanation of Positive Control Data

The EPA neurotoxicity test guidelines require that positive control data from the laboratory performing the testing should provide evidence that the Functional Observational Battery (FOB) used can detect major neurotoxic endpoints, that the activity measuring device and testing procedures can detect chemically induced increases and decreases in activity, and that the histopathology procedures can lead to the detection of central and peripheral nervous system pathology.

Two studies were conducted to achieve these ends. The abstract, cover page, GLP compliance statement, quality assurance audit statement, report signature page, and selected summary tables from the complete reports for these two studies are included in this appendix.

The study summarized in Exhibit 2 provide evidence of the ability of the FOB used by this laboratory to detect major neurotoxic endpoints including limb weakness (repeated exposure to acrylamide), tremors (p,p'-DDT), and autonomic signs (carbaryl). In addition to validation of the FOB procedures, the study in Exhibit 2 also demonstrated the sensitivity of the neurohistopathological procedures to detect central (trimethyltin) and peripheral (acrylamide) nervous system damage. The study summarized in Exhibit 3 provides positive control data demonstrating the sensitivity and reliability of the activity-measuring device and testing procedures used by this laboratory to detect increases (amphetamine) and decreases (chlorpromazine) in motor activity.

The summary tables are self-explanatory but a few clarifications are warranted.

1. The term "occurrences of descriptive observations" in Exhibit 2 more precisely refers to the total number of animals affected (each animal was observed only once during each period). For example, if 4 "occurrences" were recorded for a particular effect, then this means that 4 different animals were affected.

2. The group codes MV1, M01, MV4, and M05 listed in the pathology summary tables in Exhibit 2 refer to groups treated with vehicle for acrylamide, acrylamide, vehicle for trimethyltin, and trimethyltin, respectively.

Appendix 12, Exhibit 2

Validation of a Functional Observational Battery (FOB) and Neuropathology for Neurotoxicity Testing

Monsanto

MAG/Regulatory Science & Public Affairs/EHL
(CO./DIV./DEPT./LOCATION)

Final REPORT
(TYPE OF REPORT)

REPORT NO.: MSL-13429

JOB/PROJECT NO.: EHL 92227

DATE: March 7, 1994

TITLE: Validation of a Functional Observational Battery(FOB) and Neuropathology for Neurotoxicity Testing

AUTHORS: P. E. O'Donnell, B.S.

ABSTRACT:

This study was conducted to provide historical positive control data for the functional observational battery and neuropathology examination as required by 1991 EPA guidelines for the neurotoxicity screening battery.

Acrylamide, 1-napthyl N-methylcarbamate (carbaryl), and 1,1-bis(4-Chlorophenyl)-2,2,2-trichloroethane (p,p'-DDT) were administered to groups of 10 male rats to assess (a) the ability of the laboratory's functional observational battery to detect specific neurotoxic endpoints (FOB), (b) the proficiency of each study participant to conduct the FOB, and (c) inter-observer reliability. Additionally, groups of 10 male rats were administered the corresponding vehicle for each substance. These materials were chosen as positive controls for the FOB to demonstrate limb weakness or paralysis (acrylamide), autonomic signs (carbaryl) and tremors (p,p'-DDT). The FOB was performed after treatment at a time when neurotoxic signs would likely be detected.

Neuropathology examination was performed on five rats treated with acrylamide (a subset of the animals used for the FOB described above) and five rats treated with trimethyltin. Two control groups, each of five rats administered either the vehicle for acrylamide or the vehicle for trimethyltin, were also examined pathologically. The animals for neuropathology were sacrificed when acrylamide and trimethyltin were expected to produce abnormal pathology in the peripheral and central nervous system, respectively.

The results of this study demonstrated that this laboratory can detect the appropriate endpoints using its FOB and perfusion neuropathology procedures. Limb weakness caused by acrylamide (12 ip doses over 24 days at 40 mg/kg) was demonstrated by impairment of gait and increased landing foot splay. Neuropathological findings included axonal and myelin degeneration in the peripheral nerves of all of the animals administered acrylamide and examined microscopically.

(Continued on next page.)

REPT. NO.: MSL-13429 AUTHORS: P. E. O'Donnell, B.S.
TITLE: Validation of a Functional Observational Battery(FOB) and Neuropathology for Neurotoxicity Testing

COPY NO.:

C O M P A N Y C O N F I D E N T I A L

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ABSTRACT: cont'd.

Autonomic signs of increased salivation and urination, decreased excretion and exophthalmia occurred in the rats treated with carbaryl (single ip dose at 45 mg/kg). Other effects observed in these rats included decreased cage removal ease, alertness, rearing, reactivity to investigator, response to tail pinch, body weight, and forelimb and hindlimb grip strength; impaired gait and mobility; and localized tremors, whole body tremors and repetitive movements of mouth.

The tremorgenic effects of p,p'-DDT (single dose by oral gavage at 90 mg/kg) included myoclonic jerks or whole body tremors. Impaired gait and mobility; decreased rearing, forelimb grip strength and landing foot splay; and increased reactivity to investigator and response to clicker also occurred in these rats.

The rats administered trimethyltin (2 ip injection at 8 mg/kg and 1 ip injection at 2 mg/kg over 15 days) had clear abnormalities of the central nervous system including lesions in the hippocampus, dentate gyrus, piriform cortex, and cerebrum.

These results are consistent with previously reported findings for these substances. The objectives of this study were attained by providing positive control data for the FOB, in demonstrating observer proficiency at recognizing specific neurotoxic endpoints, and by validating the neuropathology screen for peripheral and central nervous system damage.

STUDY TITLE

VALIDATION OF A FUNCTIONAL OBSERVATIONAL BATTERY(FOB) AND NEUROPATHOLOGY FOR NEUROTOXICITY TESTING

DATA REQUIREMENT

Guideline: 81-8, Subdivision F - Neurotoxicity Screening Battery

AUTHORS

P.E. O'Donnell, D.C. Thake, A.A. Li, D.K. Branch, K.M. Shevlin

STUDY COMPLETED ON:

March 4, 1994

PERFORMING LABORATORY

Monsanto Company, The Agricultural Group
Environmental Health Laboratory (EHL)
645 S. Newstead
St. Louis, Missouri 63110

PROJECT NUMBER

Laboratory Project Number: EHL 92227

GLP COMPLIANCE STATEMENT

The study EHL 92227 was conducted in conformance with the Good Laboratory Practice (GLP) Standards of the EPA (USA, FIFRA: 40 CFR, Part 160), MAFF (Japan, 1984), and the GLP Principles of the OECD (1981) with the following exceptions:

1. Characterization of test and controls substances was not conducted according to the standards. Synthesis data are not archived at Monsanto.

2. Test and control substance concentrations and homogeneity in carrier were not confirmed.

3. The stability of test and control substances, neat and after mixing with carrier, was not determined.

Pat E O'Donnell 3-4-94

Pat E. O'Donnell Date
Study Director

R M Folk 3/7/94

R. M. Folk Date
Director, Environmental Health Laboratory

QUALITY ASSURANCE AUDIT STATEMENT

Study Number: 92227

Protocol Amendments: One - April 02, 1993

Study Title: Validation of a Functional Observational Battery (FOB) and Neuropathology for Neurotoxicity Testing

Dates of Inspections and Communication of Findings:

January 26, 1993
February 11, 1993
March 09, 26, 1993
June 15, 1993
October 18, 26, 1993
November 10, 1993
December 23, 1993
January 06, 1994
February 15, 21, 23, 1994

Quality Assurance Review Conducted by:

N.K. Harakas
S.H. McClain
C.K. Russell
P.A. Winzenburger

This signed statement indicates the ESH Quality and Compliance Assurance Unit has monitored this study and reviewed the data and final report. These reviews indicate the final report accurately presents the raw data as developed during the study.

March 3, 1994

John L. Henshaw — Date
Director Quality & Compliance Assurance

REPORT SIGNATURE PAGE

This report accurately represents the data developed during the study.

Pat E. O'Donnell — 3-4-94
Pat E. O'Donnell
Study Director
Date

3-4-94
Abby A. Li, Ph.D.
Neurotoxicology Team Leader
Date

3/4/94
Daryl C. Thake, D.V.M., Dipl. A.C.V.P.
Pathologist
Date

3/7/94
Roger M. Folk, Ph.D.
Director, Environmental Health Laboratory
Date

Group Designations and Dosing Administration:

Chemical	Group	N	Target Dose (mg/kg)	Route of Administration	Volume (ml/kg)	Vehicle
Acrylamide	M01	10	40	12 ip doses over 24 days	1	sterile water
	MV1	10	0	12 ip doses over 24 days	1	sterile water
Carbaryl	M02	10	45	single ip	1	emulphor(a) ethanol (a) 0.9% saline
	MV2	10	0	single ip	1	emulphor(a) ethanol (a) 0.9% saline
p,p'DDT	M03	10	90	single gavage	1	corn oil
	MV3	10	0	single gavage	1	corn oil
Trimethyltin	M04	5(b)	8&2&8	3 ip doses over 15 days	1	sterile water
	MV4	5	0	3 ip doses over 15 days	1	sterile water

(a) The mixture of emulphor, ethanol and saline was made to contain 5% emulphor and 5% ethanol by volume.

(b) Although 5 animals were dosed, only 4 animals survived for neuropathology examination.

EHL 92227 - Statistically Significant Results

Category	Acrylamide 15 x 40 mg/Kg ip Obs 21 days after first dosing	Carbaryl 45 mg/Kg ip Obs 1 hr after dosing	p,p' DDT 90 mg/Kg po Obs 4 hrs after dosing
Cage removal ease		↓★★	
Reactivity toward investigator		↓★	↑★★
Salivation		↑★★	
Exophthalmia		↑★★	
Alertness		↓★★	
Gait score	↓★★	↓★★	↓★★
Mobility score		↓★★	↓★
Rearing*		↓★★	↓★★
Excretion		↓★★	
Urination		↑★★	
Response to clicker			↑★★
Tail pinch response		↓★★	
Body weight	↓★	↓★	
Forelimb grip strength		↓★	↓★★
Hindlimb grip strength		↓★★	
Landing foot splay	↑★★	↑★★	↓★

Note: the arrows refer to the direction of difference from control
Stars indicate significant differences from control values at probability levels of less than or equal to 0.05 (one star) or 0.01 (two stars)
*Levine's Test significant at p less than or equal to 0.01 for carbaryl

EHL 92227 - Occurrences of Descriptive Observations

Category	Acrylamide 15 x 40 mg/Kg ip Obs 21 Days after first dose	Carbaryl 45 mg/Kg ip Obs 1 hr after dosing	p, p' - DDT 90 mg/Kg po Obs 4 Hrs after dosing
Activity in home cage			
Dead			1
Flattened; limbs may be spread out		4	5
Hunched over		1	
Clonic movements in home cage			
Repetitive movements of mouth and jaws		2	
Myoclonic jerks			5
Localized tremors		1	
Whole body tremors		8	9
Total # animals with clonic movements		10	9
Miscellaneous Observations			
Red nasal discharge/staining		1	6
Red ocular discharge		1	2
Polyuria		10	
Dyspnea		2	1
Rales		1	
Ocular cloudiness/opacity		1	
Clonic movements in open field			
Repetitive movements of mouth and jaws		4	
Myclonic jerks			6
Localized tremors			
Whole body tremors		7	9
Total # animals with clonic movements		8	9

Number of animals refers to dosed group unless otherwise noted.

EHL 92227 - Occurrences of Descriptive Observations

Category	Acrylamide 15 x 40 mg/Kg ip Obs 21 Days after first dose	Carbaryl 45 mg/Kg ip Obs 1 hr after dosing	p, p' - DDT 90 mg/Kg po Obs 4 Hrs after dosing
Tonic movements in open field			
Explosive jumps			1
Description of gait			
Waddles, rocks or lurches	9	9	4
Feet markedly point outwards from body	1		1
Hunched or crouched body position			
Moves with body flattened		1	4
Misuse/disuse of hind limbs	1		
Total # animals with impaired gait	**9**	**10**	**7**
Unusual behavior			
Flopping			1
Static flattened attitude		1	
Static foot splay		1	
Gait & mobility score assessed after stimulation		1	

Number of animals refers to dosed group unless otherwise noted.

THIS REPORT GENERATED FROM DATA LOCKED THRU 1-DEC-93

STUDY NO: 92227 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 1

P A T H O L O G Y S E C T I O N

STUDY TYPE: AC SPECIES: RAT SUBSTANCE: NO SUBSTANCE PRINTED: 4-JAN-94

*** SUMMARY INCIDENCE OF MICROSCOPIC FINDINGS ***

SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 9-MAR-1993:10-MAR-1993 :

T I S S U E S W I T H F I N D I N G S	ANIMAL SEX :	----- N U M B E R O F A N I M A L S A F F E C T E D -------- M A L E S ---------									
	DOSAGE GROUP:	MV1	M01	MV2	M02	MV3	M03	MV4	M04	MV5	M05
	NO. IN GROUP:	5	5	0	0	0	0	0	0	0	0
NERVE, SCIATIC -DEGENERATION, FIBER		0	5 **								
ROOT, CERVICAL -DEGENERATION, NERVE FIBER		0	3								
ROOT, LUMBAR -DEGENERATION, NERVE FIBER		0	5 **								
NERVE, SURAL -DEGENERATION, NERVE FIBER		0	5 **								
NERVE, TIBIAL -DEGENERATION, NERVE FIBER		0	5 **								

NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROUP.

* - SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.05] FROM CONTROL USING FISHER'S EXACT TEST.
** - SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.01] FROM CONTROL USING FISHER'S EXACT TEST.

THIS REPORT GENERATED FROM DATA LOCKED THRU 1-DEC-93

STUDY NO: 92227 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 1

P A T H O L O G Y S E C T I O N

STUDY TYPE: AC SPECIES: RAT SUBSTANCE: NO SUBSTANCE PRINTED: 4-JAN-94

*** SUMMARY INCIDENCE OF MICROSCOPIC FINDINGS ***

SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: 19-FEB-1993:24-FEB-1993 : :

T I S S U E S W I T H F I N D I N G S	ANIMAL SEX :	----- N U M B E R O F A N I M A L S A F F E C T E D -------									
		---- M A L E S ---------									
	DOSAGE GROUP:	MV4	M04	MV1	M01	MV2	M02	MV3	M03	MV5	M05
	NO. IN GROUP:	5	4	0	0	0	0	0	0	0	0
BRAIN,CEREBELLUM											
SP.CORD,CERVICAL											
-DEGENERATION, MYELIN; VENTRAL FUNICULUS		0	3 *								
-CHROMATOLYSIS, CENTRAL, NEURON		0	2								
FORE BRAIN											
-DEGENERATION, NEURON; HIPPOCAMPUS		0	4 **								
-DILATATION LATERAL VENTRICLE		0	2								
-VACUOLATION, MOLECULAR LAYER; HIPPOCAMPUS		0	3 *								
-DILATATION, 3RD VENTRICLE		0	1								
-DEGENERATION, NEURON; DENTATE GYRUS		0	4 **								
-DEGENERATION, NEURON; PIRIFORM CORTEX		0	4 **								
-DEGENERATION, NEURON		0	2								
SP.CORD,LUMBAR											
-DEGENERATION, MYELIN; VENTRAL FUNICULUS		0	3 *								
-CHROMATOLYSIS, CENTRAL, NEURON		0	2								
SP.CORD,THORACIC											
-DEGENERATION, MYELIN; VENTRAL FUNICULUS		2	2								
-DEGENERATION, MYELIN; DORSAL FUNICULUS		0	1								
-CHROMATOLYSIS, CENTRAL, NEURON		0	1								

NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROUP.

* - SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQUAL TO 0.05) FROM CONTROL USING FISHER'S EXACT TEST.
** - SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQUAL TO 0.01) FROM CONTROL USING FISHER'S EXACT TEST.

Appendix 12, Exhibit 3

Validation of Home Cage Photobeam Motor Acitivty System for Neurotoxicity Testing

Monsanto

MAG/Regulatory Science & Public Affairs/EHL
(CO./DIV./DEPT./LOCATION)

Final REPORT
(TYPE OF REPORT)

REPORT NO.: MSL-13321

JOB/PROJECT NO.: EHL 93007

DATE: January 17, 1994

TITLE: Validation of Home Cage Photobeam Motor Activity System for Neurotoxicity Testing

AUTHORS: Terry A. Kaempfe, B.S.

ABSTRACT:

The revised EPA neurotoxicity guidelines (USEPA, 1991) require that motor activity be monitored by an automated activity recording apparatus; that the test session be long enough for motor activity to approach asymptotic levels by the last 20 percent of the session for non-treated control animals; and that the device used must be capable of detecting chemically-induced increases and decreases in activity. This study demonstrated that this laboratory's motor activity testing procedures meet the above requirements.

The motor activity of four groups of 10 male Sprague-Dawley rats was determined 1 hour after the animals were dosed with chlorpromazine HCL (intraperitoneal (i.p.), 0, 1, 2 or 4 mg/kg). After motor activity levels had returned to baseline levels, the motor activity of these animals was measured 1 hour after dosing with d-amphetamine SO4 (i.p., 0, 0.5, 1 or 2 mg/kg). Baseline levels of activity were determined 2 days prior to administration of either of the chemicals.

The results of this study indicate that 60 minutes is sufficiently long for activity to approach asymptotic levels by the last 20 percent of the session (approximately 10 minutes) for non-treated animals. Decreases in motor activity after treatment with chlorpromazine HCL (2 and 4 mg/kg) and increases after d-amphetamine SO4 (0.5, 1 and 2 mg/kg) were detected by this laboratory's automated motor activity measuring devices. The sensitivity of our activity monitoring devices in detecting chemically-induced increases and decreases in activity was comparable to those obtained by other laboratories using the same procedures.

REPT. NO.: MSL-13321 AUTHORS: Terry A. Kaempfe, B.S.
TITLE: Validation of Home Cage Photobeam Motor Activity System for Neurotoxicity Testing
COPY NO.:

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STUDY TITLE

Validation of Home Cage Photobeam Motor Activity System for Neurotoxicity Testing

DATA REQUIREMENT

Guidelines 81, 82 and 83 subdivision F: Neurotoxicity

AUTHOR

Terry A. Kaempfe

STUDY COMPLETED ON:

January 17, 1994

PERFORMING LABORATORY

Monsanto Company, The Agricultural Group
Environmental Health Laboratory (EHL)
645 S. Newstead
St. Louis, Missouri 63110

PROJECT NUMBER

Monsanto EHL Study Number: EHL 93007

GLP COMPLIANCE STATEMENT

The study EHL 93007 was conducted in accordance with the Good Laboratory Practice (GLP) Standards of the EPA (USA, FIFRA: 40 CFR, Part 160), MAFF (Japan, 1984), and the GLP Principles of the OECD (1981) with the following exceptions:

No analytical determinations were made to characterize the test materials or to verify the stability, homogeneity, or concentration of the test materials in the dosing solutions. Characterization of the test materials consisted of the information supplied by the manufacturer.

Terry A. Kaempfe, B.S. 1/17/94
Study Director Date

R. M. Folk 1/17/94
Director, Environmental Health Laboratory Date

ESH QUALITY ASSURANCE AUDIT STATEMENT

Study Number: EHL 93007

Protocol Amendments: NONE

Study Title: Validation of Home Cage Photobeam Motor Activity System of Neurotoxicity Testing

Dates of Inspections and Communication of Findings:
February 09, 1993
March 04, 23, 1993
July 12, 1993
September 09, 1993
December 17, 23, 1993

Quality Assurance Review Conducted by:
S. M. Haag
N. K. Harakas
C. K. Russell
P. A. Winzenburger

Results: The Quality Assurance review indicates the final report accurately presents the raw data as developed during the study. There appears to be no significant deviation from applicable GLP regulations that adversely affected study quality or integrity.

John L. Henshaw
Director Quality & Compliance Assurance

December 23, 1993
Date

REPORT SIGNATURE PAGE

This report accurately represents the data developed during the study.

Terry A. Kaempfe 1/17/94

Terry A. Kaempfe, B.S. **Date**
Study Director

R.M. Folk 1/17/94

Roger M. Folk, Ph. D. **Date**
Director, Environmental Health Laboratory

Table 1
EHL 93007 - Effects of Chlorpromazine HCl and d-Amphetamine SO4 on Motor Activity (counts per 60 minutes)

Chlorpromazine HCl

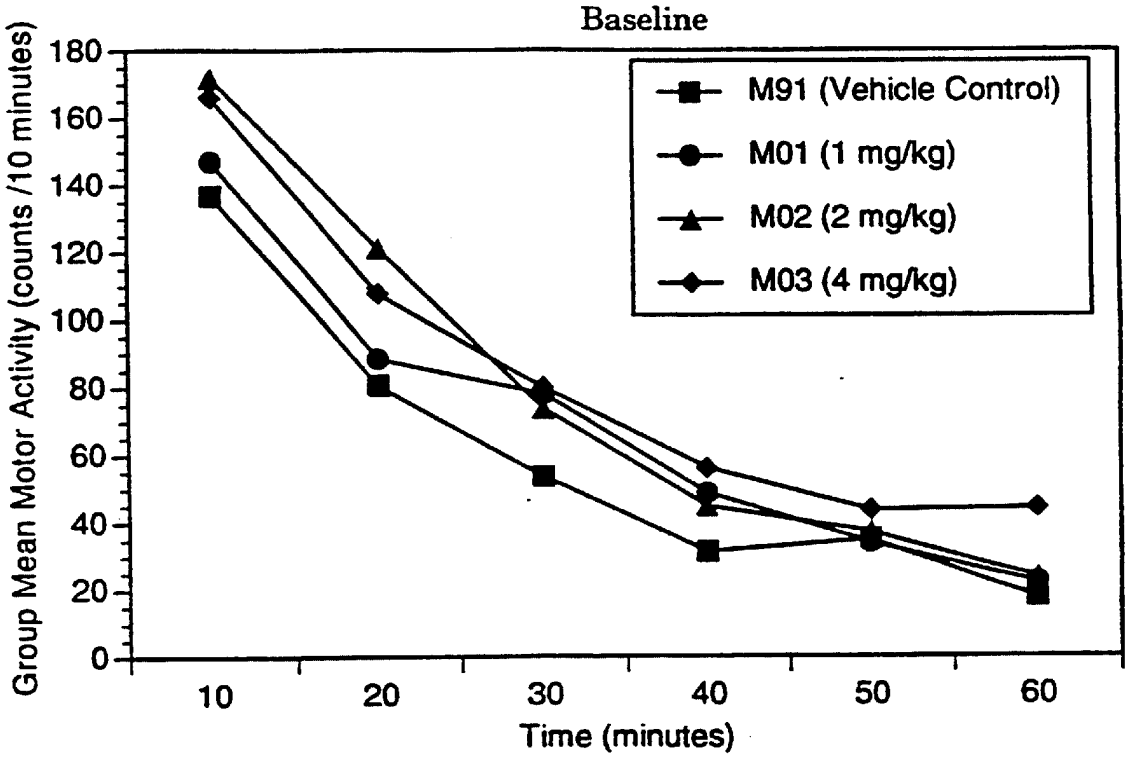
Dose Level (mg/Kg)		Baseline	Dosed
0.0	Mean	354.9	329.3
	SD	130.3	138.1
	Count	10	10
1.0	Mean	418.6	272.8
	SD	155.8	106.9
	Count	10	10
2.0	Mean	472.4	175.8**
	SD	160.6	71.0
	Count	10	10
4.0	Mean	497.8	105.4**
	SD	198.5	60.2
	Count	10	10

d-Amphetamine SO4

Dose Level (mg/Kg)		Baseline	Dosed
0.0	Mean	404.9	382.7
	SD	164.9	153.6
	Count	10	10
0.5	Mean	435.3	656.4*
	SD	195.3	209.0
	Count	10	10
1.0	Mean	376.6	1046.7**
	SD	117.0	179.5
	Count	10	10
2.0	Mean	465.8	1148.0**
	SD	191.2	340.0
	Count	10	10

* Dunnett's Test significant at p less than or equal to 0.05
** Dunnett's Test significant at p less than or equal to 0.01
LT Levene's Test significant at p less than or equal to 0.01

Figure 1
Intersession Motor Activity of Animals Dosed with Chlorpromazine HCl



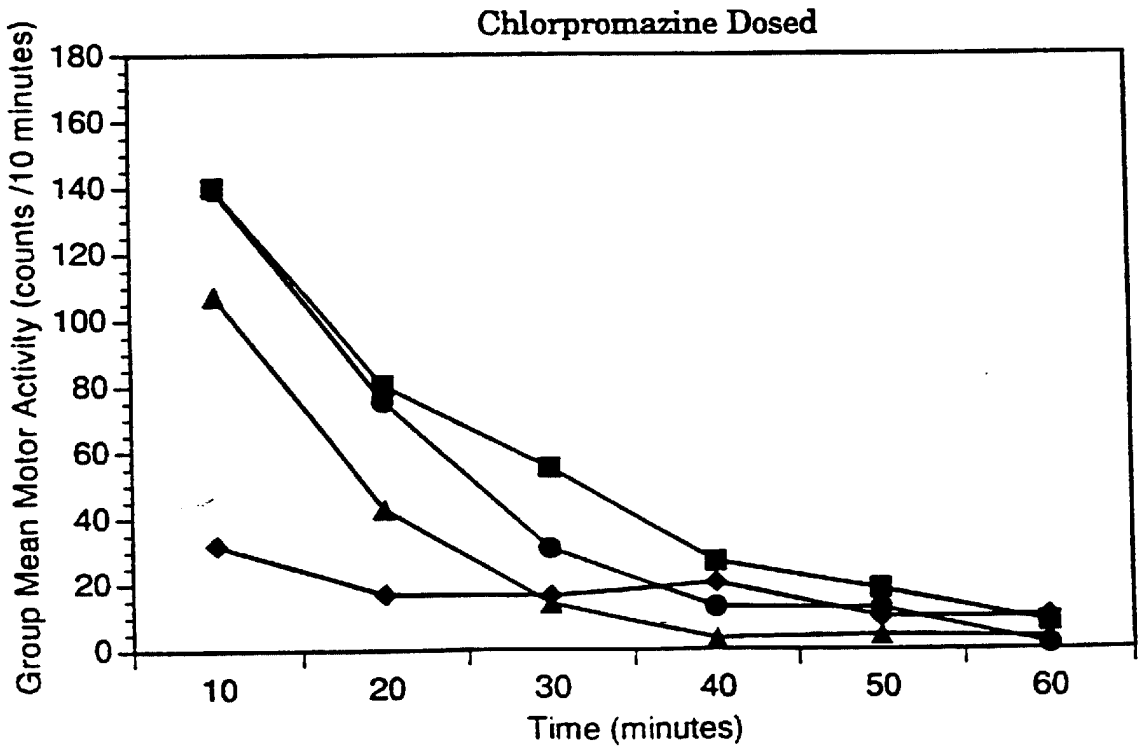


Figure 2
Effect of Chlorpromazine HCl on Motor Activity

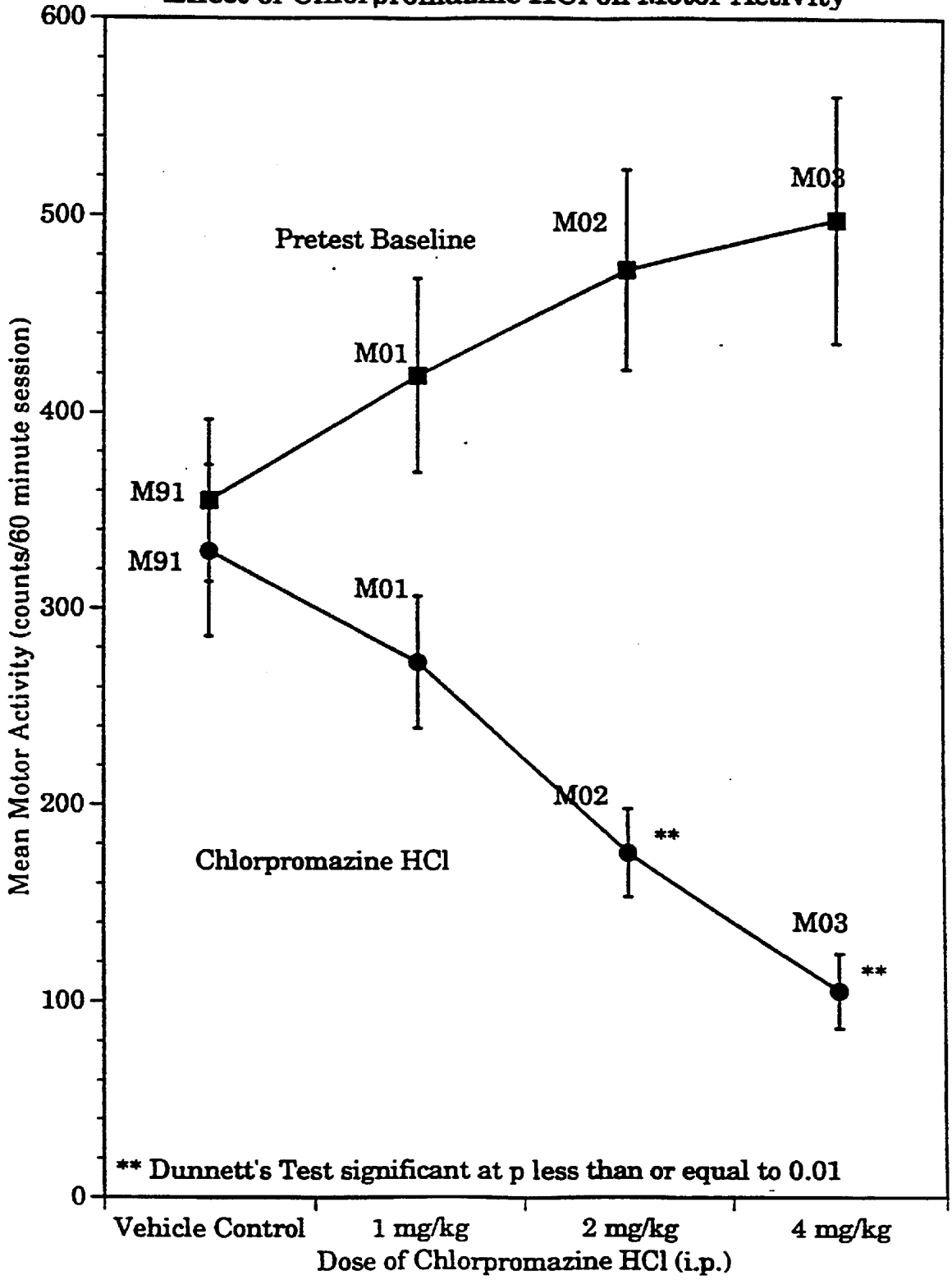


Figure 3
Intersession Motor Activity of Animals Dosed with Amphetamine SO4

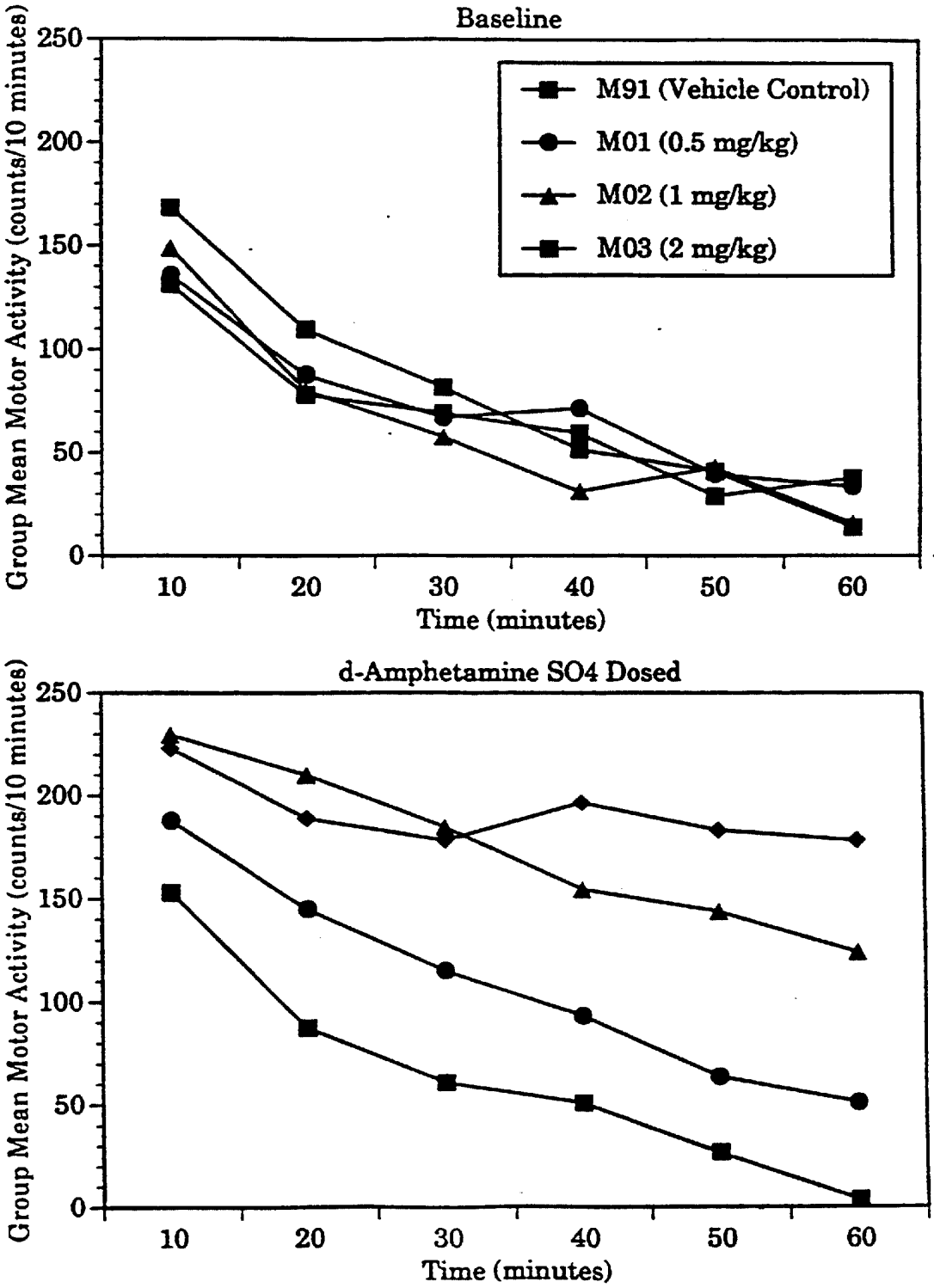
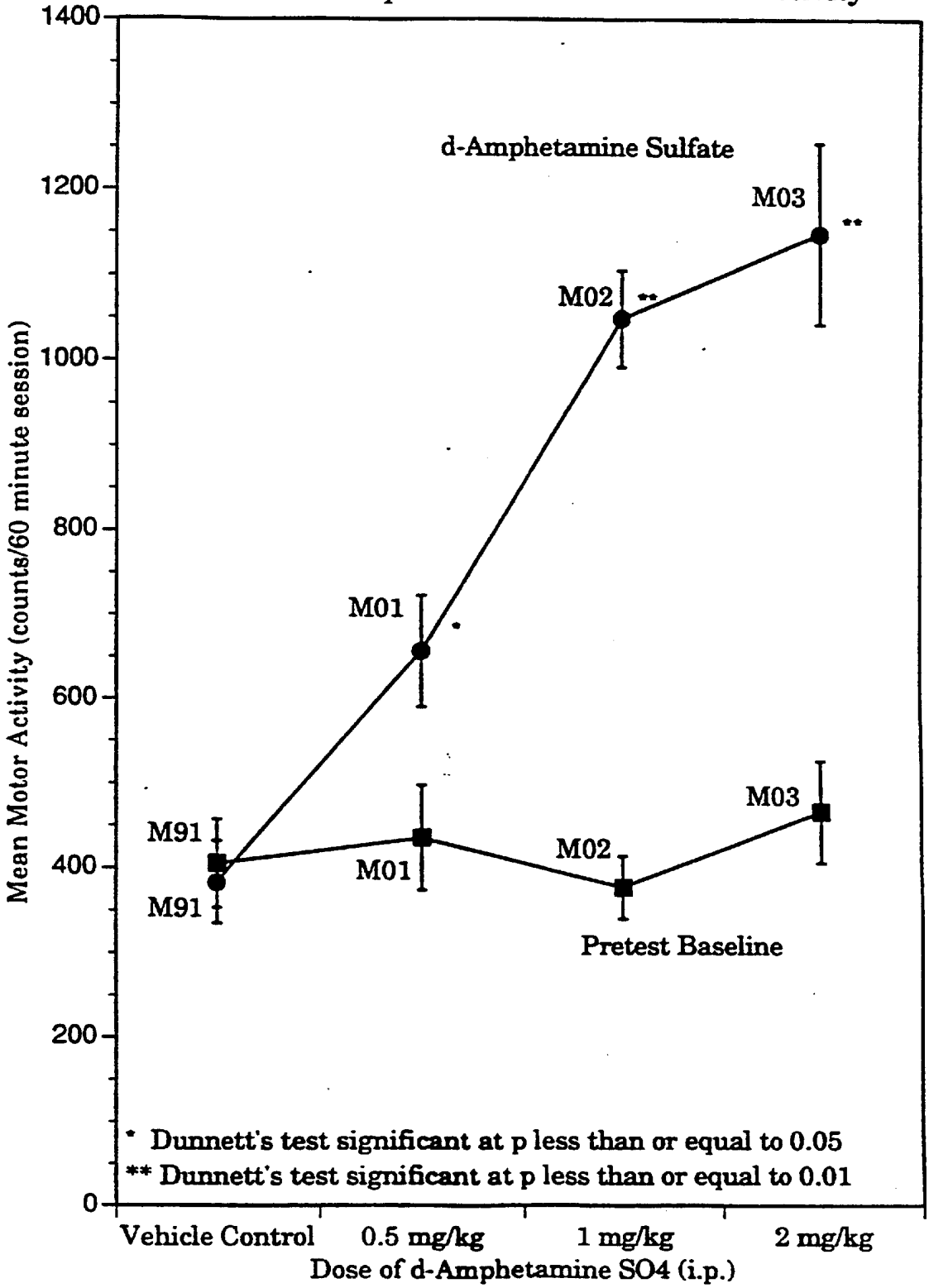



Figure 4
Effect of d-Amphetamine SO4 on Motor Activity