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Submitting Organization		
SHELL OIL CO		
Contractor		
Document Title		
ANALYSIS OF WASTE WATER SAMPLES & INHALATION REPRODUCTION RANGE-FINDING STUDY IN MATED RATS WITH C9 AROMATIC HYDROCARBONS WITH COVER LETTER DATED 051089		
Chemical Category		
1,1,1-TRICHLOROETHANE (71-55-6)		

CONTAINS NO CBI

Shell Oil Company

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

EPA-OTS

0006175185

86-890000228

May 10, 1989

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Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

SUBJECT: TSCA SECTION 8(D), HEALTH AND SAFETY DATA REPORTING

As required by Toxic Substances Control Act, Section 8(d), Shell is submitting copies of health and safety studies as outlined in 40 CFR 716. Two reports are enclosed (Report Numbers 382 and 383). Each individual study is accompanied by a cover page as requested under 716.7(b). An index is also enclosed which includes the study title, date, specific chemical substance, CAS number, and Shell's report reference number for ease of future identification. Report Number 382 contains confidential information, and, therefore, two copies are enclosed and marked as required by 716.55.

Sincerely,

J. C. Willett
Manager, Product Safety and Compliance
Oil and Chemical Products
Health, Safety and Environment

JWH/jll

Enclosures

INDEX OF HEALTH AND SAFETY STUDIES SUBMITTED TO EPA
SORTED BY SUBMISSION NUMBER

SUB. NO.	TITLE	RPT. DATE	CHEMICAL	CAS NUMBER	SHELL REF.
382	ANALYSIS OF WASTE WATER SAMPLES. I - DEER PARK MANUFACTURING C OMPLEX CHEMICAL PLANT.	770900	TRICHLOROETHANE, 1,1,1-	000071-55-6	WRC TPR 108-77
			CHLOROFORM	000067-66-3	
			DICHLORO-1,2-ETHANE	000107-06-2	
			ACETONITRILE	000075-05-8	
			TOLUENE	000108-88-3	
			ISOBUTYL ALCOHOL	000078-83-1	
			ETHYLBENZENE	000100-41-4	
			XYLENE	001330-20-7	
			EPICHLOROHYDRIN	000106-89-8	
			CUMENE	000098-82-8	
383	INHALATION REPRODUCTION RANGE-FINDING STUDY IN MATED RATS WITH C9 AROMATIC HYDROCARBONS (FINAL REPORT).	880400	XYLENE, O-	000095-47-6	HSE-88-0129
			CUMENE	000098-82-8	
			ETHYLTOLUENE, 4-	000622-96-8	
			ETHYLTOLUENE, 2-	000611-14-3	
			TRIMETHYLBENZENE, 1,3,5-	000108-67-8	
			TRIMETHYLBENZENE, 1,2,4-	000095-63-6	
			TRIMETHYLBENZENE, 1,2,3-	000526-73-8	
			ETHYLTOLUENE, 3-	000620-14-4	

ITEMS RETRIEVED 2

REPORT NO. 332

SUBMISSION OF LISTS AND COPIES OF HEALTH AND SAFETY STUDIES

NAMES OF REQUESTED SUBSTANCES(S)	CAS NUMBER(S)
TRICHLOROETHANE, 1,1,1-	000071-55-6
CHLOROFORM	000067-66-3 - OWRS
DICHLORO-1,2-ETHANE	000107-06-2
ACETONITRILE	000075-05-8 - OWRS
TOLUENE	000108-88-3
ISOBUTYL ALCOHOL	000078-83-1
ETHYLBENZENE	000100-41-4
XYLENE	001330-20-7
EPICHLOROHYDRIN	000106-89-8
CUMENE	000098-82-8

OTHER COMPONENT(S)

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J. W. HARRISON, STAFF TECHNOLOGIST
(713) 241-0734

REPORT NO. 383

SUBMISSION OF LISTS AND COPIES OF HEALTH AND SAFETY STUDIES

NAMES OF REQUESTED SUBSTANCES(S)	CAS NUMBER(S)
XYLENE, O-	000095-47-6
CUMENE	000098-82-8
ETHYLTOLUENE, 4-	000622-96-8
ETHYLTOLUENE, 2-	000611-14-3
TRIMETHYLBENZENE, 1,3,5-	000108-67-8
TRIMETHYLBENZENE, 1,2,4-	000095-63-6
TRIMETHYLBENZENE, 1,2,3-	000526-73-8
ETHYLTOLUENE, 3-	000620-14-4

OTHER COMPONENT(S)

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American Petroleum Institute
1220 L Street, Northwest
Washington, D.C. 20005
202-682-9000

HESD Publ. No.:

Health and Environmental
Sciences Department

INHALATION REPRODUCTION RANGE FINDING STUDY IN MATED RATS WITH C9 AROMATIC HYDROCARBONS

Final Report

Study Conducted Under Contract PS-64 By:
International Research and Development Corporation
Mattawan, Michigan

April 1988

An equal opportunity employer

FOREWORD

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American Petroleum Institute
Health and Environmental Sciences Department

QUALITY ASSURANCE STATEMENT

Study Title: Inhalation Reproduction Range-Finding Study In Mated Rats with C9 Aromatic Hydrocarbons

Testing Facility Number: IRDC No. 418-035

API Product Safety Number: PS-64

This study was reviewed by API Quality Assurance personnel on the dates indicated below for compliance with applicable Good Laboratory Practice regulations.

Copies of report by API Quality Assurance personnel are available upon written request to the Director of the Health and Environmental Sciences Department of the American Petroleum Institute or his designee.

Date(s) of Inspection/Review	Type of Inspection
December 7-8, 1987	Draft Final Report Review
January 25, 1988	Data Inventory
April 15, 1988	Final Report Review and acceptance

Rodney C. Anderson, M.S.
Quality Assurance Associate

Date

MATERIAL SPECIFICATION

ASTM D3734 TYPE I

C-9 AROMATIC HYDROCARBONS

CONSCI

American Petroleum Institute
1220 L Street N.W.
Washington, D.C. 20005

February 14, 1986

Attn: Dr. C. E. Holdsworth

Certificate # : 51219001
Sample Discription : C9 Aromatic Naphtha
Date Received : December 19, 1985

CAPILLARY GAS CHROMATOGRAPHY ANALYSIS *

Component Name	Wt.%	LV.%
Total non-aromatics	< 0.10	< 0.12
C6 + C7 aromatics	0.01	0.01
m-Xylene	0.05	0.05
p-Xylene	0.02	0.02
o-Xylene	3.17	3.14
Isopropylbenzene	2.76	2.79
n-Propylbenzene	3.95	3.99
1-Methyl-3-ethylbenzene	15.85	15.98
1-Methyl-4-ethylbenzene	6.13	6.19
1,3,5-Trimethylbenzene	8.09	8.14
1-Methyl-2-ethylbenzene	5.78	5.72
1,2,4-Trimethylbenzene	39.18	39.13
tert-Butylbenzene	<0.20	<0.20 #
Isobutylbenzene	0.12	0.12
sec-Butylbenzene	0.11	0.11
1-Methyl-2-isopropylbenzene	0.01	0.01
1,2,3-Trimethylbenzene	5.49	5.35
1-Methyl-4-isopropylbenzene	0.07	0.07
Indane (2,3-Dihydroindene)	0.96	0.87
1,3-Diethylbenzene	1.16	1.18
1-Methyl-3-n-propylbenzene	0.60	0.60
1-Methyl-4-n-propylbenzene/n-Butylbenzene	0.82	0.83
1,2-Diethylbenzene	0.89	0.89
1,4-Diethylbenzene/1,3-Dimethyl-5-ethylbenzene	0.12	0.12
1-Methyl-2-n-propylbenzene	0.17	0.17
1,4-Dimethyl-2-ethylbenzene	0.48	0.48
1,3-Dimethyl-4-ethylbenzene	0.59	0.59
1,2-Dimethyl-4-ethylbenzene	2.28	2.28
1,3-Dimethyl-2-ethylbenzene	0.04	0.04
1,2-Dimethyl-3-ethylbenzene	0.23	0.22

Component Name	Wt.%	LV.%
1,2,4,5-Tetramethylbenzene	0.18	0.18
Unidentified C11 compounds	0.14	0.17
1,2,3,5-Tetramethylbenzene	0.19	0.19
5-Methylindan	0.04	0.03
Naphthalene	0.02	0.02
	100.00	100.00

* All peak ID's confirmed by GC/MS analysis.
# Quantified by GC/MS due to coelution with 1,2,4 TMB peak.

ASTM D-86 Distillation

Volume % Distilled	deg F @760mm *
IBP	320
5	322
10	323
20	324
30	325
40	326
50	327
60	328
70	329
80	331
90	335
95	339
Dry Point	3[illegible]
End Point	350
Recovered	99.0%
Residue	1.0%
Loss	0.0%

* Average of duplicate runs.

International Research
and Development Corporation
MATTAWAN, MICHIGAN, U.S.A. 49071 TELEPHONE (616) 668-3336

SPONSOR: The American Petroleum Institute

TEST ARTICLE: C_9 Aromatic Hydrocarbons

SUBJECT: Inhalation Reproduction Range-Findi
Mated Rats with C_9 Aromatic Hydrocar

DATE OF SUBMISSION: April 8, 1988

418-035

"credence through research"

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International Research and Development Corporation

I. QUALITY ASSURANCE STATEMENT

Study Title: Inhalation Reproduction Range-Finding Study in Mated Rats with C_9 Aromatic Hydrocarbons

Test Article: C_9 Aromatic Hydrocarbons

This report has been reviewed by the International Research and Development Corporation Quality Assurance Department in accordance with the United States Environmental Protection Agency Good Laboratory Practice Standards of May 2, 1984.

Approved By: Margery J. Wirth, B.S. 4/7/85
Director of Quality Assurance
Date

418-035

II. SYNOPSIS

Male and female Charles River COBS® CD® rats, randomly assigned to one control and five treatment groups of five animals per sex each were used in this inhalation reproduction range-finding study to determine dosage levels of C_9 Aromatic Hydrocarbons for a multigeneration reproduction study. Exposure concentrations of 100, 250, 500, 1,000 and 1,500 ppm were administered by whole-body inhalation exposure for five days a week, six hours per day. Exposure began 14 days prior to mating and continued until sacrifice except that females were not exposed from day 21 of gestation to day 4 of lactation. The control group was exposed to filtered air on a comparable regimen. Each male was allowed to mate with one female from the same control or treatment group, and the females were allowed to give birth. Parental females and their litters were examined daily until day 4 of lactation.

Maternal toxicity was observed at the 1,500 ppm exposure level. These effects were seen in body weight losses during lactation and a decrease in food consumption during study week 1.

Changes noted in male rats at the 1,500 ppm exposure level included reductions in body weight gains and mean and relative food consumption during most or all of the measured study weeks.

Slight reductions in offspring development were present at the 1,500 ppm exposure level as evidenced by reduced pup body weights on lactation days 0 and 4. The effects were seen in pups of both sexes.

In conclusion, when administered to male and female Charles River COBS® CD® rats at a exposure concentration of 1,500 ppm, C_9 Aromatic Hydrocarbons induced reductions in body weights in paternal animals, slight maternal toxicity and may have inhibited offspring development. Similar effects were not seen at the lower exposure levels. Based on the results of this study, exposure levels of 100, 500 and 1,500 ppm were

selected for the two-generation reproduction study with C_9 Aromatic Hydrocarbons.

III. INTRODUCTION

A. OBJECTIVE

The objective of this study was to determine the dosage levels to be employed in a multigeneration reproduction study in rats.

B. TEST ARTICLE IDENTIFICATION

The test article was received in two shipments from Experimental Pathology Laboratories, Inc., Herndon, Virginia as indicated below:

Receipt Date	IRDC Test Article Identification Number	Label	Description
July 1, 1986	8953 Drum 6	C-9 AROMATIC NAPHTHA ASTM D-3734 TYPE 1 UN-1299 FLASH 117°F EPL - 388 Additional label on container FLAMMABLE LIQUID Drum number 6 labeled as above.	clear liquid [a]6 55-gallon drums received
February 17, 1987	8953B Drum 1 Drum 2 Drum 3	C-9 AROMATIC NAPHTHA ASTM D-3734 TYPE 1 Additional information on barrel UN-1299 FLASH 117°F	clear liquid [a]6 55-gallon drums received

[a]Only portions of drum number 6 from the first shipment and drum numbers 1-3 from the second shipment were used on this study.

IV. METHODS AND PROCEDURES

This study was conducted in accordance with the protocol as approved by the Sponsor and in compliance with the Standard Operating Procedures of International Research and Development Corporation (IRDC). Procedures pertinent to this study are described herein.

A. EXPERIMENTAL DESIGN

1. Animal Receipt and Maintenance

Forty seven untreated male and forty seven untreated virgin female Sprague-Dawley derived Charles River COBS® CD® rats were received from The Charles River Breeding Laboratories, Inc., Portage, Michigan. All rats were 42-days old at receipt on April 21, 1987. Upon receipt, the animals were assigned temporary animal numbers and housed individually in suspended wire-mesh cages. During the 13-day acclimation period, the animals were carefully observed for changes in appearance and behavior. From acquisition until sacrifice, each animal was provided with basal laboratory diet of Purina® Certified Rodent Chow® #5002 and tap water available ad libitum, except during the exposure periods when diet was not available.

The basal laboratory diet was analyzed by the manufacturer for the presence of pesticides, heavy metals and aflatoxins, each diet-lot used was recorded. The drinking water at IRDC is analyzed quarterly for the presence of pesticides, heavy metals and coliforms. The results of these analyses are stored in the IRDC Archives in Mattawan, Michigan and are available upon request. The Study Director was not aware of any potential contaminants of either diet or drinking water which might have interfered with the results of this study.

When not in the exposure chambers, all animals were kept in an environmentally controlled room. Temperature ranged between 23°C and 25°C, with a mean temperature ± standard deviation of 24 ± 0.7°C; humidity ranged between 31% and 53%, with a mean humidity ± standard

deviation of 48 ± 6.2%. Fluorescent lighting provided illumination 12 hours per day. All rats were individually housed, except during mating, gestation and lactation, in suspended wire-mesh cages. During mating, males and females were cohabitated in suspended wire-mesh cages. Females were housed in plastic breeding cages with wood chip (Beta-Chip®) bedding starting gestation day 20 and during lactation. Each adult rat was identified by cage, group and individually by a Monel® metal ear tag bearing its animal number. The individual animal number plus the IRDC study number comprised a unique identification number for each animal. Each rat was assigned a unique number and ear-tagged for identification when placed on study. At study initiation (first test article exposure) the rats were 55 days of age. Male rats weighed from 230 to 262 grams and female rats weighed from 174 to 198 grams.

The study initiated on May 4, 1987 and terminated (last F_0 female sacrifice) on June 20, 1987.

2. Rationale for Selection of Species and Strain

The rat is a standard laboratory animal for reproduction studies. This laboratory has historical control data on fertility and survival indices and reproductive performance for rats of this strain and source.

B. ORGANIZATION OF TEST GROUPS

Parental male and female animals were randomly assigned to one control and five treatment groups of 5 males and 5 females each by the following method: animal numbers and their corresponding body weights were entered onto magnetic tape which was used as the data source for the randomization procedure. The mean body weight and standard deviation were calculated by sex and a computer-generated edit developed a listing of those animals whose body weights were within ± 1.5 standard deviations of the mean. From the qualifying animals, the randomization procedure selected and assigned the required number of animals. Bartlett's test

for homogeneity of variances was performed on these groups. The group variances were judged homogeneous.

C. TEST ARTICLE ADMINISTRATION

1. Animal Exposure

The selected route of administration was by whole-body inhalation exposure because this was considered the most closely equivalent to the typical route of human exposure.

Animals were exposed to the test article five days a week for a 6-hour period. Dosing began 14 days prior to mating and continued through gestation day 20 for females and until sacrifice for males. Control animals received filtered air on a comparable regimen.

The animals were exposed in six $16m^3$ stainless steel and glass exposure chambers. Each chamber was dedicated for use with one group for the duration of exposure. The animals were housed in the exposure chambers approximately 24 hours per day. During the exposure phase of the study the rats were individually housed in stainless steel wire-mesh cages. Before each daily exposure the animals were removed from the chamber, excreta pans were removed from the cage racks, the food jars were capped and excreta was removed from the chamber. The animals were then placed in the exposure chamber for the duration of the exposure. After the completion of the daily exposure, the animals were again removed from the chamber, the chambers were cleaned, excreta pans were returned, and caps on the food jars were removed. The animals were then returned to the chamber. Chamber ventilation air was provided from an HVAC system separate from the general laboratory air-handling system. Chamber airflow rate, temperature and relative humidity were recorded at approximately half-hour intervals during each day's exposure.

2. Generation of Exposure Atmospheres

The exposure atmospheres were generated with the system shown schematically in Figure 1. Nitrogen, heated to 200°C by passage through

a 1L stainless steel cylinder fitted with a 1500 watt band heater, was introduced at the bottom of a glass column 7.6 cm in diameter and 30 cm long which was packed with glass beads. The liquid test material was delivered by a fluid metering pump (FMI) from a stainless steel safety can, through Teflon® tubing, to the bottom quarter of the column. The test material was vaporized as it flowed up the column co-current with the nitrogen flow. The vapors were passed to the chamber inlet where they were diluted with chamber ventilation air to the desired exposure concentration. The operating parameters for the generation system are shown in the following table:

Chamber Number	C-4	C-9	C-11	C-10	C-12	C-3
Desired Conc. (ppm)	0	100	200	500	1,000	1,500
FMI Pump Type:	-	RPG-20-1/4	RPG-20-1/4	RPG-50-3/8	RPG-50-3/8	STX-72-3/8
FMI Pump Setting:	-	3.0	8.5	2.5	5.0	9.5
Approximate Liquid Flow Rate (ml/min):	-	2.1	5.1	9.0	17.8	27.4
Ammeter Setting for heater (amps):	-	10	10	10	10	10
Nitrogen Flow Rate (L/min):	150	150	150	150	150	150
Chamber Airflow Rate (L/min):	3200-4000	3200-4000	3200-4000	3200-4000	3200-4000	3200-4000
Ammeter Setting for heat tape (amps):	N/A	N/A	N/A	N/A	N/A	2

3. Analysis of Exposure Atmospheres

a. Nominal

A nominal exposure concentration was determined for each exposure by weighing the test material reservoir before and after each day's exposure and dividing the difference in weight by the total volume of air. The total air volume was calculated by multiplying the arithmetic mean of the half-hourly measurements of chamber flowrate by the exposure duration. The nominal concentration was converted from g/L to ppm by use of the following equation:

$$ppm = \frac{g}{L} \times \frac{R}{M} \times \frac{T}{P} \times 10^6$$

$$= g/L \times 2.06 \times 10^5$$

Where: g = weight of test material used during the exposure, in grams

L = volume of air that passed through the chamber during the exposure, in liters

R = universal gas constant, $\frac{62.36L - mm\ Hg}{mole - {}^{\circ}K}$

M = gram molecular weight of the test material, 120 g/mole

T = nominal laboratory temperature, 294 °K

P = nominal laboratory barometric pressure, 740 mm Hg

10^6 = ppm conversion factor

b. Actual

The actual exposure concentrations were monitored with a gas-phase infrared spectrophotometer (IR). Each chamber, including the control, was sampled by drawing chamber atmosphere through a Teflon® sample line, through an automatic sampling system, into the IR. The automatic sampling system allowed, by means of solenoid valves, each chamber to be sampled sequentially for approximately seven minutes of every hour. Both the automatic sampling system and the recording of actual concentrations were controlled by a Hewlett-Packard Model 2388A laboratory computer. The operating conditions for the IR were as follows.

Instrument:	Miran 1A
Wavelength:	3.44 mcm
Range:	1 Absorbance Unit Full Scale
Slit Width:	1 mm
Closed-Loop Volume:	5.64L
Pathlength Setting:	1.54
Gain Setting:	X10
Cell Pressure:	-1 psig
Meter Response Time:	10 seconds
Zero Gas:	Chamber Supply Air

The IR was calibrated by use of the closed loop technique as recommended by the manufacturer. The closed-loop calibration consisted of injections of various volumes of the test material into the closed loop. The concentration of test material in the closed loop was calculated as follows:

$$\text{conc. (ppm)} = \frac{V}{L} \times \frac{R \times T}{M} \times \frac{D}{P} \times 10^{-3} \times 10^{6}$$

$$= V \times 34.176$$

V = liquid volume of test material, in mcl

L = volume of closed loop, 5.64L

R = universal gas constant, $\frac{62.36L - mmHg}{mole - {}^{\circ}K}$

M = gram molecular weight of the test material, 120 g/mole

T = nominal laboratory temperature, 294 °K

D = density of test material, 0.868 g/ml

P = IR cell pressure, 1 psig below laboratory barometric pressure or 688 mmHg

10^{-3} = mL to mcl conversion factor

10^{6} = ppm conversion factor

The volumes of test material injected into the closed loop and the corresponding vapor concentrations are shown in the following table:

Volume of Test Material Injected (mcl)	Cumulative Injection Volume (mcl)	Vapor Concentration in Closed Loop (ppm)
1.5	1.5	51
1.5	3	103
5	8	273
5	13	444
10	23	786
10	33	1130
10	43	1470
10	53	1810

Each calibration point was replicated three times, and a standard curve of mean instrument response versus closed-loop vapor concentration was generated. Before each day's exposure the standard curve was verified by the injection of liquid test material into the closed loop at the concentrations shown in the following table:

Volume of Test Material Injected (mcl)	Cumulative Injection Volume (mcl)	Vapor Concentration in Closed Loop (ppm)
3	3	103
12	15	513
30	45	1540

If the measured concentrations for all three points were within ±10% of the actual closed-loop concentrations, the IR was considered to be in calibration.

In addition the accuracy of the analytical system was checked by the use of vapor standards prepared by vaporizing liquid test material into Tedlar® gas bags and then analyzing the bag atmosphere. The gas bag was sampled from the end of the sample line within the appropriate chamber. The concentration of the test material vapors in the gas bags were calculated as follows

[illegible]

$$ppm = \frac{V}{L} \times \frac{R \times T}{M} \times \frac{D}{P} \times 10^{-3} \times 10^{-6}$$

$$= \frac{V}{L} \times 179.2$$

Where: V = liquid volume of test material, in mcl
L = volume of air added to gas bag, in liters
R = universal gas constant, $\frac{62.36\ L\text{-}mmHg}{mole - {}^{\circ}K}$
M = gram molecular weight, 120 g/mole
T = nominal laboratory temperature, 294 °K
P = nominal laboratory barometric pressure, 740 mmHg
D = test material density, 0.868 g/ml
10^{-3} = conversion factor, ml to mcl
10^{-6} = ppm conversion factor

The gas bags were prepared as shown below:

Desired Exposure Concentration (ppm)	Bag Volume (L)	Volume of Liquid Test Material (mcl)	Calculated Bag Conc. (ppm)	Acceptable Analyzed Range (ppm)
100	100	56	100	90-110
250	100	140	251	226-276
500	100	280	502	450-550
1000	100	560	1000	900-1100
1500	100	840	1510	1350-1660

If the analyzed concentration of the gas bag was not within ±10% of the calculated concentration, a second bag was prepared and analyzed. If the second bag was also not within ± 10% of the calculated concentration, the Study Director was notified. The results of the gas bag checks are presented in Table 3.

c. Gas Chromatographic Analysis of Chamber Atmospheres

Once each day for the first five (5) exposure days and then weekly during the exposure period, the composition (on a weight percentage basis) of the test material within each exposure chamber was determined by use of gas chromatography (GC).

The compositional analysis was performed to demonstrate complete vaporization of the test material, not to define exposure concentrations.

The chamber samples for GC analysis were collected on two-stage (400 mg stage 1, 200 mg stage 2) charcoal tubes (SKC, Inc.) under the following sampling regimens:

Desired Exposure Conc. (ppm)	Sample Flow Rate (cc/min)	Sample Duration (min)	Total Volume of Sample (L)
0	200	300	60
100	200	300	60
250	200	150	30
500	200	75	15
1000	200	37	7.4
1500	200	25	5

After the samples were collected, the charcoal from each stage was placed in separate 5 cc vials. Internal Standard Solution, prepared by adding 300 mcl of styrene to a 200 ml volumetric flask and diluting to the mark with carbon disulfide, was added to each vial (4 ml for stage 1, 1 ml for stage 2). Each vial was then capped and the charcoal was allowed to desorb on a shaker for at least 150 min. Approximately 1 mcl aliquots were drawn from the vials and injected into a calibrated GC (see below for details of calibration). The ratio of the peak area for the component to peak area of internal standard was determined for the following compounds/components: o-xylene, cumene, n-propylbenzene (PB), 4-ethyltoluene (4-ET), 3-ethyltoluene (3-ET), 2-ethyltoluene (2-ET),

1,3,5-trimethylbenzene (1,3,5-TMB), 1,2,4-trimethylbenzene (1,2,4-TMB) and 1,2,3-trimethylbenzene (1,2,3-TMB). In addition, unidentified components with retention times greater than 1,2,3-TMB were defined as $\geq$C10's. The weight percent for each compound was calculated by dividing the amount of each compound by the sum of the amounts of the individually quantitated compound and multiplying by 100 minus the weight percent of the $\geq$C10's. The calculations are shown below:

$$RFy = \frac{[CM]}{[ISS]} \times \frac{AIS}{Ay} \times \frac{wt.\%yCM}{1}$$

$$Amt.\ y = \frac{Ay \times RFy \times [ISS] \times EV}{AIS}$$

$$wt.\ \% \geq C10 = \frac{\Sigma AC10}{\Sigma Ay + \Sigma AC10} \times 100$$

$$wt.\ \%\ y = \frac{Amt.\ y}{\Sigma Amt.\ y} \times (100 - wt.\ \% \geq C10)$$

Where: RFy = response factor for compound y
[CM] = concentration of calibration mixture in working standard in mg/ml
[ISS] = concentration of internal standard, 1.36 mg/ml
AIS = area of internal standard from chromatogram
Ay = area from chromatogram for an individual compound (o-xylene, cumene, PB, 1,3,5-TMB, 1,2,3-TMB, 1,2,4-TMB, 2-ET, 3-ET, 4-ET)
wt.%yCM = weight percent of individual compound y in calibration mixture
Amt. y = amount of individual compound y, in mg
EV = elution volume, 4 ml for stage 1 samples and 1 ml for stage 2 samples
wt. % $\geq$ C10 = weight percent of compounds with retention times > 1,2,3-TMB
AC10 = area from chromatogram for compounds with retention times > 1,2,3-TMB
wt. % y = weight percent of individual compound y

Both stages of the charcoal tubes were evaluated. At no time was there any evidence of breakthrough into the second stage.

The GC was calibrated with a mixture of known composition prepared to be similar to the test material.

The GC operating parameters for the charcoal tube analysis and for analysis of the neat liquid (as described above under Test Material) are shown in the following table:

Instrument:	Varian 2400 Gas Chromatograph
Column:	6' x 2mm ID glass
Packing:	5% SP-1200/1.75% Bentone 34 on 100/120 mesh supelcoport
Detector:	Flame ionization
Temperatures	
Injector:	160°C
Column:	75°C
Detector:	200°C
Gas Flow Rates	
N_2:	30 cc/min at 60 psig
H_2:	40 cc/min at 40 psig
Air:	300 cc/min at 60 psig
Electrometer Attenuation	
Setting:	16×10^{-11} A
Injection Volume:	1mcl
Integrator:	HP3388A
Chart Speed:	0.5 cm/min
Chart Display	
0-15 min	16
15-40 min	12
Threshold Setting	
0-15 min	6
15-40 min	1

The results of the GC analysis of the vapor composition of the exposure atmospheres are presented in Table 4.

D. TEST MATERIAL ANALYSIS

The composition of the test material in each drum used during the animal exposures was analyzed using methods described below. As each drum was opened (not more than two weeks before use), three 1 ml aliquots were accurately weighed into separate 50 ml volumetric flasks, diluted to the mark with internal standard solution, and then diluted again 5:10. Each solution was injected into the GC and the weight percent of each compound, including the ≥C10's was calculated as described above. The weight percents for the three aliquots were averaged and the results were reported to the Study Director before the drum was used on study. The results for all drums used on study were in agreement with the test material composition defined by the protocol, which is shown in the following table.

Compound	Weight Percent
o-xylene	3.20
cumene	2.74
n-propylbenzene	3.97
4-ethyltoluene	7.05
3-ethyltoluene	15.1
2-ethyltoluene	5.44
1,3,5 - trimethylbenzene	8.37
1,2,4 - trimethylbenzene	40.5
1,2,3 - trimethylbenzene	6.18
≥C10's	6.19
	98.74

E. MATING

After 14-days of test article exposure each male was housed with one female from the same control or treated group in wire-mesh cages for mating. All animals in the study were the same strain and source. The occurrence of copulation was determined by daily inspection for a copulatory plug or by vaginal inspection for sperm. The day that evidence of mating was detected was designated day 0 of gestation.

F. F_0 PARENTAL OBSERVATIONS

1. Appearance and Behavior

Throughout the study, both male and female rats were observed twice daily for mortality and overt changes in appearance and behavior. During treatment, all parental animals were observed weekly in detail for clinical signs of toxicity.

2. Body Weights

Individual male body weights were recorded weekly from randomization until sacrifice. Individual female body weights were recorded weekly until evidence of copulation was observed. Maternal body weights were recorded on gestation days 0, 7, 14 and 21, and lactation days 0 and 4.

3. Food Consumption

Individual male and female food consumption was recorded weekly. Maternal food consumption was recorded for the gestation day intervals 0 to 7, 7 to 14 and 14 to 21, and lactation days 0 to 4. Food consumption was not measured during mating.

G. DISPOSITION OF MALES

Upon completion of mating, all surviving parental males were examined externally, sacrificed, necropsied and discarded.

H. F_0 PARTURITION AND F_1 LITTER OBSERVATIONS

All bred females were allowed to give birth. During the period of expected parturition, the F_0 females were observed twice daily for

newborn litters. Lactation day 0 was designated as the day the entire litter was found and delivery was judged complete. The duration of gestation was calculated and any difficulties occurring at parturition were recorded. On lactation day 0, the litters were examined for litter size, stillbirths, live births and any gross anomalies. During lactation, the dams and pups were observed daily for survival and the presence of dead pups was recorded. Pups were weighed individually on lactation days 0 and 4.

Intact pups found dead during the lactation period were necropsied, examined for anomalies and discarded.

On lactation day 4, all dams were sacrificed, a gross necropsy was performed and the number of uterine implantation sites were recorded.

All surviving pups were examined externally, sacrificed and discarded on lactation day 4.

On the 25th day after separation from the male, a gross necropsy was performed on all females which failed to deliver. Any condition which would have prevented pregnancy was recorded. Uteri from females that appeared nongravid were opened and placed in 10% ammonium sulfide solution for detection of implantations[1].

All nongravid females were excluded from the summary of group mean body weight and body weight changes during gestation and lactation.

I. DATA RETENTION

All raw data, a sample of the test article and copies of the final report are retained in the Archives of International Research and Development Corporation, 500 N. Main, Mattawan, Michigan, 49071.

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[1]Kopf, R., Lorenz, D., and Salewski, E. (1964). The effects of thalidomide on the fertility of rats studied in two generations. Naunyn Schmiedebergs Arch. Pharmacol., 247:121-135.

V. RESULTS

A. MATERNAL OBSERVATIONS

1. Appearance and Behavior (Tables 6 and 7)

Survival was 100% for males and females in all study groups including the control group.

Two females at the 1,500 ppm exposure level had yellow staining on the anogenital haircoat. Similar findings were not evident in females at lesser exposure levels or males at any level. No relation to treatment was determined. No other notable findings in appearance or behavior were evident in the study groups. Some of the additional incidental findings included scabbing or matter around the eyes, hair loss, and malocclusion or malaligned incisors.

The only abnormal postmortem findings were a focus on the stomach of one high-dose female and a focus on the liver of one control female. All other necropsy findings were normal.

2. Body Weights (Tables 8 and 9)

Mean body weights of males at the 1,500 ppm exposure level were lower than control values over the three weeks of exposure. Similar effects were not evident in any of the lower treatment levels. No meaningful differences in mean body weights were noted in female rats during any study week measured.

Various fluctuations in maternal body weight change were noted among the study groups during gestation, but none occurred with sufficient regularity to be considered a meaningful treatment effect. Body weight change during lactation showed a concentration-related body weight loss at the 500, 1,000 and 1,500 ppm exposure levels. Due to the high number of nongravid animals, values at the 1,000 ppm exposure concentration were based on one animal.

3. Food Consumption (Tables 10 and 11)

Reductions in mean (g/animal/day) and relative (g/kg/day) food consumption were noted in male rats at the 1,500 ppm exposure level during most study weeks measured and in female rats at the 1,500 ppm level, study week 1. No other meaningful changes in weekly food consumption were noted in either sex.

Various slight depressions in maternal food consumption were present in high-exposure females during gestation and lactation but no consistent pattern was seen that would indicate a test article effect.

4. Gestation and Lactation (Table 12)

No meaningful effects on either male or female fertility were noted in any study group. The lowest fertility occurred at the 1,000 ppm exposure level where four out of five rats were nongravid. At both the 250 and 1,500 ppm exposure levels, only two out of five rats were nongravid. Differences in copulatory intervals were not large enough between control and treated animals to be considered meaningful. Mean gestation length and the mean numbers of liveborn and stillborn pups were comparable between treated and control animals.

Mean survival of male and female pups on lactation days 0 and 4 showed no meaningful effects attributable to the test article at any exposure level. Reductions noted at the 250 ppm exposure level were due to the total loss of one litter.

Slight depressions in mean pup body weight at birth (lactation day 0) and on lactation day 4 were present at the 1,500 ppm exposure concentration. Both male and female values were less than respective controls. Pup body weights at the 1,000 ppm exposure level were also slightly lower than in the control group but a definite effect is not clear because the data were based on only one litter. The depressed day 0 body weights noted at the 250 ppm exposure level were due to the undersized pups in one litter. These pups all died prior to lactation day 4.

No effects on pup body weights were evident at the 100 and 500 ppm exposure concentrations.

In addition to the death of one litter at the 250 ppm dosage level, one male pup each at the 0 and 250 ppm dosage level, one female pup at the 100 ppm dosage level and two female pups each at the 250 and 1500 ppm dosage levels died during lactation. At necropsy, one female at the 250 ppm dosage level was found with an interventricular septal defect of the anterior portion of the heart and a reduced retroesophageal right subclavian. No visible abnormalities were noted for any other pup which died.

5. Uterine Examinations (Table 13)

Uterine examination observations gave no indication of any treatment induced deviations in uterine implantations, postimplantation loss or the number of pups delivered.

B. EXPOSURE CONCENTRATIONS

1. Exposure Chamber Environment

The chamber environment data (airflow, temperature and relative humidity) are summarized as the mean and standard deviation of the weekly means, in the following table:

Chamber Number	Air Flow (L/min)		Temperature (°C)		Relative Humidity (%RH)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
C-4	3418	115	24	0.6	54	9.1
C-9	3772	109	23	0.5	48	6.0
C-11	3665	15	24	0.4	42	4.6
C-10	3217	32	23	0.6	47	3.1
C-12	3300	30	23	0.5	40	5.1
C-3	3683	96	23	0.5	52	5.4

The weekly means (± S.D.) for the chamber environment data are presented in Table 5.

2. Exposure Concentrations

Nominal and actual exposure concentrations for each exposure day can be found in Tables 1 and 2, and are presented in summary (mean ± S.D. of the daily nominal and the daily mean actual concentration) below:

Chamber Number	Desired Conc.	Nominal		Actual	
		Mean	S.D.	Mean	S.D.
C-4	0	Control Chamber			
C-9	100	102	3.0	102	2.7
C-11	250	246	3.6	251	3.1
C-10	500	463	8.7	487	12.8
C-12	1,000	962	31.0	1000	17.9
C-3	1,500	1355	47.4	1516	23.5

S.D. - Standard deviation

The fact that the nominal exposure concentrations were lower than the actual measured levels, particularly at the highest level, was quite unusual. After completion of the study, it was determined that calibration of the analytical instrumentation was slightly in error. Based on the gas bag calibration check data, collected a few days prior to study initiation and again toward the end of the the study, this error appeared to be somewhat less than 10%. Therefore, the actual concentrations were considered to be the best estimate of animal exposure levels.

VI. SIGNATURES

Prepared By: _____ 4/6/88
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Department of Report Writing
Date

Reviewed By: _____
Kit A. Keller, Ph.D.
Staff Teratologist, Reproduction
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Date

Reviewed By: _____ 4/7/88
James L. Schardein, M.S.
Scientific Director, Reproduction
and Teratology Division
Date

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VII. DISCUSSION AND CONCLUSION

Slight maternal toxicity was present for rats at the 1,500 ppm exposure concentration. These effects were seen in body weight losses during lactation and a decrease in food consumption during study week 1.

Changes noted in male rats included reductions in body weight gains and mean and relative food consumption during most or all of the measured study weeks in the high-dose (1,500 ppm) group.

Slight reductions in offspring development were present at the 1,500 ppm exposure level as evidenced by reduced pup body weights on lactation days 0 and 4. The effects were seen in pups of both sexes.

In conclusion, when administered to male and female Charles River COBS® CD® rats at an exposure concentration of 1,500 ppm, C_9 Aromatic Hydrocarbons induced reductions in body weight in parental animals, slight maternal toxicity and inhibited offspring development. Similar effects were not seen at the lower exposure levels.

To the best of my knowledge, there were no significant deviations from the Good Laboratory Practice Regulations which affected the quality and integrity of the study. This study was conducted in conformance with the Good Laboratory Practice Regulations. This report accurately reflects the raw data obtained during the performance of the study.

James L. Schardein, M.S.
Scientific Director, Reproduction and Teratology Division
Study Director

4/7/88
Date

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FIGURE NO. 1. SCHEMATIC DIAGRAM OF GENERATION AND EXPOSURE SYSTEM

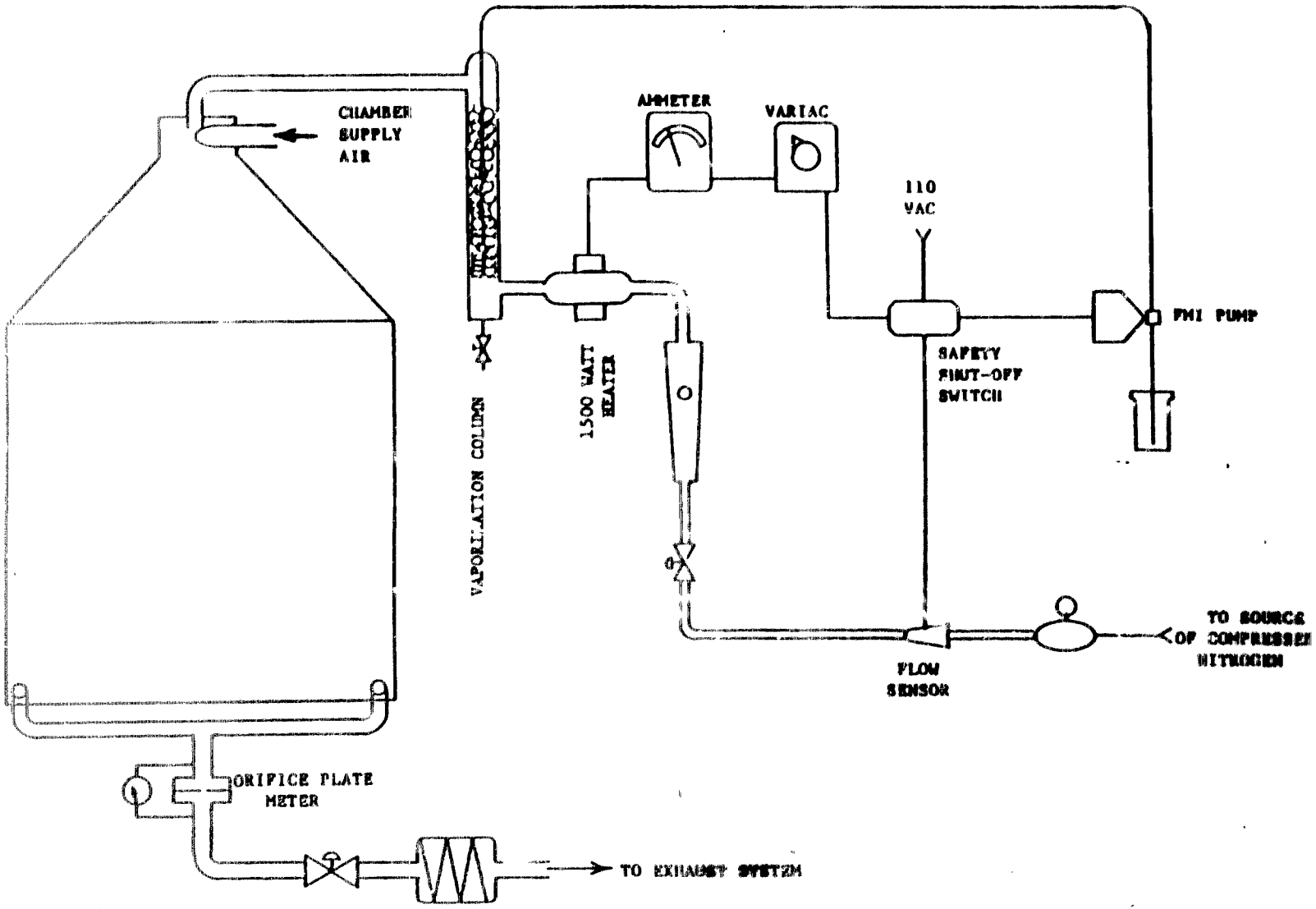

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TABLE 1. Daily Nominal Exposure Concentrations in ppm

Date	C-9	C-11	C-10	C-12	C-3
5-04-87	103	236	456	953	1280
5-05-87	102	241	469	949	1290
5-06-87	103	243	470	957	1440
5-07-87	102	244	453	819	1430
5-08-87	104	248	446	982	1360
5-11-87	106	251	470	970	1350
5-12-87	107	247	465	958	1400
5-13-87	106	252	477	959	1390
5-14-87	100	249	466	966	1400
5-15-87	101	242	466	950	1370
5-18-87	101	244	476	967	1440
5-19-87	102	245	463	959	1370
5-20-87	98	246	469	958	1360
5-21-87	100	246	467	1030	1360
5-22-87	101	246	462	965	1430
5-25-87	102	245	463	957	1380
5-26-87	101	247	461	971	1350
5-27-87	102	251	455	970	1360
5-28-87	101	249	457	975	1380
5-29-87	98	243	465	963	1320
6-01-87	98	240	461	969	1310
6-02-87	104	244	460	967	1310
6-03-87	110	250	492	972	1370
6-04-87	106	245	455	961	1350
6-05-87	108	249	458	973	1320
6-08-87	99	248	459	974	1300
6-09-87	103	249	458	965	1330
6-10-87	101	245	464	960	1280
6-11-87	-	244	455	971	1290
6-12-87	-	-	455	-	-

- - No exposure scheduled

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TABLE 2.

Daily Actual Exposure Concentrations in ppm (Mean ± Standard Deviation)

Date	C-9		C-11		C-10		C-12		C-3	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
5-04-87	104	0.5	248	0.5	492	7.2	1010	0.0	1500	44.2
5-05-87	103	5.1	247	0.4	497	2.8	997	11.6	1520	13.4
5-06-87	103	1.9	250	1.1	499	3.1	1010	4.5	1550	7.7
5-07-87	102	1.2	250	1.8	477	6.4	917	245.6	1560	14.8
5-08-87	105	1.8	253	1.2	469	2.4	1030	6.3	1580	97.3
5-11-87	107	2.0	259	1.5	509	7.5	1010	17.9	1490	10.0
5-12-87	107	1.1	254	1.5	501	2.1	1020	14.8	1480	6.3
5-13-87	105	3.0	258	2.2	507	1.4	1000	0.4	1520	14.8
5-14-87	102	5.6	254	6.0	499	12.7	1010	7.7	1500	14.8
5-15-87	102	4.6	247	2.8	498	4.5	997	11.3	1520	54.8
5-18-87	101	2.4	249	0.9	499	11.1	1010	12.0	1520	71.6
5-19-87	101	0.9	248	1.1	493	12.4	997	2.6	1510	18.4
5-20-87	99	1.9	251	0.9	496	6.7	1000	4.5	1500	15.5
5-21-87	99	2.2	252	1.3	502	1.7	1000	22.2	1510	22.8
5-22-87	100	2.9	249	1.4	492	7.3	1010	7.7	1530	43.4
5-25-87	104	1.0	252	1.0	497	4.0	1000	7.8	1570	36.1
5-26-87	101	0.6	252	2.5	482	4.9	1000	31.9	1500	17.9
5-27-87	100	1.3	254	0.9	481	4.2	1000	0.0	1500	34.1
5-28-87	99	1.3	252	1.1	479	6.6	1000	6.3	1530	31.6
5-29-87	98	2.3	249	2.9	492	1.1	1000	0.4	1520	35.7
6-01-87	98	2.4	246	1.1	484	4.3	1000	22.8	1490	13.4
6-02-87	103	3.2	246	3.9	483	6.3	997	2.9	1510	11.8
6-03-87	102	2.4	251	1.3	460	52.2	991	18.1	1500	53.3
6-04-87	107	3.5	250	0.9	474	13.0	1000	0.4	1560	45.0
6-05-87	106	3.5	252	1.0	475	6.8	1000	0.6	1500	21.0
6-08-87	99	2.8	252	1.8	484	9.8	999	2.0	1490	21.9
6-09-87	102	1.3	252	2.8	477	6.2	1000	10.0	1510	21.4
6-10-87	101	2.6	251	1.0	482	4.2	996	2.4	1530	26.5
6-11-87	-	-	250	1.0	473	12.4	1000	15.3	1500	23.2
6-12-87	-	-	-	-	464	8.6	-	-	-	-

S.D. - Standard deviation
- - No exposure scheduled

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TABLE 3. Gas Bag Checks of Analytical System

Date	Calculated Concentration (ppm)	Instrument Response (MV)	Measured Concentration (ppm)	% of Calculated Concentration
4-29-87	100	77.7	98	98
4-29-87	250	151.7	244	98
4-29-87	500	381.9	529	106
4-29-87	1000	592.8	1080	108
4-29-87	1510	988.3	1630	108
6-03-87	100	77.0	97	97
6-03-87	250	165.6	267	107
6-03-87	500	394.2	548	110
6-04-87	1000	596.7	1080	108
6-05-87	1510	998.9	1650	109

TABLE 4. Gas Chromatographic Analysis of Chamber Atmospheres (wt. %)

Chamber	Compound	Date Sample Collected 5-4-87	5-5-87	5-6-87	5-7-87	5-8-87	5-11-87
C-9 (100 ppm desired)	o-xylene	3.17	3.16	3.13	3.17	3.17	3.15
	cumene	2.83	2.81	2.80	2.82	2.83	2.81
	NPB	4.08	4.05	4.07	4.08	4.08	4.07
	4ET	7.31	7.27	7.30	7.27	7.31	7.29
	3ET	15.6	15.5	15.5	15.5	15.6	15.5
	2ET	5.40	5.39	5.40	5.40	5.40	5.39
	1,3,5 TMB	8.31	8.30	8.31	8.30	8.33	8.28
	1,2,4 TMB	40.5	40.7	40.7	40.7	40.6	40.6
	1,2,3 TMB	5.93	5.93	5.91	5.94	5.91	5.97
	≥C10's	6.86	6.89	6.89	6.84	6.78	6.93
C-11 (250 ppm desired)	o-xylene	*	3.16	3.16	3.16	3.15	3.15
	cumene	*	2.83	2.82	2.84	2.81	2.82
	NPB	*	4.07	4.07	4.07	4.09	4.06
	4ET	*	7.30	7.31	7.31	7.30	7.27
	3ET	*	15.5	15.5	15.5	15.5	15.5
	2ET	*	5.41	5.42	5.41	5.40	5.41
	1,3,5 TMB	*	8.31	8.32	8.31	8.32	8.29
	1,2,4 TMB	*	40.6	40.5	40.4	40.7	40.5
	1,2,3 TMB	*	5.97	5.96	5.95	5.94	5.99
	≥C10's	*	6.84	6.87	7.09	6.80	7.06
C-10 (500 ppm desired)	o-xylene	*	3.18	3.18	3.17	3.17	3.17
	cumene	*	2.82	2.83	2.83	2.82	2.85
	NPB	*	4.08	4.07	4.08	4.08	4.10
	4ET	*	7.31	7.29	7.31	7.29	7.34
	3ET	*	15.5	15.5	15.5	15.5	15.5
	2ET	*	5.40	5.40	5.41	5.41	5.41
	1,3,5 TMB	*	8.31	8.29	8.31	8.30	8.31
	1,2,4 TMB	*	40.5	40.5	40.6	40.6	40.4
	1,2,3 TMB	*	5.96	5.99	5.95	5.96	5.97
	≥C10's	*	6.91	7.04	6.78	6.83	6.93
C-12 (1,000 ppm desired)	o-xylene	3.14	3.15	3.15	3.15	3.[illegible]	3.17
	cumene	2.82	2.83	2.80	2.82	2.81	2.85
	NPB	4.07	4.09	4.08	4.09	4.08	4.10
	4ET	7.32	7.34	7.33	7.32	7.30	7.31
	3ET	15.6	15.6	15.6	15.5	15.5	15.6
	2ET	5.39	5.40	5.41	5.39	5.41	5.41
	1,3,5 TMB	8.30	8.28	8.33	8.28	8.32	8.32
	1,2,4 TMB	40.9	40.8	40.8	40.6	40.5	40.5
	1,2,3 TMB	5.92	5.94	5.95	5.94	5.96	5.92
	≥C10's	6.55	6.53	6.56	6.84	6.94	6.80
C-3 (1,500 ppm desired)	o-xylene	3.17	3.18	3.19	3.19	3.18	3.17
	cumene	2.82	2.83	2.83	2.83	2.[illegible]	2.85
	NPB	4.08	4.09	4.09	4.09	4.[illegible]	4.08
	4ET	7.30	7.32	7.32	7.32	7.31	7.30
	3ET	15.5	15.6	15.6	15.5	15.5	15.6
	2ET	5.40	5.41	5.41	5.42	5.41	5.42
	1,3,5 TMB	8.32	8.32	8.33	8.33	8.32	8.28
	1,2,4 TMB	40.6	40.6	40.7	40.6	40.6	40.5
	1,2,3 TMB	5.95	5.92	5.93	5.97	5.95	5.95
	≥C10's	6.83	6.73	6.65	6.79	6.81	6.90

418-035 *Samples collected, but analytical results were unreliable

TABLE 4. Cont. Gas Chromatographic Analysis of Chamber Atmospheres (wt. %) - Continued

Chamber	Compound	Date Sample Collected 5-18-87	5-26-87	6-1-87	6-8-87
C-9 (100 ppm desired)	o-xylene	3.15	3.19	3.14	3.13
	cumene	2.82	2.85	2.83	2.81
	NPB	4.06	4.10	4.08	4.08
	4ET	7.27	7.31	7.30	7.27
	3ET	15.6	15.7	15.6	15.6
	2ET	9.39	9.42	9.40	9.40
	1,3,5 TMB	8.29	8.32	8.31	8.32
	1,2,4 TMB	40.7	40.7	40.6	40.8
	1,2,3 TMB	5.93	5.92	5.89	5.89
	>C10's	6.84	6.57	6.84	6.71
C-11 (250 ppm desired)	o-xylene	3.17	3.17	3.19	[illegible]
	cumene	2.84	2.85	2.84	[illegible]
	NPB	4.08	4.08	4.07	4.06
	4ET	7.29	7.28	7.30	7.28
	3ET	15.6	15.6	15.6	15.6
	2ET	9.41	9.42	9.41	9.41
	1,3,5 TMB	8.31	8.32	8.32	8.31
	1,2,4 TMB	40.5	40.5	40.5	40.6
	1,2,3 TMB	5.93	5.96	5.94	5.96
	>C10's	6.87	6.88	6.81	6.81
C-10 (500 ppm desired)	o-xylene	3.16	3.17	3.17	3.17
	cumene	2.79	2.82	2.83	2.82
	NPB	4.07	4.06	4.08	4.06
	4ET	7.27	7.25	7.28	7.27
	3ET	15.5	15.5	15.6	15.6
	2ET	9.40	9.40	9.40	9.40
	1,3,5 TMB	8.27	8.29	8.30	8.30
	1,2,4 TMB	40.7	40.6	40.6	40.6
	1,2,3 TMB	5.96	5.96	5.94	5.92
	>C10's	6.87	6.92	6.78	6.85
C-12 (1,000 ppm desired)	o-xylene	3.17	3.18	3.16	3.23
	cumene	2.83	2.83	2.82	2.88
	NPB	4.09	4.07	4.07	4.12
	4ET	7.29	7.27	7.27	[illegible]
	3ET	15.6	15.6	15.6	15.8
	2ET	9.42	9.42	9.40	9.41
	1,3,5 TMB	8.32	8.31	8.30	[illegible]
	1,2,4 TMB	40.6	40.6	40.7	40.4
	1,2,3 TMB	5.91	5.95	5.94	5.84
	>C10's	6.82	6.85	6.74	6.69
C-3 (1,500 ppm desired)	o-xylene	3.18	3.17	3.16	3.15
	cumene	2.84	2.84	2.84	2.84
	NPB	4.09	4.09	4.07	[illegible]
	4ET	7.29	7.29	7.27	7.29
	3ET	15.6	15.6	15.6	15.6
	2ET	9.40	9.39	9.40	9.42
	1,3,5 TMB	[illegible]	8.30	8.31	8.32
	1,2,4 TMB	[illegible]	40.5	40.6	40.7
	1,2,3 TMB	5.93	5.90	5.92	[illegible]
	>C10's	6.86	6.94	6.81	6.65

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The data for this table can be found on the indicated pages of Book No. 3-1 for Study No. 418-037

TABLE 5. Weekly Mean Chamber Environment Data

Monday Date	Chamber Number	Temp. (°C) Mean	Temp. (°C) S.D.	Relative Humidity (%) Mean	Relative Humidity (%) S.D.	Chamber-Air Flow Rate (LPM) Mean	Chamber-Air Flow Rate (LPM) S.D.
5-4-87	C-4	24	0.8	55	10.7	3390	164
	C-9	23	0.4	40	1.9	3630	152
	C-10	23	0.5	45	3.9	3180	68
	C-3	23	0.7	51	5.8	3570	161
	C-11	24	0.5	41	6.8	3670	82
	C-12	23	0.4	39	7.5	3270	99
5-11-87	C-4	24	1.2	56	7.6	3410	51
	C-9	23	0.4	47	7.0	3750	117
	C-10	22	0.8	46	3.8	3260	19
	C-3	22	1.8	53	9.6	3640	89
	C-11	24	0.8	42	5.1	3650	77
	C-12	22	0.8	40	6.0	3330	32
5-18-87	C-4	24	0.4	68	7.9	3270	18
	C-9	23	0.4	57	5.6	3900	31
	C-10	22	0.6	52	3.6	3240	15
	C-3	22	0.5	61	6.5	3610	96
	C-11	23	0.4	50	5.3	3690	25
	C-12	22	0.4	48	5.3	3330	16
5-25-87	C-4	25	1.3	58	8.6	3350	72
	C-9	22	2.4	51	4.8	3880	32
	C-10	23	1.7	48	2.4	3220	24
	C-3	23	1.7	54	5.5	3690	49
	C-11	24	1.6	45	4.0	3670	33
	C-12	23	1.6	42	4.1	3310	21
6-01-87	C-4	24	1.3	43	8.4	3490	132
	C-9	22	1.3	43	9.1	3670	149
	C-10	23	1.1	44	4.4	3180	110
	C-3	23	1.3	45	9.8	3770	86
	C-11	24	1.3	39	7.4	3650	135
	C-12	23	1.2	35	7.6	3260	104
6-08-87*	C-4	23	1.3	43	11.6	3600	18
	C-9	22	1.4	48	12.4	3800	70
	C-10	24	0.5	44	4.8	3220	15
	C-3	23	0.9	49	14.6	3820	85
	C-11	24	0.2	37	8.0	3600	38
	C-12	23	0.5	34	9.2	3300	26

*The chambers were only operated for 4 days during this week

418-035 S.D. - Standard deviation

Temp. - Temperature

TABLE 6. Summary of Antemortem and Necropsy Observations - Males

Observation	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)											
	0 (Control)		100		250		500		1,000		1,500	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Number of animals observed	5	-	5	-	5	-	5	-	5	-	5	-
No visible abnormalities[a]	4	80	5	100	3	60	5	100	5	100	3	60
Antemortem Observations												
Matter eye	1	20			1	20						
Scabbing					1	20					1	20
Staining											1	20
Incisors misaligned												
Necropsy Observations												
Gross lesions	5	100	5	100	5	100	5	100	3	100	4	80
Broken incisors											1	20

[a]Includes animals with no visible abnormalities during the entire observation period

No. - Number
% - Percent based on number of animals at beginning of observation period
- - Not applicable

4.8-0.55

TABLE [illegible]

Summary of Maternal Antemortem and Necropsy Observations - Females

Observation	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)											
	0 (Control)		100		250		500		1,000		1,500	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Number of animals observed	5	-	5	-	5	-	5	-	5	-	5	-
No visible abnormalities[a]	4	80	3	60	2	40	2	40	3	60	1	20
Antemortem Observations												
Hair loss	1	20	2	40	3	60	3	60	1	20	2	40
Staining											2	40
Matter eye			1	20								
Scabbing											1	20
Eye closed			1	20								
Malocclusion											1	20
Toe missing									1	20		
Necropsy Observations												
No gross lesions	4	80	5	100	5	100	5	100	5	100	4	80
Stomach, focus											1	20
Liver, focus	1	20										

[a]Includes animals with no visible abnormalities during the entire observation period

No. - Number
% - Percent based on number of animals at beginning of observation period
- - Not applicable

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TABLE 8. Summary of Weekly Body Weight Values (g) - Males

Week of Study	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)																	
	0 (Control)			100			250			500			1,000			1,200		
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N
0	245	8.8	5	244	13.4	5	248	9.3	5	247	10.0	5	249	7.8	5	246	5.3	5
1	298	18.0	5	282	36.9	5	308	21.5	5	309	14.2	5	306	12.6	5	276	8.0	5
2	340	26.6	5	320	23.9	5	351	23.0	5	350	15.7	5	344	22.9	5	311	12.5	5
3	376	36.1	5	364	33.5	5	391	32.0	5	386	16.7	5	377	28.9	5	343	11.6	5

S.D. - Standard deviation
N - Number of animals

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TABLE B. Cont.

Summary of Weekly Body Weight Values (g) - Females

Week of Study	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)																	
	0 (Control)			100			250			500			1,000			1,500		
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N
0	183	2.2	5	187	7.8	5	192	2.9	5	185	6.4	5	182	6.9	5	188	7.5	5
1	206	7.8	5	216	11.5	5	219	5.3	5	197	17.2	5	203	4.1	5	208	9.6	5
2	227	12.3	5	234	11.6	5	239	8.1	5	222	10.6	5	218	10.3	5	232	12.5	5

S.D. - Standard deviation
N - Number of animals

TABLE 9. Summary of Group Mean Maternal Body Weights and Body Weight Changes During Gestation and Lactation

Day of Gestation	Group Mean Maternal Body Weights (grams)					
	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)					
	0 (Control)	100	250	500	1,000	1,500
	Mean	Mean	Mean	Mean	Mean	Mean
0	228	239	252	225	228	250
7	263	270	276	258	250	286
14	298	305	319	285	286	305
21	356	372	383	360	321	376
Day of Lactation						
0	283	276	305	272	270	299
4	284	292	309	264	241	239
Days of Gestation	Group Mean Maternal Body Weight Change (grams)[a]					
0 to 7	35	30	25	33	22	36
7 to 14	35	36	43	28	36	20
14 to 21	68	67	64	75	35	71
Days of Lactation						
0 to 4	1	16	4	-8	-29	-60

[a]Values represent the mean of the individual changes in maternal body weight for these intervals

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TABLE 10.

Summary of Food Consumption Values - Males

	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)														
	0 (Control)					100					250				
Week of Study	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N
1	24.4	3.67	89.8	15.64	5	23.7	6.10	83.0	12.19	5	25.3	4.90	81.5	10.70	5
2	25.0	2.63	73.4	2.50	5	27.5	4.04	83.2	7.57	5	26.2	3.38	74.5	5.11	5

S.D. - Standard deviation
N - Number of animals

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TABLE 10. Cont.

Summary of Food Consumption Values - Males

	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)														
	500					1,000					1,200				
Week of Study	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N
1	24.2	2.02	77.6	6.00	5	23.5	2.35	76.8	6.48	5	20.3	3.27	73.3	11.72	5
2	25.3	1.45	72.2	5.31	5	24.6	1.47	71.5	2.93	5	22.1	2.06	70.9	4.71	5

S.D. - Standard deviation
N - Number of animals

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TABLE 10. Cont.

Summary of Food Consumption Values - Females

	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)														
	0 (Control)					100					250				
Week of Study	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N
1	16.8	0.90	81.6	3.32	5	17.7	1.12	82.0	3.89	5	16.3	0.73	74.4	3.47	5
2	18.6	1.60	83.6	3.25	5	16.7	5.09	71.8	23.48	5	18.6	8.46	76.6	33.00	5

S.D. - Standard deviation
N - Number of animals

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TABLE 10. Cont.

Summary of Food Consumption Values - Females

	Aromatic Hydrocarbons (Desired Concentration) (ppm)														
	500					1,000					1,500				
Week of Study	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N	g/ animal/ day	S.D.	g/ kg/ day	S.D.	N
1	15.4	0.72	78.5	4.73	5	15.3	2.64	75.0	11.53	5	12.7	5.86	61.8	29.00	5
2	18.3	0.76	82.7	6.69	5	17.7	2.42	81.0	7.87	5	17.9	1.62	76.9	3.93	5

S.D. - Standard deviation
N - Number of animals

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Day of Gestation	0 (control) g/animal/day	S.D.	g/kg/day	S.D.	N	100 g/animal/day	S.D.	g/kg/day	S.D.	N	250 g/animal/day	S.D.	g/kg/day	S.D.	N
0-7	22.5	1.93	85.6	4.74	4	23.9	2.33	83.5	6.51	5	23.9	2.79	86.5	9.37	3
7-14	23.4	0.99	78.6	2.92	4	23.8	4.00	77.8	7.27	5	25.7	2.39	80.5	5.47	3
14-21	25.4	1.86	69.6	7.39	4	21.6	6.30	57.5	11.07	5	27.4	1.38	71.9	6.66	3
0-21	23.8	1.13	65.1[a]	5.09	4	23.1	3.27	62.0[a]	2.93	5	25.7[a]	1.44	67.2[a]	3.79	3
Day of Lactation															
0-4	30.9	3.53	110.7	23.81	4	37.5	7.85	127.6	17.14	5	24.5	5.97	78.9	14.80	3

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S.D. - Standard deviation
N - Number of animals
[a]0-21 day g/kg/day food consumption = $\frac{\text{total food consumed (days 0-21)}}{\text{day 21 body weight}}$ /21 (days)

TABLE 11. Cont. Summary of Maternal Food Consumption Values During Gestation and Lactation

	C_9 Aromatic Hydrocarbons (Desired Concentration) (ppm)														
	500					1,000					1,500				
Day of Gestation	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N	g/animal/day	S.D.	g/kg/day	S.D.	N
0- 7	24.6	7.16	96.0	20.67	4	18.7	-	74.9	-	1	22.2	2.41	77.7	4.59	3
7-14	22.8	1.57	80.1	7.81	4	20.0	-	69.9	-	1	24.7	1.03	81.7	10.00	3
14-21	25.5	1.32	70.8	1.89	4	22.4	-	69.9	-	1	27.6	2.14	73.3	4.41	3
0-21	24.3	2.87	67.4[a]	7.40	4	20.4	-	63.5[a]	-	1	24.8	1.78	65.9[a]	2.52	3
Day of Lactation															
0- 4	29.9	4.17	113.4	10.17	4	24.0	-	99.6	-	1	23.4	5.13	97.3	12.32	3

S.D. - Standard deviation
N - Number of animals
- Not applicable
[a]0-21 day g/kg/day food consumption = $\frac{\text{total food consumed (days 0-21)}}{\text{day 21 body weight}}$ /21 (days)

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TABLE 12. Summary of Gestation and Lactation Data - F_0 Dams, F_1 Pups

Test Article, Desired Conc. (ppm)	Female Fertility Index: Gravid Females Total Females Mated		Male Fertility Index: Fertile Males Total Males Mated		Mean Gestation Length (days)	Mean No. Dead Pups at Day 0		Mean No. Live Pups at Day 4		Pup Survival Index (Lactation Days) 0: No. Live Pups at Day 0 / Total Born, Male		Female		4: No. Live Pups at Day 4 / No. Live Pups at Day 0, Male		Female	
						M	F	M	F	No.	%	No.	%	No.	%	No.	%
Polycyclic Aromatic Hydrocarbons																	
0 (Control)	4/5	80.0	4/5	80.0	20.8	0.3	0.0	7.5	4.3	30/31	96.8	17/17	100.0	30/30	100.0	17/17	100.0
100	5/5	100.0	5/5	100.0	21.0	0.0	0.2	6.8	7.0	34/34	100.0	35/36	97.2	34/34	100.0	34/35	97.1
250	3/5	60.0	3/5	60.0	21.0	0.3	0.3	5.7	7.0	17/18	94.4	21/22	95.5	9/17	52.9	13/21	61.9
500	4/5	80.0	4/5	80.0	21.0	0.0	0.0	7.0	6.0	28/28	100.0	24/24	100.0	28/28	100.0	24/24	100.0
1,000	1/5	20.0	1/5	20.0	21.0	0.0	0.0	5.0	6.0	5/5	100.0	6/6	100.0	5/5	100.0	6/6	100.0
1,500	3/5	60.0	3/5	60.0	21.0	0.0	0.3	6.7	7.0	20/20	100.0	21/22	95.5	20/20	100.0	20/21	95.2

	Copulatory Interval (days) Mean	Copulatory Index: Total Females Mated / Total Females Paired	%	Group Mean Body Weight (grams) of Live Pups During Lactation (Lactation Days) 0 Mean M	F	4 Mean M	F
0 (Control)	2.3	5/5	100.0	6.6[a]	6.2	11.2	10.6
100	2.8	5/5	100.0	6.6	6.2	10.7	10.3
250	2.7	5/5	100.0	5.8	5.5	12.4	11.7
500	3.5	5/5	100.0	6.5	6.4	10.4	10.1
1,000	4.0	5/5	100.0	6.3	6.1	10.3	9.5
1,500	3.0	5/5	100.0	6.2	6.0	9.7	9.3

[a]Does not include data from litter with alsexed pup

No. - Number
Conc. - Concentration

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TABLE 13. Summary of Group Mean Uterine Observations on Lactation Day 4

Test Article Desired Concentration (ppm)	Number of Implantation Sites Mean	Number of Pups Delivered Mean	Number Remaining Sites[a] Mean
C_9 Aromatic Hydrocarbons			
0 (Control)	14	12	2
100	15	14	1
250	14	13	1
500	14	13	1
1,000	12	11	1
1,500	14	14	0

[a]Implantation sites not corresponding to delivered pups; values represent postimplantation loss and/or complete cannibalization

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APPENDIX A

Individual Experimental Data

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Record of Fate - Males

Test Article, Desired Concentration, Male Number	Age at Start of Study (weeks)	Fate	Death Date	Study Week	Age at Death (weeks)
0 ppm (Control):					
27162	8	SS	5-27-87	4	12
27163	8	SS	5-27-87	4	12
27164	8	SS	5-27-87	4	12
27165	8	SS	5-27-87	4	12
27166	8	SS	5-27-87	4	12
C_9 Aromatic Hydrocarbons 100 ppm:					
27167	8	SS	5-27-87	4	12
27168	8	SS	5-27-87	4	12
27169	8	SS	5-27-87	4	12
27170	8	SS	5-27-87	4	12
27171	8	SS	5-27-87	4	12
C_9 Aromatic Hydrocarbons 250 ppm:					
27172	8	SS	5-27-87	4	12
27173	8	SS	5-27-87	4	12
27174	8	SS	5-27-87	4	12
27175	8	SS	5-27-87	4	12
27176	8	SS	5-27-87	4	12
C_9 Aromatic Hydrocarbons 500 ppm:					
27177	8	SS	5-27-87	4	12
27178	8	SS	5-27-87	4	12
27179	8	SS	5-27-87	4	12
27180	8	SS	5-27-87	4	12
27181	8	SS	5-27-87	4	12
C_9 Aromatic Hydrocarbons 1,000 ppm:					
27182	8	SS	5-27-87	4	12
27183	8	SS	5-27-87	4	12
27184	8	SS	5-27-87	4	12
27185	8	SS	5-27-87	4	12
27186	8	SS	5-27-87	4	12
C_9 Aromatic Hydrocarbons 1,500 ppm:					
27187	8	SS	5-27-87	4	12
27188	8	SS	5-27-87	4	12
27189	8	SS	5-27-87	4	12
27190	8	SS	5-27-87	4	12
27191	8	SS	5-27-87	4	12

SS - Scheduled sacrifice

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Record of Fate - Females

Test Article, Desired Concentration, Female Number	Age at Start of Study (weeks)	Fate	Death Date	Study Week	Age at Death (weeks)
0 ppm (Control):					
27192	8	SS	6-17-87	6	14
27193	8	SS	6-13-87	6	14
27194	8	SS	6-16-87	6	14
27195	8	SS	6-14-87	6	14
27196	8	SS	6-14-87	6	14
C_9 Aromatic Hydrocarbons 100 ppm:					
27197	8	SS	6-16-87	6	14
27198	8	SS	6-15-87	6	14
27199	8	SS	6-16-87	6	14
27200	8	SS	6-16-87	6	14
27201	8	SS	6-16-87	6	14
C_9 Aromatic Hydrocarbons 250 ppm:					
27202	8	SS	6-14-87	6	14
27203	8	SS	6-17-87	6	14
27204	8	SS	6-14-87	6	14
27205	8	SS	6-16-87	6	14
27206	8	SS	6-14-87	6	14
C_9 Aromatic Hydrocarbons 500 ppm:					
27207	8	SS	6-17-87	6	14
27208	8	SS	6-14-87	6	14
27209	8	SS	6-20-87	7	15
27210	8	SS	6-14-87	6	14
27211	8	SS	6-15-87	6	14
C_9 Aromatic Hydrocarbons 1,000 ppm:					
27212	8	SS	6-17-87	6	14
27213	8	SS	6-14-87	6	14
27214	8	SS	6-15-87	6	14
27215	8	SS	6-14-87	6	14
27216	8	SS	6-14-87	6	14
C_9 Aromatic Hydrocarbons 1,500 ppm:					
[illegible]	8	SS	6-14-87	6	14
27218	8	SS	6-17-87	6	14
27219	8	SS	6-17-87	6	14
27220	8	SS	6-14-87	6	14
27221	8	SS	6-15-87	6	14

SS - Scheduled sacrifice

Individual Autopsies and Necropsy Observations - Males

Test Article, Desired Conc., Male Number	Study Week	Autopsies Observations	Week of Sacrifice	Necropsy Observations
0 ppm (Control):				
27162	1-3 4	No visible abnormalities Matter, left eye, corner, dark	4	No gross lesions
27163	1-4	No visible abnormalities	4	No gross lesions
27164	1-4	No visible abnormalities	4	No gross lesions
27165	1-4	No visible abnormalities	4	No gross lesions
27166	1-4	No visible abnormalities	4	No gross lesions
C_9 Aromatic Hydrocarbons **100 ppm:**				
27167	1-4	No visible abnormalities	4	No gross lesions
27168	1-4	No visible abnormalities	4	No gross lesions
27169	1-4	No visible abnormalities	4	No gross lesions
27170	1-4	No visible abnormalities	4	No gross lesions
27171	1-4	No visible abnormalities	4	No gross lesions
C_9 Aromatic Hydrocarbons **250 ppm:**				
27172	1-3 4	No visible abnormalities Scabbing, right lateral abdomen	4	No gross lesions
27173	1-4	No visible abnormalities	4	No gross lesions
27174	1-4	No visible abnormalities	4	No gross lesions
27175	1-4	No visible abnormalities	4	No gross lesions
27176	1-3 2-3 4	Matter around left eye, red Matter around right eye, red No visible abnormalities	4	No gross lesions
C_9 Aromatic Hydrocarbons **500 ppm:**				
27177	1-4	No visible abnormalities	4	No gross lesions
27178	1-4	No visible abnormalities	4	No gross lesions
27179	1-4	No visible abnormalities	4	No gross lesions
27180	1-4	No visible abnormalities	4	No gross lesions
27181	1-4	No visible abnormalities	4	No gross lesions

Conc. - Concentration

Individual Antemortem and Necropsy Observations - Males

Test Article, Desired Conc., Male Number	Study Week	Antemortem Observations	Week of Sacrifice	Necropsy Observations
C_9 Aromatic Hydrocarbons 1,000 ppm:				
27182	1-4	No visible abnormalities	4	No gross lesions
27183	1-4	No visible abnormalities	4	No gross lesions
27184	1-4	No visible abnormalities	4	No gross lesions
27185	1-4	No visible abnormalities	4	No gross lesions
27186	1-4	No visible abnormalities	4	No gross lesions
C_9 Aromatic Hydrocarbons 1,500 ppm:				
27187	1-4	No visible abnormalities	4	No gross lesions
27188	1-2,4	No visible abnormalities	4	No gross lesions
	3	Staining around mouth, brown		
27189	1-4	No visible abnormalities	4	No gross lesions
27190	1	No visible abnormalities	4	Broken dorsal incisors, bilateral moderate
	2-4	Malaligned upper incisors		
27191	1-4	No visible abnormalities	4	No gross lesions

Conc. - Concentration

Individual Antemortem and Necropsy Observations - Females

Test Article, Desired Conc., Dam Number	Study Week	Antemortem Observations	Week of Sacrifice	Necropsy Observations
0 ppm (Control):				
27192	1-7	No visible abnormalities	7	Liver[a]: focus, tan, 2 mm in diameter, left lateral lobe
27193	1-7	No visible abnormalities	6	No gross lesions
27194	1-7	No visible abnormalities	7	No gross lesions
27195	1-7	No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
27196	1-4,7 5-6	No visible abnormalities Hair loss, left forelimb	6	No gross lesions
C_9 Aromatic Hydrocarbons 100 ppm:				
27197	1-7	No visible abnormalities	7	No gross lesions
27198	1-3 4-7 5 6-7	No visible abnormalities Matter around right eye, red Right eye closed Hair loss, upper part of right forelimb	7	No gross lesions
27199	1-7	No visible abnormalities	7	No gross lesions
27200	1-2 3-7	No visible abnormalities Hair loss, both forelimbs	7	No gross lesions
27201	1-7	No visible abnormalities	7	No gross lesions
C_9 Aromatic Hydrocarbons 250 ppm:				
27202	1-5 6-7	No visible abnormalities Hair loss, left side of head, neck	6	No gross lesions Uterus: nongravid[b]
27203	1 2-7 5-7	No visible abnormalities Hair loss, left forelimb Hair loss, right forelimb	7	No gross lesions
27204	1-7	No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
27205	1-4 5-7	No visible abnormalities Hair loss, right forelimb	7	No gross lesions
27206	1-7	No visible abnormalities	6	No gross lesions

[a]Tissues saved in formalin, subsequently discarded
[b]Confirmed by ammonium sulfide test

418-035 Conc. - Concentration

Individual Antemortem and Necropsy Observations - Females

Test Article, Desired Conc., Dam Number	Study Week	Antemortem Observations	Week of Sacrifice	Necropsy Observations
C_9 Aromatic Hydrocarbons 500 ppm:				
27207	1-2,5-7 3-4	No visible abnormalities Hair loss, both forelimbs	7	No gross lesions
27208	1-5 6-7	No visible abnormalities Hair loss, ventral abdomen	6	No gross lesions
27209	1-7	Hair loss, both forelimbs	8	No gross lesions
27210	1-7	No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
27211	1-7	No visible abnormalities	7	No gross lesions
C_9 Aromatic Hydrocarbons 1,000 ppm:				
27212	1-4 5-7	No visible abnormalities Hair loss, both forelimbs	7	No gross lesions
27213	1-6 7	No visible abnormalities Toe missing, left forelimb	6	No gross lesions Uterus: nongravid[b]
27214	1-7	No visible abnormalities	7	No gross lesions Uterus: nongravid[b]
27215	1-7	No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
27216	1-7	No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
C_9 Aromatic Hydrocarbons 1,500 ppm:				
27217	1-2 3-7	Staining, anogenital area, yellow No visible abnormalities	6	No gross lesions Uterus: nongravid[b]
27218	1 1 2-3,5-7 4	Scabbing, both forelimbs Hair loss, both forelimbs No visible abnormalities Staining, anogenital area, yellow	7	Stomach[a]: focus, black, 3 mm in diameter mucosa, mild
27219	1-7	No visible abnormalities	7	No gross lesions
27220	1-5 6-7	No visible abnormalities Hair loss, chin	6	No gross lesions
27221	1-2,5-7 3-4	No visible abnormalities Malocclusion	7	No gross lesions Uterus: nongravid[b]

[a]Tissues saved in formalin, subsequently discarded
[b]Confirmed by ammonium sulfide test
Conc. - Concentration

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Individual Weekly Body Weights (g) - Males

Test Article, Desired Concentration, Male Number	Week 0	Week 1	Week 2	Week 3
0 ppm (Control):				
27162	248	300	350	394
27163	244	315	354	401
27164	231	268	294	316
27165	254	308	360	401
27166	250	299	343	369
C_9 Aromatic Hydrocarbons 100 ppm:				
27167	230	221	310	338
27168	240	293	332	369
27169	253	280	306	330
27170	262	319	366	415
27171	234	297	333	369
C_9 Aromatic Hydrocarbons 250 ppm:				
27172	234	287	324	353
27173	256	332	381	424
27174	243	284	340	378
27175	255	321	368	420
27176	251	317	342	377
C_9 Aromatic Hydrocarbons 500 ppm:				
27177	239	299	340	374
27178	255	320	366	404
27179	260	329	368	404
27180	238	298	334	371
27181	242	301	343	376
C_9 Aromatic Hydrocarbons 1,000 ppm:				
27182	254	321	374	409
27183	252	297	323	353
27184	251	305	340	369
27185	235	291	322	347
27186	252	316	360	405
C_9 Aromatic Hydrocarbons 1,500 ppm:				
27187	248	282	318	358
27188	247	285	325	350
27189	245	272	315	333
27190	251	265	297	343
27191	237	277	298	330

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Individual Weekly Body Weights (g) - Females

Test Article, Desired Concentration, Female Number	Study Week Number 0	1	2
0 ppm (Control):			
27192	185	194	205
27193	185	210	230
27194	181	202	221
27195	185	214	217
27196	181	208	237
C_9 Aromatic Hydrocarbons 100 ppm:			
27197	179	216	233
27198	181	198	215
27199	185	215	237
27200	191	222	245
27201	198	229	241
C_9 Aromatic Hydrocarbons 250 ppm:			
27202	196	222	242
27203	194	216	228
27204	189	217	238
27205	191	227	250
27206	190	214	236
C_9 Aromatic Hydrocarbons 500 ppm:			
27207	186	173	218
27208	185	202	221
27209	175	186	207
27210	192	210	226
27211	189	214	235
C_9 Aromatic Hydrocarbons 1,000 ppm:			
27212	184	202	213
27213	175	209	231
27214	174	202	215
27215	189	212	225
27216	187	191	205
C_9 Aromatic Hydrocarbons 1,500 ppm:			
27217	183	201	224
27218	192	214	237
27219	197	222	252
27220	178	201	228
27221	189	202	221

Individual Maternal Body Weights During Gestation and Lactation

Test Article, Desired Conc., Dam Number	Body Weight (grams) Day of Gestation 0	7	14	21	Day of Lactation 0	4
0 ppm (Control):						
27192	223	259	300	356	276	239
27193	233	257	296	384	294	299
27194	219	259	292	357	289	249
27195[a]	234	246	258	242	b	
27196	235	275	303	367	274	309
C_9 Aromatic Hydrocarbons 100 ppm:						
27197	234	266	292	377	276	239
27198	219	239	261	310	228	278
27199	241	264	300	356	269	293
27200	248	283	330	390	295	304
27201	254	298	341	427	313	348
C_9 Aromatic Hydrocarbons 250 ppm:						
27202[a]	251	264	270	280	b	
27203	273	274	321	381	284	293
27204[a]	236	248	260	262	b	
27205	251	289	336	417	321	319
27206	231	266	301	352	310	314
C_9 Aromatic Hydrocarbons 500 ppm:						
27207	231	252	291	365	268	247
27208	226	258	262	371	284	281
27209	204	246	279	342	262	233
27210[a]	241	250	254	262	b	
27211	239	274	309	363	272	295

[a]Nongravid, not included in calculation of means
[b]Did not deliver, sacrificed 25 days following termination of mating
Conc. - Concentration

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Individual Maternal Body Weights During Gestation and Lactation

Test Article, Desired Conc., Dam Number	Body Weight (grams) Day of Gestation 0	7	14	21	Day of Lactation 0	4
C_9 Aromatic Hydrocarbons 1,000 ppm:						
27212	228	250	286	321	270	241
27213[a]	238	244	254	269	b	
27214[a]	230	247	252	260	b	
27215[a]	226	238	245	254	b	
27216[a]	212	219	244	250	b	
C_9 Aromatic Hydrocarbons 1,500 ppm:						
27217[a]	229	226	246	257	b	
27218	252	284	318	362	309	246
27219	266	311	343	394	311	261
27220	232	263	256	373	277	209
27221[a]	220	234	247	250	b	

[a]Nongravid, not included in calculation of mean
[b]Did not deliver, sacrificed 25 days following termination of mating
Conc. - Concentration

Desired Conc., Dam Number	Lactation Day	Total Born No. Viable	Individual Pup Weights (grams) Pup Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14
0 ppm (Control):																
27192	0	14/13	6.0	6.2	6.3	6.0	6.1	6.4	6.2	7.0	6.7	5.4	5.0	6.1	6.2	
	4		10.8	11.2	11.3	10.6	11.3	10.4	10.8	11.6	10.4	11.5	9.5	10.8	10.8	
27193	0	14/14	5.2	5.4	5.2	5.4	4.7	5.6	5.5	5.3	5.0	5.5	4.7	5.1	[illegible]	[illegible]
	4		9.2	9.6	10.1	11.2	9.2	9.4	10.0	8.5	9.7	7.5	9.6	9.2	[illegible]	[illegible]
27194	0	9/9	7.4	7.4	7.9	7.2	7.9	7.1	7.5	7.5	7.4					
	4		13.5	13.1	12.1	12.7	12.4	12.4	12.8	12.2	12.8					
27195	0	Nongravid														
	4															
27196	0	11/11	7.5	7.1	6.7	6.3	7.4	7.0	6.7	6.5	6.5	6.6	5.0			
	4		12.4	12.4	9.7	11.1	10.4	12.4	10.7	9.9	10.7	9.0	9.0			

Conc. - Concentration
No. - Number

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Individual Pup Weights (grams)

Test Article, Desired Conc., Dam Number	Lactation Day	Total Born / No. Viable	Fetus Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
C_9 Aromatic Hydrocarbons 100 ppm:																	
27197	0	14/14	6.7	7.7	7.6	6.8	7.7	7.1	7.0	7.1	7.0	7.2	7.0	6.8	7.0	7.4	
	4		9.9	10.5	9.7	10.0	10.3	9.8	10.0	9.8	9.8	9.9	9.8	9.3	9.1		
27198	0	13/13	5.8	5.6	6.3	6.2	6.2	6.2	6.1	5.8	4.5	5.6	5.4	5.9	6.1		
	4		8.6	10.0	9.8	9.2	9.7	9.4	9.2	8.5	8.9	9.8	9.2	9.5	7.6		
27199	0	14/13	6.5	6.1	6.1	6.1	6.8	6.4	6.4	5.9	6.2	6.4	5.9	6.1	6.1		
	4		8.9	10.4	11.2	11.0	11.0	10.9	10.2	10.5	10.5	11.4	9.4	10.4	10.4		
27200	0	14/14	6.7	5.9	6.7	6.4	5.9	6.0	6.5	5.8	6.3	6.0	5.9	6.5	5.9	5.2	
	4		11.5	11.5	10.6	11.1	10.0	11.8	11.4	11.2	10.6	11.1	11.7	9.2	10.4	10.5	
27201	0	15/15	7.2	6.3	7.1	7.9	7.2	6.7	6.6	6.6	6.1	6.9	7.0	6.3	6.3	6.7	7.0
	4		11.8	13.2	12.1	13.0	12.5	11.3	12.4	11.0	12.7	12.8	13.0	11.5	12.5	9.7	11.5

Conc. - Concentration
No. - Number

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Individual Pup Weights (grams)

Test Article, Desired Conc., Dam Number	Lactation Day	Total Born No. Viable	Pup No. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
C_9 Aromatic Hydrocarbons 250 ppm:																		
27202	0	Nongravid																
	4																	
27203	0	18/16	4.3	4.2	4.7	4.2	4.2	4.4	4.0	4.0	4.0	3.8	4.6	4.0	4.2	4.1	4.2	3.6
	4																	
27204	0	Nongravid																
	4																	
27205	0	16/16	6.7	6.4	6.9	6.4	6.4	6.4	6.4	5.4	6.1	6.6	6.1	5.9	5.7	5.4	5.8	6.3
	4		10.9	10.0	9.3	9.8	10.6	9.7	9.6	9.2	9.6	9.7	9.8	9.4	7.6	9.3	9.5	8.3
27206	0	6/6	6.8	6.7	6.5	5.9	6.6	6.3										
	4		14.5	15.0	14.5	14.8	13.8	14.1										

Conc. - Concentration
No. - Number

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Individual Pup Weights (grams)

Test Article, Desired Conc., Dam Number	Lactation Day	Total Born / No. Viable	Fetus Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
C_9 Aromatic Hydrocarbons																	
500 ppm:																	
27207	0	13/13	6.5	7.0	6.6	6.8	6.3	6.6	6.9	7.3	6.6	7.0	6.5	6.8	6.3		
	4		10.6	10.5	10.9	10.5	9.8	10.2	10.7	11.1	9.9	10.3	10.6	9.3	9.9		
27208	0	13/13	5.4	6.7	6.9	5.9	6.2	5.8	6.7	6.4	6.7	6.8	6.5	6.6	6.4		
	4		8.7	8.9	12.[illegible]	12.7	9.4	8.5	12.2	12.6	12.1	12.7	12.1	12.2	8.6		
27209	0	11/11	6.0	6.2	6.0	6.0	4.6	5.6	5.0	6.1	5.9	5.9	6.0				
	4		10.7	10.1	10.7	10.6	6.1	10.[illegible]	10.4	10.4	10.7	7.6	10.5				
27210	0	Nongravid															
	4																
27211	0	15/15	7.2	7.0	7.8	7.9	5.5	7.3	6.7	7.5	6.4	6.9	6.9	6.4	6.9	6.1	6.1
	4		10.9	9.5	9.6	10.7	11.0	10.2	11.1	10.1	10.1	9.5	8.3	9.5	9.9	9.8	8.8

Conc. - Concentration
No. - Number

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Individual Pup Weights (grams)

Test Article, Desired Conc., Dam Number	Lactation Day	Total Born No. Viable	Fetus Number 1	2	3	4	5	6	7	8	9	10	11
C_9 Aromatic Hydrocarbons 1,000 ppm:													
27212	0	11/11	6.9	6.3	6.1	5.7	6.0	6.1	6.2	6.2	6.2	5.7	6.0
	4		10.3	9.8	10.5	10.8	10.2	10.6	9.9	10.0	10.2	10.3	9.8
2721[illegible]	0	Nongravid											
	4												
2[illegible]4	0	Nongravid											
	4												
27215	0	Nongravid											
	4												
27216	0	Nongravid											
	4												

Conc. - Concentration
No. - Number

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Individual Pup Weights (grams)

Test Article, Desired Conc., Dam Number	Lactation Day	Total Born / No. Viable	Fetus Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
C_9 Aromatic Hydrocarbons																	
1,500 ppm:																	
27217	0	Nongravid															
	4																
27218	0	15/15	5.5	5.5	6.0	5.9	4.8	5.6	4.7	5.3	5.1	5.7	6.0	5.5	5.1	5.2	4.8
	4		9.7	8.3	10.0	8.4	9.2	8.6	8.9	8.6	8.0	9.0	9.7	8.7	8.6	8.8	9.1
27219	0	14/14	7.0	6.6	7.1	6.4	5.9	6.7	6.5	6.6	6.5	6.3	6.1	6.3	4.9	6.3	
	4		11.3	11.4	11.7	10.4	11.5	10.9	11.0	10.8	10.2	7.9	11.0	10.5	10.5		
27220	0	13/12	6.5	6.5	7.3	6.3	6.4	7.0	6.5	6.4	6.3	6.1	6.9	6.8			
	4		7.2	8.7	9.0	8.8	9.6	9.1	9.1	9.0	8.7	8.8	8.7	8.6			
27221	0	Nongravid															
	4																

Conc. - Concentration
No. - Number

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0 PPM

27	M	186	188
27	M	200[a,b]	188
27164	M	141	145
27165	M	38[b]	195
27166	M	186	178
27192	F	110	117
27193	F	116	135
27194	F	115	123
27195	F	119	129
27196	F	127	148

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[a]3 day measurement
[b]unreliable value, not included in mean calculation

Individual Food Consumption, Grams

GROUP, ANIMAL NO.	SEX	OBSERVATION PERIODS 1	2
100 PPM			
27167	M	101	189
27168	M	171	181
27169	M	171	170
27170	M	221	240
27171	M	167	172
27197	F	119	123
27198	F	116	79
27199	F	124	139
27200	F	136	54
27201	F	126	129

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Individual Food Consumption, Grams

GROUP, ANIMAL NO.	SEX	OBSERVATION PERIODS 1	2
250 PPM			
27172	M	148	157
27173	M	207	206
27174	M	134	174
27175	M	200	211
27176	M	187	170
27202	F	108	130
27203	F	118	NA
27204	F	110	127
27205	F	120	205
27206	F	115	66

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NA - Not available

Individual Food Consumption, Grams

GROUP, ANIMAL NO.	SEX	OBSERVATION PERIODS 1	2
500 PPM			
27177	M	167	172
27178	M	188	167
27179	M	165	182
27180	M	153	171
27181	M	179	192
27207	F	103	130
27208	F	105	125
27209	F	106	135
27210	F	109	121
27211	F	116	129

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Individual Food Consumption, Grams

GROUP, ANIMAL NO.	SEX	OBSERVATION PERIODS 1	2
1000 PPM			
27182	M	168	178
27183	M	175	164
27184	M	152	181
27185	M	144	158
27186	M	184	178
27212	F	86	111
27213	F	136	153
27214	F	108	120
27215	F	108	122
27216	F	98	113

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Individual Food Consumption, Grams

GROUP, ANIMAL NO.	SEX	OBSERVATION PERIODS 1	2
1500 PPM			
27187	M	156	173
27188	M	161	161
27189	M	121	156
27190	M	158	134
27191	M	113	149
27217	F	94	118
27218	F	111	126
27219	F	18	141
27220	F	122	131
27221	F	99	113

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Individual Maternal Food Consumption
During Gestation and Lactation (g)

Test Article, Desired Conc., Dam Number	Gestation Days 0-7	Gestation Days 7-14	Gestation Days 14-21	Lactation Days 0-4
0 ppm (Control):				
27192	157	174	187	139
27193	144	160	161	118
27194	153	159	189	107
27195[a]	129	117	122	
27196	176	162	174	131
C_9 Aromatic Hydrocarbons 100 ppm:				
27197	150	141	164	103
27198	155	146	107	157
27199	165	153	139	136
27200	191	203	126	181
27201	174	190	221	173
C_9 Aromatic Hydrocarbons 250 ppm:				
27202[a]	141	135	161	
27203	186	195	181	74
27204[a]	130	127	145	
27205	169	183	199	118
27206	147	162	196	102
C_9 Aromatic Hydrocarbons 500 ppm:				
27207	247	171	182	121
27208	155	152	181	137
27209	142	166	165	97
27210[a]	130	129	138	
27211	145	148	186	124
C_9 Aromatic Hydrocarbons 1,000 ppm:				
27212	131	140	157	96
27213[a]	146	134	161	
27214[a]	142	130	137	
27215[a]	126	123	141	
27216[a]	118	117	154	
C_9 Aromatic Hydrocarbons 1,500 ppm:				
27217[a]	116	112	132	
27218	144	168	193	106
27219	175	181	208	105
27220	148	169	178	70
27221[a]	116	114	119	

[a]Nongravid, not included in calculation of means
Conc. - Concentration

Individual Litter Data - F_0 Dams, F_1 Pups

Test Article, Desired Conc., Dam Number	First Male Used	Copulatory Interval (days)	Gestation Length (Days)	No. Pups Dead on Day 0		Number of Live Pups Lactation Day 0		Number of Live Pups Lactation Day 4		Mean Body Weight of Live Pups Lactation Day 0		Mean Body Weight of Live Pups Lactation Day 4	
				M	F	M	F	M	F	M	F	M	F
0 ppm (Control):													
27192	27162	4	21	1	0	9	4	9	4	6.2[b]	6.1[a]	11.0	10.7
27193	27163	1	20	0	0	8	6	8	6	5.3	5.2	9.6	9.0
27194	27164	3	21	0	0	5	4	5	4	7.6	7.3	12.9	12.6
27195	27165	2		Did not deliver									
27196	27166	1	21	0	0	8	3	8	3	6.9	6.3	11.1	10.1
C_9 Aromatic Hydrocarbons 100 ppm:													
27197	27167	3	21	0	0	5	9	5	8[c]	7.3	7.1	10.1	9.7
27198	27168	2	21	0	0	8	5	8	5	6.0	5.5	9.3	9.0
27199	27169	3	21	0	1	9	4	9	4	6.3	6.1	10.4	10.4
27200	27170	3	21	0	0	7	7	7	7	6.3	5.9	11.1	10.7
27201	27171	3	21	0	0	5	10	5	10	7.1	6.6	12.5	11.8
C_9 Aromatic Hydrocarbons 250 ppm:													
27202	27172	2		Did not deliver									
27203	27173	4	21	1	1	8	8	0	0	4.3	4.1	-	-
27204	27174	2		Did not deliver									
27205	27175	3	21	0	0	6	10	6	10	6.5	6.0	10.1	9.2
27206	27176	1	21	0	0	3	3	3	3	6.7	6.3	14.7	14.2

No. - Number
Conc. - Concentration
- - Not applicable

[a]Body weight does not represent total number of pups
[b]Value includes weight of misnamed pup, not included in calculation of mean
[c]One pup missing

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Individual Litter Data - F_0 Dams, F_1 Pups

Test Article, Desired Conc., Dam Number	First Male Used	Copulatory Interval (days)	Gestation Length (Days)	No. Pups Dead on Day 0		Number of Live Pups Lactation Day 0		Number of Live Pups Lactation Day 4		Mean Body Weight of Live Pups Lactation Day 0		Mean Body Weight of Live Pups Lactation Day 4	
				M	F	M	F	M	F	M	F	M	F
C_9 Aromatic Hydrocarbons 500 ppm:													
27207	27177	4	21	0	0	11	2	11	2	6.7	6.6	10.5	9.6
27208	27178	1	21	0	0	6	7	6	7	6.2	6.6	10.1	10.0
27209	27179	7	21	0	0	2	9	2	9	6.1	5.7	10.4	9.7
27210	27180	2		Did not deliver									
27211	27181	2	21	0	0	9	6	9	6	7.1	6.6	10.4	9.5
C_9 Aromatic Hydrocarbons 1,000 ppm:													
27212	27182	4	21	0	0	5	6	5	6	6.3	6.1	10.3	9.9
27213	27183	2		Did not deliver									
27214	27184	3		Did not deliver									
27215	27185	2		Did not deliver									
27216	27186	2		Did not deliver									
C_9 Aromatic Hydrocarbons 1,500 ppm:													
27217	27187	2		Did not deliver									
27218	27188	4	21	0	0	7	8	7	8	5.4	5.3	9.0	8.8
27219	27189	4	21	0	0	6	8	6	7	5.6	6.2	11.2	10.3
27220	27190	1	21	0	1	7	5	7	5	6.6	6.5	8.8	8.8
27221	27191	3		Did not deliver									

No. - Number
Conc. - Concentration
- - Not applicable

418-035

Individual Uterine Observations on Lactation Day 4

Test Article, Desired Conc., Dam Number	Total Implantation Sites	Number of Pups Delivered	Remaining Sites[a]
0 ppm (Control):			
27192	17	14	3
27193	14	14	0
27194	10	9	1
27195	Did not deliver (nongravid)		
27196	16	11	5
C_9 Aromatic Hydrocarbons 100 ppm:			
27197	17	14	3
27198	13	13	0
27199	14	14	0
27200	15	14	1
27201	18	15	3
C_9 Aromatic Hydrocarbons 250 ppm:			
27202	Did not deliver (nongravid)		
27203	18	18	0
27204	Did not deliver (nongravid)		
27205	17	16	1
27206	7	6	1
C_9 Aromatic Hydrocarbons 500 ppm:			
27207	13	13	0
27208	17	13	4
27209	11	11	0
27210	Did not deliver (nongravid)		
27211	15	15	0

[a]Implantation sites not corresponding to delivered pups; values represent postimplantation loss and/or complete cannibalization.

Conc. - Concentration

418-035

Individual Uterine Observations on Lactation Day 4

Test Article, Desired Conc., Dam Number	Total Implantation Sites	Number of Pups Delivered	Remaining Sites[a]
C_9 Aromatic Hydrocarbons 1,000 ppm:			
27212	12	11	1
27213	Did not deliver (nongravid)		
27214	Did not deliver (nongravid)		
27215	Did not deliver (nongravid)		
27216	Did not deliver (nongravid)		
C_9 Aromatic Hydrocarbons 1,500 ppm:			
27217	Did not deliver (nongravid)		
27218	16	15	1
27219	14	14	0
27220	13	13	0
27221	Did not deliver (nongravid)		

[a]Implantation sites not corresponding to delivered pups; values represent postimplantation loss and/or complete cannibalization.

Conc. - Concentration

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APPENDIX B

Historical Control Data

Individual Studies have been subjected to Quality Assurance audit; the following historical compilation of data has not.

FILE #42
IRDC REPRODUCTIVE HISTORICAL CONTROL DATA
Charles River CD®® CD® Rats

Sex, (When Applicable) Reproductive/Litter Parameter		Number	Value	Range
MALE				
Fertility Index	Fertile Males / Total Males Mated	391 / 433	90.3%	(90.3% - 100.0%)
FEMALE				
Fertility Index	No. of Females Pregnant / No. of Females Mated	591 / 676	87.4%	(40.9% - 100.0%)
Copulatory Index	Females with Evidence of Copulation / Total Females Mated	308 / 325	94.8%	(77.3% - 100.0%)
Copulatory Interval (Days)	Total No. of Days / No. of Females Mated	1009 / 306	3.3	(2.1 - 4.9)
Gestation Length (Days)	Total No. of Days / No. of Pregnant Dams	10712 / 486	22.0	(21.7 - 22.5)
No. Implantation Sites at Weaning/Dam	Total No. of Implantation Sites / No. of Pregnant Dams	4209 / 294	14.3	(11.0 - 15.3)
Postimplantation Loss/Dam	No. of Implantation Sites at Weaning - Total No. Pups at Birth / No. of Implantation Sites	268 / 294	0.9%	(0.6% - 1.0%)
LITTER SIZE				
Viable Pups/Litter at Day 0	Total No. of Viable Pups / No. of Pregnant Dams	6610 / 509	13.0	(10.6 - 14.7)
Stillborn Pups/Litter	Total No. of Stillborn Pups / No. of Pregnant Dams	115 / 508	0.2	(0.0 - 0.5)
PUP SEX DISTRIBUTION AT WEANING	Total No. of Males: Total No. of Females	Total No. of Males: Total No. of Females 2200:2192	%Male:%Female 50.1:49.9	%Male:%Female - %Male:%Female (45.6:44.4 - 55.6:54.4)

The historical control data compiled January 9, 1987 includes data from studies terminating January, 1984 to January, 1986.

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FILE #42
IRDC REPRODUCTIVE HISTORICAL CONTROL DATA
Charles River COBS® CD® Rats

Sex, (When Applicable) Reproductive/Litter Parameter		Number	Value	Range
PUP SURVIVAL AT BIRTH				
Gestation Survival Index	Total No. of Viable Pups at Birth / Total No. of Pups Born	6610 / 6723	98.3%	(95.7% - 100.0%)
PUP SURVIVAL INDICES THROUGH WEANING				
Lactation Day 4 (Before Reduction)	Total No. of Viable Pups on Day 4 (B.R.) / Total No. of Viable Pups on Day 0	6512 / 6610	98.5%	(96.0% - 99.5%)
Lactation Day 7	Total No. of Viable Pups on Day 7 / Total No. of Viable Pups on Day 4 (A.R.)	4185 / 4200	99.6%	(95.3% - 100.0%)
Lactation Day 14	Total No. of Viable Pups on Day 14 / Total No. of Viable Pups on Day 4 (AR), 5 (AR) or 7	4157 / 4162	99.9%	(99.0% - 100.0%)
Lactation Day 21	Total No. of Viable Pups on Day 21 / Total No. of Viable Pups on Day 12 or 14	4253 / 4255	99.9%	(99.1% - 100.0%)
PUP BODY WEIGHT (g) AT BIRTH				
Litter Weight (Males and Females)	Total Mean Viable Litter Weight at Birth / Total No. of Litters	2604.2 / 420	6.2 g	(6.0 g - 6.7 g)
PUP BODY WEIGHT (g) THROUGH WEANING				
Lactation Day 4 (Before Reduction)				
Litter Weight (Males and Females)	Total Mean Viable Litter Weight on Day 4 (B.R.) / Total No. of Litters on Day 4 (B.R.)	3601.1 / 359	10.0 g	(9.2 g - 11.4 g)
Litter Weight (Males and Females)	Total Mean Viable Litter Weight on Day 4 (A.R.) / Total No. of Litters on Day 4 (A.R.)	3335.0 / 334	10.0 g	(9.2 g - 11.4 g)
Lactation Day 7				
Litter Weight (Males and Females)	Total Mean Viable Litter Weight on Day 7 / Total No. Litters on Day 7	6474.1 / 420	15.4 g	(14.3 g - 17.3 g)

Sex, (When Applicable) Reproductive/Litter Parameter		Number	Value	Range
Lactation Day 14				
Litter Weight (Males and Females)	Total Mean Viable Litter Weight on Day 14 / Total No. Litters on Day 14	11880.7 / 305	38.1 g	(26.5 g - 54.8 g)
Lactation Day 21				
Male	Total Mean Viable Male Pup Weight on Day 21 / Total No. of litters on Day 21	19038.1 / 399	47.7 g	(36.1 g - 53.8 g)
Female	Total Mean Viable Female Pup Weight on Day 21 / Total No. of litters on Day 21	18311.5 / 400	45.8 g	(34.8 g - 52.8 g)