

24719

BROMINATED SOLVENTS COMMITTEE

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Phone: 202-637-9040 • Fax: 202-637-9178

July 16, 1999

VIA CERTIFIED MAIL

8EHQ-0799-14346

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Document Control Office (7407)
U.S. Environmental Protection Agency
ATTN: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
401 M Street, SW
Washington, DC 20460

pdw

RE: Follow-up Submission to an Earlier TSCA Section 8(e)
Notification for 1-Bromopropane (CAS No. 106-94-5)
TSCA Section 8(e) Document Control No. 8EHQ-98-14346

Dear TSCA 8(e) Coordinator:

The Brominated Solvents Committee (BSOC) is submitting the attached final report entitled, "A Range-Finding Developmental/ Reproductive Toxicity Study of 1-Bromopropane in Rats via Whole Body Inhalation Exposure" as a follow-up to a previous TSCA Section 8(e) substantial risk notification dated March 9, 1999, (TSCA Section 8(e) Document Control No. 8EHQ-98-14346).

If you have any questions, please contact me at (202) 637-9040.

Sincerely,

Robert J. Fensterheim
Robert J. Fensterheim
Executive Director



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Huntingdon
Life Sciences

STUDY NO. 98 - 4140

**A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY
STUDY OF 1-BROMOPROPANE IN RATS VIA WHOLE BODY
INHALATION EXPOSURE**

Final Report

Submitted to: Brominated Solvents Committee (BSOC)
c/o John A. Bieseimer
Regulatory Toxicologist
Great Lakes Chemical Corp.
P.O. Box 2200
One Great Lakes Boulevard
West Lafayette, IN 47906

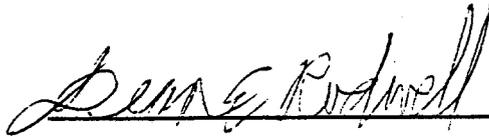
Date: 07 June 1999

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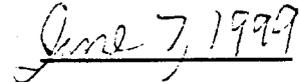
STATEMENT OF COMPLIANCE

This study was conducted in accordance with the Environmental Protection Agency Toxic Substances Control Act (TSCA) Good Laboratory Practice Standards Part 792 of 40 CFR and the Organization for Economic Cooperation and Development Principles of Good Laboratory Practice (as revised in 1997) ENV/MC/CHEM (98) 17 with the exception of Day 0 gestation body weights provided by the animal supplier.

Portions of the study conducted by Huntingdon Life Sciences were performed according to the protocol and Huntingdon Life Science's Standard Operating Procedures (SOP's).



Dean E. Rodwell, M.S.
Study Director



Date

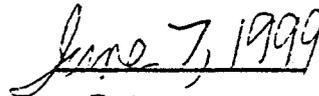
SIGNATURE PAGE

SCIENTIST

The following Scientist was responsible for the overall conduct of this study. Departmental supervisory personnel are listed on the personnel page of this report (Appendix DD).



Dean E. Rodwell, M.S.
Study Director



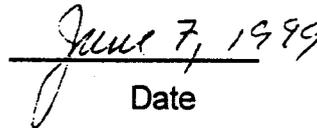
Date

SCIENTIFIC REVIEW

The following Scientist has reviewed and approved this report.



Sylvie J. Gosselin, DVM, Ph. D., ACVP
Vice President of Research and Pathology



Date

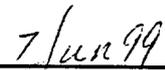
QUALITY ASSURANCE STATEMENT

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management. This report reflects the raw data as far as can be reasonably established.

<u>Type of Inspection</u>	<u>Date(s) of Inspection</u>	<u>Reported to Study Director and Management</u>
GLP Protocol Review	20 Aug 98	20 Aug 98
Exposure and Monitoring	22 Sep 98	22 Sep 98
Litter Evaluations and Pup Body Weights	12 Oct 98	12 Oct 98
Day 21L Hematology and Clinical Chemistry Blood Collection	28 Oct 98	28 Oct 98
F1 Sacrifice and Evaluation	05 Nov 98	06 Nov 98
Final In-Life and Pathology Report	25 Jan 99 to 04 Feb 99	04 Feb 99
Analytical Report	05 Feb 99	05 Feb 99



Nicki S. Iacono
Quality Assurance Senior Auditor



Date

ABSTRACT

The purpose of this study, conducted for the Brominated Solvents Committee (BSOC), was designed to detect potential adverse effects of inhaled 1-Bromopropane on the pregnant/lactating female rat and the developing of the conceptus and the offspring following exposure. F₀ parental dams were exposed from implantation of the zygote through weaning of the F₁ pups. The F₁ pups were exposed for a one week period beginning 1 day post-weaning (Lactation Day 22). Fifty pregnant timed mated female rats (10 per group) were placed on study. 1-Bromopropane was administered via whole-body inhalation as a vapor for 6 hours daily at target exposure levels of 0.0, 0.50, 1.0, 3.0 and 5.0 mg/L. These exposure levels are equivalent to 0.0, 100, 199, 598 and 996 ppm, respectively. F₀ parental rats were exposed on Gestation Days (GD) 6 - 19 and on Lactation Days (LD) 4-20. The F₁ pups were also administered 1-Bromopropane via whole-body inhalation as a vapor for six hours daily on post-weaning days 1-7. Animals were exposed to the vapor approximately the same time each day in a whole-body exposure chamber with an air volume of approximately 1000 liters and a minimum flow rate of 200 liters per minute. Control animals received room air for the 6 hour daily exposure.

F₀ parental animals were observed twice daily for mortality, morbidity and for obvious pharmacological and/or toxicological effects. F₀ parental body weights were recorded on Gestation Days 0 (provided by supplier), 4, 6, 10, 14 and 20, and on Lactation Days 1, 4, 7, 14 and 21. Food consumption was reported for the following intervals: Gestation Days 0-4, 4-6, 6-10, 10-14 and 14-20. These animals were given a physical evaluation daily from the day of receipt to GD 19 and then from LD 4-21.

F₀ parental animals were allowed to deliver and nurse the pups over a 21 day period. On Lactation Day 0, the F₁ pups were examined for survival and abnormalities and then subsequently observed twice daily for survival. On LD 4, litters were culled to 10 animals (5/sex/litter). F₁ pups were given detailed physical examinations, including sexing, on Lactation Days 0, 4, 7, 14 and 21 and on post-weaning days 1, 4 and 8. Body weights were recorded on Lactation Days 1, 4, 7, 14 and 21 and on post-weaning days 1, 4 and 8. F₀ parental animals were sacrificed on LD 21 and F₁ pups were sacrificed on post-weaning day 8 by carbon dioxide inhalation and given a macroscopic postmortem evaluation.

Effects noted in the F₀ females included the following: salivation and lacrimation post-exposure at the 996 ppm exposure level; reduced body weight gain over days 6-20 of gestation at exposure levels of 199, 598 and 996 ppm; reduced F₁ pup body weights on days 14 and 21 of lactation at the 996 ppm exposure level;

and increased relative kidney and liver weights (to body weight) at the 598 and 996 ppm exposure levels. In the F₁ pups, which were exposed for one week post weaning (postnatal days 22-29), the following effects were noted: reduced body weight gain in male pups postnatal days 22-29 at the 598 ppm exposure level and in both male and female pups at the 996 ppm exposure level; lowered platelet levels in female pups at 598 ppm and in both male and female pups at 996 ppm; lower glucose levels in male pups at all exposure levels and in female pups at 996 ppm; elevated GGT levels in both male and female pups at 996 ppm; and increased relative adrenal weights (to body weight) in male pups at all exposure levels. There were a few other changes in clinical chemistry parameters for one or more of the treated groups that differed statistically from control data but in the absence of a dose-response relationship or because of the direction of the response, the significance in relation to treatment was unclear.

In this range-finding reproduction study in rats with 1-Bromopropane, the no-observed-effect level (NOEL) for maternal toxicity was 100 ppm. At 996 ppm, some maternal toxicity (reduced body weight gain during gestation) was noted, but in the absence of an effect on parturition data, litter size or pup body weights at birth, should not preclude this being a high-exposure level for a developmental toxicity study. Considering effects noted for the F₁ pups during the postnatal exposure period, the 996 ppm exposure level may possibly be suitable for the high exposure level for a 2-generation reproduction study.

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1. INTRODUCTION

The purpose of this study, conducted for the Brominated Solvents Committee (BSOC), was to detect potential adverse effects of inhaled 1-Bromopropane on the pregnant/lactating female rat and the developing of the conceptus and the offspring following exposure. F₀ parental dams were exposed from implantation of the zygote through weaning of the F₁ pups. The F₁ pups were exposed for a one week period beginning 1 day post-weaning (Lactation Day 22). Fifty pregnant timed mated female rats (10 per group) were placed on study. 1-Bromopropane was administered via whole-body inhalation as a vapor for 6 hours daily at target exposure levels of 0.0, 0.50, 1.0, 3.0 and 5.0 mg/L. These exposure levels are equivalent to 0.0, 100, 199, 598 and 996 ppm, respectively. F₀ parental rats were exposed on Gestation Days (GD) 6 - 19 and on Lactation Days (LD) 4-20. The F₁ pups were also administered 1-Bromopropane via whole-body inhalation as a vapor for six hours daily on post-weaning days 1-7. Animals were exposed to the vapor approximately the same time each day in a whole-body exposure chamber with an air volume of approximately 1000 liters and a minimum flow rate of 200 liters per minute. Control animals received room air for the 6 hour daily exposure.

2. MATERIALS AND METHODS

2.1. REGULATORY REFERENCES

2.1.1. TEST GUIDELINES

There are no specific guidelines for the performance of a range-finding developmental/reproductive toxicity study. The maternal dosing during gestation in this protocol followed a modification of the study design for the EPA (Environmental Protection Agency) OPPTS (Office of Prevention, Pesticides and Toxic Substances) 870.3600. Inhalation Developmental Toxicity Study (draft 1996) and OECD Guidelines No. 414 (Draft Document, August, 1996). Exposure of female rats from day 4 - 20 of lactation and exposure of the F₁ pups for one week post-weaning provided data useful in establishing exposure concentrations for the two generation study.

2.1.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with EPA TSCA Good Laboratory Practices Part 792 of 40 CFR and OECD Good Laboratory Practices [ENV/MC/CHEM(98)17].

2.1.3. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

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

2.1.4. ANIMAL WELFARE ACT COMPLIANCE

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

2.2. STUDY MANAGEMENT

2.2.1. SPONSOR

Brominated Solvents Committee (BSOC)

Albemarle Corporation
Health and Environment
451 Florida Street
Baton Rouge, LA 70801

Dead Sea Bromine Group/Bromine Compounds Ltd.
Health, Safety & Environment Division
PO Box 180
Beer Sheva 84101
Israel

Great Lakes Chemical Corporation
Regulatory Affairs
One Great Lakes Boulevard
West Lafayette, IN 47906

2.2.2. SPONSOR REPRESENTATIVE

John A. Biesemeier

Great Lakes Chemical Corporation
P.O. Box 2200
One Great Lakes Boulevard
West Lafayette, IN 47906

2.2.3. TESTING FACILITY

Huntingdon Life Sciences
P.O. Box 2360
Mettlers Road
East Millstone, NJ 08875-2360

2.2.4. STUDY DIRECTOR

Dean E. Rodwell, M.S.

2.3. EXPERIMENTAL DESIGN

Exposure Groups			Number of Exposed Animals			
Group	Group Designation	Exposure Levels (mg/L) ^a	Exposure Schedule	Mated Females	Females that Deliver	F ₁ Pups Male/Female
I	Control	0.0 (air only)	F ₀ Gestation Days 6-19 F ₀ Lactation Days 4-20 F ₁ Post-weaning Days 1-7	10	All	10/10
II	Low	0.50	F ₀ Gestation Days 6-19 F ₀ Lactation Days 4-20 F ₁ Post-weaning Days 1-7	10	All	10/10
III	Low-mid	1.0	F ₀ Gestation Days 6-19 F ₀ Lactation Days 4-20 F ₁ Post-weaning Days 1-7	10	All	10/10
IV	High-mid	3.0	F ₀ Gestation Days 6-19 F ₀ Lactation Days 4-20 F ₁ Post-weaning Days 1-7	10	All	10/10
V	High	5.0	F ₀ Gestation Days 6-19 F ₀ Lactation Days 4-20 F ₁ Post-weaning Days 1-7	10	All	10/10

^a Exposures were 6 hours per day. These exposure levels were selected by the Sponsor based on available toxicity data and are equivalent to 0.0, 100, 199, 598 and 996 ppm in air.

2.4. STUDY DATES**2.4.1. STUDY INITIATION**

03 September 1998 (Date the Study Director signed the Protocol)

2.4.2. DATE OF ANIMAL RECEIPT

17 September 1998

2.4.3. DOSING INITIATION

First day 6 of gestation:	22 September 98
F ₀ lactation exposure:	10 October 1998
F ₁ exposure:	28 October 1998

2.4.4. DOSING TERMINATION

Last day 19 of gestation:	05 October 1998
F ₀ lactation exposure:	28 October 1998
F ₁ exposure:	05 November 1998

2.4.5. TERMINAL SACRIFICE

F ₀ parental:	30 October 1998
F ₁ pups:	07 November 1998

2.4.6. STUDY COMPLETION

Date final report is signed by the Study Director.

2.5. TEST ARTICLE

1-Bromopropane (n-propyl bromide)

2.5.1. MANUFACTURER

Dead Sea Bromine Group
P.O.B. 180
Beer Sheva 84101
Israel

2.5.2. SUPPLIER

AmeriBrom, Inc.
A Member of Dead Sea Bromine Group
52 Vanderbilt Avenue
New York, New York 10017

2.5.3. LOT NUMBER

980104

2.5.4. DATE RECEIVED

13 August 1998

2.5.5. EXPIRATION DATE

Stable as per Material Safety Data Sheet

2.5.6. CHARACTERISTICS

Liquid

Documentation of the identity, strength, purity, composition, stability, synthesis, fabrication and/or derivation of the test material used on study is presented in Appendix EE.

2.5.7. STORAGE

Stored at room temperature.

2.5.8. ARCHIVAL SAMPLE

An archival sample (approximately 13.7 g) was taken from the lot of test material used on study and is maintained in the Archives of the Testing Facility.

2.5.9. DISPOSITION

Remaining test article was saved for use in future toxicology studies.

2.6. ANALYSIS OF TEST MATERIAL PURITY

Prior to and at the end of the study, a purity and stability analysis was performed by the Analytical Department of Huntingdon Life Sciences using a modified method provided by the Sponsor. Results are contained in Appendix BB.

2.7. TEST ANIMALS**2.7.1. SPECIES**

Albino Rats CrI: CD® (SD) IGS BR

2.7.2. SUPPLIER

Charles River Laboratories
Kingston, New York

2.7.3. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model commonly utilized in reproduction/developmental toxicity studies, as recommended in the referenced guidelines. In addition, for comparative evaluation, a historical data base is available within the Testing Facility for this strain of rat.

2.7.4. ANIMAL RECEIPT INFORMATION

A total of 54 timed mated females were received on Gestation Day 1. Fifty timed mated females were placed on study.

2.7.5. AGE AND WEIGHT AT RECEIPT

Females were approximately 10-12 weeks of age at receipt and approximately 210-275 grams on Day 0 of gestation. Animals outside this range were used at the discretion of the Study Director.

2.8. ACCLIMATION PERIOD

Animals were acclimated for approximately five days from the time of receipt until initiation of test article exposure.

2.9. ASSIGNMENT OF ANIMALS INTO GROUPS

F₀ females were placed into study groups at receipt using a manual randomization procedure, which ranked Gestation Day 0 body weights (provided by the supplier) and randomly assigned each animal within the block into groups. Animals were replaced based on physical examinations and/or body weight changes up to Gestation Day 6. Disposition of all animals not utilized in the study is maintained in the study file.

2.10. ANIMAL IDENTIFICATION

Each F₀ female was ear-tagged with a unique identification number by the supplier. This ear-tag number served as the animals' permanent identification for the duration of the study. This number plus the study number comprised a unique identification for each animal. If the tag was lost, it was replaced. Each study animal cage was also fitted to retain a cage card which was color-coded for dose level identification and contained the study number and animal number.

2.11. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions were identified, a staff veterinarian was notified for an examination and evaluation. Animals were treated as outlined in the Animal Welfare Act Compliance section of this report.

2.12. ANIMAL HUSBANDRY

2.12.1.Housing

Animals were housed individually in suspended stainless steel wire mesh cages except as follows: after exposure on Day 19 of gestation, females were transferred to solid plastic cages and bedding provided. Females were housed in these cages for delivery and with their litter during the 21-day lactation period.

2.12.2.Food

Purina Certified Rodent Diet, No. 5022; (meal) as supplied by PMI Nutrition International, St. Louis, MO was provided *ad libitum* except during exposure.

Analytical certification of batches of food provided by the manufacturer are being maintained on file at the Testing Facility. There are no known contaminants in the feed which were considered capable of interfering with the results of this study.

2.12.3.Water

Facility water (supplied by Elizabethtown Water Company, Westfield, NJ); was provided *ad libitum* to individual animal cages via an automated watering system.

Water analyses were conducted by Elizabethtown Water Company to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water analyses, provided by the supplier, are being maintained on file at the Testing Facility. In addition, water samples are collected biannually from representative rooms in the Testing Facility. Chemical and microbiological water analyses were conducted on these samples by a subcontract laboratory. These analytical data for all water analyses are maintained on file at the Testing Facility.

2.12.4. Bedding Material:

Ground corncob bedding (Bed-O'-Cobs® Irradiated-Certified ¼ inch, The Andersons, Maunee, OH) were provided for each mated female on Day 19 of gestation. Fresh bedding was provided as needed during the lactation period (litters weaned on Day 21 of lactation). A copy of the bedding material analysis is maintained at the Testing Facility. There are no known contaminants in the bedding which are considered capable of interfering with the results of this study.

2.12.5. Environmental Conditions

2.12.5.1. Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

2.12.5.2. Temperature

Temperature was monitored and recorded twice daily and maintained within the desired range (19 to 25°C) to the maximum extent possible.

Desired: 19-25°C

Actual: 19-23°C

2.12.5.3. Relative Humidity

Relative humidity was monitored and recorded once daily and maintained within the desired range (30 to 70°C) to the maximum extent possible.

Desired: 30-70°C

Actual: 30-69°C

2.12.5.4. Air Changes (Non-chamber Vivarium Room Conditions)

Animal quarters had 10-15 air changes/hour. The actual number of air changes/hour in the animal room was recorded twice during the study.

2.13. TEST ARTICLE ADMINISTRATION

2.13.1. FREQUENCY AND DURATION OF ADMINISTRATION

The F₀ mated female rats were exposed daily from Gestation Day 6-19. The day of parturition was observed as Lactation Day 0. F₀

females with litters were exposed daily during the lactation period (Lactation Day 4-20). F₁ pups were exposed once daily from post-weaning day 1-7 (Postnatal Day 22-28). All animals were exposed for 6 hours per day.

2.13.2.JUSTIFICATION FOR FREQUENCY AND DURATION OF EXPOSURE

Test article exposure of females from day 6 of gestation (implantation of zygote) to day 21 of lactation provides for potential exposure of the fetus *in utero* and of the developing neonate throughout lactation to weaning in the study guidelines referenced in Section 2.1.1 of this report.

2.13.3.ROUTE OF ADMINISTRATION OF TEST ARTICLE

The inhalation route of administration was selected for this study because it is the potential route of human exposure.

2.13.4.TEST ARTICLE ADMINISTRATION

The test article was administered as a vapor in the breathing zone of the animals. Trials were performed to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the targeted exposure levels. During this time, samples were taken to determine the distribution of the test article in the exposure chamber.

Animals were individually housed in stainless steel, wire mesh cages within a 1000 liter stainless steel and glass whole-body exposure chamber. The placement of the animals in the whole-body exposure chamber was rotated at each exposure to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

The exposure chambers were operated dynamically under slight negative pressure. The chamber airflow rate, time for air change and 99% equilibrium time (T99) for each group are summarized below:

Group	Airflow Rate (Lpm)	Air Change (min)	T99 (min)
I	218	4.6	21
II	212	4.7	22
III	207	4.8	22
IV	210	4.8	22
V	210	4.8	22

The chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and an oxygen level of at least 19%. The chambers were exhausted through a system consisting of a coarse filter, a HEPA filter and an activated charcoal bed.

All animals remained in the chambers for a minimum of 30 minutes at the end of the exposure. During this time the chambers were operated at the same flow rate as used during the exposure.

Recordings of airflow rate and static pressure were made every half-hour during exposure.

EXPOSURE PROCEDURE

Group I

Houseline nitrogen was delivered from a regulator and backpressure gauge via 1/4" tubing to a metering valve. The metering valve regulated the nitrogen flow into the inlet of the flowmeter at a rate of 20 Lpm. The nitrogen entered the inlet of the turret of the exposure chamber.

Groups II - V

Houseline nitrogen was delivered from a regulator and backpressure gauge via 1/4" tubing to a metering valve. The metering valve regulated the nitrogen flow into the inlet of a flowmeter at a rate of 20 Lpm. The nitrogen then entered the bottom of the volatilization chamber with a coiled glass rod via 1/4" tubing to a ground glass ball and socket joint.

The test article (used as received) was delivered from an Erlenmeyer flask via 1/8" tubing to a pump with a piston. The test article then entered the volatilization chamber onto the coiled glass rod via 1/8" tubing. The resultant vapor entered the inlet turret of the exposure chamber via 1/2" tubing and stopper.

Initial Settings

Pump settings were selected in order to achieve the target exposure levels. Specific initial settings for each group are summarized below:

Group	Initial Pump Setting (%)	Piston Size (inch)
II	10	$\frac{1}{8}$
III	17	$\frac{1}{8}$
IV	20	$\frac{1}{4}$
V	35	$\frac{1}{4}$

Refer to Appendix A for diagram and equipment details.

2.13.5. EXPOSURE CONCENTRATION DETERMINATION

The nominal concentrations (mg/L) were determined by weighing the generation apparatus containing the test article before and after the exposure and calculated as follows:

$$\text{Conc (mg/L)} = \frac{\text{amount consumed (g)} \times 1000 \text{ mg/g}}{\text{exposure duration (min)} \times \text{airflow (Lpm)}}$$

Chamber air samples were drawn 4 times during each exposure using a Miran air analyzer, with a strip chart recorder. The chamber air samples were drawn through a glass fiber filter in a filter holder and then through $\frac{1}{4}$ " tubing to the inlet of the Miran. A vacuum gauge was connected to the outlet of the Miran. The gauge was connected via $\frac{1}{4}$ " tubing to a flowmeter equipped with a metering valve. A pump was turned off and the absorbance was read off the multimeter which was attached to the Miran.

Refer to Appendix A for equipment details.

2.13.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

Particle size samples were drawn once during each exposure at a flowrate of 5.00 Lpm using a TSI Aerodynamic Particle Sizer. A computer was used to program the system prior to sampling and a printer was used to record the information. The samples were collected for 20 seconds through the routine sampling port using a stopper, $\frac{1}{2}$ " stainless steel tubing and plastic tubing which connected the particle sizer to the exposure chamber. The particle size distributions were calculated by the computer and printed out

based on the amount of test article collected by the particle sizer.

Refer to Appendix A for equipment details.

2.13.7. CHAMBER ENVIRONMENT

Chamber temperature and relative humidity were recorded every half-hour during exposure and maintained to the maximum extent possible within the ranges presented below. Excursions outside the specified ranges did not affect the integrity of the study.

Temperature

Desired:	20 to 24°C
Actual:	16 to 24°C

Relative Humidity

Desired:	40 to 60%
Actual:	29 to 75%

2.14. EXPERIMENTAL EVALUATION

2.14.1. VIABILITY OBSERVATIONS (CAGESIDE)

Observations for mortality, morbidity and signs of severe toxicity were made twice daily. Animals in extremely poor health or in a possible moribund condition were identified for further monitoring and possible euthanasia.

2.14.2. CLINICAL OBSERVATIONS

F₀ females were removed from their cages and observed daily (prior to exposure during the treatment period). For the F₀ females this was days 6-19 of gestation and days 4 - 21 of lactation and for the F₁ pups selected to continue on study (10/sex/group) this was post-weaning days 1, 4 and prior to sacrifice (post-weaning day 8). Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia as well as evaluations of respiration.

2.14.3. EXPOSURE AND POST-EXPOSURE OBSERVATIONS

During the treatment period, exposure and postexposure observations for toxicity and pharmacotoxic signs were performed. General signs relating to activity were made at hourly intervals during the exposure period. Postexposure observations were made

at approximately one-half hour following daily exposure (F_0 females and F_1 pups). These observations were tabulated separately for reporting.

2.14.4.BODY WEIGHTS

Body weights, for F_0 females were recorded on Days 0 (provided by the supplier), 4, 6, 10, 14 and 20 of gestation and on days 1, 4, 7, 14 and 21 of lactation.

Individual pup weights were recorded on Days 1, 4 (presented for both pre- and postcull intervals), 7, 14 and 21 of lactation. Following weaning, the ten male and ten female selected pups from each group were weighed on post-weaning days 1, 4 and 8 (postnatal days 22, 25 and 29).

2.14.5.FOOD CONSUMPTION

Food consumption was recorded for each F_0 during the following intervals of gestation: days 4-6, 6-10, 10-14 and 14-20. Food consumption was also recorded for each F_0 during the following intervals of lactation: days 1-4, 4-7, 7-14 and 14-21. Food consumption was not recorded for F_1 pups selected to continue on study for the one week of post-weaning exposures.

2.14.6.PARTURITION AND LACTATION

On day 19 of gestation, a few days prior to expected parturition, each female was transferred to a solid plastic "shoebox" cage. Bedding material was provided and changed at least weekly and as needed. Examination for signs of parturition were made twice daily. The day on which parturition was first observed was defined as day 0 of lactation.

2.14.7.LITTER EVALUATIONS (F_1)

2.14.7.1.OBSERVATIONS

Litters were observed as soon as possible after delivery for the number of live and dead pups, pup abnormalities and each pup was sexed. Thereafter, litters were observed twice daily. All pups in the litter were uniquely identified by toe tattoo on Lactation Day 0. The presence of dead pups was recorded, and then they were removed from the litter. Pups in each litter were counted daily through Lactation Day 21.

2.14.7.2.Culling

On Day 4 of lactation, each litter with more than 10 pups was culled to that number with sex distribution equalized (five/sex) when possible. Pups were culled randomly. Preferential culling of runts was not performed. Culled pups were examined externally for abnormalities and if externally within normal limits were euthanized by an intraperitoneal injection of sodium pentobarbital. If external abnormalities were noted an internal examination was performed at the discretion of the Study Director.

2.14.7.3.Physical Examinations

Each pup was given a gross physical examination on Days 0, 4, 7, 14 and 21. Following weaning, ten randomly selected males and ten female pups from each exposure level were given a physical examination on post-weaning days 1, 4 and 8.

2.14.7.4.Pup Body Weight Data

Individual pup weights were recorded on Days 1, 4 (presented for both pre- and postcull intervals), 7, 14 and 21 of Lactation. Following weaning, the ten male and ten female selected pups from each group were weighed on post-weaning days 1, 4 and 8 (Postnatal Days 22, 25 and 29).

2.14.7.5.Pup Sexing Data

Individual sexing data were recorded on Days 0, 4, 7, 14 and 21 of lactation.

2.14.8.SELECTION OF F₁ ANIMALS

Pups (one/sex/litter) were selected using a random numbers table at weaning (Lactation Day 21) to continue on study for the one week post-weaning growth phase of the selected F₁ pups (10 pups/sex/group). If less than 10 litters were available at weaning, additional pups were selected randomly to provide the 10 pups/sex.

Selected pups were individually identified using a metal eartag and housed two or three per cage throughout the one week exposure prior to sacrifice. Runts, if otherwise normal, were not excluded from the selection procedure.

2.15. CLINICAL LABORATORY STUDIES

Blood for hematology and clinical chemistry analyses was obtained from lightly anesthetized (isoflurane) animals via puncture of the orbital sinus (retrobulbar). Animals were not fasted and were sacrificed immediately after blood collection. Blood was collected and studies performed as follows:

2.15.1. Hematology

Blood (~ 0.3 mL for maternal and F₁ pups) for hematology studies was collected into tubes containing EDTA anticoagulant.

2.15.1.1. Number of Animals

F₀ females: all 10/group

F₁ pups: all surviving pups (10/sex/group)

2.15.1.2. Collection Intervals

F₀ females: Day 21 of lactation following weaning of the litter;

F₁ pups: postnatal Day 29 (following the 7 day postweaning exposure)

2.15.1.3. Parameters Evaluated^a

erythrocyte count
hematocrit
hemoglobin concentration
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin concentration
leukocyte count (total and differential)
platelet count
reticulocyte count

^a If inadequate volume of sample available, these parameters are in priority order.

2.15.2. Clinical Chemistry

Blood (~1 mL for maternal and F₁ pups) for clinical chemistry studies was collected into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum.

2.15.2.1. Number of Animals

F₀ females: all 10/group

F₁ pups: all surviving pups (10/sex/group)

2.15.2.2. Collection Intervals

F₀ females: Day 21 of lactation following weaning of the litter

F₁ pups: postnatal Day 29 (following the 7 day postweaning exposure)

2.15.2.3. Parameters Evaluated^a

alanine aminotransferase

alkaline phosphatase

aspartate aminotransferase

gamma-glutamyl transferase

lactate dehydrogenase

sorbitol dehydrogenase

urea nitrogen

bilirubin (total)

glucose

total protein

albumin

globulin (calculated as total protein - albumin = globulin)

albumin/globulin ratio (calculated)

creatinine

bilirubin conjugated (direct)

bilirubin unconjugated (indirect)

^a If inadequate volume of sample available, these parameters are in priority order.

2.15.3. Stains

Slides for differential leukocyte counts were stained with Wright stain. Slides for reticulocyte counts were stained with New Methylene Blue.

2.15.4. Retention/Storage of Specimens:

Reticulocyte slides and any remaining (frozen) serum, which may have limited storage stability, will be stored for up to six months after completion of assays and will then be discarded. Differential slides were retained and archived with the study.

3. POSTMORTEM

3.1. MACROSCOPIC POSTMORTEM EXAMINATION

A macroscopic postmortem examination was performed on all F₀ females and all F₁ pups retained to postnatal Day 29.

3.2. SACRIFICE SCHEDULE/TERMINAL NECROPSY

3.2.1. Method of Euthanasia

Adults and Pups: Overdose of inhaled CO₂
Culled Pups: Euthanized by intraperitoneal injection of sodium pentobarbital (approximately 0.1 cc/pup).

3.2.2. F₀ Females

F₀ females that failed to deliver a litter were sacrificed on Day 25 of gestation (post-mating). F₀ females that weaned litters were sacrificed on Day 21 of lactation. A macroscopic postmortem examination was performed on all animals.

Gross lesions identified during the macroscopic postmortem evaluations were saved in 10% neutral buffered formalin (NBF); corresponding tissues were saved from several control animals for comparative purposes.

3.2.3. F₁ Pups (prior to weaning)

The culled F₁ pups (Day 4) were examined externally, sacrificed and discarded.

F₁ pups not selected for the one week post-weaning phase were sacrificed on Day 21 of lactation, examined externally and were discarded.

3.2.4. F₁ Pups (post-weaning phase)

A macroscopic postmortem examination was performed on all F₁ pups the day following the last exposure (postnatal day 29).

3.2.5. Organ Weights

Organs indicated below were taken from all survivors at the scheduled necropsy (F₀ females at Day 21 of lactation and F₁ pups on postnatal Day 29) and weighed. Organ/body and organ/brain

weight ratios were calculated. Prior to weighing, all organs were carefully dissected and properly trimmed to remove fat and other contiguous tissue in a uniform manner. Organs were weighed as soon as possible after dissection to avoid drying.

- Adrenals (right and left organs weighed together)
- Brain
- Liver
- Kidneys (right and left organs weighed separately)

3.3. STATISTICAL EVALUATIONS

The following items were analyzed statistically in the final report:

CONTINUOUS DATA

An ANOVA followed by a Dunnett's test was performed to identify differences between the control and test groups. A Kruskal-Wallis test was performed to test equality of means. All statistical tests were conducted at the 5% and 1%, two-sided risk levels.

- Body weights: F_0 - gestation, lactation and post-mating periods; F_1 animals lactation and post-weaning^a
- Body weight change: F_0 - between all weighing intervals during gestation and lactation; F_1 lactation and post-weaning^a
- Food consumption values: all recorded intervals (F_0 and F_1)^a
- F_1 pup weights (each weighing interval during lactation and post-weaning)^a
- Parturition and litter data^a
- Hematology^b

^aStatistical evaluation of equality of means were made by the appropriate one-way analysis of variance (ANOVA) technique, followed by a multiple comparison procedure, if needed. If ANOVA showed no difference, no additional comparisons were made. If ANOVA was significant, Dunnett's test was used to determine which data, if any, differed from the control.

^bStatistical evaluation of equality of means was made by the appropriate one way analysis of variance (ANOVA) technique, followed by a multiple comparison procedure, if needed. First, Bartlett's test (Snedecor and Cochran, 1967) was performed to determine if groups have equal variance. If the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. The parametric procedures were the standard one way ANOVA (Snedecor and Cochran, 1967) using the F distribution to assess significance. If significant differences among the means were indicated, Dunnett's test (Dunnett, 1955, 1964) was used to determine which means were significantly different from the control. If a

nonparametric procedure for testing equality of means was needed, the Kruskal-Wallis test (Hollander and Wolfe, 1973) was used, and if differences were indicated Dunn's summed rank test (Hollander and Wolfe, 1973) was used to determine which test group, if any, differed from the control group.

A statistical test for trend in the exposure levels was also performed. In the parametric case (i.e., equal variance) standard regression techniques with a test for trend and lack of fit were used (Snedecor, and Cochran, 1967). In the nonparametric case Jonckheere's test (Hollander and Wolfe, 1973) for monotonic trend was used.

The test for equal variance (Bartlett's) was conducted at the 1%, two-sided risk level. All other statistical tests were conducted at the 5% and 1%, two-sided risk level.

3.4. DATA STORAGE

All data documenting experimental details and study procedures and observations were recorded and maintained as raw data.

At the completion of the study, all reports, study protocol and amendments, raw data to include animal receipt data, feed analysis, water analysis, room maintenance, records, etc. preserved specimens and retained samples are maintained in the Testing Facility's Archives for a period of five years after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these articles. The Sponsor is responsible for all costs associated with the storage of these articles beyond five years from the issuance of the final report and for any costs associated with the shipment of these articles to the Sponsor or to any other facility designated by the Sponsor.

3.5. PROTOCOL DEVIATIONS

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

1. During pre-exposure observations on 25 Sep 98, animal #648 was found in animal #643's cage, and #643 was found in #648's cage. Food consumption for the GD 6-10 interval was excluded.

2. On 5 Oct 98, one animal, #655, was recorded in the post-exposure observation record, but no adverse observations were recorded.
3. On 12 Oct 98, one pup day 4 lactation body weight, Pup #6 from litter #631, was not recorded prior to culling.
4. On 5 Nov 98 three hematology samples (#3711, 4107, and 5110) and three clinical chemistry samples (#2708, 2110, and 2113) were not obtained.
5. On 29 Oct 98, the weight of the adrenals for one dam (#640) was recorded incorrectly.
6. On 21 Sept. 98, humidity was not recorded.

4. RESULTS

4.1. ANALYTICAL RESULTS - PURITY ANALYSIS

Duplicate assays of the Test Material gave identical means of 99.87% purity during the prestudy and poststudy assays. Therefore, the test material was considered of acceptable purity and stability during the study.

4.2. MATERNAL AND F₁ DATA

4.2.1. EXPOSURE DATA

(Appendix A)

Prestudy chamber distribution analyses showed the test material was evenly distributed within each chamber. The target, the mean analytical and the nominal concentrations are summarized as follows:

Group	Target ^a (mg/L)	Gestation		Lactation	
		Analytical (mg/L)	Nominal (mg/L)	Analytical (mg/L)	Nominal (mg/L)
I	0.0	0.00±0.00	-	0.00±0.00	-
II	0.5	0.51±0.03	0.5±0.0	0.52±0.07	0.5±0.0
III	1.0	1.03±0.07	1.0±0.1	1.04±0.12	1.0±0.0
IV	3.0	3.05±0.21	2.8±0.1	3.04±0.08	2.9±0.1
V	5.0	5.01±0.11	5.0±0.2	5.07±0.13	4.9±0.1

^aThese exposure levels were equivalent to 0.0, 100, 199, 598, and 996 ppm in air, respectively.

The IR measured exposure levels of 1-Bromopropane were reasonably close to the targeted exposure levels and to the nominal concentrations for all test groups. The differences between measured and nominal concentrations were typical for this type of exposure.

Chamber environmental conditions averaged 21°C and 47% relative humidity.

Particle size distribution measurements for the exposures are summarized as follows:

Group	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m ³)
I	4.576	2.077	3.53E-03
II	4.738	2.052	3.54E-03
III	4.422	2.075	2.92E-03
IV	4.011	2.056	2.93E-03
V	4.623	2.048	3.58E-03

These results indicated that the atmospheres were vapor only, as expected, since the test material atmospheres were comparable to the air control (Group I) atmosphere.

4.2.2. MATERNAL MORTALITY

(Table 1, Appendix B)

No F₀ females in the control or 1-Bromopropane-test groups died.

4.2.3. MATERNAL CLINICAL OBSERVATIONS

(Tables 2 and 3, Appendices C and D)

With the exception of excessive salivation and lacrimation noted in several F₀ females in the high-exposure (996 ppm) group post-exposure, no other exposure-related clinical findings were seen in the 1-Bromopropane-test groups.

4.2.4. PREGNANCY DATA

(Table 12, Appendix M)

Pregnancy rates were comparable between the control and 1-Bromopropane-test groups. These rates for the control, 100, 199,

598, and 996 ppm groups were 80%, 90%, 80%, 80%, and 100%, respectively.

4.2.5. BODY WEIGHTS DURING GESTATION AND LACTATION

(Gestation - Tables 4 and 5; Appendices E and F; Lactation - Tables 6 and 7; Appendices G and H)

No statistically significant differences in body weight or body weight gain data were seen between the control and 1-Bromopropane-test groups during the gestation or lactation periods. Lower body weight gains during gestation were noted over the exposure period (days 6-20) at levels of 199 ppm, 598 ppm and 996 ppm. This difference for the 199 ppm exposure group was slight, about 8% in comparison to control data, and between 16-18% at the 598 and 996 ppm exposure levels. Mean body weights and weight gain data during lactation for the exposure groups were comparable to control data and unaffected by treatment.

Dam No. 88 in the 199 ppm group and Dam No. 900 in the 598 ppm group delivered full-size, term pups on Gestation Day 20. These dams are footnoted in the individual tables and have been excluded from all calculations during the gestation period. The time-mated rats supplied by Charles River were obviously one to two days more advanced in gestation when delivered to our facility. Dam No. 98 in the 598 ppm group had only early resorptions as identified by an ammonium sulfide stain at the time of cesarean section. Since this condition was not noted in the 996 ppm group, it was considered a spontaneous event and was not considered exposure related. Therefore, the data from this dam (98) and the two dams (88 and 900), which were supplied with incorrect gestational age, were all excluded from calculations including body weights, body weight gains, and food consumption during gestation.

4.2.6. FOOD CONSUMPTION DURING GESTATION AND LACTATION

(Gestation - Tables 8 and 9, Appendices I and J; Lactation - Tables 10 and 11, Appendices K and L)

No effect of test article with 1-Bromopropane at an exposure up to and inclusive of 996 ppm was indicated from food consumption data during either gestation or lactation periods. Mean food consumption, absolute or relative to body weight, for the exposure groups was comparable to control during these periods.

4.2.7. GESTATION LENGTH AND LITTER DATA

(Table 12, Appendix M)

No effect of test article with 1-Bromopropane at an exposure level up to and inclusive of 996 ppm was evident from gestation length or parturition data. Gestation length, litter size (total pups delivered and live pups), and live birth indices for the exposure groups were comparable to control data. Pup mortality at birth was minimal and comparable for all exposure groups to the control group. Pup survival for lactation days 0-4 and 5-21 were comparable.

4.2.8. PUP CLINICAL OBSERVATIONS

(Table 13, Appendix N)

No test article effect with 1-Bromopropane was evident from the clinical examination of F₁ pups at birth and during the lactation period.

4.2.9. PUP BODY WEIGHTS - THROUGH LACTATION

(Table 15, Appendix P)

The only effect of exposures on F₁ pup body weights during the lactation period was a slight, non-statistically significant decrease at days 14 and 21 in the high-exposure (996 ppm) group. Mean pup body weights for the combined sexes on these days for this group were about 6-7% lower than control data. No test article effect on F₁ pup body weights were seen at the lower exposure levels of 1-Bromopropane evaluated.

4.2.10.F₁ CLINICAL OBSERVATIONS AND BODY WEIGHTS - POST-WEANING DAYS

(Tables 14 and 16, Appendix O and Q)

There were no clinical observations attributed to exposure in any of the four test groups during exposure or following exposure.

Lower mean F₁ pup body weights on postnatal days 25 and 29 were noted in the 996 ppm exposure group; however, only for the male pups were these differences from control data statistically significant. At postnatal day 29, mean body weight for the F₁ male and female pups in the 996 ppm exposure group were about 16% and 11%, respectively, lower than control data. In the remaining test groups, mean F₁ pup body weights during the postnatal period

were considered comparable to control data and unaffected by exposure.

4.2.11.F, BODY WEIGHT GAIN - POST-WEANING DAYS

(Table 17, Appendix R)

Effects on F₁ pup body weight gain during the one week postweaning exposure period were noted at the 598 and 996 ppm exposure levels. F₁ male pups in the 598 ppm group and both male and female F₁ pups in the 996 ppm group, gained significantly less body weight over the day 22-29 postnatal period in comparison to control data. Body weights and body weight gain data over the one week postnatal period for the F₁ pups in the 100 and 199 ppm treated groups were comparable to control data and unaffected by exposure.

4.3. HEMATOLOGY, CLINICAL CHEMISTRY AND POSTMORTEM DATA

4.3.1. MATERNAL HEMATOLOGY

(Table 18, Appendix S)

No test article effect with 1-Bromopropane at an exposure level up to and inclusive of 996 ppm was indicated from hematology data for the F₀ maternal animals.

4.3.2. MATERNAL CLINICAL CHEMISTRY

(Table 19, Appendix T)

A statistically significant decrease in LD (lactate dehydrogenase) levels was noted in each test group in comparison to control data and a dose response relationship was evident. There was also a dose-related decrease in AST (aspartate aminotransferase) levels in each of the test groups and these differences from control data were statistically significant at exposure levels of 199, 598, and 996 ppm. BUN (blood urea nitrogen) levels for the F₀ females were also lower than control in each of the exposure groups and these differences were statistically significant at the 100, 598 and 996 ppm exposure levels. This type of response (lower LD, AST, and BUN levels) in the exposure groups may not be toxicologically significant as the typical toxic response would be to elevate the levels of these parameters. A few other statistically significant differences in clinical chemistry parameters were noted in the test

groups in comparison to control data, but in the absence of a similar response at the higher exposure levels, these were not considered exposure-related.

4.3.3. MATERNAL MACROSCOPIC POSTMORTEM EVALUATIONS

(Table 20, Appendix U)

No test article effect with 1-Bromopropane at an exposure level up to and inclusive of 996 ppm was indicated from the macroscopic postmortem examinations of the F₀ females.

4.3.4. MATERNAL ORGAN WEIGHT DATA

(Table 21, Appendix V)

The absolute organ weights for adrenals, brains, livers, and kidneys (right and left) did not differ significantly for any groups when compared to the control group. However, when the organ to body weight ratios were compared, the liver and kidney to body weight ratios were significantly elevated in the 598 and 996 ppm groups. When organ to brain weight ratios were compared, the kidney to brain weight ratio in the high test group (996 ppm) was significantly increased while the liver to brain weight ratio was increased, but the difference was not significant.

4.3.5. F₁ LACTATION DAY 21 MACROSCOPIC POSTMORTEM EVALUATIONS

(Table 22, Appendix W)

No test article effect with 1-Bromopropane at an exposure level up to and inclusive of 996 ppm was evident from the macroscopic examination of F₁ pups sacrificed on Day 21.

4.3.6. F₁ HEMATOLOGY

(Table 23, Appendix X)

A decrease in platelets was noted in the F₁ female pups at the 598 ppm exposure level and in both male and female F₁ pups in the 996 ppm group. This decrease in females at the 598 and 996 ppm exposure levels was not dose-responsive (i.e., lowest at 598 ppm), but platelet levels for both groups differed statistically from control data. There was also a statistically significant decrease in MCV (mean corpuscular volume) and MCH (mean corpuscular hemoglobin) in male F₁ pups at the 996 ppm exposure level, but in

the absence of an effect of treatment on hemoglobin, hematocrit, and red blood cell count in the male pups in this group and in the absence of similar changes in the female pups, these decreases in MCV and MCH were not considered dose-related. There were a few other instances when hematological parameters for one or more of the exposure groups differed statistically from control data, but in the absence of a similar response at the higher exposure levels, these were not considered test article-related.

4.3.7. F₁ CLINICAL CHEMISTRY

(Table 24, Appendix Y)

F₁ male pups at all exposure levels and female pups at the 996 ppm exposure level had lower glucose levels. The response in glucose levels for the F₁ male pups was dose-related, and differences from control data were statistically significant at exposure levels of 199, 598, and 996 ppm. The glucose level for female F₁ pups at the 100 ppm exposure level was statistically significantly lower than control but in the absence of a similar trend in glucose levels in the 199 and 598 ppm exposure groups, this was not considered biologically significant. GGT levels for both male and female F₁ pups at the 996 ppm exposure level were statistically significantly increased in comparison to control data. For all other exposure groups, GGT levels for the F₁ pups were comparable to control data.

There were several other clinical chemistry parameters for the 1-Bromopropane-exposed F₁ pups that differed statistically from control data but in the absence of a dose-response relationship, the changes were not considered to be exposure-related. This applied to the following parameters: 1) LD (lactate dehydrogenase) levels for F₁ male pups were statistically significantly higher than control in each of the exposure groups but the response was not exposure-related, a similar response in LD levels was not seen in female pups; 2) albumin levels and albumin/globulin ratios for male F₁ pups were lower than control at each exposure level and many of these differences were statistically significant, but the response was not exposure-related and not seen in the F₁ female pups; and 3) direct bilirubin levels were increased for F₁ female pups in the 598 and 996 ppm exposure groups, but the response was not exposure-related.

ALT (alanine aminotransferase) levels were lower than control in the F₁ male and female pups at exposure levels of 199, 598 and 996 ppm and most of these differences from control data were statistically significant, while the levels of other enzymes (AST

[aspartate aminotransferase] and ALK [alkaline phosphatase]) for the test F₁ male and female pups were comparable to control data. BUN (blood urea nitrogen) levels were statistically significantly lower than control data for both male and female F₁ pups in the 996 ppm exposure group. This type of response (lower ALT and BUN levels) in the exposure groups has no apparent biological significance.

Other clinical chemistry parameters for F₁ pups in the 1-Bromopropane test groups were considered comparable to control data and unaffected by test article exposure.

4.3.8. MACROSCOPIC POSTMORTEM EVALUATIONS F₁ PUPS POSTNATAL DAY 29

(Table 25, Appendix Z)

No test article effect with 1-Bromopropane at an exposure level up to and inclusive of 996 ppm was indicated from the macroscopic postmortem examination of postnatal day 29 F₁ pups.

4.3.9. F₁ ORGAN WEIGHT DATA

(Tables 26, Appendix AA)

The only suggestion of a treatment-related change in organ weight data for the F₁ pups sacrificed on postnatal day 29 was an increase in adrenal weights for the male pups. This was seen at all exposure levels. Absolute and relative (to body weight) adrenal weights for the F₁ male pups in the 100 and 199 ppm exposure groups were statistically significantly increased in comparison to control data while in the 598 and 996 ppm exposure groups, only the adrenal to body weight ratios were increased in comparison to control and only at the 996 ppm exposure level was this difference statistically significant. Absolute and relative adrenal weights for the F₁ female pups in the 1-Bromopropane exposure groups were comparable to control data.

Absolute brain weights for the F₁ pups in the 996 ppm group were statistically significantly lower than control data but the day 29 body weights for these pups (male and female) were also statistically significantly lower than controls. Brain weights relative to body weight for the F₁ pups in the 996 ppm exposure group were comparable to control data.

Other organ weight data for the F₁ pups in the 1-Bromopropane test groups were comparable to control data.

5. DISCUSSION AND CONCLUSION

In this range-finding study mated F₀ female rats were exposed to 1-Bromopropane from days 6-19 of gestation and from days 4-20 of lactation. Animals were exposed 6 hours/day at levels of 0 (chamber housed, room air control), 100, 199, 598 and 996 ppm. Test article-related effects noted in the F₀ females included the following: salivation and lacrimation post-exposure at the 996 ppm exposure level; reduced body weight gain over days 6-20 of gestation at exposure levels of 199, 598 and 996 ppm; reduced F₁ pup body weights on days 14 and 21 of lactation at the 996 ppm exposure level; and increased relative kidney and liver weights (to body weight) at the 598 and 996 ppm exposure levels. In the F₁ pups exposed for one week post weaning (postnatal days 22-29), the following effects were noted: reduced body weight gain in male pups postnatal days 22-29 at the 598 ppm exposure level and in both male and female pups at the 996 ppm exposure level; lowered platelet levels in female pups at 598 ppm and in both male and female pups at 996 ppm; lower glucose levels in male pups at all exposure levels and in female pups at 996 ppm; elevated GGT levels in both male and female pups at 996 ppm; and increased relative adrenal weights (to body weight) in male pups at all exposure levels. There were a few other changes in clinical chemistry parameters for one or more of the test groups that differed statistically from control data but in the absence of a dose-response relationship or because of the direction of the response, the significance in relation to test article exposure was unclear.

In this range-finding reproduction study in rats with 1-Bromopropane, the no-observed-effect level (NOEL) for maternal toxicity was 100 ppm. At 996 ppm, some maternal toxicity (reduced body weight gain during gestation) was noted, but in the absence of an effect on parturition data, litter size or pup body weights at birth, should not preclude this being a high-exposure level for a developmental toxicity study. Considering effects noted for the F₁ pups during the postnatal exposure period, the 996 ppm exposure level may possibly be suitable for the high exposure level for a 2-generation reproduction study.

CALCULATIONS AND REFERENCES

CALCULATIONS

Food Consumption:

grams of food consumed per interval ÷ no. of days = grams/animal/day

grams of food consumed/kilogram of body weight/day (g/kg/day) =
$$\frac{\text{grams of food consumed}}{\text{previous body weight (kg)}} \div \text{no. of days}$$

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TABLE 1 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF SURVIVAL AND PREGNANCY

DOSE LEVEL (PPM)	GROUP	I	II	III	IV	V
		0	100	199	598	996
No. of females mated	N	10	10	10	10	10
Pregnant	N	8	9	8	8	10
- Died/sacrificed moribund	N	0	0	0	0	0
- Died delivering	N	0	0	0	0	0
- Died/sac.mor. post partum	N	0	0	0	0	0
- Elective sacrifice	N	0	0	0	0	0
Nonpregnant	N	2	1	2	2	0
- Died/sacrificed moribund	N	0	0	0	0	0
- Elective sacrifice	N	0	0	0	0	0
Total no. of females died/ sacrificed moribund	%	0.0	0.0	0.0	0.0	0.0
Dams delivering	N	8	9	8	7	10
- With liveborn pups	N	8	9	8	7	10
%	%	100.0	100.0	100.0	100.0	100.0
- With all pups stillborn	N	0	0	0	0	0
%	%	0.0	0.0	0.0	0.0	0.0

No statistically significant differences

TABLE 2 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION (frequency/animals)

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996

DAY 6 to 19

Normal

WITHIN NORMAL LIMITS

	140/10	135/10	140/10	132/10	140/10
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Dermal-General

ALOPECIA - EXTREMITIES/SNOUT

	0/0	5/1	0/0	8/1	0/0
--	-----	-----	-----	-----	-----

Post-dose Findings

POST-DOSE: EXCESSIVE SALIVATION
 POST-DOSE: LACRIMATION; UNILATERAL
 POST-DOSE: LACRIMATION; BILATERAL

	0/0	0/0	0/0	0/0	25/7
	0/0	0/0	0/0	0/0	3/2
	0/0	0/0	0/0	0/0	5/2

TABLE 3 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING LACTATION (frequency/animals)

DOSE LEVEL (PPM)	GROUP					V
	I	II	III	IV	V	
0	0	100	199	598	996	
133/ 8		144/ 9	131/ 8	126/ 7	180/10	
8/ 8		9/ 9	8/ 8	7/ 7	10/10	
7/ 1 0/ 0		15/ 2 3/ 1	13/ 1 0/ 0	0/ 0 0/ 0	0/ 0 0/ 0	0/ 0 0/ 0
1/ 1		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
4/ 1		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
0/ 0 0/ 0		0/ 0 0/ 0	0/ 0 0/ 0	0/ 0 0/ 0	35/ 7 2/ 2	

DAY 4 to 21

Normal

WITHIN NORMAL LIMITS

TERMINAL SACRIFICE

Dermal-General

ALOPECIA - EXTREMITIES/SNOUT
SCABS

Ocular

CHROMODACRYORRHEA - UNILATERAL

Oral/Buccal

INCISORS BROKEN/MISSING

Post-dose Findings

POST-DOSE: EXCESSIVE SALIVATION
POST-DOSE: LACRIMATION; BILATERAL

TABLE 4-F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

DAY	GROUP	DOSE LEVEL (PPM)	SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)				
			I	II	III	IV	V
DAY 0	MEAN		235	235	237	234	234
	S.D.		14.2	12.2	17.0	17.4	18.4
	N		8	9	7	6	10
DAY 4	MEAN		247	249	248	244	246
	S.D.		12.6	10.4	16.2	13.5	20.2
	N		8	9	7	6	10
DAY 6	MEAN		263	266	265	260	263
	S.D.		12.2	12.3	15.4	16.1	20.4
	N		8	9	7	6	10
DAY 10	MEAN		278	282	282	272	271
	S.D.		9.6	13.6	16.0	18.5	22.8
	N		8	9	7	6	10
DAY 14	MEAN		302	309	306	292	293
	S.D.		11.5	17.5	16.0	17.1	23.3
	N		8	9	7	6	10
DAY 20	MEAN		366	365	358	346	347
	S.D.		11.8	22.0	25.9	22.8	30.7
	N		8	9	7	6	9

No statistically significant differences

TABLE 5 - FO GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)

DAYS	GROUP	DOSE LEVEL (PPM)	SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)				
			I	II	III	IV	V
0 TO 4	MEAN	0	12	15	11	10	12
	S.D.		4.6	6.4	6.7	7.9	5.2
	N		8	9	7	6	10
4 TO 6	MEAN		17	16	17	16	17
	S.D.		2.7	5.6	5.9	3.5	3.7
	N		8	9	7	6	10
6 TO 10	MEAN		15	17	17	12	9
	S.D.		7.2	2.7	5.0	3.9	6.7
	N		8	9	7	6	10
10 TO 14	MEAN		24	27	24	21	21
	S.D.		6.8	5.3	4.8	2.7	4.6
	N		8	9	7	6	10
14 TO 20	MEAN		64	56	53	54	54
	S.D.		6.8	10.7	10.6	11.6	9.6
	N		8	9	7	6	9
6 TO 20	MEAN		102	99	94	86	84
	S.D.		12.6	15.5	13.2	10.2	17.6
	N		8	9	7	6	9

No statistically significant differences

TABLE 6-F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

DAY	GROUP	DOSE LEVEL (PPM)	SUMMARY OF LACTATION BODY WEIGHTS (GRAMS)				
			I	II	III	IV	V
DAY 1	MEAN	280	287	283	269	273	
	S.D.	16.1	17.8	15.2	14.4	19.3	
	N	8	9	8	7	10	
DAY 4	MEAN	300	311	304	293	299	
	S.D.	16.4	19.4	25.9	16.7	22.4	
	N	8	9	8	7	10	
DAY 7	MEAN	308	320	314	297	302	
	S.D.	22.6	18.7	23.0	14.7	23.2	
	N	8	9	8	7	10	
DAY 14	MEAN	329	343	338	327	325	
	S.D.	26.8	20.0	23.5	15.4	25.7	
	N	8	9	8	7	10	
DAY 21	MEAN	331	329	333	312	330	
	S.D.	25.2	14.3	32.0	24.8	16.1	
	N	8	9	8	7	10	

No statistically significant differences							

TABLE 7 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF LACTATION BODY WEIGHT GAIN (GRAMS)

DAYS	GROUP	DOSE LEVEL (PPM)	SUMMARY OF LACTATION BODY WEIGHT GAIN (GRAMS)				
			I	II	III	IV	V
1 TO 4	MEAN	0	24	21	24	26	
	S.D.	9.2	5.9	11.9	6.4	8.4	
	N	8	9	8	7	10	
4 TO 7	MEAN	8	9	10	4	3	
	S.D.	7.8	7.8	8.0	8.5	8.7	
	N	8	9	8	7	10	
7 TO 14	MEAN	21	23	23	30	23	
	S.D.	14.6	10.0	2.9	7.4	3.7	
	N	8	9	8	7	10	
14 TO 21	MEAN	2	-14	-5	-15	5	
	S.D.	13.1	20.6	15.5	14.4	19.6	
	N	8	9	8	7	10	
4 TO 21	MEAN	31	18	29	19	30	
	S.D.	21.0	20.5	16.8	24.1	15.0	
	N	8	9	8	7	10	

No statistically significant differences

TABLE 8 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF GESTATION FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

DAYS	GROUP	DOSE LEVEL (PPM)	I					II					III					IV					V				
			MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	
DAYS 4 TO 6	I	0	20			20			21			21			20			20			20			21			
			1.0			2.0			2.6			2.6			2.2			2.2			2.2			2.1			
			8			9			7			7			6			6			6			7			
DAYS 6 TO 10	I		21			21			21			21			19			19			19			19			
			1.5			2.3			2.4			2.4			1.9			1.9			1.9			2.5			
			8			9			7			7			4			4			4			10			
DAYS 10 TO 14	I		23			24			24			24			22			22			22			23			
			1.6			2.4			2.8			2.8			1.6			1.6			1.6			2.9			
			8			9			7			7			6			6			6			10			
DAYS 14 TO 20	I		25			25			24			24			23			23			23			24			
			1.5			2.2			3.2			3.2			1.2			1.2			1.2			2.7			
			8			9			7			7			6			6			6			10			
DAYS 6 TO 20	I		23			23			23			23			22			22			22			22			
			1.3			2.3			2.7			2.7			1.5			1.5			1.5			2.6			
			8			9			7			7			6			6			6			10			

No statistically significant differences

TABLE 9 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

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

GROUP	DOSE LEVEL (PPM)				
	I	II	III	IV	V
DAYS 4 TO 6	0	100	199	598	996
MEAN	79	78	84	80	84
S.D.	5.1	8.2	12.0	6.4	5.8
N	8	9	7	6	7
DAYS 6 TO 10	79	79	81	72	74
S.D.	7.3	6.3	8.2	4.7	8.8
N	8	9	7	4	10
DAYS 10 TO 14	81	83	84	81	84
S.D.	4.8	6.1	8.6	5.6	8.2
N	8	9	7	6	10
DAYS 14 TO 20	82	80	79	80	82
S.D.	3.6	4.1	7.8	3.5	5.8
N	8	9	7	6	10
DAYS 6 TO 20	81	81	81	78	80
S.D.	4.3	5.4	7.9	3.9	7.1
N	8	9	7	6	10

No statistically significant differences

TABLE 10 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF LACTATION FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

DAYS	GROUP	DOSE LEVEL (PPM)				
		I	II	III	IV	V
		0	100	199	598	996
DAYS 1 TO 4	MEAN	30	32	30	33	35
	S.D.	2.8	5.0	5.1	3.0	6.8
	N	8	9	8	7	9
DAYS 4 TO 7	MEAN	38	38	39	39	37
	S.D.	4.7	4.1	5.8	3.7	4.0
	N	8	8	8	7	10
DAYS 7 TO 14	MEAN	50	50	52	51	50
	S.D.	5.0	6.1	3.6	3.6	2.4
	N	7	9	8	7	10
DAYS 14 TO 21	MEAN	62	62	64	64	62
	S.D.	3.7	4.6	3.7	4.7	3.5
	N	8	7	8	5	9
DAYS 4 TO 21	MEAN	50	51	52	51	50
	S.D.	3.9	4.9	3.9	3.1	2.7
	N	8	7	8	5	9

No statistically significant differences

TABLE 11 - F0 GENERATION
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

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

DAYS	GROUP	DOSE LEVEL (PPM)	I					II					III					IV					V				
			MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	
DAYS 1 TO 4	I	0	109	8.8	8	II	100	110	14.8	9	III	199	104	13.0	8	IV	598	121	9.1	7	V	996	130	30.7	9		
			126	11.0	8			121	10.8	8			127	9.7	8			134	15.5	7			125	15.6	10		
			160	11.5	7			157	16.2	9			165	5.3	8			172	13.1	7			165	10.6	10		
DAYS 4 TO 7	I	0	188	18.5	8	II	183	183	10.8	7	III	190	190	12.6	8	IV	196	196	15.8	5	V	190	190	21.8	9		
			158	7.6	8			157	14.5	7			161	5.4	8			164	6.6	5			159	15.0	9		
			158	7.6	8			157	14.5	7			161	5.4	8			164	6.6	5			159	15.0	9		

No statistically significant differences

TABLE 12 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF DELIVERY AND LITTER DATA

DOSE LEVEL (PPM)	GROUP				
	I	II	III	IV	V
	0	100	199	598	996
Females on Study	N 10	10	10	10	10
Females Mated	N 10	10	10	10	10
Mating Index	% 100.0	100.0	100.0	100.0	100.0
Females Pregnant	N 8	9	8	8	10
Female Fertility Index	% 80.0	90.0	80.0	80.0	100.0
Females with Liveborn Gestation Index	N 8	9	8	7	10
	% 100.0	100.0	100.0	87.5	100.0
Females Completing Delivery	N 8	9	8	7	10
	% 100.0	100.0	100.0	87.5	100.0
with Stillborn Pups	N 2	0	0	0	1
	% 25.0	0.0	0.0	0.0	10.0
with all Stillborn	N 0	0	0	0	0
	% 0.0	0.0	0.0	0.0	0.0
Litters with Liveborn, but no Pups Alive	N 0	0	0	0	0
	% 0.0	0.0	0.0	0.0	0.0
day 4	N 0	0	0	0	0
	% 0.0	0.0	0.0	0.0	0.0
day 21	N 0	0	0	0	0
	% 0.0	0.0	0.0	0.0	0.0
Duration of Gestation	MEAN 21.3	21.3	21.1	21.4	21.1
S.D.	0.46	0.50	0.64	0.79	0.32
N	8	9	8	7	10

No statistically significant differences

TABLE 12 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF DELIVERY AND LITTER DATA

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996
Litters with Liveborn Pups	8	9	8	7	10
Pups Delivered (total)	109	105	101	88	126
MEAN	13.6	11.7	12.6	12.6	12.6
S.D.	1.51	2.06	2.20	2.82	2.41
Liveborn	107	105	101	88	125
Live Birth Index	98.2	100.0	100.0	100.0	99.2
Stillborn	2	0	0	0	1
%	1.8	0.0	0.0	0.0	0.8
Culled day 4	27	17	18	20	23
Liveborn, not culled prior to day 21	80	88	83	68	102
Pups Dying, Missing, and/or Cannibalized					
day 0	0	0	0	0	0
%	0.0	0.0	0.0	0.0	0.0
days 1-4	0	0	4	0	3
%	0.0	0.0	4.0	0.0	2.4
days 5-21	0	0	0	0	0
%	0.0	0.0	0.0	0.0	0.0
days 0-4	0	0	4	0	3
%	0.0	0.0	4.0	0.0	2.4
days 0-21	0	0	4	0	3
%	0.0	0.0	4.0	0.0	2.4
Pups Surviving 4 days	107	105	97	88	122
Viability Index	100.0	100.0	96.0	100.0	97.6
Pups Surviving 21 days	80	88	79	68	99
Lactation Index	100.0	100.0	100.0	100.0	100.0

No statistically significant differences

TABLE 12 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF DELIVERY AND LITTER DATA

GROUP	DOSE LEVEL (PPM)				
	I	II	III	IV	V
Live Pups/Litter					
day 0	13.4 S.D.: 1.41 N 8	11.7 2.06 9	12.6 2.20 8	12.6 2.82 7	12.5 2.42 10
day 4 preculling	13.4 S.D.: 1.41 N 8	11.7 2.06 9	12.1 2.17 8	12.6 2.82 7	12.2 1.93 10
day 4 postculling	10.0 S.D.: 0.00 N 8	9.8 0.44 9	9.9 0.35 8	9.7 0.76 7	9.9 0.32 10
day 7	10.0 S.D.: 0.00 N 8	9.8 0.44 9	9.9 0.35 8	9.7 0.76 7	9.9 0.32 10
day 14	10.0 S.D.: 0.00 N 8	9.8 0.44 9	9.9 0.35 8	9.7 0.76 7	9.9 0.32 10
day 21	10.0 S.D.: 0.00 N 8	9.8 0.44 9	9.9 0.35 8	9.7 0.76 7	9.9 0.32 10
Sex Ratio - Male Pups:Total Pups					
day 0	N 54 % 50.5	N 51 % 48.6	N 49 % 48.5	N 39 % 44.3	N 65 % 52.0
day 21	N 40 % 50.0	N 45 % 51.1	N 38 % 48.1	N 34 % 50.0	N 52 % 52.5

No statistically significant differences

TABLE 12 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF DELIVERY AND LITTER DATA

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996
Pup Weight/Litter (grams)					
day 1	6.6 0.37 8	7.3 0.86 9	6.7 0.55 8	7.0 0.76 7	6.6 0.54 10
day 4 preculling	9.5 0.88 8	10.4 1.34 9	9.6 0.85 8	10.3 1.51 7	9.7 0.87 10
day 4 postculling	9.5 0.85 8	10.4 1.30 9	9.6 0.86 8	10.4 1.47 7	9.7 0.89 10
day 7	13.4 1.16 8	14.0 1.81 9	13.2 1.01 8	14.5 1.78 7	13.1 0.94 10
day 14	24.3 2.07 8	25.4 3.08 9	24.2 1.60 8	25.5 3.33 7	22.9 1.18 10
day 21	37.2 4.21 8	39.3 5.81 9	37.7 3.44 8	41.6 6.36 6	34.6 2.52 10

No statistically significant differences

Huntingdon Life Sciences 98-4140
 BROMINATED SOLVENTS COMMITTEE (BSOC)

TABLE 13-F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING LACTATION (frequency/animals)

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996
DAY 0 to 21					
Normal					
WITHIN NORMAL LIMITS	40/ 8	45/ 9	35/ 7	35/ 7	50/10
Gen. Appearance					
PALE	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
Respiration					
LABORED BREATHING	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
Pup observations					
NO MILK IN STOMACH	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0

TABLE 14 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MALES	SUMMARY OF CLINICAL OBSERVATIONS DURING STUDY (frequency/animals)				
GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996

DAY 22 to 29

Normal

WITHIN NORMAL LIMITS

TERMINAL SACRIFICE

30/10 30/10 30/10 30/10 30/10

10/10 10/10 10/10 10/10 10/10

TABLE 14 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

FEMALES	SUMMARY OF CLINICAL OBSERVATIONS DURING STUDY (frequency/animals)				
DOSE LEVEL (PPM)	I	II	III	IV	V
0	0	100	199	598	996

DAY 22 to 29

Normal

WITHIN NORMAL LIMITS

30/10 30/10 30/10 30/10 30/10

TERMINAL SACRIFICE

10/10 10/10 10/10 10/10 10/10

TABLE 15 - F1 GENERATION
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

DOSE LEVEL (PPM)	GROUP	I					II					III					IV					V				
		MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	
day 1	males	6.9	0.44	8	7.5	0.83	9	6.9	0.57	8	7.4	0.78	7	7.4	0.52	10	6.7	0.52	10	6.7	0.52	10	6.7	0.52	10	
1	females	6.2	0.39	8	7.1*	0.89	9	6.5	0.59	8	6.8	0.72	7	6.8	0.59	10	6.3	0.59	10	6.3	0.59	10	6.3	0.59	10	
1	males+females	6.6	0.37	8	7.3	0.86	9	6.7	0.55	8	7.0	0.76	7	7.0	0.54	10	6.6	0.54	10	6.6	0.54	10	6.6	0.54	10	
day 4	males preculling	9.8	0.98	8	10.7	1.29	9	9.9	0.87	8	10.7	1.44	7	10.7	0.87	10	9.9	0.87	10	9.9	0.87	10	9.9	0.87	10	
4	females preculling	8.9	0.75	8	10.2	1.39	9	9.4	0.89	8	10.0	1.52	7	10.0	0.90	10	9.5	0.90	10	9.5	0.90	10	9.5	0.90	10	
4	males+females preculling	9.5	0.88	8	10.4	1.34	9	9.6	0.85	8	10.3	1.51	7	10.3	0.87	10	9.7	0.87	10	9.7	0.87	10	9.7	0.87	10	
day 4	males postculling	9.8	0.99	8	10.6	1.25	9	9.9	0.86	8	10.7	1.47	7	10.7	0.87	10	9.9	0.87	10	9.9	0.87	10	9.9	0.87	10	
4	females postculling	8.9	0.74	8	10.2	1.36	9	9.4	0.90	8	10.1	1.48	7	10.1	0.92	10	9.4	0.92	10	9.4	0.92	10	9.4	0.92	10	
4	males+females postculling	9.5	0.85	8	10.4	1.30	9	9.6	0.86	8	10.4	1.47	7	10.4	0.89	10	9.7	0.89	10	9.7	0.89	10	9.7	0.89	10	

Statistical key: * = p<0.05

Huntingdon Life Sciences 98-41140
 BROMINATED SOLVENTS COMMITTEE (BSOC)

TABLE 15 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)

DOSE LEVEL (PPM)	GROUP	SUMMARY OF MEAN PUP BODY WEIGHTS (GRAMS)				
		I 0	II 100	III 199	IV 598	V 996
day 7 males	MEAN	13.8	14.2	13.5	15.0	13.4
	S.D.	1.39	1.79	1.04	1.76	0.91
	N	8	9	8	7	10
7 females	MEAN	12.7	13.7	12.9	14.1	12.8
	S.D.	0.92	1.86	1.00	1.80	0.97
	N	8	9	8	7	10
7 males+females	MEAN	13.4	14.0	13.2	14.5	13.1
	S.D.	1.16	1.81	1.01	1.78	0.94
	N	8	9	8	7	10
day 14 males	MEAN	25.1	25.7	24.7	26.2	23.3
	S.D.	2.20	3.05	1.75	3.19	1.31
	N	8	9	8	7	10
14 females	MEAN	23.3	25.1	23.7	24.8	22.5
	S.D.	1.60	3.15	1.41	3.49	1.19
	N	8	9	8	7	10
14 males+females	MEAN	24.3	25.4	24.2	25.5	22.9
	S.D.	2.07	3.08	1.60	3.33	1.18
	N	8	9	8	7	10
day 21 males	MEAN	38.2	39.9	38.3	42.5	35.0
	S.D.	4.43	5.89	3.73	6.61	2.74
	N	8	9	8	6	10
21 females	MEAN	35.5	38.7	37.0	40.7	34.0
	S.D.	3.13	5.92	3.41	6.16	2.53
	N	8	9	8	6	10
21 males+females	MEAN	37.2	39.3	37.7	41.6	34.6
	S.D.	4.21	5.81	3.44	6.36	2.52
	N	8	9	8	6	10

No statistically significant differences

TABLE 15 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF PUP BODY WEIGHT CHANGES -- GRAMS

DOSE LEVEL (PPM)	GROUP				
	I	II	III	IV	
	0	100	199	598	
				V	
				996	
day 1-4 males	MEAN 3.0	3.2	3.0	3.4	3.2
	S.D. 0.64	0.60	0.62	0.79	0.48
	N 8	9	8	7	10
females	MEAN 2.7	3.1	2.9	3.2	3.1
	S.D. 0.47	0.64	0.54	0.88	0.46
	N 8	9	8	7	10
males+females	MEAN 2.8	3.1	2.9	3.3	3.2
	S.D. 0.57	0.62	0.58	0.84	0.47
	N 8	9	8	7	10
day 4-7 males	MEAN 4.0	3.6	3.7	4.3	3.5
	S.D. 0.57	0.70	0.89	1.05	0.59
	N 8	9	8	7	10
females	MEAN 3.8	3.5	3.5	4.0	3.3
	S.D. 0.36	0.67	0.78	1.03	0.57
	N 8	9	8	7	10
males+females	MEAN 3.9	3.5	3.6	4.1	3.4
	S.D. 0.48	0.67	0.83	1.04	0.58
	N 8	9	8	7	10
day 4-21 males	MEAN 28.4	29.3	28.4	31.4	25.1
	S.D. 3.59	4.89	3.42	5.83	2.52
	N 8	9	8	6	10
females	MEAN 26.6	28.5	27.7	30.3	24.6
	S.D. 2.79	4.92	3.04	5.32	2.09
	N 8	9	8	6	10
males+females	MEAN 27.7	28.9	28.1	30.8	24.9
	S.D. 3.52	4.80	3.12	5.55	2.23
	N 8	9	8	6	10

No statistically significant differences

TABLE 15 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF PUP BODY WEIGHT CHANGES -- GRAMS

GROUP	DOSE LEVEL (PPM)	SUMMARY OF PUP BODY WEIGHT CHANGES -- GRAMS				
		I 0	II 100	III 199	IV 598	V 996
day 7-14 males	MEAN	11.2	11.5	11.1	11.2	9.9
	S.D.	1.44	1.55	1.20	1.87	1.08
	N	8	9	8	7	10
females	MEAN	10.6	11.4	10.8	10.8	9.7
	S.D.	1.22	1.57	0.97	1.97	0.86
	N	8	9	8	7	10
males+females	MEAN	10.9	11.5	11.0	11.0	9.8
	S.D.	1.40	1.56	1.09	1.90	0.94
	N	8	9	8	7	10
day 14-21 males	MEAN	13.2	14.2	13.6	16.2	11.7
	S.D.	3.22	2.93	2.94	3.54	2.23
	N	8	9	8	6	10
females	MEAN	12.3	13.6	13.3	15.6	11.6
	S.D.	2.65	2.94	2.79	2.61	2.08
	N	8	9	8	6	10
males+females	MEAN	12.9	13.9	13.5	15.9	11.7
	S.D.	3.10	2.80	2.76	3.06	2.12
	N	8	9	8	6	10

No statistically significant differences

TABLE 16 - F1 GENERATION
 A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MALES MEAN BODY WEIGHT VALUES -- grams

DAY	DOSE LEVEL (PPM)	GROUP	MEAN BODY WEIGHT VALUES -- grams				
			I	II	III	IV	V
22		MEAN	42	43	43	45	39
		S.D.	5.1	5.7	4.4	6.5	4.3
		N	10	10	10	10	10
25		MEAN	58	60	59	58	49**
		S.D.	6.1	7.3	5.3	7.7	5.3
		N	10	10	10	10	10
29		MEAN	81	83	82	78	68**
		S.D.	8.2	10.5	7.6	10.5	6.4
		N	10	10	10	10	10

Statistical key: ** = p<0.01

TABLE 16 - F1 GENERATION
 A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

FEMALES	DAY	GROUP	DOSE LEVEL (PPM)	MEAN BODY WEIGHT VALUES -- grams				
				I	II	III	IV	V
			0		100	199	598	996
	22	MEAN	38	43	39	46**	37	
		S.D.	4.3	6.8	6.7	7.1	3.4	
		N	10	10	10	10	10	
	25	MEAN	53	58	54	59	46	
		S.D.	5.2	7.2	7.8	9.0	3.1	
		N	10	10	10	10	10	
	29	MEAN	71	78	74	78	63	
		S.D.	6.7	9.2	10.5	11.6	4.2	
		N	10	10	10	10	10	

Statistical key: ** = p<0.01

TABLE 17 - F1 GENERATION
 A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MALES		MEAN BODY WEIGHT GAIN (GRAMS)				
DAY	DOSE LEVEL (PPM)	I	II	III	IV	V
22 TO 25	0	17	17	16	13**	10**
		1.8	2.1	1.5	1.9	1.9
		10	10	10	10	10
			100	199	598	996
25 TO 29	2.3	22	23	23	20	19*
		2.3	3.9	3.4	3.2	1.7
		10	10	10	10	10

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

TABLE 17 - F1 GENERATION
 A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

FEMALES		MEAN BODY WEIGHT GAIN (GRAMS)				
DAY	DOSE LEVEL (PPM)	I	II	III	IV	V
22 TO 25	0	15	16	15	12	9**
		2.5	1.8	1.7	2.6	2.2
		10	10	10	10	10
			100	199	598	996
25 TO 29	18	18	20	20	19	17
		2.0	3.1	3.5	3.1	1.5
		10	10	10	10	10

Statistical key: ** = p<0.01

T 18-1
TABLE 18
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN HEMATOLOGY VALUES - F0 FEMALES

	H G B	H C T	R B C	P L T	M C V	M C H	M C H C	W B C	A N E U	A L Y M	R E T I C
UNITS>>>>>	g/dL	%	mil/uL	thous/uL	fL	pg	g/dL	thous/uL	thous/uL	thous/uL	% RBC
GROUP I - 0 PPM											
MEAN	14.5	42.8	7.55	797	56.7	19.3	34.0	8.67	1.69	6.27	1.1
S.D.	0.5	1.2	0.14	62	2.1	0.8	0.8	2.47	0.87	1.47	1.0
N	8	8	8	8	8	8	8	8	8	8	8
GROUP II - 100 PPM											
MEAN	15.1	43.6	7.76	784	56.2	19.4	34.6	7.45	1.67	5.14	0.8
S.D.	0.5	1.8	0.25	208	1.5	0.3	1.1	2.11	0.62	1.59	0.8
N	9	9	9	9	9	9	9	9	9	9	9
GROUP III - 199 PPM											
MEAN	14.7	43.0	7.56	851	56.9	19.5	34.2	7.84	1.53	5.54	1.3
S.D.	0.6	1.0	0.40	131	2.9	1.0	0.7	0.78	0.37	0.63	0.8
N	8	8	8	8	8	8	8	8	8	8	8
GROUP IV - 598 PPM											
MEAN	14.8	43.2	7.63	855	56.7	19.4	34.3	8.48	1.80	5.94	1.5
S.D.	0.4	1.1	0.25	162	1.1	0.6	0.5	1.85	0.45	1.49	1.4
N	7	7	7	7	7	7	7	7	7	7	7
GROUP V - 996 PPM											
MEAN	14.6	43.2	7.44	739	58.1	19.6	33.8	7.62	1.84	5.23	1.1
S.D.	0.5	1.3	0.30	218	2.0	0.6	0.6	1.56	0.61	1.42	0.7
N	10	10	10	10	10	10	10	10	10	10	10

RUN ON 29-JAN-99 AT 09:28:35

Key:

HGB	Hemoglobin Concentration	g/dL	MCH	Mean Corpuscular Hemoglobin	pg
HCT	Hematocrit	percent	MCHC	Mean Corpuscular Hemoglobin Concentration	g/dL
RBC	Erythrocyte Count	10 ⁶ /microliter(mil/μL)	WBC	Total Leukocyte Count	10 ³ /microliter(thous/μL)
PLT	Platelet Count	10 ³ /microliter(thous/μL)	RETIC	Reticulocyte Count	% RBC
MCV	Mean Corpuscular Volume	fL	ANEU	Absolute Neutrophils	thous/μL
ALYM	Absolute Lymphocytes	thous/μL			

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences

T 19-1
TABLE 19
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F0 FEMALES

	A S T	A L T	A L K P	L D	S D H	B U N	C R E A T	G L U	T P R O T	A L B	G L O B	A / G
UNITS>>>>>	IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL	g/dL	g/dL	g/dL	
GROUP	I - 0 PPM											
MEAN	125	99	304	812	9.8	24.3	0.4	112	5.9	4.1	1.8	2.3
S.D.	13	40	129	300	4.6	1.5	0.1	16	0.3	0.2	0.2	0.3
N	8	8	8	8	7	8	8	8	8	7	7	7
GROUP	II - 100 PPM											
MEAN	111	103	283	524	11.7	21.0	0.3	119	6.0	4.3	1.7	2.4
S.D.	11	24	87	211	5.6	3.0	0.1	18	0.1	0.1	0.2	0.3
N	9	9	9	9	9	9	9	9	9	9	9	9
GROUP	III - 199 PPM											
MEAN	107	103	237	401	10.6	21.6	0.3	116	6.2	4.3	1.9	2.3
S.D.	16	18	40	278	4.1	2.8	0.0	7	0.1	0.2	0.2	0.4
N	8	8	8	8	8	8	8	8	8	8	8	8
GROUP	IV - 598 PPM											
MEAN	99	100	344	306	16.8	20.7	0.3	125	5.7	4.2	1.5	2.8
S.D.	8	15	141	109	5.4	2.1	0.1	17	0.2	0.1	0.2	0.4
N	7	7	7	7	7	7	7	7	7	7	7	7
GROUP	V - 996 PPM											
MEAN	97	95	288	217	11.2	20.0	0.3	129	6.1	4.3	1.8	2.4
S.D.	15	21	86	130	3.3	2.2	0.1	7	0.3	0.2	0.2	0.3
N	10	10	10	10	10	10	10	10	10	10	10	10

RUN ON 27-JAN-99 AT 15:00:07

Key:

AST	Aspartate Aminotransferase	IU/L	CREAT	Creatinine	mg/dL
ALT	Alanine Aminotransferase	IU/L	GLU	Glucose	mg/dL
ALKP	Alkaline Phosphatase	IU/L	T PROT	Total Protein	g/dL
LD	Lactate Dehydrogenase	IU/L	ALB	Albumin	g/dL
SDH	Sorbitol Dehydrogenase	IU/L	GLOB	Globulin (calculated)	g/dL
BUN	Blood Urea Nitrogen	mg/dL	A/G	Albumin/Globulin Ratio (calculated)	

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

T 19-2
TABLE 19 (cont.)
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F0 FEMALES

	T B I L I	D B I L I	I B I L I	G G T
UNITS>>>>>	mg/dL	mg/dL	mg/dL	IU/L
GROUP	I - 0 PPM			
MEAN	0.2	0.0	0.2	0
S.D.	0.1	0.0	0.1	1
N	8	8	8	8
GROUP	II - 100 PPM			
MEAN	0.1	0.0	0.1	0
S.D.	0.0	0.0	0.0	1
N	9	9	9	9
GROUP	III - 199 PPM			
MEAN	0.2	0.0	0.2	0
S.D.	0.0	0.0	0.0	0
N	8	8	8	8
GROUP	IV - 598 PPM			
MEAN	0.2	0.0	0.2	1
S.D.	0.1	0.0	0.1	1
N	7	7	7	7
GROUP	V - 996 PPM			
MEAN	0.2	0.0	0.2	0
S.D.	0.1	0.0	0.1	1
N	10	10	10	10

RUN ON 27-JAN-99 AT 15:00:07

Key:

T BILI	Total Bilirubin	mg/dL	I BILI	Indirect Bilirubin	mg/dL
D BILI	Direct Bilirubin	mg/dL	GGT	Gamma-Glutamyl Transferase	IU/L

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

TABLE 20-F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996
N	10	10	10	10	10
FEMALES					
GROSS EXAM	N 1	1	1	0	0
INCISORS BROKEN/MISSING	N 1 % 10.0	0 0.0	0 0.0	0 0.0	0 0.0
ALOPECIA EXTREMITIES/SNOUT	N 0 % 0.0	1 10.0	1 10.0	0 0.0	0 0.0

No statistically significant differences

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BROMINATED SOLVENTS COMMITTEE (BSOC)

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TABLE 21 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ABSOLUTE ORGAN WEIGHTS

FEMALES	GROUP	DOSE LEVEL (PPM)					V
		I	II	III	IV	V	
		0	100	199	598	996	
FINAL BODY WEIGHT g	MEAN	331	329	333	312	330	
	S.D.	25.2	14.3	32.0	24.8	16.1	
	N	8	9	8	7	10	
ADRENALS g	MEAN	0.0937	0.0929	0.0967	0.0898	0.0938	
	S.D.	.01402	.00827	.02170	.01767	.01302	
	N	8	9	8	6	10	
BRAIN g	MEAN	1.8447	1.9079	1.8869	1.8561	1.8291	
	S.D.	.06724	.09182	.11649	.12646	.07014	
	N	8	9	8	7	10	
LIVER g	MEAN	14.981	14.224	15.434	15.314	16.361	
	S.D.	1.3483	1.2415	2.4114	1.2085	1.3201	
	N	8	9	8	7	10	
RIGHT KIDNEY g	MEAN	1.2084	1.2445	1.3019	1.2620	1.3488	
	S.D.	.13805	.07302	.10312	.10627	.14670	
	N	8	9	8	7	10	
LEFT KIDNEY g	MEAN	1.1632	1.2098	1.2359	1.2203	1.2713	
	S.D.	.13405	.08768	.10765	.11154	.11599	
	N	8	9	8	7	10	

No statistically significant differences

TABLE 21 - F0 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE
 ORGAN WEIGHT TO BRAIN WEIGHT RATIO

FEMALES	GROUP	DOSE LEVEL (PPM)				
		I	II	III	IV	V
FINAL BODY WEIGHT	g	331	329	333	312	330
	MEAN	25.2	14.3	32.0	24.8	16.1
	S.D.	8	9	8	7	10
	N	8	9	8	7	10
ADRENALS Ratio	MEAN	0.0508	0.0488	0.0512	0.0475	0.0513
	S.D.	.00754	.00457	.01054	.00770	.00722
	N	8	9	8	6	10
LIVER Ratio	MEAN	8.1284	7.4801	8.2142	8.2566	8.9435
	S.D.	.77008	.82525	1.4812	.49600	.60736
	N	8	9	8	7	10
RIGHT KIDNEY Ratio	MEAN	0.6555	0.6525	0.6918	0.6816	0.7369*
	S.D.	.07665	.02823	.06651	.06057	.06936
	N	8	9	8	7	10
LEFT KIDNEY Ratio	MEAN	0.6312	0.6345	0.6567	0.6585	0.6948
	S.D.	.07681	.04278	.06579	.05621	.05563
	N	8	9	8	7	10

Statistical key: * = p<0.05

Huntingdon Life Sciences 98-4140
 BROMINATED SOLVENTS COMMITTEE (BSOC)

TABLE 22 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
 IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF PUP NECROPSY OBSERVATIONS

GROUP	I	II	III	IV	V
DOSE LEVEL (PPM)	0	100	199	598	996
Litters Evaluated	8	9	8	7	10
Pups Evaluated	60	67	59	48	79
Live	60	67	59	48	79
TOTAL PUP NECROPSY OBSERVATIONS	0	0	0	0	0

No statistically significant differences

T 23-1
TABLE 23
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN HEMATOLOGY VALUES - F1 PUPS

	H G B	H C T	R B C	P L T	M C V	M C H	M C H C	W B C	A N E U	A L Y M	R E T I C
UNITS>>>>>	g/dL	%	mil/uL	thous/uL	fL	pg	g/dL	thous/uL	thous/uL	thous/uL	% RBC
MALE											
GROUP	I - 0 PPM										
MEAN	11.1	34.0	5.09	1017	66.8	21.9	32.7	7.63	1.26	5.73	8.7
S.D.	0.9	2.7	0.40	74	2.1	0.7	0.8	1.17	0.32	0.99	6.1
N	10	10	10	10	10	10	10	10	10	10	10
GROUP	II - 100 PPM										
MEAN	10.6	32.6	4.86	922	67.1	21.9	32.7	6.31	1.13	4.00	11.2
S.D.	1.0	3.3	0.43	183	2.8	0.6	0.8	2.28	0.68	2.33	5.1
N	9	9	9	9	9	9	9	9	9	9	9
GROUP	III - 199 PPM										
MEAN	11.7	36.1	5.33	907	67.8	22.1	32.6	7.90	1.25	6.02	14.0
S.D.	0.3	1.3	0.19	87	2.8	0.7	0.5	1.00	0.25	0.91	3.6
N	10	10	10	10	10	10	10	10	10	10	10
GROUP	IV - 598 PPM										
MEAN	11.8	35.6	5.47	964	65.2	21.6	33.2	7.11	1.21	5.36	10.3
S.D.	0.5	1.6	0.26	137	1.7	0.6	0.7	0.78	0.47	1.21	1.7
N	9	9	9	9	9	9	9	9	9	9	9
GROUP	V - 996 PPM										
MEAN	11.4	34.4	5.46	803	63.2	21.0	33.1	6.84	1.31	4.95	8.9
S.D.	1.6	4.8	0.81	198	1.4	0.7	0.7	1.89	0.38	1.34	2.8
N	8	8	8	8	8	8	8	8	8	8	7

RUN ON 29-JAN-99 AT 09:31:53

Key:

HGB	Hemoglobin Concentration	g/dL	MCH	Mean Corpuscular Hemoglobin	pg
HCT	Hematocrit	percent	MCHC	Mean Corpuscular Hemoglobin Concentration	g/dL
RBC	Erythrocyte Count	10 ⁶ /microliter(mil/μL)	WBC	Total Leukocyte Count	10 ³ /microliter(thous/μL)
PLT	Platelet Count	10 ³ /microliter(thous/μL)	RETIC	Reticulocyte Count	% RBC
MCV	Mean Corpuscular Volume	fL	ANEU	Absolute Neutrophils	thous/μL
ALYM	Absolute Lymphocytes	thous/μL			

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences

T 23-2
TABLE 23 (cont.)
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN HEMATOLOGY VALUES - F1 PUPS

		H G B	H C T	R B C	P L T	M C V	M C H	M C H C	W B C	A N E U	A L Y M	R E T I C
UNITS>>>>>		g/dL	%	mil/uL	thous/uL	fL	pg	g/dL	thous/uL	thous/uL	thous/uL	% RBC
FEMALE												
GROUP	I - 0 PPM											
MEAN		11.5	34.8	5.37	1060	64.8	21.4	33.0	6.71	1.11	5.04	10.1
S.D.		0.5	1.5	0.29	110	1.4	0.6	1.1	1.63	0.40	1.08	3.9
N		9	9	9	9	9	9	9	9	9	9	9
GROUP	II - 100 PPM						*					*
MEAN		10.8	32.2	4.89	873	65.8	22.2	33.8	6.50	1.18	4.86	14.8
S.D.		1.3	4.2	0.62	368	1.4	0.6	0.8	1.51	0.42	1.23	3.0
N		10	10	10	10	10	10	10	10	10	10	8
GROUP	III - 199 PPM											
MEAN		11.6	35.5	5.31	897	67.0	21.9	32.7	7.88	1.23	5.97	14.0
S.D.		0.4	1.4	0.35	149	4.2	1.0	0.7	1.60	0.40	1.38	3.1
N		9	9	9	9	9	9	9	9	9	9	9
GROUP	IV - 598 PPM		*		**							
MEAN		12.2	36.5	5.63	742	64.9	21.6	33.4	7.54	1.42	5.48	11.8
S.D.		0.3	0.5	0.20	179	1.8	0.4	0.5	1.80	0.58	1.21	2.7
N		10	10	10	10	10	10	10	10	10	10	9
GROUP	V - 996 PPM					*						
MEAN		11.7	34.9	5.52	852	63.4	21.2	33.4	7.98	1.22	6.15	10.9
S.D.		1.4	4.0	0.71	167	1.7	0.5	0.4	2.36	0.33	1.93	3.2
N		10	10	10	10	10	10	10	10	10	10	9

RUN ON 29-JAN-99 AT 09:31:53

Key:

HGB	Hemoglobin Concentration	g/dL	MCH	Mean Corpuscular Hemoglobin	pg
HCT	Hematocrit	percent	MCHC	Mean Corpuscular Hemoglobin Concentration	g/dL
RBC	Erythrocyte Count	10 ⁶ /microliter(mil/μL)	WBC	Total Leukocyte Count	10 ³ /microliter(thous/μL)
PLT	Platelet Count	10 ³ /microliter(thous/μL)	RETIC	Reticulocyte Count	% RBC
MCV	Mean Corpuscular Volume	fL	ANEU	Absolute Neutrophils	thous/μL
ALYM	Absolute Lymphocytes	thous/μL			

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences

T 24-1
TABLE 24
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F1 PUPS

	AST	ALT	ALKP	LD	SDH	BUN	CREAT	GLU	T PROT	ALB	GLOB	A/G
UNITS>>>>>	IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL	g/dL	g/dL	g/dL	
MALE												
GROUP	I - 0 PPM											
MEAN	118	55	402	272	16.9	12.6	0.2	160	4.9	4.0	0.9	4.6
S.D.	28	7	49	173	8.0	3.3	0.1	14	0.1	0.1	0.1	0.7
N	10	10	10	10	10	10	10	10	10	10	10	10
GROUP	II - 100 PPM											
MEAN	143	51	375	668*	10.6	12.2	0.1	149	4.6	3.7**	0.9	4.2
S.D.	34	7	99	164	3.0	2.0	0.0	15	0.3	0.2	0.1	0.5
N	10	10	10	8	8	8	8	8	8	8	8	8
GROUP	III - 199 PPM											
MEAN	120	46	404	659*	12.8	9.1	0.1	144	4.8	3.9	0.9	4.1
S.D.	20	12	98	298	3.3	4.2	0.1	13	0.1	0.1	0.1	0.5
N	10	10	10	10	10	10	10	10	10	10	10	10
GROUP	IV - 598 PPM											
MEAN	129	39**	419	803**	11.5	10.8	0.2	141	4.8	3.8**	1.0	3.8*
S.D.	32	10	73	480	4.8	4.0	0.1	10	0.1	0.1	0.1	0.6
N	10	10	10	10	10	10	10	10	10	10	10	10
GROUP	V - 996 PPM											
MEAN	134	38**	434	733**	14.6	6.7**	0.1	135*	4.8	3.8**	1.0	3.8*
S.D.	52	14	84	342	9.6	2.9	0.1	28	0.2	0.2	0.1	0.5
N	10	10	10	10	10	10	10	10	10	10	10	10

RUN ON 5-FEB-99 AT 11:26:21

Key:

AST	Aspartate Aminotransferase	IU/L	CREAT	Creatinine	mg/dL
ALT	Alanine Aminotransferase	IU/L	GLU	Glucose	mg/dL
ALKP	Alkaline Phosphatase	IU/L	T PROT	Total Protein	g/dL
LD	Lactate Dehydrogenase	IU/L	ALB	Albumin	g/dL
SDH	Sorbitol Dehydrogenase	IU/L	GLOB	Globulin (calculated)	g/dL
BUN	Blood Urea Nitrogen	mg/dL	A/G	Albumin/Globulin Ratio (calculated)	

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

T 24-2
TABLE 24 (cont.)
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F1 PUPS

	T B I L I	D B I L I	I B I L I	G G T
UNITS>>>>>	mg/dL	mg/dL	mg/dL	IU/L
MALE				
GROUP	I - 0 PPM			
MEAN	0.2	0.0	0.2	1
S.D.	0.0	0.1	0.1	0
N	10	10	10	10
GROUP	II - 100 PPM			
MEAN	0.1	0.0	0.1	2
S.D.	0.1	0.1	0.0	4
N	8	8	8	10
GROUP	III - 199 PPM			
MEAN	0.2	0.1	0.1	1
S.D.	0.1	0.0	0.1	0
N	10	10	10	10
GROUP	IV - 598 PPM			
MEAN	0.2	0.1	0.1	1
S.D.	0.1	0.1	0.1	1
N	10	10	10	10
GROUP	V - 996 PPM			
MEAN	0.2	0.1	0.1	**
S.D.	0.1	0.0	0.1	3
N	10	10	10	2
				10

RUN ON 5-FEB-99 AT 11:26:21

Key:

T BILI	Total Bilirubin	mg/dL	I BILI	Indirect Bilirubin	mg/dL
D BILI	Direct Bilirubin	mg/dL	GGT	Gamma-Glutamyl Transferase	IU/L

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

T 24-3
TABLE 24 (cont.)
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F1 PUPS

	AST	ALT	ALKP	LD	SDH	BUN	CREAT	GLU	T PROT	ALB	GLOB	A/G
UNITS>>>>>	IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL	g/dL	g/dL	g/dL	
FEMALE												
GROUP	I - 0 PPM											
MEAN	116	48	408	367	13.9	11.8	0.1	151	4.8	3.9	0.9	4.5
S.D.	15	5	94	294	3.2	1.8	0.0	6	0.2	0.2	0.1	0.6
N	10	10	10	10	10	10	10	10	10	10	10	10
GROUP	II - 100 PPM											
	**			*				*				
MEAN	154	48	376	966	10.2	9.6	0.1	139	4.7	3.9	0.9	4.6
S.D.	40	8	67	694	4.8	2.3	0.1	12	0.1	0.2	0.1	0.7
N	10	10	10	10	10	9	9	9	9	9	9	9
GROUP	III - 199 PPM											
		*				*						
MEAN	115	39	359	553	12.1	7.7	0.1	142	4.8	3.8	1.0	4.1
S.D.	17	14	46	327	3.0	4.7	0.0	8	0.2	0.1	0.1	0.5
N	10	10	10	10	10	9	9	9	9	9	9	9
GROUP	IV - 598 PPM											
		*										
MEAN	118	38	414	550	12.4	10.1	0.2	141	4.9	4.0	0.9	4.5
S.D.	16	5	71	267	3.4	3.5	0.1	15	0.2	0.2	0.2	1.2
N	10	10	10	10	10	10	10	10	10	10	10	10
GROUP	V - 996 PPM											
		**				**		**				
MEAN	116	35	422	380	14.5	5.3	0.1	128	4.9	3.9	1.0	4.1
S.D.	28	4	120	209	3.8	2.9	0.0	10	0.2	0.2	0.1	0.5
N	10	10	10	10	10	10	10	10	10	10	10	10

RUN ON 5-FEB-99 AT 11:26:21

Key:

AST	Aspartate Aminotransferase	IU/L	CREAT	Creatinine	mg/dL
ALT	Alanine Aminotransferase	IU/L	GLU	Glucose	mg/dL
ALKP	Alkaline Phosphatase	IU/L	T PROT	Total Protein	g/dL
LD	Lactate Dehydrogenase	IU/L	ALB	Albumin	g/dL
SDH	Sorbitol Dehydrogenase	IU/L	GLOB	Globulin (calculated)	g/dL
BUN	Blood Urea Nitrogen	mg/dL	A/G	Albumin/Globulin Ratio (calculated)	

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

T 24-4
TABLE 24 (cont.)
A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

MEAN CLINICAL CHEMISTRY VALUES - F1 PUPS

	T B I L I	D B I L I	I B I L I	G G T
UNITS>>>>	mg/dL	mg/dL	mg/dL	IU/L
FEMALE				
GROUP	I - 0 PPM			
MEAN	0.1	0.0	0.1	1
S.D.	0.1	0.0	0.1	1
N	10	10	10	10
GROUP	II - 100 PPM			
MEAN	0.2	0.0	0.1	2
S.D.	0.1	0.1	0.1	3
N	9	9	9	10
GROUP	III - 199 PPM			
MEAN	0.2	0.1	0.1	1
S.D.	0.1	0.1	0.1	0
N	9	9	9	10
GROUP	IV - 598 PPM			
MEAN	0.2	0.1	0.1	2
S.D.	0.1	0.0	0.1	0
N	10	10	10	10
GROUP	V - 996 PPM			
MEAN	0.2	0.1	0.1	3
S.D.	0.0	0.0	0.0	1
N	10	10	10	10

RUN ON 5-FEB-99 AT 11:26:21

Key:

T BILI	Total Bilirubin	mg/dL	I BILI	Indirect Bilirubin	mg/dL
D BILI	Direct Bilirubin	mg/dL	GGT	Gamma-Glutamyl Transferase	IU/L

Statistical Key: * = p < 0.05 ** = p < 0.01. If no asterisks, no statistically significant differences.

TABLE 25-F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF PARENTAL NECROPSY OBSERVATIONS

GROUP	DOSE LEVEL (PPM)					V
	I	II	III	IV	V	
	0	100	199	598	996	
MALES	N	10	10	10	10	10
TRACHEA	N	0	0	0	1	0
FLUID FILLED	N	0	0	0	1	0
	%	0.0	0.0	0.0	10.0	0.0
THYMUS	N	0	0	0	0	0
DISCOLORED	N	0	0	0	0	0
	%	0.0	0.0	0.0	0.0	0.0
KIDNEY	N	0	1	1	0	2
DISCOLORED	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	10.0
DISTENDED PELVIS	N	0	0	0	0	1
	%	0.0	0.0	0.0	0.0	10.0
CYST	N	0	1	1	0	0
	%	0.0	10.0	10.0	0.0	0.0

No statistically significant differences

TABLE 25-F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE

SUMMARY OF PARENTAL NECROPSY OBSERVATIONS

DOSE LEVEL (PPM)	GROUP				
	I	II	III	IV	V
	0	100	199	598	996
N	10	10	10	10	10
FEMALES					
TRACHEA	N 0	0	0	0	0
FLUID FILLED	N 0	0	0	0	0
	% 0.0	0.0	0.0	0.0	0.0
THYMUS	N 0	0	0	1	0
DISCOLORED	N 0	0	0	1	0
	% 0.0	0.0	0.0	10.0	0.0
KIDNEY	N 1	0	1	1	0
DISCOLORED	N 1	0	0	0	0
	% 10.0	0.0	0.0	0.0	0.0
DISTENDED PELVIS	N 0	0	1	0	0
	% 0.0	0.0	10.0	0.0	0.0
CYST	N 0	0	0	1	0
	% 0.0	0.0	0.0	10.0	0.0

No statistically significant differences

TABLE 26 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ABSOLUTE ORGAN WEIGHTS

FEMALES	GROUP	DOSE LEVEL (PPM)	DOSE LEVEL (PPM)					V
			I	II	III	IV	V	
FINAL BODY WEIGHT g	MEAN	71	78	74	78	63		
	S.D.	6.7	9.2	10.5	11.6	4.2		
	N	10	10	10	10	10		
ADRENALS g	MEAN	0.0193	0.0236	0.0199	0.0215	0.0196		
	S.D.	.00427	.00449	.00431	.00479	.00248		
	N	10	10	10	10	10		
BRAIN g	MEAN	1.489	1.541	1.475	1.420	1.376**		
	S.D.	0.0855	0.0791	0.1006	0.0490	0.0451		
	N	10	10	10	10	10		
LIVER g	MEAN	3.23	3.43	3.40	3.82	2.95		
	S.D.	0.294	0.558	0.847	0.768	0.425		
	N	10	10	10	10	10		
RIGHT KIDNEY g	MEAN	0.423	0.450	0.444	0.462	0.393		
	S.D.	0.0470	0.0701	0.0529	0.0720	0.0366		
	N	10	10	10	10	10		
LEFT KIDNEY g	MEAN	0.419	0.443	0.432	0.445	0.387		
	S.D.	0.0522	0.0553	0.0530	0.0741	0.0314		
	N	10	10	10	10	10		

Statistical key: ** = p<0.01

TABLE 26 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ORGAN WEIGHT TO BODY WEIGHT RATIO

MALES

	DOSE LEVEL (PPM)	GROUP				
		I	II	III	IV	V
		0	100	199	598	996
FINAL BODY WEIGHT g	MEAN	81	83	82	78	68**
	S.D.	8.2	10.5	7.6	10.5	6.4
	N	10	10	10	10	10
ADRENALS Ratio	MEAN	0.0002	0.0003*	0.0003*	0.0003	0.0003**
	S.D.	.00003	.00003	.00008	.00002	.00006
	N	10	10	10	10	10
BRAIN Ratio	MEAN	0.0193	0.0192	0.0191	0.0195	0.0213
	S.D.	.00155	.00190	.00158	.00219	.00168
	N	10	10	10	10	10
LIVER Ratio	MEAN	0.0483	0.0450	0.0476	0.0468	0.0477
	S.D.	.00187	.00336	.00408	.00422	.00410
	N	10	10	10	10	10
RIGHT KIDNEY Ratio	MEAN	0.0059	0.0059	0.0060	0.0059	0.0061
	S.D.	.00035	.00048	.00033	.00034	.00047
	N	10	10	10	10	10
LEFT KIDNEY Ratio	MEAN	0.0058	0.0059	0.0058	0.0057	0.0059
	S.D.	.00033	.00053	.00041	.00030	.00035
	N	10	10	10	10	10

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

TABLE 26 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ORGAN WEIGHT TO BODY WEIGHT RATIO

FEMALES	GROUP	DOSE LEVEL (PPM)	DOSE LEVEL (PPM)					V
			I	II	III	IV	V	
FINAL BODY WEIGHT	MEAN	g	71	78	74	78	63	
	S.D.		6.7	9.2	10.5	11.6	4.2	
	N		10	10	10	10	10	
ADRENALS Ratio	MEAN		0.0003	0.0003	0.0003	0.0003	0.0003	
	S.D.		.00006	.00005	.00006	.00005	.00005	
	N		10	10	10	10	10	
BRAIN Ratio	MEAN		0.0213	0.0199	0.0202	0.0186*	0.0218	
	S.D.		.00239	.00184	.00193	.00218	.00124	
	N		10	10	10	10	10	
LIVER Ratio	MEAN		0.0458	0.0437	0.0457	0.0490	0.0466	
	S.D.		.00292	.00251	.00534	.00489	.00655	
	N		10	10	10	10	10	
RIGHT KIDNEY Ratio	MEAN		0.0060	0.0057	0.0061	0.0059	0.0062	
	S.D.		.00062	.00046	.00047	.00033	.00057	
	N		10	10	10	10	10	
LEFT KIDNEY Ratio	MEAN		0.0060	0.0057	0.0059	0.0057	0.0061	
	S.D.		.00080	.00035	.00057	.00046	.00054	
	N		10	10	10	10	10	

Statistical key: * = p<0.05

TABLE 26 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ORGAN WEIGHT TO BRAIN WEIGHT RATIO

MALES	DOSE LEVEL (PPM)	GROUP	I					II					III					IV					V				
			MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	MEAN	S.D.	N	
FINAL BODY WEIGHT	g		81	8.2	10	83	10.5	10	82	7.6	10	82	7.6	10	78	10.5	10	78	10.5	10	78	10.5	10	68**	6.4	10	
ADRENALS Ratio			0.0116	.00211	10	0.0146*	.00177	10	0.0148*	.00378	10	0.0148*	.00378	10	0.0141	.00146	10	0.0141	.00146	10	0.0141	.00146	10	0.0150*	.00278	10	
LIVER Ratio			2.5179	.27451	10	2.3749	.35316	10	2.5228	.41054	10	2.5228	.41054	10	2.4519	.49709	10	2.4519	.49709	10	2.4519	.49709	10	2.2560	.30948	10	
RIGHT KIDNEY Ratio			0.3075	.03040	10	0.3145	.05629	10	0.3146	.01946	10	0.3146	.01946	10	0.3092	.05219	10	0.3092	.05219	10	0.3092	.05219	10	0.2851	.02513	10	
LEFT KIDNEY Ratio			0.2998	.03171	10	0.3120	.05785	10	0.3065	.02335	10	0.3065	.02335	10	0.2961	.04122	10	0.2961	.04122	10	0.2961	.04122	10	0.2757	.01419	10	

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

TABLE 26 - F1 GENERATION

A RANGE-FINDING DEVELOPMENTAL/REPRODUCTIVE TOXICITY STUDY
IN RATS VIA WHOLE BODY INHALATION EXPOSURE
ORGAN WEIGHT TO BRAIN WEIGHT RATIO

FEMALES	DOSE LEVEL (PPM)	GROUP				
		I	II	III	IV	V
FINAL BODY WEIGHT g		71	78	74	78	63
MEAN		6.7	9.2	10.5	11.6	4.2
S.D.		10	10	10	10	10
N		10	10	10	10	10
ADRENALS Ratio		0.0130	0.0153	0.0135	0.0151	0.0143
MEAN		.00267	.00270	.00265	.00321	.00195
S.D.		10	10	10	10	10
N		10	10	10	10	10
LIVER Ratio		2.1667	2.2243	2.2878	2.6875**	2.1409
MEAN		.16055	.30846	.43545	.48900	.30146
S.D.		10	10	10	10	10
N		10	10	10	10	10
RIGHT KIDNEY Ratio		0.2839	0.2919	0.3006	0.3249	0.2855
MEAN		.02263	.04202	.02002	.04580	.02585
S.D.		10	10	10	10	10
N		10	10	10	10	10
LEFT KIDNEY Ratio		0.2809	0.2874	0.2923	0.3131	0.2812
MEAN		.02562	.03364	.02066	.04817	.02228
S.D.		10	10	10	10	10
N		10	10	10	10	10

Statistical key: * = p<0.05

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		Chamber Monitoring Results				Appendix A					
Gestation Day	Date	Exposure Number	Chamber Concentration		Particle Size Determinations		Chamber Environment				
			Daily Mean (mg/L)	Miran (IR)	MMAD (µm)	GSD	TMC (mg/m ³)	Daily Mean Temperature (°C)	Humidity (%)		
										Individual Concentrations (mg/L)	
6	22-Sep-98	1	0.00	0.0	0.0	0.0	0.6985	1.504	3.25E-03	22	62
7	23-Sep-98	2	0.00	0.0	0.0	0.0	1.723	1.796	7.05E-04	23	47
8	24-Sep-98	3	0.00	0.0	0.0	0.0	10.10	2.354	2.62E-03	22	46
9	25-Sep-98	4	0.00	0.0	0.0	0.0	1.116	1.772	7.86E-04	20	59
10	26-Sep-98	5	0.00	0.0	0.0	0.0	0.7030	1.622	8.19E-03	21	59
11	27-Sep-98	6	0.00	0.0	0.0	0.0	0.6830	1.524	6.90E-03	22	62
12	28-Sep-98	7	0.00	0.0	0.0	0.0	1.111	2.611	9.32E-04	22	52
13	29-Sep-98	8	0.00	0.0	0.0	0.0	6.533	2.671	1.05E-03	22	46
14	30-Sep-98	9	0.00	0.0	0.0	0.0	0.8892	1.859	9.08E-04	21	51
15	1-Oct-98	10	0.00	0.0	0.0	0.0	5.374	2.111	9.28E-04	22	55
16	2-Oct-98	11	0.00	0.0	0.0	0.0	1.902	2.241	5.69E-04	21	38
17	3-Oct-98	12	0.00	0.0	0.0	0.0	1.838	2.037	8.14E-04	21	45
18	4-Oct-98	13	0.00	0.0	0.0	0.0	12.86	2.386	3.33E-03	21	52
19	5-Oct-98	14	0.00	0.0	0.0	0.0	5.481	2.619	1.10E-03	20	52
			Mean ^a :	0.00 ^b		3.644		2.079	2.29E-03	21	52
			SD ^a :	0.00		3.901		-	2.43E-03	0.9	7.1

^aMean and standard deviation of the values presented from Exposure Day 1 to 14

^bMean and standard deviation of the individual concentrations from Exposure Day 1 to 14

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

		Chamber Monitoring Results				Appendix A					
Lactation Period	Date	Exposure Number	Chamber Concentration			Particle Size Determinations		Chamber Environment			
			Daily Mean (mg/L)	Miran (IR)		MMAD (µm)	GSD	TMC (mg/m ³)	Daily Mean Temperature (°C)	Humidity (%)	
				Individual Concentrations (mg/L)							
			Group 1 - 0.0 mg/L								
	11-Oct-98	15	0.00	0.0	0.0	0.0	3.332	2.387	7.24E-04	20	54
	12-Oct-98	16	0.00	0.0	0.0	0.0	2.472	2.145	1.05E-03	21	51
	13-Oct-98	17	0.00	0.0	0.0	0.0	5.800	2.319	2.72E-03	21	50
	14-Oct-98	18	0.00	0.0	0.0	0.0	2.963	2.233	5.31E-03	22	50
	15-Oct-98	19	0.00	0.0	0.0	0.0	4.324	2.355	1.11E-03	22	47
	16-Oct-98	20	0.00	0.0	0.0	0.0	1.758	2.317	1.49E-03	21	45
	17-Oct-98	21	0.00	0.0	0.0	0.0	1.619	2.189	1.75E-03	20	46
	18-Oct-98	22	0.00	0.0	0.0	0.0	1.782	3.406	5.31E-03	21	49
	19-Oct-98	23	0.00	0.0	0.0	0.0	1.345	1.772	1.07E-03	21	47
	20-Oct-98	24	0.00	0.0	0.0	0.0	2.289	2.053	1.14E-03	21	44
	21-Oct-98	25	0.00	0.0	0.0	0.0	1.964	1.973	5.98E-04	21	41
	22-Oct-98	26	0.00	0.0	0.0	0.0	4.072	1.984	1.03E-03	21	38
	23-Oct-98	27	0.00	0.0	0.0	0.0	8.193	2.719	1.67E-03	23	38
	24-Oct-98	28	0.00	0.0	0.0	0.0	1.115	1.847	1.05E-03	23	43
	25-Oct-98	29	0.00	0.0	0.0	0.0	1.523	2.115	1.40E-03	23	40
	26-Oct-98	30	0.00	0.0	0.0	0.0	1.325	1.819	3.12E-03	23	46
	27-Oct-98	31	0.00	0.0	0.0	0.0	6.074	2.215	2.70E-03	23	50
	28-Oct-98	32	0.00	0.0	0.0	0.0	1.018	2.226	2.41E-03	22	51
	29-Oct-98	33	0.00	0.0	0.0	0.0	5.481	1.723	1.81E-03	22	41
	30-Oct-98	34	0.00	0.0	0.0	0.0	8.035	1.572	1.56E-02	22	37
	31-Oct-98	35	0.00	0.0	0.0	0.0	11.22	1.525	1.67E-02	22	36
	1-Nov-98	36	0.00	0.0	0.0	0.0	15.22	1.666	1.25E-02	22	40
	2-Nov-98	37	0.00	0.0	0.0	0.0	8.431	1.996	6.57E-03	22	37
	3-Nov-98	38	0.00	0.0	0.0	0.0	15.42	1.896	1.09E-02	22	32
	4-Nov-98	39	0.00	0.0	0.0	0.0	13.74	1.669	8.67E-03	22	31
	5-Nov-98	40	0.00	0.0	0.0	0.0	1.510	1.838	5.18E-04	21	32
			Mean ^a :	0.00 ^b			5.078	2.075	4.19E-03	22	43
			SD ^a :	0.00			4.502	-	4.76E-03	0.9	6.5
			Mean ^c :	0.00 ^b			4.576	2.077	3.53E-03	22	46
			SD ^c :	0.00			4.306	-	4.17E-03	0.9	7.9

^aMean and standard deviation of the values presented from Exposure Day 15 to 40.

^bMean and standard deviation of the individual concentrations from Exposure Day 15 to 40.

^cMean and standard deviation of the entire study (Exposure Days 1 to 40).

^dMean and standard deviation of the individual concentrations of the entire study (Exposure Days 1 to 40).

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

		Chamber Monitoring Results										Appendix A	
Gestation Day	Date	Exposure Number	Chamber Concentration				Particle Size Determinations				Chamber Environment		
			Miran (IR)		Nominal (mg/L)	MMAD (µm)	GSD	TMC (mg/m ³)	Daily Mean Temperature (°C)	Humidity (%)			
			Daily Mean (mg/L)	Individual Concentrations (mg/L)									
6	22-Sep-98	1	0.518	0.52	0.52	0.51	0.53	0.7332	2.178	4.55E-03	21	70	
7	23-Sep-98	2	0.523	0.44	0.58	0.54	0.54	3.084	2.187	1.45E-03	23	54	
8	24-Sep-98	3	0.543	0.57	0.53	0.54	0.53	4.625	2.243	1.48E-03	21	55	
9	25-Sep-98	4	0.525	0.56	0.52	0.52	0.50	11.56	2.537	3.46E-03	20	64	
10	26-Sep-98	5	0.523	0.52	0.53	0.52	0.50	0.7017	1.503	8.09E-03	20	66	
11	27-Sep-98	6	0.470	0.48	0.46	0.48	0.46	0.6788	1.293	6.71E-03	21	69	
12	28-Sep-98	7	0.525	0.53	0.53	0.51	0.53	0.8313	1.859	7.23E-04	21	60	
13	29-Sep-98	8	0.513	0.56	0.50	0.49	0.50	1.281	1.876	5.35E-04	21	49	
14	30-Sep-98	9	0.498	0.49	0.51	0.50	0.49	0.7721	2.156	7.74E-04	21	52	
15	1-Oct-98	10	0.538	0.55	0.53	0.54	0.53	2.277	1.797	6.10E-04	21	55	
16	2-Oct-98	11	0.503	0.48	0.52	0.51	0.50	1.054	2.212	7.37E-03	21	42	
17	3-Oct-98	12	0.513	0.54	0.52	0.50	0.49	2.676	1.906	1.11E-03	21	46	
18	4-Oct-98	13	0.493	0.49	0.50	0.48	0.50	1.778	1.198	5.26E-04	21	53	
19	5-Oct-98	14	0.518	0.53	0.52	0.52	0.50	1.593	2.044	7.53E-04	21	51	
			Mean ^a :	0.514 ^b				2.396	1.928	2.72E-03	21	56	
			SD ^a :	0.027				2.872	-	2.80E-03	0.7	8.5	

^aMean and standard deviation of the values presented from Exposure Day 1 to 14

^bMean and standard deviation of the individual concentrations from Exposure Day 1 to 14

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

Chamber Monitoring Results												Appendix A		
Lactation Period	Date	Exposure Number	Chamber Concentration				Particle Size Determinations			Chamber Environment				
			Daily Mean (mg/L)	Miran (fR)			MMAD (µm)	GSD	TMC (mg/m ³)	Temperature (°C)	Humidity (%)			
				Individual Concentrations (mg/L)								Nominal (mg/L)		
	11-Oct-98	15	0.523	0.56	0.51	0.52	0.50	6.009	2.426	2.00E-03	19	55		
	12-Oct-98	16	0.530	0.53	0.53	0.53	0.53	7.132	2.148	3.97E-03	19	53		
	13-Oct-98	17	0.520	0.55	0.52	0.51	0.50	2.516	2.151	1.84E-03	20	52		
	14-Oct-98	18	0.505	0.52	0.52	0.52	0.46	6.335	2.846	6.24E-03	21	52		
	15-Oct-98	19	0.520	0.52	0.53	0.53	0.50	4.836	2.287	1.86E-03	21	49		
	16-Oct-98	20	0.510	0.48	0.52	0.53	0.51	12.52	2.654	5.14E-03	21	45		
	17-Oct-98	21	0.530	0.55	0.55	0.50	0.52	8.983	2.902	4.29E-03	21	45		
	18-Oct-98	22	0.503	0.50	0.49	0.48	0.54	0.7807	1.643	3.91E-03	21	47		
	19-Oct-98	23	0.508	0.49	0.52	0.53	0.49	2.304	2.216	1.23E-03	21	46		
	20-Oct-98	24	0.500	0.50	0.47	0.54	0.49	4.814	2.080	2.21E-03	22	44		
	21-Oct-98	25	0.525	0.53	0.52	0.52	0.53	2.881	2.205	9.97E-04	22	42		
	22-Oct-98	26	0.523	0.54	0.53	0.52	0.52	1.847	1.872	3.50E-04	21	39		
	23-Oct-98	27	0.513	0.52	0.52	0.51	0.50	1.656	1.924	1.13E-03	22	37		
	24-Oct-98	28	0.503	0.50	0.51	0.50	0.50	7.049	2.057	6.57E-03	22	40		
	25-Oct-98	29	0.658	1.2	0.44	0.46	0.53	3.704	2.111	3.11E-03	22	39		
	26-Oct-98	30	0.505	0.44	0.53	0.53	0.52	8.279	2.500	8.47E-03	22	43		
	27-Oct-98	31	0.505	0.57	0.47	0.50	0.48	3.249	2.481	2.04E-03	22	44		
	28-Oct-98	32	0.523	0.48	0.55	0.53	0.53	1.112	2.077	2.90E-03	21	46		
	29-Oct-98	33	0.510	0.51	0.49	0.52	0.52	6.087	1.706	1.19E-03	21	41		
	30-Oct-98	34	0.493	0.50	0.50	0.48	0.49	9.630	1.637	1.54E-02	21	37		
	31-Oct-98	35	0.500	0.49	0.50	0.50	0.51	10.37	1.634	8.35E-03	22	37		
	1-Nov-98	36	0.508	0.53	0.51	0.50	0.49	11.77	1.810	6.62E-03	22	39		
	2-Nov-98	37	0.508	0.52	0.46	0.54	0.51	11.34	2.205	5.63E-03	22	38		
	3-Nov-98	38	0.520	0.54	0.52	0.52	0.50	5.668	1.977	2.89E-03	22	33		
	4-Nov-98	39	0.498	0.50	0.49	0.51	0.49	5.611	1.701	1.52E-03	22	23		
	5-Nov-98	40	0.503	0.50	0.51	0.50	0.50	9.511	1.821	3.62E-03	21	33		
			Mean ^a :	0.517 ^b			0.51			6.000	2.118	3.98E-03	21	42
			SD ^a :	0.072			0.01			3.488	-	3.27E-03	0.9	7.1
			Mean ^c :	0.516 ^d			0.51			4.738	2.052	3.54E-03	21	47
			SD ^c :	0.060			0.02			3.685	-	3.14E-03	0.8	10.1

^aMean and standard deviation of the values presented from Exposure Day 15 to 40.

^bMean and standard deviation of the individual concentrations from Exposure Day 15 to 40.

^cMean and standard deviation of the entire study (Exposure Days 1 to 40).

^dMean and standard deviation of the individual concentrations of the entire study (Exposure Days 1 to 40).
MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

Chamber Monitoring Results													Appendix A	
Gestation Day	Date	Exposure Number	Chamber Concentration						Particle Size Determinations			Chamber Environment		
			Miran (IR)		Nominal (mg/L)	TMC (mg/m ³)	MMAD (µm)	GSD	Temperature (°C)	Humidity (%)				
			Daily Mean (mg/L)	Individual Concentrations (mg/L)										
6	22-Sep-98	1	0.990	1.0	0.97	0.98	1.0	1.0	0.7011	1.397	3.65E-03	21	71	
7	23-Sep-98	2	1.06	0.92	1.1	1.1	1.1	1.1	9.526	2.209	3.17E-03	23	57	
8	24-Sep-98	3	1.01	1.1	1.0	0.95	1.0	1.0	1.696	1.761	5.95E-04	21	58	
9	25-Sep-98	4	1.08	1.2	1.1	1.0	1.0	1.0	0.9660	1.545	6.21E-04	20	66	
10	26-Sep-98	5	0.993	1.0	1.0	0.97	0.96	0.96	0.7071	1.950	8.22E-03	20	67	
11	27-Sep-98	6	0.990	1.0	1.0	1.0	0.96	1.0	0.6839	1.349	7.03E-03	21	69	
12	28-Sep-98	7	1.05	1.1	1.1	1.0	1.0	1.0	6.616	2.588	1.90E-03	20	62	
13	29-Sep-98	8	1.08	1.2	1.1	1.0	1.0	1.1	1.994	1.920	8.50E-04	21	48	
14	30-Sep-98	9	0.975	1.0	1.0	0.96	0.94	0.98	0.9630	1.847	9.27E-04	21	51	
15	1-Oct-98	10	1.10	1.2	1.1	1.1	1.0	1.1	2.098	1.667	1.54E-03	21	53	
16	2-Oct-98	11	0.995	1.0	1.0	1.0	0.98	0.96	1.050	2.068	1.29E-02	21	44	
17	3-Oct-98	12	1.10	1.2	1.1	1.1	1.0	1.0	6.153	2.237	2.42E-03	21	48	
18	4-Oct-98	13	0.963	0.99	0.97	0.92	0.97	0.95	2.537	2.188	9.51E-04	21	52	
19	5-Oct-98	14	1.08	1.2	1.1	1.0	1.0	1.0	1.101	1.982	6.90E-04	21	51	
			Mean ^a :	1.03 ^b				1.0	2.628	1.908	3.25E-03	21	57	
			SD ^a :	0.07				0.1	2.760	-	3.67E-03	0.7	8.7	

^aMean and standard deviation of the values presented from Exposure Day 1 to 14

^bMean and standard deviation of the individual concentrations from Exposure Day 1 to 14

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

		Chamber Monitoring Results										Appendix A	
Lactation Period	Date	Exposure Number	Chamber Concentration				Particle Size Determinations				Chamber Environment		
			Miran (IR)				Nominal (mg/L)	MMAD (µm)	GSD	TMC (mg/m ³)	Daily Mean Temperature (°C)	Humidity (%)	
			Daily Mean (mg/L)	Individual Concentrations (mg/L)									
Group III - 1.0 mg/L													
	10-Oct-98	15	1.05	1.1	1.1	1.0	1.0	1.0	2.413	1.814	7.26E-04	18	53
	11-Oct-98	16	1.03	1.1	1.0	1.0	1.0	1.0	2.864	2.121	1.30E-03	18	54
	12-Oct-98	17	1.03	1.1	1.0	1.0	1.0	1.0	2.864	2.410	1.65E-03	18	53
	13-Oct-98	18	1.13	1.2	1.1	1.1	1.1	1.1	1.230	2.085	9.60E-04	19	53
	14-Oct-98	19	0.983	1.0	0.98	0.96	0.99	0.96	1.817	1.760	2.80E-03	19	52
	15-Oct-98	20	1.10	1.2	1.2	1.0	1.0	1.0	3.867	2.305	2.04E-03	20	50
	16-Oct-98	21	1.02	1.1	1.0	1.0	0.99	0.99	4.251	2.306	3.55E-03	21	44
	17-Oct-98	22	0.993	1.0	1.0	0.97	1.0	0.96	8.385	2.812	5.93E-03	21	45
	18-Oct-98	23	0.955	0.97	0.93	0.98	0.94	0.93	0.7738	1.788	3.39E-03	21	47
	19-Oct-98	24	1.10	1.2	1.1	1.1	1.0	1.0	4.365	2.282	2.02E-03	20	46
	20-Oct-98	25	1.01	1.1	1.0	0.95	1.0	1.0	5.048	2.143	1.75E-03	21	43
	21-Oct-98	26	1.08	1.1	1.1	1.1	1.0	1.1	5.686	1.971	3.07E-03	21	42
	22-Oct-98	27	1.02	1.1	1.0	1.0	0.97	0.98	10.21	2.054	2.19E-03	21	39
	23-Oct-98	28	1.15	1.2	1.2	1.1	1.1	1.1	3.464	1.939	1.77E-03	22	37
	24-Oct-98	29	0.988	1.0	1.0	1.0	0.95	0.97	4.492	2.676	2.66E-03	22	40
	25-Oct-98	30	1.24	2.1	0.95	0.97	0.95	0.99	2.016	2.125	1.86E-03	23	38
	26-Oct-98	31	1.01	1.1	0.99	1.0	0.96	0.94	1.171	2.558	2.70E-03	22	42
	27-Oct-98	32	1.05	1.1	1.1	1.0	1.0	1.0	6.986	2.475	2.15E-03	22	43
	28-Oct-98	33	0.998	1.0	1.0	1.0	0.99	0.98	13.50	3.325	6.03E-03	21	44
	29-Oct-98	34	1.13	1.2	1.1	1.1	1.1	1.1	8.196	1.813	2.36E-03	21	38
	30-Oct-98	35	1.00	1.0	1.0	1.0	1.0	0.99	7.247	1.898	4.36E-03	21	37
	31-Oct-98	36	0.993	1.0	0.99	0.98	1.0	0.98	8.194	1.618	5.87E-03	22	36
	1-Nov-98	37	1.13	1.2	1.1	1.1	1.1	1.1	8.798	2.238	1.56E-03	22	39
	2-Nov-98	38	0.993	1.0	0.99	1.0	0.98	1.0	6.039	2.228	2.91E-03	22	37
	3-Nov-98	39	1.01	1.1	0.96	0.99	0.99	1.0	11.15	1.998	4.06E-03	22	34
	4-Nov-98	40	0.998	1.0	1.0	1.0	0.99	1.0	5.178	1.637	3.73E-03	22	33
	5-Nov-98	41	0.990	0.96	1.0	1.0	1.0	1.0	4.323	2.005	9.72E-04	21	33
			Mean ^a :	1.04 ^b				1.0	5.353	2.162	2.75E-03	21	43
			SD ^a :	0.12				0.0	3.268	-	1.48E-03	1.4	6.5
			Mean ^c :	1.04 ^d				1.0	4.422	2.075	2.92E-03	21	48
			SD ^c :	0.11				0.0	3.336	-	2.42E-03	1.2	10.0

^aMean and standard deviation of the values presented from Exposure Day 15 to 40.
^bMean and standard deviation of the individual concentrations from Exposure Day 15 to 40.
^cMean and standard deviation of the entire study (Exposure Days 1 to 40).
^dMean and standard deviation of the individual concentrations of the entire study (Exposure Days 1 to 40).
 MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

Chamber Monitoring Results												Appendix A	
Gestation Day	Date	Exposure Number	Chamber Concentration						Particle Size Determinations			Chamber Environment	
			Miran (IR)						MMAD (µm)	GSD	TMC (mg/m ³)	Temperature (°C)	Humidity (%)
			Daily Mean (mg/L)	Individual Concentrations (mg/L)									
Group IV - 3.0 mg/L													
6	22-Sep-98	1	3.10	3.2	3.1	3.1	3.0	2.9	0.7160	1.786	3.95E-03	21	71
7	23-Sep-98	2	3.05	2.8	3.2	3.2	3.0	2.9	1.985	1.699	8.13E-04	22	54
8	24-Sep-98	3	2.95	3.0	3.0	2.9	2.9	2.7	3.251	2.364	1.20E-03	21	55
9	25-Sep-98	4	3.05	3.1	3.3	2.9	2.9	2.6	1.058	1.846	7.58E-04	20	64
10	26-Sep-98	5	3.60	3.9	3.7	3.4	3.4	2.7	0.7063	1.599	8.72E-03	20	64
11	27-Sep-98	6	2.80	2.7	2.7	2.9	2.9	2.8	0.6932	1.381	7.70E-03	20	69
12	28-Sep-98	7	2.90	2.8	2.9	2.9	3.0	2.8	3.190	2.564	1.34E-03	20	61
13	29-Sep-98	8	2.95	2.8	3.0	3.0	3.0	3.0	8.522	2.355	3.11E-03	20	48
14	30-Sep-98	9	2.95	3.0	3.0	2.9	2.9	2.9	1.033	2.277	1.02E-03	20	51
15	1-Oct-98	10	3.00	3.0	3.0	3.1	2.9	2.8	2.433	1.965	4.74E-03	20	54
16	2-Oct-98	11	3.05	2.9	3.1	3.1	3.1	2.9	0.9448	1.606	9.21E-03	20	41
17	3-Oct-98	12	3.05	3.0	3.1	3.1	3.0	2.8	5.618	2.350	2.17E-03	20	46
18	4-Oct-98	13	3.15	3.1	3.2	3.2	3.1	3.0	1.585	2.161	6.57E-04	20	52
19	5-Oct-98	14	3.10	2.9	3.3	3.1	3.1	3.0	4.777	2.369	1.64E-03	19	51
			Mean ^a :	3.05 ^b					2.8	2.608	3.36E-03	20	56
			SD ^a :	0.21					0.1	2.312	3.08E-03	0.7	8.8

^aMean and standard deviation of the values presented from Exposure Day 1 to 14

^bMean and standard deviation of the individual concentrations from Exposure Day 1 to 14

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

		Chamber Monitoring Results										Appendix A		
Lactation Period	Date	Exposure Number	Chamber Concentration						Nominal (mg/L)		Particle Size Determinations		Chamber Environment	
			Miran (IR)						Nominal (mg/L)	MMAD (µm)	GSD	TMC (mg/m ³)	Temperature (°C)	Humidity (%)
			Daily Mean (mg/L)	Individual Concentrations (mg/L)										
	10-Oct-98	15	3.00	3.0	3.0	3.0	3.0	2.8	1.486	1.961	3.36E-04	18	54	
	11-Oct-98	16	3.10	3.2	3.1	3.1	3.0	2.9	1.625	2.079	6.83E-04	18	55	
	12-Oct-98	17	3.05	3.0	3.2	3.0	3.0	2.8	5.730	2.489	2.10E-03	19	53	
	13-Oct-98	18	3.05	3.1	3.1	3.0	3.0	2.8	1.130	1.822	9.22E-04	18	52	
	14-Oct-98	19	3.05	3.0	3.1	3.1	3.0	2.8	12.90	2.281	1.63E-02	17	52	
	15-Oct-98	20	2.98	2.8	3.0	3.1	3.0	2.9	2.607	1.930	1.47E-03	20	49	
	16-Oct-98	21	3.08	3.1	3.1	3.1	3.0	2.9	5.104	2.265	3.87E-03	18	44	
	17-Oct-98	22	3.00	3.0	3.0	3.0	3.0	2.9	1.340	2.251	2.42E-03	17	45	
	18-Oct-98	23	3.05	3.0	3.0	3.1	3.1	3.0	0.7653	1.367	3.47E-03	16	48	
	19-Oct-98	24	3.08	3.0	3.1	3.2	3.0	3.0	4.166	2.281	1.67E-03	16	46	
	20-Oct-98	25	3.10	3.1	3.1	3.1	3.1	3.0	5.077	2.080	2.12E-03	22	43	
	21-Oct-98	26	2.98	2.9	3.0	3.0	3.0	2.9	1.375	1.979	4.92E-04	22	41	
	22-Oct-98	27	3.03	2.9	3.1	3.1	3.0	2.9	6.175	2.044	1.18E-03	22	39	
	23-Oct-98	28	3.08	3.0	3.1	3.1	3.1	3.0	5.825	2.518	1.86E-03	22	37	
	24-Oct-98	29	3.00	2.9	3.2	3.0	2.9	3.0	5.679	2.387	3.46E-03	22	40	
	25-Oct-98	30	3.03	2.8	3.1	3.1	3.1	3.1	1.007	1.853	1.16E-03	22	38	
	26-Oct-98	31	3.10	3.0	3.2	3.1	3.1	2.9	1.007	1.988	2.55E-03	22	43	
	27-Oct-98	32	3.08	3.0	3.1	3.1	3.1	2.9	6.985	2.508	2.27E-03	22	44	
	28-Oct-98	33	3.00	3.0	3.0	3.0	3.0	2.8	1.239	2.297	2.84E-03	22	46	
	29-Oct-98	34	3.03	3.0	3.1	3.0	3.0	2.9	2.506	1.729	4.49E-04	21	39	
	30-Oct-98	35	3.05	3.0	3.0	3.1	3.1	2.9	5.196	1.985	2.14E-03	21	37	
	31-Oct-98	36	3.05	3.1	3.1	3.0	3.0	2.8	5.133	1.757	1.89E-03	21	36	
	1-Nov-98	37	3.00	3.0	3.0	3.0	3.0	2.9	9.120	1.945	3.52E-03	21	40	
	2-Nov-98	38	3.00	3.0	3.0	3.0	3.0	2.9	8.817	2.161	4.44E-03	22	37	
	3-Nov-98	39	3.00	3.0	3.0	3.0	3.0	3.0	7.853	1.838	6.44E-03	21	33	
	4-Nov-98	40	3.03	2.8	3.1	3.1	3.1	3.1	11.07	1.994	2.28E-03	21	33	
	5-Nov-98	41	3.10	3.1	3.1	3.1	3.1	3.1	7.014	2.187	9.63E-04	21	32	
			Mean ^a :	3.04 ^b					2.9	4.738	2.073	2.71E-03	20	43
			SD ^a :	0.08					0.1	3.340	-	3.04E-03	2.1	6.7
			Mean ^c :	3.04 ^d					2.9	4.011	2.056	2.93E-03	20	47
			SD ^c :	0.14					0.1	3.168	-	3.03E-03	1.7	9.7

^aMean and standard deviation of the values presented from Exposure Day 15 to 40.
^bMean and standard deviation of the individual concentrations from Exposure Day 15 to 40.
^cMean and standard deviation of the entire study (Exposure Days 1 to 40).
^dMean and standard deviation of the individual concentrations of the entire study (Exposure Days 1 to 40).
 MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

Chamber Monitoring Results												Appendix A	
Gestation Day	Date	Exposure Number	Chamber Concentration					Particle Size Determinations			Chamber Environment		
			Group V - 5.0 mg/L					MMAD (µm)	GSD	TMC (mg/m ³)	Temperature (°C)	Humidity (%)	
			Daily Mean (mg/L)	Miran (IR) Individual Concentrations (mg/L)									Nominal (mg/L)
6	22-Sep-98	1	4.93	5.0	4.9	4.9	4.9	4.9	0.6989	1.337	3.78E-03	21	70
7	23-Sep-98	2	4.98	4.9	5.0	5.0	4.9	4.9	3.741	2.061	1.27E-03	23	44
8	24-Sep-98	3	4.93	5.0	5.0	4.8	4.8	5.7	1.668	1.932	7.81E-04	21	45
9	25-Sep-98	4	5.18	5.2	5.5	5.0	5.0	4.8	0.9745	1.744	7.33E-04	20	61
10	26-Sep-98	5	5.05	5.0	5.2	5.0	5.0	4.8	0.7269	2.113	9.86E-03	20	61
11	27-Sep-98	6	4.93	4.8	4.9	5.1	4.9	4.9	0.7068	1.874	8.54E-03	21	67
12	28-Sep-98	7	5.00	5.0	5.0	5.0	5.0	5.0	1.237	2.157	8.79E-04	21	55
13	29-Sep-98	8	5.00	5.0	5.0	5.0	5.0	4.9	1.607	1.993	7.79E-04	21	48
14	30-Sep-98	9	4.95	4.9	5.0	5.0	4.9	5.0	1.082	2.089	1.08E-03	21	53
15	1-Oct-98	10	5.10	5.2	5.2	5.0	5.0	4.9	2.118	1.723	4.96E-03	21	59
16	2-Oct-98	11	5.05	5.0	5.1	5.1	5.0	4.8	0.9235	1.386	3.80E-03	21	38
17	3-Oct-98	12	5.05	5.2	5.0	5.0	5.0	4.9	8.228	2.479	2.01E-03	21	45
18	4-Oct-98	13	5.03	5.0	5.1	5.0	5.0	4.8	2.454	2.110	9.91E-04	21	54
19	5-Oct-98	14	5.03	5.1	5.0	5.0	5.0	4.9	11.58	2.224	4.51E-03	21	52
			Mean ^a :	5.01 ^b				5.0	2.696	1.944	3.14E-03	21	54
			SD ^b :	0.1096				0.2	3.233	-	2.99E-03	0.7	9.2

^aMean and standard deviation of the values presented from Exposure Day 1 to 14

^bMean and standard deviation of the individual concentrations from Exposure Day 1 to 14

MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

		Chamber Monitoring Results										Appendix A	
Lactation Period	Date	Exposure Number	Chamber Concentration			Particle Size			Chamber Environment				
			Miran (IR)		Nominal (mg/L)	Determinations		Temperature (°C)	Humidity (%)				
			Daily Mean (mg/L)	Individual Concentrations (mg/L)		MMAD (µm)	GSD			TMC (mg/m ³)			
				Group V - 5.0 mg/L									
	11-Oct-98	15	5.03	5.0	5.1	5.0	5.0	4.9	4.761	2.166	1.66E-03	19	56
	12-Oct-98	16	5.18	5.2	5.1	5.2	5.2	5.0	6.436	2.063	4.17E-03	19	54
	13-Oct-98	17	5.10	5.4	5.0	5.0	5.0	4.8	1.865	2.026	1.26E-03	20	52
	14-Oct-98	18	5.03	4.9	5.1	5.0	5.1	4.8	1.906	2.016	2.83E-03	21	51
	15-Oct-98	19	5.03	5.0	5.0	5.1	5.0	4.8	3.912	2.231	2.02E-03	21	47
	16-Oct-98	20	5.00	5.0	5.0	5.0	5.0	4.8	11.21	2.892	3.98E-03	21	46
	17-Oct-98	21	5.03	4.9	5.2	5.1	4.9	4.9	1.575	2.458	2.92E-03	21	47
	18-Oct-98	22	5.00	5.0	5.0	5.0	5.0	4.9	0.8275	2.565	4.87E-03	21	50
	19-Oct-98	23	4.98	5.0	5.0	4.9	5.0	4.9	3.033	2.155	2.08E-03	21	47
	20-Oct-98	24	5.03	5.0	5.0	5.1	5.0	4.9	4.988	2.226	2.19E-03	21	45
	21-Oct-98	25	5.05	5.0	5.1	5.1	5.0	4.9	11.92	2.438	2.58E-03	22	42
	22-Oct-98	26	5.13	5.2	5.1	5.1	5.1	4.9	5.423	1.790	1.85E-03	22	38
	23-Oct-98	27	5.18	5.2	5.2	5.2	5.1	5.0	6.401	2.126	3.34E-03	23	38
	24-Oct-98	28	5.13	5.2	5.4	5.0	4.9	4.9	4.202	2.252	2.70E-03	23	42
	25-Oct-98	29	5.00	4.9	5.1	5.1	4.9	5.1	1.910	2.280	1.80E-03	23	41
	26-Oct-98	30	5.25	5.3	5.1	5.4	5.2	4.8	2.507	2.778	4.27E-03	23	46
	27-Oct-98	31	5.20	5.2	5.3	5.1	5.2	4.9	1.526	2.069	1.29E-03	23	49
	28-Oct-98	32	5.20	5.2	5.2	5.2	5.2	4.9	0.9241	1.644	1.87E-03	22	49
	29-Oct-98	33	5.30	5.3	5.3	5.3	5.3	4.9	12.88	1.568	1.18E-02	22	40
	30-Oct-98	34	5.08	5.1	5.1	5.1	5.0	4.8	10.15	1.670	7.68E-03	21	37
	31-Oct-98	35	5.13	5.1	5.2	5.2	5.0	4.9	11.22	1.501	8.82E-03	21	36
	1-Nov-98	36	4.98	5.0	5.0	5.0	4.9	4.9	4.775	2.107	2.12E-03	21	41
	2-Nov-98	37	4.98	4.9	5.0	5.0	5.0	5.0	6.398	2.172	4.12E-03	22	37
	3-Nov-98	38	5.00	5.0	5.0	5.0	5.0	5.0	18.11	1.797	1.29E-02	22	31
	4-Nov-98	39	4.88	4.9	5.0	4.8	4.8	5.0	6.538	1.777	3.42E-03	21	31
	5-Nov-98	40	4.98	4.9	5.0	5.0	5.0	5.2	1.776	1.927	5.64E-04	21	30
			Mean ^a :	5.07 ^b					4.92	5.661	3.81E-03	21	43
			SD ^a :	0.13					0.10	4.436	3.13E-03	1.1	7.1
			Mean ^c :	5.05 ^d					4.93	4.623	3.58E-03	21	47
			SD ^c :	0.12					0.15	4.260	3.06E-03	1.0	9.3

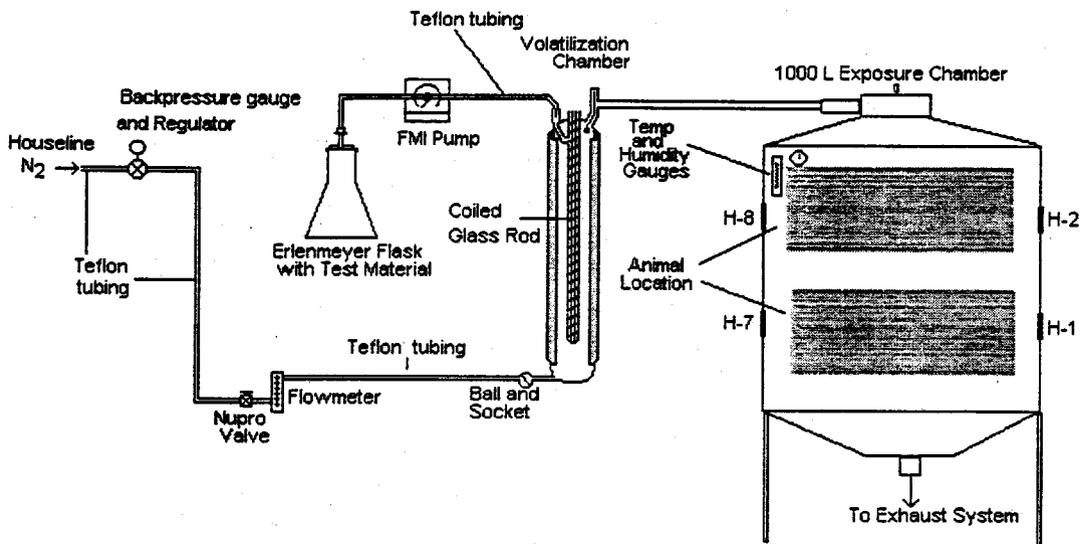
^aMean and standard deviation of the values presented from Exposure Day 15 to 40.

^bMean and standard deviation of the individual concentrations from Exposure Day 15 to 40.

^cMean and standard deviation of the entire study (Exposure Days 1 to 40).

^dMean and standard deviation of the individual concentrations of the entire study (Exposure Days 1 to 40).
MMAD = mass median aerodynamic diameter; GSD = geometric standard deviation, TMC = total mass concentration.

	Chamber Generation System and Whole-Body Exposure Chamber	Appendix A
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Notes

The Group I generation system only utilized the nitrogen flow set-up which went directly to the turret of the exposure chamber. The volatilization chamber and FMI pump were not used.

The H-12 and H-14 sampling ports are located on the opposition side of the chamber.