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National Institute of Environmental
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Contract DE-AC06-76RLO 1830

Pacific Northwest Laboratory
Operated for the U.S. Department of Energy
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INHALATION DEVELOPMENTAL TOXICOLOGY STUDIES: TERATOLOGY STUDY OF 1,3-BUTADIENE IN MICE

Final Report
No. NIH-401-ES-4D131

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ACKNOWLEDGMENTS

We wish to express our appreciation to the following members of the staff for their contributions to this project: EJ Rossignol, GR Ell, RD Swannack, LG Florek, EM Milliman, DK Hammerberg, M McCulloch, N Stamps, and KH Stoney for their work on the generation and monitoring system; WB Peterson, VL Dedmond, JT Pierce, and AE Jarrell for animal care and health screening; and J Kaschmitter and DN Rommereim for work on data-acquisition systems. We are especially appreciative of the members of the reproductive toxicology working group: TT Sherer, ML Sours, BL Champion, BJ Willemsen, RC Zangar, TA Breier, and SA Quinn.

ABSTRACT

Maternal toxicity, reproductive performance and developmental toxicology were evaluated in CD-1 mice following whole-body, inhalation exposures to 0 (filtered air), 40, 200 and 1000 ppm of 1,3-butadiene. The female mice, which had mated with unexposed males (day of detection of a copulation plug = 0 days of gestation; dg), were exposed to the chemical for 6 hours/day on 6 through 15 dg and sacrificed on 18 dg.

Maternal animals were weighed prior to mating and on 0, 6, 11 and 18 dg; the mice were observed for mortality, morbidity and signs of toxicity during exposure and examined for gross tissue abnormalities at necropsy. Reproductive measures included numbers of implantation sites, resorptions and live and dead fetuses. Live fetuses were weighed and subjected to external, visceral and skeletal examinations to detect growth retardation and morphologic anomalies.

For unknown reasons, the overall percentage of pregnant mice was low (60%), but no differences among treatments were detected in the number of pregnancies or implantation sites/dam. The incidence of early resorptions was higher in control mice than in animals exposed to 200 ppm, but no effect was observed on the percentage of total resorptions and live fetuses/litter.

Significant concentration-related decreases were detected in a number of maternal body weight measures (weight gains during the intervals encompassing the last 5 days of exposure and from the end of exposure to sacrifice, body weight at sacrifice, extragestational weight and weight gain, and weight of the gravid uterus). There was a significant concentration-related depression of fetal body weights and placental weights. Body weights of male fetuses of all exposed groups were significantly lower than values for control fetuses; weights of female fetuses were significantly depressed in the mice exposed to 200 and 1000 ppm. In the 200- and 1000-ppm exposure groups, weights of placentas of male fetuses were significantly decreased, but placental weights of female fetuses were significantly affected only in litters exposed to the highest 1,3-butadiene concentration. There were no significant differences among groups in the incidences of malformations. However, incidences of fetal variations (supernumerary ribs and reduced ossifica

tion of the sternebrae) were significantly increased in litters from mice exposed to 200 and 1000 ppm.

This exposure regimen produced significant signs of maternal toxicity at concentrations of 200 and 1000 ppm 1,3-butadiene. Fetal growth retardation, decreased placental weights, and increased incidences of morphologic variations were observed to occur in a concentration-related manner. Body weights of male fetuses of mice exposed to the lowest concentration of 1,3-butadiene (40 ppm) were significantly depressed, although no other signs of retarded fetal development or significant alterations in maternal indices were noted at this exposure level. These results may indicate that the fetus is more susceptible than the dam to 1,3-butadiene toxicity, but no evidence of teratogenicity was found in the offspring of dams exposed to 1,3-butadiene vapors on 6 through 15 dg.

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ABBREVIATIONS

ANOVA	= Analysis of variance
BNW	= Battelle, Pacific Northwest Laboratories; Battelle-Northwest
CDS	= Colorado Data Systems
CO_2	= Carbon dioxide
dg	= Day(s) of gestation
FID	= Flame ionization detector
GC	= Gas chromatography
HP	= Hewlett-Packard
IIS	= Intelligent Interface System
MRI	= Midwest Research Institute
NIEHS	= National Institute of Environmental Health Sciences
NIOSH	= National Institute of Occupational Safety and Health
NTP	= National Toxicology Program
PNL	= Pacific Northwest Laboratory
ppm	= Parts per million
RH	= Relative humidity
v/v	= Volume to volume ratio

1. INTRODUCTION

The major uses of butadiene are in the manufacture of styrene-butadiene rubber, in the production of polymers, and as a chemical intermediate (SRI, 1979). The major manufacturers in the U.S. produced about 1.5 million tons in 1980 (SRI, 1981), and it has been estimated that about 62,000 workers were exposed (National Institute of Occupational Safety and Health [NIOSH], 1980). As with most chemicals, accidental release during their transportation poses a potential for exposure of the general population. From a review of the literature, it appears that acute exposure to 1,3-butadiene is not highly toxic and that mice are more sensitive than rats when exposed by either oral or inhalation routes.

There are indications that chronic inhalation exposure to 1,3-butadiene alters the reproductive system. In a study in rats (Hazelton, 1981), euthanasia was required for females with large mammary tumors and males with severe nephropathic changes after 24 months of exposure to 1000 to 8000 ppm of butadiene. In this study, there was an increased incidence of a number of tumor types, including those of the reproductive tract (Leydig cell tumors of the testes and uterine/vaginal stromal tumors). Another study, performed by Battelle, Pacific Northwest Laboratories (Battelle-Northwest; BNW) for the National Toxicology Program (NTP) in 1981 (BNW, 1984), in which mice were exposed to 625 and 1250 ppm of butadiene, was terminated at about 60 weeks because of high mortality associated with neoplasms at multiple sites, including ovarian granulosa cell tumors. There was also a significantly increased incidence of mice with testicular or ovarian atrophy.

There appear to be only two studies reported in which the reproductive and developmental toxicity of inhaled 1,3-butadiene was specifically evaluated. In one of these studies, exposure of rats to 600, 2300 and 6700 ppm of butadiene for 8 months resulted in a concentration-related depression of body weight (Carpenter et al., 1944). Reproductive studies of male and female animals were performed at unstated times during these exposures, but no data were given concerning the number of matings, or of barren females. The number of litters/female rat in all exposed groups tended to be lower than in controls, although litter sizes were stated to slightly exceed the "expected norm" of six/litter. Limited breeding tests of the offspring in the 2300- and 6700-ppm exposure groups suggested that there was

reduced fecundity, but it was not determined whether the deficit was associated with the males or with the females. Although details were not provided, 12 guinea pigs and 4 rabbits of each exposure group were also used for reproductive studies. Animals of all groups evidently produced progeny, except for rabbits exposed to 600 and 2300 ppm. The data are not supportive of the authors' conclusion that butadiene exposure did not affect reproductive performance and that any apparent reduction in fertility was due to hereditary characteristics.

In the Hazelton study (Hazelton, 1982), female rats were exposed to 0, 200, 1000 and 8000 ppm of butadiene from 6 through 15 days of gestation (dg). There was a significant concentration-related suppression of maternal body-weight gains during exposure, but body-weight gains during gestation (adjusted for conceptus weight) were significantly depressed only in animals exposed to the two highest concentrations. Reproductive measures (pregnancy rate, gravid uterus weight, number of implantation sites, number of fetuses per dam and preimplantation loss) were not affected by butadiene exposure. Mortality of postimplantation embryos tended to be slightly higher in all groups of exposed animals than in controls but the difference was statistically significant only at the highest concentration.

Body weights and crown-rump lengths of fetuses of the highest exposure group were significantly less than those of control fetuses. There was a significant increase in minor fetal defects (hematomas and minor skeletal defects) in all groups, and exposure to 1000 or 8000 ppm resulted in significantly higher incidences of major skeletal defects. In the 8000-ppm exposure group, there were significant increases in the incidence of other anomalies, including lens opacities and irregular ossification. The incidence of wavy ribs, which was rarely observed in their historical controls, was 1.6% in the control animals for this study, and increased in a concentration-related manner for exposed animals. The authors concluded that this response was not indicative of a teratogenic effect, but was due to maternally mediated embryonic growth retardation.

These indications of deleterious reproductive and developmental effects of 1,3-butadiene, together with quantitative uncertainties in the limited literature dealing with this widely used material, suggested a need for further investigation. It was considered important to confirm and extend the findings reported by Hazelton (1982). In particular, it was desirable to evaluate developmental effects at a

level that was not overtly toxic. Therefore, experiments have been performed that included lower atmospheric concentrations than those of the Hazelton study; thus, the chamber concentrations were 40, 200 and 1000 ppm. These exposure concentrations were used in a previous study in this project to evaluate the reproductive and teratologic effects of inhalation exposure to 1,3-butadiene in the same strain of outbred rats (Sprague-Dawley-derived) as those used in the Hazelton study, but obtained from a different source. Because 1,3-butadiene appears to be more toxic in the mouse than in the rat, the present study was performed using CD-1 mice subjected to the same exposure regimen as the study in rats.

II. MATERIALS AND METHODS

A. PROCUREMENT AND CHARACTERIZATION OF 1,3-BUTADIENE

The procurement of 1,3-butadiene from Phillips Chemical Company (Borger, TX) and its initial chemical characterization by Midwest Research Institute (MRI; Kansas City, MO) were arranged by the National Institute of Environmental Health Sciences (NIEHS).

For this study, a single lot (F909) of 1,3-butadiene was packaged in three 28-gal steel cylinders and shipped directly from Phillips Chemical Company to Pacific Northwest Laboratory (PNL). The cylinders were fitted with double-entry valves, which permitted sampling of liquid 1,3-butadiene through an eductor tube or gaseous material through a valve from the cylinder headspace. As received, the test-material cylinders contained variable amounts of nitrogen, which had been used by the manufacturer to dispense the 1,3-butadiene from bulk storage into appropriate containers for off-site shipment. The nitrogen was released from the cylinders prior to the withdrawal of 1,3-butadiene for analyses or animal exposures. Two cylinders (BNW 580846-36-2 and -3) were used for the animal exposures of 14 days' duration in the study described in this report.

Procedures for reanalysis of bulk chemicals were provided by MRI, and the materials were analyzed in our laboratory prior to the initiation of the animal exposures. The infrared spectrum of Lot Number F909 of 1,3-butadiene (400 to 600 cm^{-1}, using a gas cell with NaCl windows) confirmed its identity and did not detect major impurities (Appendix A). Data were consistent with values obtained from the literature (Erley and Blake).

Gas chromatographic analysis (2 m x 2 mm Porapak QS 100/120, 100°C isothermal, flame ionization detector; FID) of 1,3-butadiene for this study determined purity to be 99.88% (Appendix A). An unidentified minor peak, which eluted from the column 2 minutes later than the 1,3-butadiene, represented 0.11% of the total peak area. Analyses for an impurity, 4-vinyl-1-cyclohexene, were also performed by gas chromatography (GC; 1 m x 2 mm Porapak QS 80/100, 150°C isothermal, FID). This impurity results from the thermally catalyzed dimerization of 1,3-butadiene,

which occurs continuously during storage. Since the rate of "dimer" formation is temperature-dependent, care was taken to assure constant storage temperatures of approximately 72°F. The dimer is considerably less volatile than 1,3-butadiene and therefore concentrates in the cylinder "heel" as the contents of the cylinder are exhausted. To prevent the appearance of high concentrations of dimer in the 1,3-butadiene atmospheres used for the exposures, cylinder usage was limited to 80% of the net contents, and the acceptable dimer concentration in material sampled from the headspace was specified to be <500 ppm. At the beginning of the study, the headspace dimer concentration of BNW 50846-36-2 was 202 ppm and that for BNW 50846-36-3 was 354 ppm (Appendix A); periodic analyses performed during mouse exposures yielded a mean headspace dimer concentration of 338 ± 72 ppm (Appendix A).

B. INHALATION EXPOSURE SYSTEM

The animals were exposed to the test atmospheres within stainless-steel chambers designed at BNW (U.S. Patent #4,216,741; Brown and Moss, 1981; Moss et al., 1982) and fabricated by Hazelton Systems, Inc. (Aberdeen, MD). The total volume of the chamber was 2.3 m^3, and the active mixing volume was 1.7 m^3. There were three levels of caging in each chamber; each level was split into two tiers, which were offset from each other and from the chamber walls. Drawer-like stainless-steel cage units, consisting of individual animal cages, were suspended in the space above each tier. Stainless-steel catch pans for collection of urine and feces were positioned below each cage unit. Mice were exposed in individual cages (60/cage unit) equipped with feed troughs and automatic watering. During exposure, the feed troughs were removed from each cage unit. The chamber was designed so that uniform atmospheric concentrations of the test material could be maintained throughout the chamber when the catch pans were in position (Moss et al., 1982; Griffis et al., 1981).

Environmental conditions of the exposure chambers and the room were monitored throughout the study. These data included temperature, which was measured by means of thermistors, and relative humidity (RH), which was determined using an EG&G Model 910 chilled-mirror dewpoint hygrometer. A multiplexed orifice meter system, in which calibrated flow orifices were installed at the inlet and exhaust outlet of each chamber, measured chamber air flow. A Validyne pressure

transducer system was used to measure chamber air flow and chamber vacuum. Data for all environmental parameters are summarized in Appendix B.

All data-acquisition and automated system controls originated from an executive computer (Hewlett-Packard [HP] Model 9816), located in the Suite Control Center. Data from GC analyses were collected and preconditioned by an HP Model 858 computer; data from all other monitoring equipment were interfaced through a Colorado Data Systems (CDS) Model 53A-IBX Intelligent Interface System (IIS). System control, by means of devices such as valves, drive motors, audible alarms, and indicator lamps, was provided from the computer by means of control relays in the CDS-IIS.

For generation of chamber atmospheres, 1,3-butadiene was withdrawn directly from the gas cylinder through a solenoid valve and, subsequently, through a check-valve filter-flow-limit switch and a flow meter, which accurately metered gas to a distribution manifold, where it was initially diluted with filtered air. An air-driven vacuum pump delivered the butadiene-air mixture to the exposure chamber inlet for final dilution to the desired concentration.

Chamber monitoring of 1,3-butadiene concentrations was performed using an HP 5840 gas chromatograph equipped with an FID, a Valco (1-ml loop) sampling valve and a Valco stream-select valve capable of sampling eight different sites. Both valves were mounted in the GC oven, which was maintained at 120°C. The 1/8- x 12-in. nickel column was packed with 1% SP-1000 on 60/80 mesh Carbopack B. The gas chromatograph was calibrated with volumetric standards prepared with calibrated syringes and gas-sampling bags. These calibrations were in good agreement with certified gas standards, the concentrations of which had been selected to bracket the range of exposure concentrations. Eight sites were sampled every 16 minutes: four exposure chambers, two "holding" chambers, the exposure room and the GC standard. Data from the monitor were accumulated by the HP 85B computer and compared with limit values for the specific sampling location. When the value exceeded the control limits, the HP 85B computer transmitted the information to the executive computer, which initiated an appropriate action to correct the concentration. A summary of the 1,3-butadiene concentrations for each chamber during the 14-day exposure is shown in Table 1. Mean daily concentrations are listed in Appendix B.

TABLE 1. Summary of Exposure Chamber Atmospheric Concentrations of 1,3-Butadiene During the Developmental Toxicology Study of Mice

Observation	Chamber Concentrations (ppm)		
	40	200	1000
Mean daily chamber concentration ± standard deviation (ppm)	39.9 ± 0.6	199.8 ± 3.0	1000 ± 13.1
Range (ppm)	42.5 to 25.8	214 to 88.0	1070 to 630
Relative standard deviation (%)	1.4	1.5	1.3
Mean of target concentrations (%)	100	100	100

Periodic measurements of the chamber atmosphere for the dimer 4-vinyl-1-cyclohexene were performed using an HP 5790 gas chromatograph equipped with an FID, a Valco sampling valve with a 5-ml loop and a column similar to that previously described for butadiene monitoring. Column temperature was programmed to 190°C at 30°C/minute, following a 0.5-minute hold at 120°C. With this system, which employed a nitrogen carrier at 20 ml/minute, 1,3-butadiene eluted at 0.33 minutes, and the dimer at 3.25 minutes. A 100 ppm v/v certified standard of dimer in nitrogen was used to calibrate the gas chromatograph. Analyses for dimer concentrations in the atmosphere of the 1000-ppm chamber are shown in Table 2. These values were consistent with the analyses of dimer concentrations in the cylinder headspace and indicated that additional dimerization did not occur during generation of the test material.

Determinations of chamber characteristics were obtained in the presence and absence of animals. These included chamber balance measurements, which demonstrated the uniformity of chamber mixing (Appendix C) and chamber buildup and decay information. These values were within 5% of the target concentrations of 1,3-butadiene or chamber evacuation (0 ppm) and were attained within 15 minutes, even when study animals were in the chamber (Figure 1).

TABLE 2. 4-Vinyl-1-Cyclohexene (Dimer) Concentrations in the Atmosphere of the 1000-ppm 1,3-Butadiene Chamber of the Teratology Study with Mice

Exposure Day	Dimer Concentration (ppm, v/v)
12/10/85	0.29
12/12/85	0.25
12/13/85	0.26
12/15/85	0.27
12/16/85	0.28
12/17/85	0.29

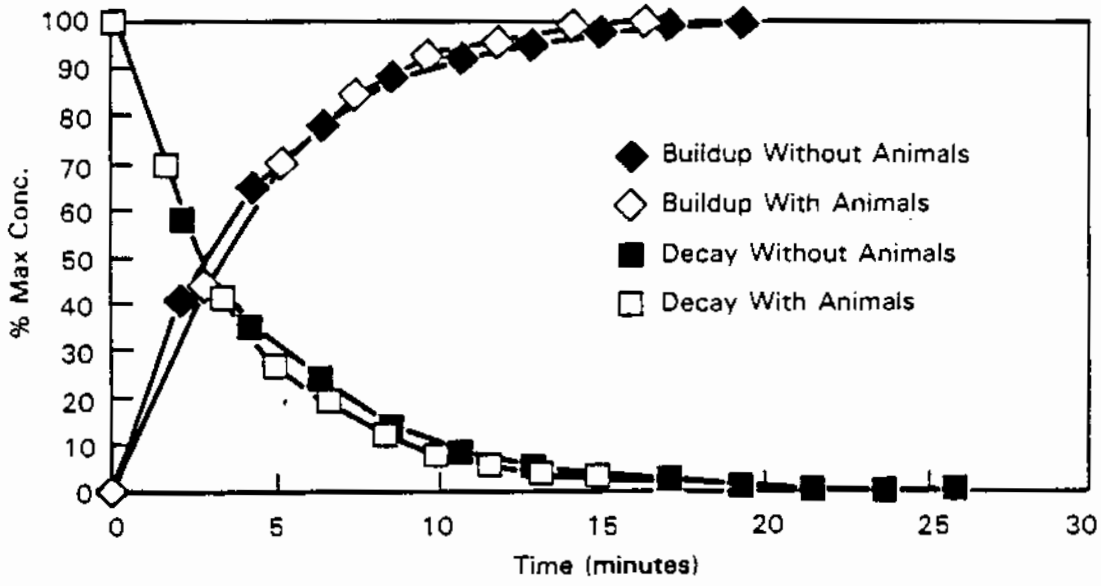

FIGURE 1. Buildup and Decay of the Atmosphere of the 1000-ppm 1,3-Butadiene Exposure Chamber in the Presence and Absence of Animals

C. ANIMAL HUSBANDRY AND EXPOSURE PROCEDURES

Salient features of the experimental design for this study are summarized in Table 3. For the study, 226, CD-1 female and 108 male (7 to 8 weeks old) mice were purchased from Charles River Laboratory, Kingston, NY Facility. The animals were isolated for 14 days, at which time five females and five males were killed and exam-

ined for internal and external parasites and bacterial pathogens; their sera were tested for antibodies to selected pathogens, and histopathologic examinations of lung, liver, kidney, ileum, colon, heart and Harderian gland were performed (Appendix D). At sacrifice, serum from five females of the control group and five of the high dose group was tested for antibodies to selected pathogens; negative results were obtained.

TABLE 3. Experimental Design for Teratology Study of Mice Exposed to 1,3-Butadiene

Chamber concentrations (ppm): 0, 40, 200, and 1000
Number of plug-positive females/exposure group: 32, 33, 31, 33
Number of days of mating: 5 (resulting in five exposure subgroups)
Exposure regimen: 6 through 15 days of gestation (dg); 6 hours/day
Day of sacrifice: 18 dg
Maternal observations: Mortality and signs of toxicity; body weights on 0, 6, 11, 16 and 18 dg; lesions at gross necropsy; weight of gravid uterus; number of implantation sites; intrauterine mortality; placental weights
Fetal observations: Body weight tabulated by sex; gross, visceral and skeletal examinations

Animal facilities and procedures at PNL were inspected and certified by the American Association of Laboratory Animal Care. During the isolation period, the animals were housed by sex, in groups of 10 mice per wire-mesh cage and provided (ad libitum) NIH-07 open formula diet; water was supplied by an automatic watering system. Temperatures and RH in the animal rooms were maintained in ranges of 72 ± 3°F and 50 ± 15%, respectively.

Following the isolation period, the females were weighed and individually identified by numbered eartags. For mating, two females were caged overnight with one male. Mating continued for 5 successive nights to obtain the desired group size of females. Copulation was established by examination for a copulation plug, and the morning of observation was designated as 0 dg. At this time, the plug-positive females were weighed and assigned to exposure groups by means of a computer-assisted randomization program, which is based on a single blocking factor, body weight. In addition to individual eartag numbers, animals in each exposure group were identified by means of a distinctive toeclip on the forepaw.

Three days prior to the initiation of exposure, the animals were housed in the exposure chambers in the exposure room. Environmental data were collected during this interval. Exposure to 1,3-butadiene atmospheres of 0 (filtered air), 40, 200 and 1000 ppm commenced on 6 dg. Each animal was exposed to its assigned treatment daily for 6 hours per day from 6 through 15 dg. From 16 dg until sacrifice at 18 dg, all animals were housed in exposure chambers with filtered-air atmospheres. The 5 days of mating resulted in staged starts and cessations of exposures. Accordingly, "filler" animals (excess males and females) were used to maintain a constant animal load in the exposure chambers. Water was provided ad libitum throughout the study; however, food was removed during the daily 6-hour exposure period.

D. TOXICOLOGIC AND DEVELOPMENTAL OBSERVATIONS

The animals were observed twice daily for mortality, morbidity and signs of toxicity. Female mice were weighed during the week prior to mating, and on 0, 6, 11 and 16 dg. On 18 dg, the animals were euthanized with CO_2, weighed, and examined for gross tissue abnormalities. The uterus was removed and weighed; apparently nongravid uteri were stained with ammonium sulfite to detect implantation sites (Kopf et al., 1964). The number, position and status of implants were recorded for gravid uteri; placentas were examined and weighed. Live fetuses were weighed, examined for gross defects, and their sex was determined. Examinations for fetal lens opacities were conducted by removing the eyelid and examining the eye in situ. In addition, the eyeballs were removed for observation under the dissecting microscope. Visceral examinations (Staples, 1977) and skeletal examinations, using specimens stained with alcian blue and alizarin red (Kimmel and Trammell, 1981; Kimmel, personal communication), were performed on all live fetuses. Approximately 50% of the fetal heads were examined by razor-blade sectioning of fixed preparations (Wilson, 1965).

E. STATISTICAL METHODS

Analysis of variance (ANOVA; Steel and Torrie, 1980) was used to analyze weight data and, if the result of the analysis was significant, a *t*-test was performed to determine if exposed groups were significantly different from the control group. Response proportions, such as the number of resorptions, implants, live or dead or

affected fetuses/litter, were also analyzed by the ANOVA method following arcsin transformation of the response proportion. An orthogonal contrast (Winer, 1971) was used to test trends for dose dependency. In the case of maternal weights, which were repeated over time, analyses for differences among growth curves employed a randomization test (Zerbe, 1979).

Binary-response variables between groups were compared, using chi-square or Fischer's exact test (Siegel, 1956), e.g., numbers of pregnant females/number of inseminated.

III. RESULTS

No signs of maternal toxicity were observed and there was no mortality other than in three mice in the 1000-ppm exposure group. During a routine inspection of the animals, these mice were observed to be dehydrated. Two of the mice died on the last day of exposure and early parturition occurred in the third after the exposure had been completed. Necropsy revealed no abnormalities other than those associated with dehydration.

There was a significant concentration-related decrease in maternal body weight gains during the last 5 days of exposure and in the interval between the cessation of exposure and sacrifice (Table 4). During the last half of the exposure interval, weight gains of mice exposed to 200 and 1000 ppm were significantly less than those of control animals. Exposure to 1,3-butadiene did not significantly affect the body weights of nonpregnant mice at any time during exposure (Table 5). Significant concentration-related decreases in body weights at sacrifice, weights of gravid uteri, extragestational weights and extragestational weight gains were detected (Table 6). For all of these parameters, values of the mice exposed to 1000 ppm were significantly lower than control values. In the case of extragestational weight gains, a significant difference was detected in animals exposed to 200 ppm.

The overall percentage of animals that were pregnant was low, ranging from 56% in control mice to 68% in females of the 1000-ppm exposure group, but the percentage did not significantly differ among treatments (Table 7). There were no remarkable differences among treatment groups in the number of implantation sites, total resorptions and live fetuses/litter. The total number of resorptions and percentage of resorptions/litter did not differ, but a slightly disproportionate partition of early and late resorptions in control and exposed groups led to apparent differences in incidence. In exposed mice, early resorptions tended to be less numerous than in the control animals, and the difference between values for 200 ppm and control groups was statistically significant. Conversely, values for late resorptions tended to be higher in exposed groups than in the controls, although none of the differences were significant.

TABLE 4. Changes in Body Weights (g, Mean ± Standard Error) of Pregnant Mice Exposed to 1,3-Butadiene

Time Interval (Day of Gestation)	1,3-Butadiene Concentration (ppm)			
	0 (N = 18)[a]	40 (N = 19)	200 (N = 21)	1000 (N = 20)
0 to 6	2.7 ± 0.3	3.0 ± 0.3	2.5 ± 0.2	2.3 ± 0.2
6 to 11	5.5 ± 0.4	5.8 ± 0.3	5.6 ± 0.3	4.8 ± 0.3
11 to 16[b]	13.3 ± 0.6[c]	12.7 ± 0.4[c,d]	11.4 ± 0.5[d,e]	10.6 ± 0.4[e]
16 to 18[b]	5.5 ± 0.3	5.7 ± 0.3	4.7 ± 0.4	4.8 ± 0.3

[a]Number of animals
[b]Significant ($P \leq 0.05$) linear trend
[c-e]Values that do not share a common letter are significantly different ($P \leq 0.05$) from one another.

TABLE 5. Changes in Body Weights (g, Mean ± Standard Error) of Nonpregnant Mice Exposed to 1,3-Butadiene

Exposure Day	1,3-Butadiene Concentration (ppm)			
	0 (N = 14)[a]	40 (N = 14)	200 (N = 10)	1000 (N = 10)
-6	28.1 ± 0.4	27.8 ± 0.3	27.6 ± 0.3	27.9 ± 0.2
1	30.2 ± 0.4	29.6 ± 0.4	29.0 ± 0.4	28.6 ± 0.3
5	30.1 ± 0.3	30.1 ± 0.3	29.5 ± 0.4	29.5 ± 0.4
10[b]	30.6 ± 0.3	29.9 ± 0.4	29.5 ± 0.4	29.1 ± 0.5
Sacrifice[c]	29.4 ± 0.4	28.5 ± 0.3	27.9 ± 0.2	28.0 ± 0.4

[a]Number of animals
[b]Last day of exposure
[c]Last day of exposure plus 2 days

Although numerical differences were small, the low within-group variability permitted the detection of statistically significant, concentration-related linear trends toward depressed fetal and placental weights (Table 8). Body weights of male fetuses from litters exposed to 1,3-butadiene differed significantly from control values and there was a significant concentration-related trend with increasing concentrations of the chemical. Weights of female fetuses were significantly lower

TABLE 6. Maternal Measures (g, Mean ± Standard Error) for Mice Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0 (N = 18)[a]	40 (N = 19)	200 (N = 21)	1000 (N = 20)
Body weight on 0 day of gestation (dg)	28.4 ± 0.25	28.3 ± 0.32	28.2 ± 0.32	28.4 ± 0.32
Body weight on 18 dg[b]	54.9 ± 1.21[c]	55.4 ± 1.09[c]	52.5 ± 1.01[c,d]	50.8 ± 0.87[d]
Weight of gravid uterus[b]	19.3 ± 1.00[c]	20.3 ± 0.80[c]	18.0 ± 0.87[c,d]	16.7 ± 0.67[d]
Extragestational weight[b,e]	35.5 ± 0.48[c]	35.1 ± 0.44[c,d]	34.5 ± 0.46[c,d]	34.1 ± 0.36[d]
Extragestational weight gain[b,f]	7.60 ± 0.48[c]	6.99 ± 0.38[c,d]	6.20 ± 0.38[d]	5.91 ± 0.28[d]

[a]Number of animals
[b]Significant ($P \leq 0.05$) linear trend
[c,d]Values that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.
[e]Extragestational weight = body weight on 18 dg - weight of gravid uterus
[f]Extragestational weight gain = extragestational weight - body weight on 0 dg

TABLE 7. Reproductive Measures (Mean ± Standard Error) for Mice Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number of:				
Mice exposed	32	33	31	33
Pregnant mice (%)	18 (56)	19 (57)	21 (68)	22 (67)
Litters examined	18	19	21	20
Litters with live fetuses	18	19	21	20
Implantations/dam	12.7 ± 0.52	13.3 ± 0.44	13.0 ± 0.64	13.1 ± 0.43
Resorptions/litter	1.06 ± 0.22	0.84 ± 0.21	0.67 ± 0.20	0.90 ± 0.19
Early	1.00 ± 0.23[a]	0.58 ± 0.21[a,b]	0.43 ± 0.13[b]	0.75 ± 0.16[a,b]
Late	0.06 ± 0.06	0.26 ± 0.10	0.24 ± 0.12	0.15 ± 0.08
Dead fetuses/litter	0	0	0	0
Live fetuses/litter	11.7 ± 0.66	12.5 ± 0.52	12.3 ± 0.62	12.2 ± 0.51
Percentage of:				
Resorptions/litter	9.75 ± 2.83	6.73 ± 1.94	4.80 ± 1.44	7.25 ± 1.59
Early	9.35 ± 2.88[a]	4.96 ± 2.00[a,b]	3.07 ± 0.96[b]	6.17 ± 1.35[a,b]
Late	0.40 ± 0.40	1.77 ± 0.70	1.73 ± 0.85	1.08 ± 0.60
Live fetuses/litter	90.3 ± 2.83	93.3 ± 1.94	95.2 ± 1.44	92.8 ± 1.59

[a,b]Values that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.

than control values in the 200- and 1000-ppm exposure groups. Placental weights were also significantly decreased following exposure to concentrations of 200 or 1000 ppm. Weights of placentas of male fetuses were significantly lower in the 200- and 1000-ppm groups, but weights of placentas of female fetuses were significantly reduced in only the highest exposure group.

TABLE 8. Fetal and Placental Measures (Mean ± Standard Error) for Mouse Litters Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number of:				
Litters examined	18	19	21	20
Fetuses examined	211	237	259	244
Body weight (g)[a]	1.34 ± 0.03[b]	1.28 ± 0.01[b]	1.13 ± 0.02[c]	1.04 ± 0.03[d]
Females[a]	1.30 ± 0.02[b]	1.25 ± 0.01[b]	1.10 ± 0.02[c]	1.02 ± 0.03[d]
Males[a]	1.38 ± 0.03[b]	1.31 ± 0.02[c]	1.13 ± 0.02[d]	1.06 ± 0.02[e]
Sex ratio (% males)	51.6 ± 3.91	49.8 ± 3.06	51.5 ± 3.68	51.8 ± 3.29
Placental weight (mg)[a]	86.8 ± 2.99[b]	85.4 ± 2.29[b,c]	78.6 ± 3.24[c,d]	72.6 ± 1.88[d]
Females[a]	83.1 ± 3.03[b]	80.9 ± 2.46[b]	74.7 ± 3.52[b,c]	70.1 ± 2.33[c]
Males[a]	89.3 ± 3.05[b]	89.5 ± 2.27[b]	80.1 ± 2.35[c]	74.5 ± 1.81[c]

[a]Significant ($P \leq 0.05$) linear trend
[b-e]Values that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.

The incidence of malformations, which included exencephalus, hydrocephalus, cleft palate and thoracogastroschisis, was not significantly different among treatment groups (Table 9). No lens opacities of the fetal eye were detected during examination. The incidence of supernumerary ribs, particularly extra rudimentary ribs, was significantly elevated in fetuses and litters of the 200- and 1000-ppm exposure groups (Tables 10 and 11). In these exposure groups, the incidence of reduced sternebral ossification was significantly increased when the tests used mean proportion of the litter affected.

TABLE 9. Fetal Malformations[a] in Mice Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number Examined				
Litters	18	19	21	20
Fetuses	211	237	259	244
Fetal heads	105	120	130	120
Malformations				
Exencephalus	1/1[b]	---[c]	---	2/2[d]
Open eye	1/1[b]	---	---	1/1[d]
External hydrocephalus	---	---	---	1/1
Cleft palate	---	1/1	---	---
Thoracogastroschisis	1/1	---	---	---
Missing left atrium	---	---	---	1/1
Limb flexure	2/1	---	---	---
Fused sternebrae	---	---	---	2/2[d]
Scrambled sternebrae	---	1/1	---	---
Fused ribs	---	2/2	---	---
TOTAL MALFORMED	4/3	4/4	0/0	6/5

[a]Expressed as number of fetuses/number of litters
[b]Fetus #10 in litter #351
[c]No malformations observed
[d]Fetus #1 in litter #264; fetus #12 in litter #317

TABLE 10. Fetal Variations[a] in Mice Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number Examined				
Litters	18	19	21	20
Fetuses	211	237	259	244
Fetal heads	105	120	130	120
Variations				
Pale	2/2	---	---	---
Hydroureter	2/2	6/3	---	---
Misaligned sternebrae	10/6	3/3	9/8	10/8[b]
Ossification site between sternebrae 5 and 6	---	1/1	1/1	3/3
Supernumerary ribs	30/11	30/9	127[d]/20	198[d]/20
Normal length	6/5	5/1	29[d]/9	68[d]/10
Rudimentary	13/6	19/8	81[d]/20	120[d]/16
Ossification site at lumbar 1	11/5	6/4	17/10	10/7
Reduced Ossification				
Skull	---	---	2/2	3/1
Sternebrae	31/13	20/9	57/16	76/19
Vertebrae (centra)	---	1/1	---	1/1
Phalanges	---	---	---	2/1

[a]Expressed as number of fetuses/number of litters
[b]Fetus #1 in litter #264; fetus #12 in litter #317

TABLE 11. Mean Percent of Reduced Ossification, Supernumerary Ribs, and Abnormal Sternebrae per Litter Following Exposure to 1,3-Butadiene (Mean ± Standard Deviation)

Observation	1,3 Butadiene Exposure Concentration (ppm)			
	0%	40%	200%	1000%
Reduced ossification[a]	1.7 ± 1.7	1.2 ± 1.5	2.7 ± 2.7	3.9 ± 2.6†
Supernumerary ribs*	1.7 ± 2.3	1.6 ± 2.1	6.0 ± 3.6†	9.9 ± 3.0†
Abnormal sternebrae[b]*	0.6 ± 0.9	0.4 ± 0.7	0.4 ± 0.8	0.8 ± 1.3†

[a]All sites of reduced ossification combined
[b]Misaligned, scrambled, or cleft sternebrae
*Linearly correlated with increasing exposure concentration at $P < 0.05$. Trend analysis performed following arcsine transformation of proportional data.
†Significantly greater than control value at $P < 0.05$, as calculated by Tukey's test following ANOVA on arcsine transformation of proportional data.

IV. DISCUSSION

Significant concentration-related trends in several indices of maternal toxicity were observed. These included depressed values for various parameters related to measures of body weight and body weight gain in the interval from 11 dg to sacrifice. Compared to control values, exposure to 1000 ppm resulted in significantly reduced body weight and extragestational weight at sacrifice and a depression in extragestational gain and weight gain from 11 to 16 dg. Significant differences in mice exposed to 200 ppm were confined to weight gain during late exposure and extragestational gain, while values for these two parameters and extragestational weight only tended to be lower in animals exposed to 40 ppm. These results suggest that 1,3-butadiene was toxic to mice at atmospheric concentrations of 200 ppm and higher.

No significant dose-related effect on the number of intrauterine deaths was observed; in fact, the incidence of early resorptions in all treated groups was lower than in the control group. The significant depression in weights of gravid uteri of the mice exposed to 1000 ppm correlated well with significant depressions in fetal body weights. Although fetal body weights of the 200-ppm treatment group were also significantly depressed, there was only a tendency for weights of gravid uteri in these animals to be lower but they were not significantly different from the controls.

Perhaps the most important aspect of the findings related to the depressed fetal body weights was that male fetuses were affected at exposure concentrations of 40 ppm, a level at which there were no clear signs of maternal toxicity. Significant decreases in body weights of females occurred at the next higher dose level (200 ppm). Differences in the depression of placental weights were also associated with the sex of the fetuses, i.e., placentas of male fetuses were significantly affected at 200 ppm and those of female fetuses at 1000 ppm.

Findings similar to the significant dose-related increase in the incidence of extra ribs in the two highest exposure groups have been reported for a number of agents and in a variety of animal species (Khera, 1981). It has been shown that this effect may be related to maternal toxicity (Kavlock et al., 1985). These authors have

stated that there was an inverse linear relationship between gestational weight gain of the dams and the incidence of extra ribs in the offspring when an increased incidence of supernumerary ribs was the only observed fetal effect. Interpretations of other studies in which the only significant finding was a dose-related increase in the incidence of supernumerary ribs have varied from considerations of no significance to suggestions of teratogenicity (Khera, 1981). Results from the present study suggest that the increased incidences of extra ribs and of reduced ossification of fetal sternebrae in the two highest exposure groups, are associated with reduced fetal body weight and with maternal toxicity as evidenced by a significant dose-related reduction in maternal weight gain during gestation.

Our overall findings are consistent with the conclusions of earlier studies. Some indication of fetotoxicity, expressed as a decrease in fetal weight, was observed following exposure of pregnant mice to 1,3-butadiene. The reduction in weight for male fetuses was statistically significant at all butadiene concentrations, and for female fetuses at the two higher exposure levels, 200 and 1000 ppm. A corresponding decrease in maternal body weight and in extragestational weight gain was observed for the 200- and 1000-ppm exposure groups. Although no treatment-related effect on fetal weight was observed in the rat, a statistically significant reduction in extragestational gain was observed in the dam at the 1000-ppm exposure level. Embryotoxicity, as evidenced by an increase in intrauterine deaths or in the incidence of fetal malformations, was not observed in either species. Fetal mice exhibited a statistically significant increase in the mean percent of supernumerary ribs per litter at 200 ppm, and an increase in the percent of reduced ossification sites and abnormal sternebrae at 1000 ppm. No treatment-related increase in the incidence of corresponding fetal variations was observed in the rat. In summary, 1,3-butadiene does not appear to be teratogenic in either the rat or the mouse, but there is some indication of fetotoxicity in the mouse.

V. REFERENCES

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APPENDIX A

ANALYTICAL DATA FOR 1,3-BUTADIENE (LOT NUMBER F909)

BULK CHEMICAL REANALYSIS FOR 1,3-BUTADIENE

Compound:	1,3-Butadiene
NTP number:	10514-J
CAS number:	106-99-0
Lot:	Phillips F909; BNW notebook number 50846-36-(2&3)
Appearance:	NA
Receipt date:	06/28/85
Analysis period:	4 months after receipt
Storage temperature:	Room temperature
Sample submittal date:	NA
Sample analysis date:	November 13 and 14, 1985
Analysis procedure:	Method #ØB-AC-3AØ3-Ø3SAØ3
Notebook reference:	BNW 50846-60 through 63

Assay: Gas chromatography, using a 2-m x 2-mm glass column packed with Porapak QS 100/120 for purity by area percent and 1-m x 2-mm glass column packed with Porapak PS 80/100 for the dimer analysis, dimer content is determined from the ratio of the area of the dimer peak versus the area of the 1,3-butadiene peak. Instrument: Hewlett-Packard 5840A

Results:

Date	Sample ID	Bulk
11/85	BNW 50846-36-2	99.88
	BNW 50846-36-3	99.88

1,3-Butadiene eluted at ~6.7 minutes. A minor peak eluted 2 minutes later; it represented 0.11% of the total peak area.

Date	Sample ID	Dimer (ppm)
11/85	BNW 50846-36-2	332[a]
	BNW 50846-36-3	189

1,3-Butadiene eluted at ~0.4 minutes, the dimer at ~4.7 minutes. The dimer retention time was confirmed by running a dimer standard.

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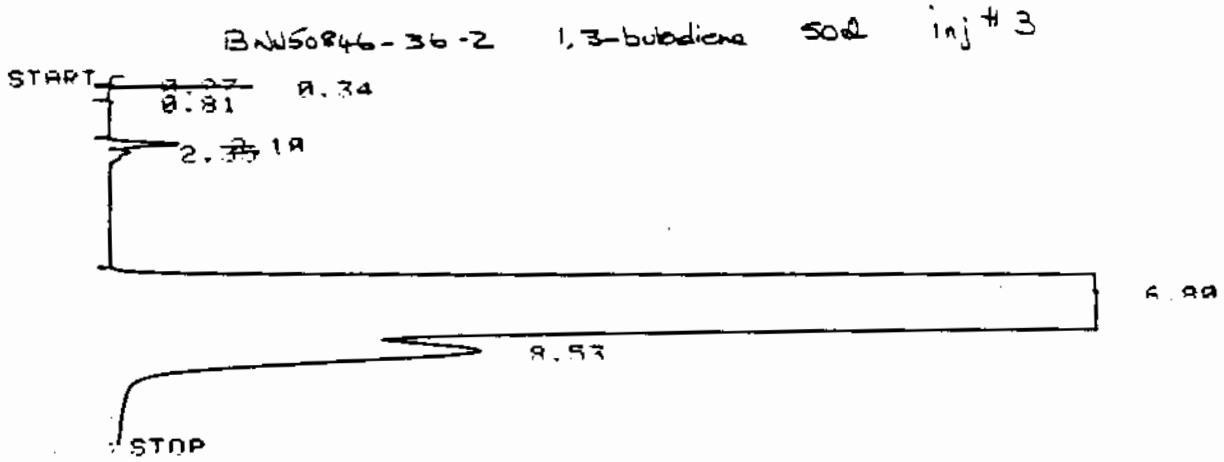
[a]Differences in values for dimer concentrations in individual cylinders reflect the thermal and usage history of each cylinder (see p. 5 of report).

HEADSPACE DIMER CONTENT OF THE 1,3-BUTADIENE CYLINDER DURING MOUSE EXPOSURES

Cylinder Number BNW 50846-36-	Date	Dimer Concentration (ppm v/v)
2	12/06/85	202
2	12/11/85	391
3	12/12/85	354
3	12/13/85	320
3	12/16/85	371
3	12/19/85	391

Purity Analysis of 1,3-butadiene
Lot# BNW 50846-36-2
BNW 50846-60 → 63 M. M'Culloch
GC: HP5840 WA 10706
Column: 2mm x 6ft glass packed:
Porapak QS 100/120.



HP RUN # 371 NOV/14/85 TIME 12:33:35
AREA %

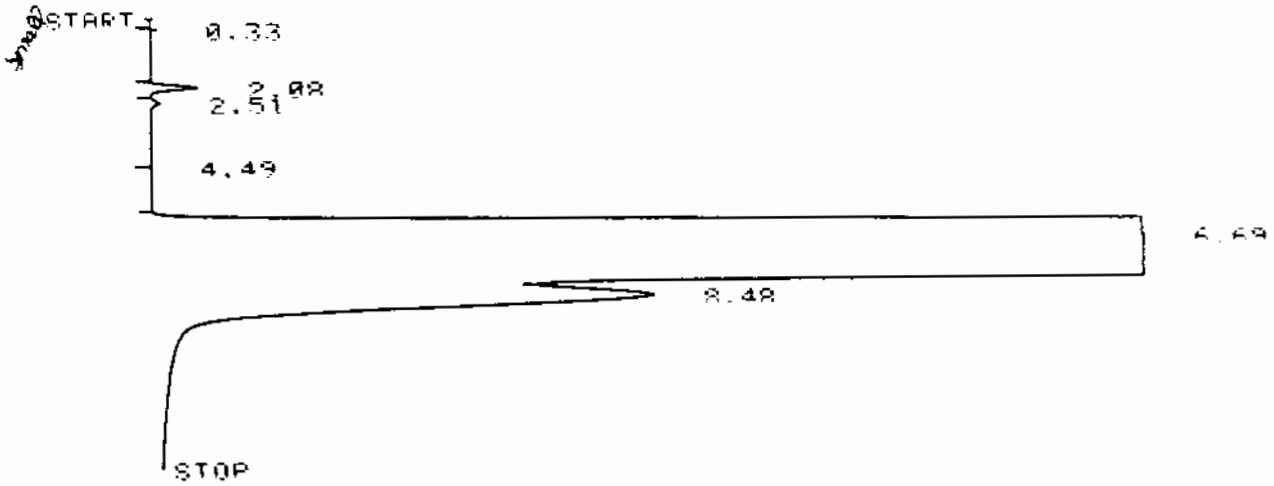
RT	AREA	AREA %
0.27	12	0.000
0.34	796	0.001
0.81	207	0.000
2.10	2959	0.005
2.35	1431	0.002
6.80	63960000	99.888
8.53	66260	0.103

DIL FACTOR: 1.0000 E+ 0

FIGURE A1. A. Gas Chromatogram of 1,3-Butadiene

Purity Analysis of 1,3-butadiene
Lot# BNW 50846-36-3.
BNW 50846-60 → 63 M.M'Culloch
GC: HP5840 WA 10706
Column: 2mm x 6ft glass packed :
Porapak QS 100/120.

BNW 50846-36-3 1,3-butadiene 5 50 ul. inj#5



HP RUN # 373 NOV/14/85 TIME 13:08:33
AREA %

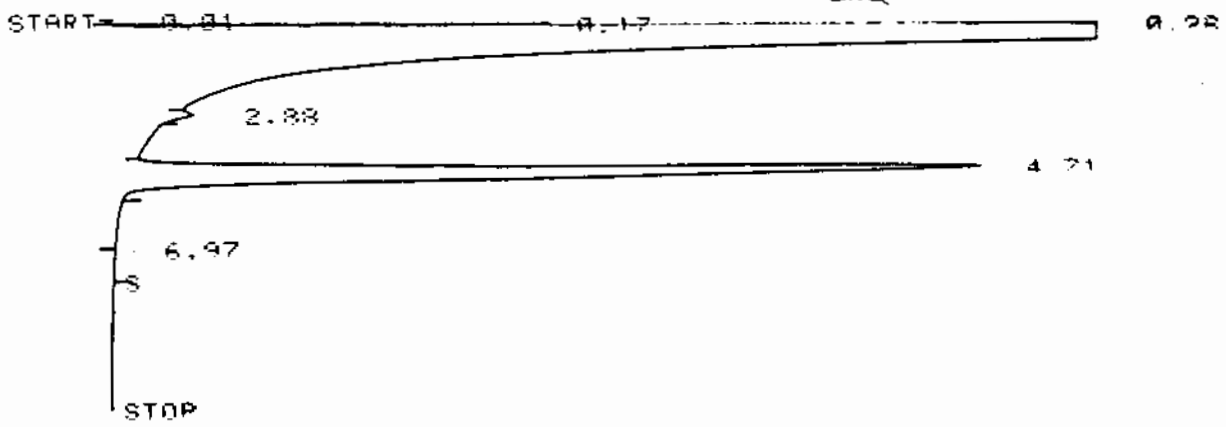
RT	AREA	AREA %
0.33	47	0.000
2.08	1949	0.002
2.51	652	0.001
4.49	69	0.000
6.69	84740000	99.880
8.48	99060	0.117

DTL FACTOR: 1.0000 E+ 0

FIGURE A1. B. Gas Chromatogram of 1,3-Butadiene

Dimer Analysis of 1,3-butadiene
Lot# BNW 50846-36-2
BNW 50846-60→63
M. M. Culbreth 11/13/85
GC HP5840 WA#10706
Column: 2mm x 3ft glass packed Porapak PS 80/100

Inj# 14 1,3-butadiene BNW 50846-36-2 0.2ml



HP RUN # 364 NOV/13/85 TIME 14:15:10
AREA %

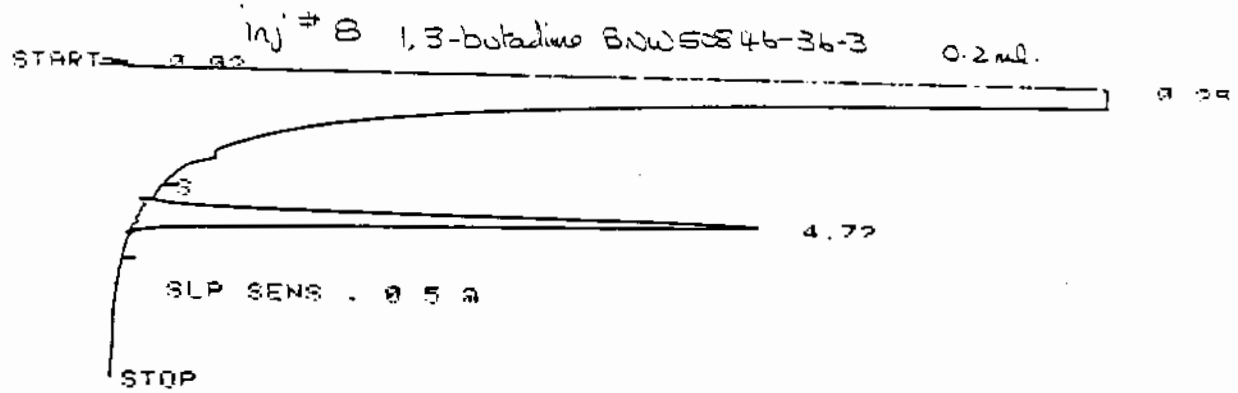
RT	AREA	AREA %
0.17	2457	0.001
0.22	9648	0.004
0.26	233000000	99.961
2.88	921	0.000
4.71	78560	0.034
6.97	10	0.000

DIL FACTOR: 1.0000 E+ 0

TEMP1 3 5 0
TEMP1 250 35 37
TEMP1 1 0 0 0

FIGURE A2. A. Gas Chromatogram of 1,3-Butadiene Dimer

Dimer Analysis of 1,3-butadiene.
Lot# BNW 50846-36-3.
BNW 50846-60→63
M. M. Cullock 11/13/85
GC HP5840 WA# 10706
Column: 2mm x 3ft glass packed Chromosorb PS 80/100



HP RUN # 358 NOV/13/85 TIME 13:12:51
AREA %

RT	AREA	AREA %
0.25	31000000000	99.982
4.72	55530	0.018

DIL FACTOR: 1.0000 E+ 0

FIGURE A2. B. Gas Chromatogram of 1,3-Butadiene Dimer

FIGURE A3. A. Infrared Spectrum of 1,3-Butadiene (Beckman Acculab 8, 10-cm Gas Cell)

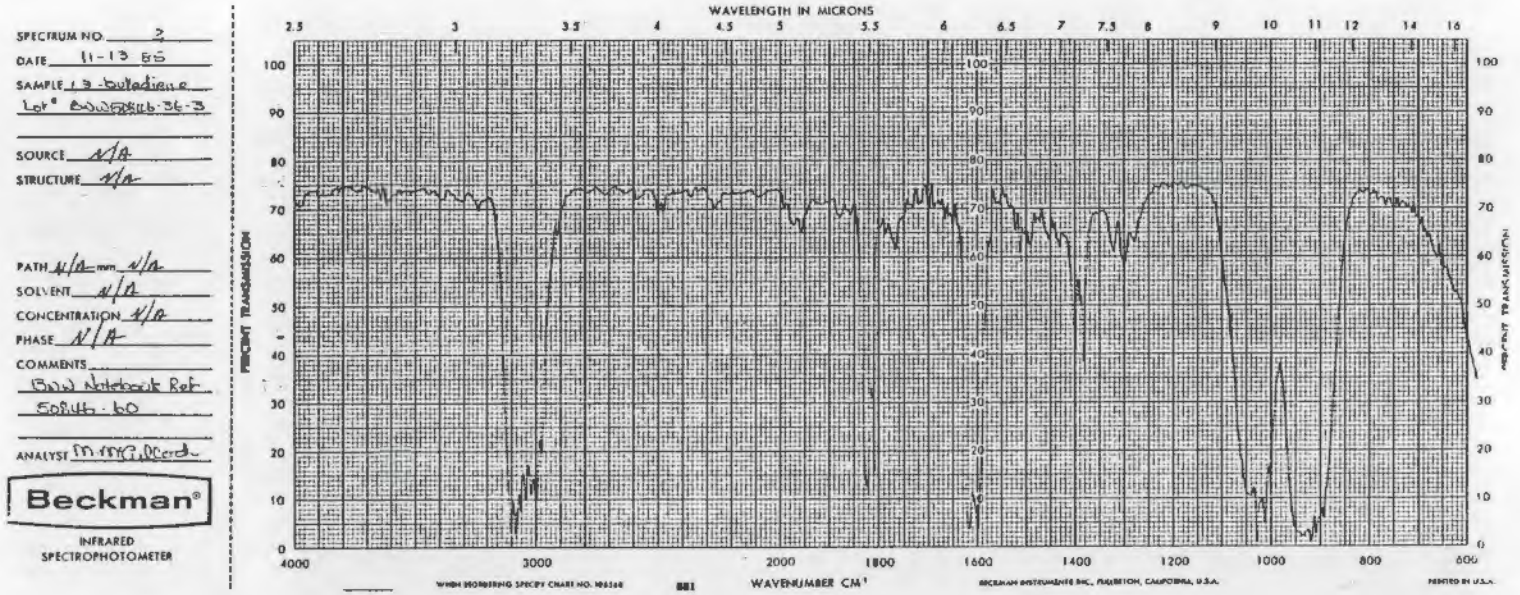


FIGURE A3. B. Infrared Spectrum of 1,3-Butadiene (Beckman Acculab 8, 10-cm Gas Cell)

APPENDIX B

BUTADIENE CONCENTRATIONS, TEMPERATURE, AND RELATIVE HUMIDITY MEASUREMENTS IN THE EXPOSURE CHAMBERS

TABLE B1. Exposure Chamber Atmospheric Concentrations (Mean Daily Concentration ± Standard Deviation) of 1,3-Butadiene During the Teratology Study in Mice

Exposure Day	Chamber Concentrations (ppm)		
	40	200	1000
12/06/85	40.6 ± 0.71	202 ± 3.30	1020 ± 15.0
12/07/85	40.0 ± 0.75	199 ± 3.19	1010 ± 23.8
12/08/85	40.0 ± 0.61	199 ± 2.66	1010 ± 8.80
12/09/85	39.9 ± 0.58	200 ± 2.30	1000 ± 11.2
12/10/85	39.6 ± 0.45	199 ± 2.35	997 ± 8.52
12/11/85	40.4 ± 0.93	202 ± 4.86	1020 ± 19.87
12/12/85	39.0 ± 3.36[a]	194 ± 8.33	993 ± 30.5
12/13/85	40.1 ± 0.43	197 ± 4.05	1000 ± 17.9
12/14/85	40.9 ± 0.18	202 ± 2.10	1010 ± 14.8
12/15/85	39.9 ± 0.47	199 ± 2.17	998 ± 7.04
12/16/85	38.8 ± 3.90[b]	192 ± 2.76[b]	968 ± 10.8[b]
12/17/85	40.1 ± 0.86	202 ± 3.77	1010 ± 15.2
12/18/85	39.9 ± 0.41	201 ± 2.49	1010 ± 10.4
12/19/85	39.8 ± 0.66	199 ± 3.44	1000 ± 13.0

[a]One reading of 25.8 ppm occurred during a 1-minute shutdown caused by a blown fuse in the system's power supply.

[b]A period of sporadic variation in airflow was caused by a flameout in the building's boiler; this resulted in three system shutdowns during this 30-minute period in which the following chamber concentrations were recorded:

Target Concentration (ppm)	Recorded Value (ppm)
40	26.7
40	30.0
200	88.0
1000	699
1000	630

TABLE B2. Exposure Chamber Temperatures (°F, Daily Mean ± Standard Deviation) for the Teratology Study of 1,3-Butadiene in Mice

Exposure Day	Exposure Chamber (ppm)			
	0	40	200	1000
12/06/85	74.7 ± 0.78	74.2 ± 0.55	74.1 ± 0.71	74.0 ± 0.75
12/07/85	75.5 ± 0.47	74.7 ± 0.42	74.4 ± 0.60	73.7 ± 0.79
12/08/85	74.8 ± 0.59	74.6 ± 0.53	74.2 ± 0.75	73.3 ± 0.74
12/09/85	74.4 ± 1.38	72.3 ± 1.28	72.1 ± 1.47	72.4 ± 1.67
12/10/85	74.3 ± 0.37	72.7 ± 0.13	72.7 ± 0.14	72.9 ± 0.15
12/11/85	74.1 ± 0.43	72.7 ± 0.14	72.6 ± 0.25	72.9 ± 0.33
12/12/85	74.4 ± 1.04	73.1 ± 0.35	73.1 ± 0.44	73.5 ± 0.48
12/13/85	74.1 ± 0.71	73.4 ± 0.74	73.5 ± 0.76	73.9 ± 0.51
12/14/85	74.0 ± 0.15	73.4 ± 0.39	73.4 ± 0.37	73.9 ± 0.34
12/15/85	73.9 ± 0.25	73.4 ± 0.20	73.3 ± 0.14	73.9 ± 0.26
12/16/85	74.3 ± 0.67	72.8 ± 0.34	72.6 ± 0.43	73.9 ± 0.36
12/17/85	73.9 ± 0.46	72.9 ± 0.13	72.7 ± 0.30	74.1 ± 0.25
12/18/85	73.9 ± 0.38	72.8 ± 0.31	72.6 ± 0.31	74.1 ± 0.19
12/19/85	73.9 ± 0.36	72.9 ± 0.40	72.6 ± 0.33	74.0 ± 0.28

TABLE B3. Exposure Chamber Relative Humidity (RH; %, Daily Mean ± Standard Deviation) for the Teratology Study of 1,3-Butadiene in Mice

Exposure Day	Exposure Chamber (ppm)			
	0[a]	40	200	1000[b]
12/06/85	58.4 ± 3.4	59.3 ± 3.3	51.6 ± 3.5	59.1 ± 5.1
12/07/85	57.7 ± 4.3	57.0 ± 5.9	51.9 ± 4.5	56.6 ± 8.9
12/08/85	57.7 ± 5.3	61.7 ± 5.4	53.4 ± 3.8	49.4 ± 2.9
12/09/85	53.7 ± 5.6	56.7 ± 10.2	46.1 ± 8.1	39.4 ± 7.3
12/10/85	48.0 ± 5.1	51.9 ± 6.2	52.3 ± 14.7	50.8 ± 13.7
12/11/85	47.1 ± 3.9	50.6 ± 3.6	61.0 ± 6.9	56.6 ± 7.1
12/12/85	35.4 ± 6.0	46.0 ± 7.8	52.8 ± 10.9	48.3 ± 9.3
12/13/85	34.1 ± 3.1	48.0 ± 6.3	44.9 ± 6.9	42.7 ± 8.5
12/16/85	41.8 ± 9.8	52.9 ± 8.4	47.9 ± 8.9	43.7 ± 5.8
12/17/85	53.0 ± 5.5	48.0 ± 8.0	46.3 ± 5.8	44.5 ± 5.5
12/18/85	47.6 ± 4.8	53.5 ± 7.0	51.0 ± 9.5	43.1 ± 5.2
12/19/85	49.7 ± 6.5	55.4 ± 5.4	51.0 ± 7.0	37.6 ± 5.4
12/20/85	51.6 ± 6.0	55.6 ± 6.3	54.7 ± 7.9	37.8 ± 4.0
12/21/85	46.5 ± 3.3	54.6 ± 7.7	51.4 ± 7.1	37.1 ± 3.2

[a]On exposure days 7 through 9, three to five recorded RH values (minimal values of 29 to 31%) were less than the lower operating limit (40%) specified in the protocol. On day 9, a loose nut was found in the RH control motor.

[b]On exposure days 4, 12, 13 and 14, the daily mean RH value was less than the minimum operating limit specified in the protocol (40%); the minimal RH recorded was 32%. On day 5, one low value of 34% was recorded. The cause of these variances could not be determined.

APPENDIX C

CHAMBER UNIFORMITY TESTS FOR 1,3-BUTADIENE CONCENTRATIONS

CHAMBER UNIFORMITY DATA SHEET

COMPOUND: IRT 1,3 BUTADIENE **EXPOSURE ROOM NUMBER:** 436

TPV MEASUREMENTS

CHAMBER:	40 ppm		200 ppm		1000 ppm					
DATE:	11/4/85		11/4/85		11/4/85					
SAMPLE PORT	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD
BACK: 1B	39.9	100.2%	203.9	99.6%	996.5	99.8%				
2B	39.9	100.2%	203.9	99.6%	999.3	100.1%				
3B	40	100.4%	204.7	100.0%	998.2	100.0%				
4B	40.1	100.7%	205.1	100.2%	1002.1	100.4%				
5B	40	100.4%	205.4	100.3%	994.5	99.6%				
6B	40	100.4%	205.7	100.5%	993.3	99.5%				
FRONT: 1F	39.6	99.4%	204.8	100.0%	1000.7	100.2%				
2F	39.5	99.2%	205	100.1%	995.9	99.7%				
3F	39.7	99.7%	204.7	100.0%	1000.2	100.2%				
4F	39.8	99.9%	205.3	100.3%	1001.4	100.3%				
5F	39.4	98.9%	204.2	99.7%	1000.2	100.2%				
6F	40	100.4%	204.4	99.8%	1000.3	100.2%				
MEAN:	39.8	100.0%	204.8	100.0%	998.6	100.0%				
TPV:	0.23	0.6%	0.58	0.3%	2.86	0.3%				
BPV:	//////////	0.5%	//////////	≤0%	//////////	≤0%	//////////		//////////	

WPV MEASUREMENTS

IN-LINE 1st	40	100.3%	206	100.5%	985	99.2%				
2nd	40	100.0%	204	99.5%	997	100.4%				
3rd	40	99.7%	205	100.0%	996	100.4%				
MEAN:	39.9	100.0%	204.9	100.0%	992.3	100.0%				
WPV:	0.10	0.3%	1.00	0.5%	6.70	0.7%				

MONITOR TYPE: GC 809569 SERIAL #:

MONITOR DATA LOCATION:

COMMENTS: GC monitor port 2B 6' long 1/4" OD Teflon line added to the regular GC sampling line without animals

ENTERED BY: ML Clark DATE: 12/31/85 REVIEWED BY: MKCRL DATE: 1/3/86

FIGURE C1. Chamber Uniformity Data Sheet--Gas Chromatography Monitoring

TJM-607A

CHAMBER UNIFORMITY DATA SHEET

COMPOUND: IRT 1,3 BUTADIENE **EXPOSURE ROOM NUMBER:** 436

TPV MEASUREMENTS

CHAMBER:	40 ppm		200 ppm		1000 ppm					
DATE:	11/26/85		11/26/85		11/26/85					
SAMPLE PORT	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD
BACK: 1B	39.9	100.9%	198	101.3%	1006.5	100.5%				
2B										
3B	39.8	100.6%	197.7	101.1%	988.6	98.7%				
4B	39	98.6%	197.5	101.0%	1007.9	100.6%				
5B										
6B										
FRONT: 1F										
2F										
3F	39.5	99.8%	190.2	97.3%	1002	100.1%				
4F	39.6	100.1%	194.3	99.4%	1002	100.1%				
5F										
6F										
MEAN:	39.6	100.0%	195.5	100.0%	1001.4	100.0%				
TPV:	0.35	0.9%	3.34	1.7%	7.63	0.8%				
HTPV:	//////////	0.9%	//////////	0.4%	//////////	0.7%	//////////		//////////	

WPV MEASUREMENTS

IN-LINE: 1st	40	99.9%	198	100.4%	1007	100.1%		
2nd	40	99.9%	194	98.2%	1004	99.8%		
3rd	40	100.2%	200	101.4%	1007	100.1%		
MEAN:	39.9	100.0%	197.1	100.0%	1005.7	100.0%		
WPV:	0.06	0.1%	3.29	1.7%	1.84	0.2%		

MONITOR TYPE: GC-N809569 SERIAL #:

MONITOR DATA LOCATION: BNW Lab notebook #51192, page 71

COMMENTS: Chamber balance performed with chambers containing animals

ENTERED BY: ML Clark DATE: 12/31/85 REVIEWED BY: MRCLL DATE: 1/3/86

C-2

FIGURE C2. Chamber Uniformity Data Sheet--Chamber Balance

APPENDIX D

HEALTH EVALUATIONS OF EXPERIMENTAL ANIMALS

Battelle
Pacific Northwest Laboratories

Project Number

Internal Distribution

File/LB

Date December 12, 1985

To Pat Hackett

From Steve Rowe SER

Subject PRE-EXPOSURE HEALTH EVALUATION OF MICE FOR 1,3 BUTADIENE TERATOLOGY STUDY

Mice for this study were received in good condition on 11/12/85 from Charles River's Kingston, NY facility, area 96. On 11/25, 5 males and 5 females were randomly selected for health evaluation. Examination included culture of nasopharyngial wash for bacterial pathogens, serologic tests for viral antibodies, gross necropsy and microscopic examination of selected tissues.

Rare tiny foci of hepatocellular necrosis were found in livers of 5 mice. I have found these lesions are very common in recently shipped mice and believe they are caused by shipping stress without intercurrent infection. I am not especially concerned about these findings particularly since serologic tests for mouse hepatitis virus antibodies were negative.

No other significant lesions or pathogens were found and the mice were verbally released from quarantine on 11/27/85. Detailed results can be found in the attached lab report (N-123).

APPENDIX E

INDIVIDUAL VALUES FOR FETAL STATUS, SEX AND BODY WEIGHT, AND PLACENTAL WEIGHT

TABLE E1. Individual Values for Fetal Status, Sex and Body Weight, and Placental Weight[a]

[a]Column Headings:

CASE - Sequential number of samples
DAM ID - Eartag number of maternal animals
TMT GRP - Exposure concentration of 1,3-butadiene (ppm)

1 = 0
2 = 40
3 = 200
4 = 1000

SAC DATE - Year/month/day of sacrifice
SAC TIME - Hour of sacrifice
SITE# - Fetal identification by position in uterus
STATUS - Viability of fetuses or embryos at sacrifice

1 = live fetus
2 = early resorption
4 = late resorption
5 = dead fetus

SEX - Sex of fetuses

1 = male
2 = female

FETAL WT - Fetal body weight in g (-1.000 = no value determined)
PLAC WT - Placental y weight in g (-1.000 = no value determined)

TMT=Ø ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
228	1	1	1	1.611	Ø.101
228	2	1	2	1.393	Ø.106
228	3	1	1	1.524	Ø.095
228	4	1	1	1.512	Ø.103
228	5	1	2	1.573	Ø.087
228	6	1	1	1.526	Ø.092
228	7	1	1	1.563	Ø.080
228	8	2	.	.	.
228	9	1	2	1.311	Ø.080
228	10	1	1	1.550	Ø.084
256	1	1	1	1.406	Ø.110
256	2	1	2	1.277	Ø.097
256	3	1	2	1.272	Ø.088
256	4	1	1	1.220	Ø.090
256	5	2	.	.	.
256	6	1	1	1.362	Ø.095
256	7	1	2	1.273	Ø.090
256	8	1	2	1.293	Ø.102
256	9	2	.	.	.
256	10	1	1	1.336	Ø.100
256	11	1	1	1.312	Ø.126
256	12	1	1	1.316	Ø.108
270	1	1	2	1.433	Ø.122
270	2	1	1	1.763	Ø.131
270	3	2	.	.	.
270	4	2	.	.	.
270	5	1	1	1.613	Ø.123
270	6	2	.	.	.
273	1	1	2	1.352	Ø.078
273	2	2	.	.	.
273	3	1	2	1.215	Ø.068
273	4	1	2	1.181	Ø.069
273	5	1	1	1.425	Ø.078
273	6	1	2	1.204	Ø.080
273	7	1	2	1.183	Ø.055
273	8	1	1	1.108	Ø.068
273	9	1	2	1.372	Ø.095
273	10	1	1	1.370	Ø.062
273	11	1	1	1.379	Ø.089
273	12	1	2	1.355	Ø.078
273	13	1	2	Ø.664	Ø.069
273	14	1	1	1.436	Ø.095
304	1	1	2	1.189	Ø.081
304	2	1	1	1.165	Ø.095
304	3	1	2	1.140	Ø.071
304	4	1	1	1.172	Ø.091
304	5	1	1	1.289	Ø.090
304	6	1	2	1.179	Ø.086
304	7	1	1	1.098	Ø.073
304	8	1	1	1.105	Ø.078

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TWT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
304	9	1	2	1.231	0.071
304	10	1	2	1.183	0.073
304	11	1	1	1.349	0.093
304	12	1	1	1.118	0.085
320	1	1	1	1.322	0.098
320	2	1	2	1.132	0.083
320	3	1	2	1.281	0.076
320	4	1	1	1.354	0.090
320	5	1	1	1.383	0.089
320	6	1	1	1.338	0.098
320	7	1	2	1.016	0.080
320	8	1	2	1.273	0.082
320	9	1	2	1.390	0.089
320	10	1	2	1.249	0.075
320	11	1	1	1.444	0.088
320	12	1	2	1.310	0.087
320	13	1	2	1.381	0.098
321	1	1	2	1.294	0.077
321	2	1	1	1.299	0.098
321	3	1	2	1.342	0.092
321	4	1	2	1.294	0.086
321	5	1	1	1.308	0.072
321	6	1	1	1.336	0.087
321	7	1	1	1.285	0.078
321	8	1	2	1.153	0.078
321	9	1	2	1.151	0.081
321	10	1	1	1.300	0.086
321	11	1	1	1.459	0.092
321	12	1	1	1.477	0.094
321	13	1	2	1.259	0.073
321	14	1	1	1.276	0.081
321	15	1	2	1.184	0.081
341	1	1	1	1.493	0.105
341	2	1	1	1.492	0.109
341	3	1	1	1.469	0.112
341	4	1	2	1.379	0.097
341	5	1	1	1.429	0.107
341	6	1	2	1.381	0.096
341	7	1	2	1.269	0.084
341	8	1	1	1.429	0.092
341	9	1	2	1.381	0.087
341	10	1	1	1.404	0.090
341	11	1	2	1.311	0.085
341	12	1	2	1.403	0.094
341	13	1	1	1.426	0.093
351	1	1	2	1.285	0.086
351	2	1	2	1.180	0.069
351	3	1	1	1.180	0.078
351	4	1	1	1.148	0.085
351	5	1	2	1.117	0.079

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
361	6	1	1	1.234	0.080
361	7	1	2	1.128	0.069
361	8	1	2	1.218	0.084
361	9	1	2	1.169	0.082
361	10	1	1	0.932	0.066
361	11	1	2	1.214	0.074
361	12	2	.	.	.
361	13	1	2	1.158	0.073
361	14	1	2	1.214	0.089
372	1	1	2	1.430	0.079
372	2	1	2	1.252	0.070
372	3	1	1	1.200	0.078
372	4	1	1	1.354	0.079
372	5	1	2	1.322	0.070
372	6	1	2	1.380	0.082
372	7	1	1	1.451	0.081
372	8	1	1	1.316	0.089
372	9	1	2	1.262	0.098
372	10	1	1	1.353	0.076
372	11	1	2	1.240	0.093
372	12	4	.	.	.
372	13	1	2	1.305	0.075
372	14	1	1	1.410	0.083
378	1	1	1	1.338	0.091
378	2	1	1	1.402	0.092
378	3	1	1	1.464	0.100
378	4	1	1	1.460	0.083
378	5	1	2	1.348	0.066
378	6	2	.	.	.
378	7	1	1	1.350	0.079
378	8	2	.	.	.
378	9	1	1	1.346	0.083
378	10	1	1	1.398	0.139
378	11	1	1	1.400	0.091
378	12	1	1	1.347	0.080
378	13	1	1	1.332	0.099
378	14	1	1	1.245	0.073
380	1	1	2	1.337	0.070
380	2	1	1	1.360	0.072
380	3	2	.	.	.
380	4	1	2	1.276	0.074
380	5	1	1	1.429	0.080
380	6	1	2	1.295	0.064
380	7	1	2	1.284	0.075
380	8	1	1	1.482	0.073
380	9	1	2	1.334	0.060
380	10	1	2	1.236	0.074
380	11	1	1	1.365	0.067
380	12	1	1	1.357	0.086
380	13	1	2	1.360	0.089

Status: 1 = Live, 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=Ø ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
380	14	1	1	1.275	Ø.084
388	1	2	.	.	.
388	2	1	1	1.511	Ø.080
388	3	1	2	1.370	Ø.094
388	4	1	1	1.459	Ø.100
388	5	1	2	1.428	Ø.087
388	6	1	2	1.345	Ø.095
388	7	1	2	1.441	Ø.097
388	8	1	2	1.376	Ø.090
388	9	1	1	1.279	Ø.104
388	10	1	2	1.419	Ø.087
391	1	1	2	1.208	Ø.059
391	2	1	1	1.341	Ø.060
391	3	1	2	1.362	Ø.084
391	4	1	1	1.482	Ø.087
391	5	1	2	1.480	Ø.077
391	6	1	1	1.281	Ø.083
391	7	1	1	1.179	Ø.061
391	8	2	.	.	.
391	9	1	2	1.070	Ø.058
391	10	1	2	1.261	Ø.083
391	11	1	1	1.269	Ø.057
391	12	1	1	1.344	Ø.064
391	13	1	1	1.489	Ø.082
391	14	1	1	1.502	Ø.098
415	1	1	1	1.459	Ø.088
415	2	2	.	.	.
415	3	2	.	.	.
415	4	1	1	1.364	Ø.085
415	5	2	.	.	.
415	6	1	2	1.288	Ø.085
415	7	1	1	1.226	Ø.089
415	8	1	2	1.332	Ø.082
415	9	1	2	1.137	Ø.082
415	10	1	1	1.333	Ø.094
415	11	1	1	1.217	Ø.074
415	12	1	1	1.458	Ø.102
418	1	1	2	1.154	Ø.109
418	2	1	2	1.281	Ø.073
418	3	1	2	1.383	Ø.091
418	4	1	1	1.354	Ø.090
418	5	1	2	1.318	Ø.094
418	6	1	2	Ø.957	Ø.073
418	7	1	2	1.311	Ø.103
418	8	1	2	1.300	Ø.077
418	9	1	1	1.370	Ø.090
418	10	1	1	1.298	Ø.082
418	11	1	2	1.218	Ø.078
418	12	2	.	.	.
418	13	1	2	1.220	Ø.074

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=Ø ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
418	14	1	2	1.328	Ø.Ø61
422	1	1	2	1.475	Ø.Ø99
422	2	1	2	1.511	Ø.Ø69
422	3	1	1	1.490	Ø.Ø91
422	4	1	2	1.405	Ø.Ø94
422	5	1	1	1.500	Ø.Ø85
422	6	1	2	1.413	Ø.Ø89
422	7	1	1	1.518	Ø.Ø94
422	8	1	1	1.524	Ø.1Ø4
422	9	1	1	1.498	Ø.Ø87
422	1Ø	1	2	1.368	Ø.Ø97
422	11	1	2	1.36Ø	Ø.Ø92
422	12	1	2	1.351	Ø.Ø89
422	13	1	1	1.478	Ø.Ø92
422	14	2	.	.	.
422	15	1	1	1.497	Ø.Ø84
444	1	1	2	1.343	Ø.Ø8Ø
444	2	1	2	1.347	Ø.Ø79
444	3	1	1	1.372	Ø.Ø69
444	4	1	2	1.311	Ø.Ø83
444	5	1	1	1.357	Ø.Ø87
444	6	1	2	1.259	Ø.Ø69
444	7	1	1	1.350	Ø.Ø82
444	8	1	2	1.275	Ø.Ø65
444	9	1	1	1.310	Ø.Ø69
444	1Ø	1	1	1.138	Ø.Ø8Ø
444	11	1	2	1.278	Ø.Ø74
444	12	1	1	1.444	Ø.1Ø1
444	13	1	2	1.304	Ø.Ø83
444	14	1	2	1.332	Ø.Ø84

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
242	1	1	1	1.470	0.091
242	2	2	.	.	.
242	3	1	1	1.377	0.100
242	4	1	1	1.429	0.105
242	5	1	2	1.363	0.083
242	6	1	2	1.325	0.089
242	7	1	1	1.269	0.091
242	8	1	1	1.319	0.090
242	9	1	2	1.330	0.086
242	10	1	1	1.381	0.084
242	11	1	2	1.214	0.073
242	12	1	2	1.302	0.100
242	13	2	.	.	.
246	1	1	2	1.422	0.112
246	2	1	2	1.394	0.103
246	3	1	2	1.237	0.102
246	4	1	1	1.329	0.094
246	5	1	2	1.372	0.108
246	6	1	2	0.940	0.084
246	7	1	2	1.287	0.105
246	8	1	1	1.356	0.106
246	9	1	2	1.290	0.092
246	10	1	2	1.304	0.096
246	11	1	1	1.168	0.109
263	1	1	2	1.308	0.083
263	2	1	1	1.313	0.084
263	3	1	2	1.373	0.085
263	4	1	2	1.275	0.076
263	5	1	2	1.378	0.078
263	6	1	2	1.295	0.068
263	7	1	2	1.301	0.083
263	8	1	1	1.267	0.081
263	9	2	.	.	.
263	10	1	2	1.326	0.084
263	11	1	1	1.383	0.097
263	12	1	2	1.312	0.086
263	13	1	2	1.321	0.078
263	14	1	2	1.048	0.080
286	1	1	1	1.429	0.095
286	2	1	2	1.233	0.188
286	3	1	1	1.320	0.086
286	4	1	1	1.326	0.083
286	5	1	1	1.359	0.095
286	6	1	2	1.334	0.088
286	7	1	2	1.321	0.083
286	8	1	1	1.426	0.106
286	9	1	1	1.407	0.081
286	10	1	2	1.283	0.088
286	11	1	2	1.356	0.076
286	12	1	2	1.142	0.055

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
288	13	1	1	1.409	0.090
288	14	1	1	1.313	0.098
295	1	1	1	1.428	0.108
295	2	1	1	1.292	0.091
295	3	1	1	1.250	0.074
295	4	1	1	1.443	0.076
295	5	1	2	1.241	0.090
295	6	1	2	1.230	0.089
295	7	1	1	1.289	0.102
295	8	4	.	.	.
295	9	1	1	1.378	0.108
295	10	1	1	1.287	0.084
295	11	1	2	1.157	0.080
295	12	1	2	1.291	0.088
295	13	1	1	1.349	0.090
295	14	1	2	1.264	0.086
302	1	1	1	1.133	0.098
302	2	1	1	1.140	0.104
302	3	1	2	1.085	0.088
302	4	1	1	1.193	0.105
302	5	1	2	1.079	0.091
302	6	1	1	1.108	0.084
302	7	4	.	.	.
302	8	1	1	1.183	0.082
302	9	1	2	1.191	0.091
302	10	1	1	1.172	0.098
302	11	1	2	1.121	0.081
302	12	1	1	1.038	0.077
302	13	1	1	1.130	0.083
302	14	1	1	1.220	0.105
302	15	1	1	1.167	0.090
302	16	1	1	1.173	0.093
307	1	1	2	1.343	0.091
307	2	1	2	1.227	0.099
307	3	1	1	1.358	0.130
307	4	1	1	1.423	0.113
307	5	1	1	1.351	0.096
307	6	1	2	1.179	0.078
307	7	1	2	1.364	0.093
307	8	1	1	1.397	0.112
307	9	1	1	1.362	0.102
307	10	1	1	1.384	0.114
307	11	1	2	1.252	0.095
307	12	1	2	1.265	0.107
307	13	1	2	1.350	0.116
311	1	1	1	1.378	0.083
311	2	1	1	1.337	0.083
311	3	1	1	1.400	0.089
311	4	1	2	1.315	0.078
311	5	1	2	1.297	0.082

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
311	6	1	1	1.430	0.079
311	7	1	1	1.380	0.087
311	8	1	2	1.294	0.077
311	9	1	2	1.298	0.074
311	10	1	2	1.310	0.066
311	11	1	1	1.280	0.078
311	12	1	2	1.063	0.078
312	1	1	1	1.344	0.095
312	2	1	1	1.239	0.067
312	3	1	2	1.273	0.083
312	4	1	2	1.249	0.072
312	5	1	2	1.259	0.089
312	6	1	2	1.149	0.063
312	7	1	1	1.312	0.083
312	8	1	2	1.217	0.072
312	9	1	2	1.386	0.098
312	10	1	1	1.235	0.098
312	11	1	2	1.151	0.070
312	12	1	1	1.215	0.085
312	13	1	1	1.291	0.075
312	14	1	1	1.148	0.092
312	15	1	2	1.199	0.066
312	16	4	.	.	.
312	17	1	1	1.305	0.075
314	1	1	1	1.405	0.093
314	2	1	2	1.184	0.077
314	3	1	1	1.184	0.092
314	4	1	1	1.424	0.082
314	5	1	2	1.300	0.077
314	6	1	1	1.313	0.094
314	7	1	1	1.416	0.100
314	8	1	1	1.437	0.090
314	9	1	2	1.288	0.085
314	10	2	.	.	.
314	11	1	2	1.287	0.071
314	12	1	2	1.321	0.080
318	1	1	1	1.482	0.110
318	2	1	2	1.289	0.086
318	3	1	1	1.245	0.073
318	4	1	1	1.379	0.095
318	5	1	2	1.256	0.075
318	6	1	1	1.217	0.093
318	7	1	2	1.339	0.092
318	8	1	2	1.308	0.081
318	9	4	.	.	.
318	10	1	2	1.205	0.073
318	11	1	1	1.490	0.169
318	12	1	2	1.284	0.105
318	13	1	1	1.321	0.078
348	1	1	2	1.092	0.079

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TJM 60/A

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
346	2	2	.	.	.
346	3	2	.	.	.
346	4	2	.	.	.
346	5	1	1	1.310	0.103
346	6	1	1	1.322	0.094
346	7	1	1	1.048	0.089
346	8	1	2	1.238	0.088
346	9	1	2	1.167	0.089
349	1	1	2	1.015	0.063
349	2	1	2	1.227	0.055
349	3	1	1	1.249	0.098
349	4	1	2	1.394	0.072
349	5	1	2	1.334	0.070
349	6	1	1	1.404	0.081
349	7	1	1	1.344	0.074
349	8	1	1	1.395	0.099
349	9	1	1	1.391	0.081
349	10	1	1	1.246	0.071
349	11	1	1	1.411	0.072
349	12	1	2	1.349	0.064
349	13	1	2	1.354	0.082
368	1	1	2	1.283	0.080
368	2	1	2	1.396	0.078
368	3	1	1	1.421	0.084
368	4	1	2	1.253	0.055
368	5	1	1	1.355	0.070
368	6	1	1	1.391	0.087
368	7	1	1	1.379	0.059
368	8	1	1	1.480	0.097
368	9	1	2	1.365	0.074
368	10	1	1	1.235	0.078
368	11	1	1	1.369	0.070
369	1	1	2	1.286	0.078
369	2	1	2	1.237	0.091
369	3	1	1	1.292	0.097
369	4	1	2	1.218	0.089
369	5	1	1	1.230	0.088
369	6	2	.	.	.
369	7	1	1	1.278	0.085
369	8	1	1	1.127	0.089
369	9	1	2	1.345	0.097
369	10	2	.	.	.
369	11	1	2	1.251	0.081
369	12	1	2	1.287	0.081
373	1	1	1	1.421	0.087
373	2	1	2	1.307	0.081
373	3	1	2	1.260	0.062
373	4	1	1	1.342	0.078
373	5	1	2	1.315	0.061
373	6	1	1	1.382	0.093

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
373	7	1	1	1.391	0.078
373	8	1	1	1.338	0.069
373	9	1	1	1.301	0.080
373	10	1	1	1.289	0.067
373	11	1	1	1.266	0.066
373	12	1	2	1.270	0.068
373	13	1	2	1.308	0.065
373	14	1	2	1.268	0.057
373	15	1	2	1.259	0.061
381	1	2	.	.	.
381	2	1	1	1.401	0.075
381	3	1	2	1.243	0.074
381	4	1	2	1.077	0.082
381	5	1	1	1.278	0.088
381	6	1	1	1.283	0.072
381	7	1	1	1.289	0.080
381	8	1	1	1.399	0.073
381	9	1	2	1.238	0.059
381	10	1	1	1.234	0.059
381	11	1	1	1.344	0.082
381	12	1	2	1.410	0.074
381	13	1	2	1.390	0.075
381	14	1	2	0.902	0.059
381	15	1	2	1.370	0.089
390	1	1	2	1.277	0.077
390	2	1	1	1.338	0.095
390	3	1	2	1.250	0.072
390	4	1	2	1.211	0.058
390	5	1	2	1.215	0.079
390	6	1	2	1.058	0.051
390	7	1	2	1.082	0.064
390	8	1	2	1.078	0.063
390	9	1	2	1.085	0.071
390	10	1	1	1.009	0.078
390	11	1	1	1.187	0.058
390	12	1	2	1.351	0.084
390	13	1	2	1.303	0.067
390	14	1	2	1.298	0.080
433	1	1	1	1.314	0.101
433	2	1	1	1.225	0.100
433	3	1	2	1.115	0.093
433	4	1	1	1.141	0.088
433	5	1	2	1.202	0.112
433	6	1	2	1.214	0.089
433	7	1	1	1.230	0.092
433	8	1	1	1.194	0.088
433	9	1	1	1.293	0.098
433	10	1	1	1.358	0.110
433	11	1	2	1.168	0.078
433	12	2	.	.	.

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
433	13	4	.	.	.
433	14	1	2	1.239	0.085
433	15	1	2	1.252	0.086

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
251	1	1	2	1.124	0.054
251	2	1	1	1.228	0.096
251	3	1	1	1.142	0.095
251	4	1	1	1.183	0.100
251	5	1	1	1.080	0.086
251	6	1	1	1.190	0.087
251	7	1	1	1.061	0.072
251	8	1	2	1.127	0.067
251	9	1	2	1.064	0.079
251	10	1	1	1.123	0.068
251	11	1	2	1.000	0.069
251	12	1	2	1.068	0.070
251	13	1	2	0.984	0.057
258	1	1	1	1.198	0.099
258	2	1	2	1.122	0.074
258	3	1	1	1.141	0.078
258	4	1	1	1.157	0.080
258	5	1	1	1.146	0.057
258	6	2	.	.	.
258	7	1	1	1.169	0.078
258	8	1	1	1.180	0.080
258	9	1	2	1.127	0.076
258	10	1	2	1.178	0.083
258	11	1	1	1.164	0.073
258	12	1	1	1.121	0.071
258	13	1	2	1.140	0.057
260	1	1	1	1.229	0.097
260	2	4	.	.	.
260	3	1	1	1.255	0.133
260	4	1	2	1.224	0.075
260	5	1	1	1.137	0.105
260	6	2	.	.	.
260	7	1	1	1.294	0.101
260	8	1	2	1.088	0.077
260	9	1	2	1.223	0.081
260	10	1	2	1.175	0.067
260	11	1	1	1.181	0.093
260	12	1	2	1.130	0.067
260	13	1	1	1.186	0.094
260	14	1	1	1.217	0.094
265	1	1	2	1.075	0.077
265	2	1	1	1.049	0.077
265	3	1	2	1.131	0.083
265	4	1	1	1.139	0.091
265	5	1	1	1.118	0.082
265	6	1	2	1.038	0.066
265	7	1	2	1.078	0.075
265	8	1	2	1.064	0.057
265	9	1	2	0.988	0.065
265	10	1	1	0.974	0.095

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
265	11	1	2	0.978	0.073
265	12	1	2	0.921	0.050
265	13	1	2	1.051	0.058
272	1	1	1	1.041	0.073
272	2	1	1	0.953	0.080
272	3	1	2	1.051	0.084
272	4	1	2	1.016	0.076
272	5	1	2	1.037	0.071
272	6	1	2	1.010	0.066
272	7	1	1	0.953	0.055
272	8	1	2	0.962	0.068
272	9	1	2	1.026	0.067
272	10	1	1	1.127	0.065
272	11	1	1	0.993	0.066
272	12	1	1	1.122	0.071
272	13	1	2	0.905	0.068
272	14	1	2	1.060	0.082
274	1	1	1	1.135	0.073
274	2	1	1	1.192	0.083
274	3	1	1	1.130	0.066
274	4	1	2	0.983	0.062
274	5	1	1	1.187	0.087
274	6	1	2	0.995	0.082
274	7	1	2	1.115	0.080
274	8	1	1	0.826	0.058
274	9	1	2	0.967	0.047
274	10	1	1	1.150	0.070
274	11	1	1	1.178	0.079
274	12	1	2	1.108	0.089
274	13	1	1	1.167	0.089
274	14	1	2	1.038	0.069
274	15	1	1	1.138	0.081
298	1	1	2	1.190	0.108
298	2	1	1	1.100	0.103
298	3	1	1	1.159	0.106
298	4	1	2	1.124	0.116
298	5	1	1	1.092	0.081
298	6	1	1	1.180	0.106
298	7	1	2	1.083	0.095
298	8	1	2	1.113	0.112
298	9	1	2	1.097	0.110
298	10	1	1	1.094	0.106
298	11	1	2	1.060	0.083
319	1	1	2	1.071	0.071
319	2	1	2	1.207	0.085
319	3	1	2	1.175	0.060
319	4	1	2	1.139	0.077
319	5	1	1	1.148	0.074
319	6	1	1	1.144	0.083
319	7	1	2	1.092	0.079

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
319	8	2	.	.	.
319	9	1	2	0.951	0.054
319	10	1	1	1.182	0.087
319	11	1	1	1.148	0.070
319	12	1	1	1.186	0.070
319	13	1	2	0.973	0.034
319	14	1	1	1.073	0.068
319	15	1	1	1.121	0.055
328	1	2	.	.	.
328	2	1	2	0.975	0.072
328	3	1	1	1.028	0.089
328	4	1	2	1.007	0.101
328	5	1	1	1.033	0.101
328	6	4	.	.	.
328	7	1	1	1.100	0.113
328	8	1	2	0.906	0.078
328	9	1	1	0.843	0.072
328	10	4	.	.	.
328	11	1	1	0.990	0.081
328	12	1	2	1.064	0.088
328	13	1	2	1.026	0.107
328	14	1	1	1.002	0.100
337	1	1	1	1.205	0.080
337	2	1	2	1.102	0.053
337	3	1	1	1.231	0.076
337	4	1	2	1.112	0.088
337	5	1	2	1.098	0.066
337	6	1	2	1.087	0.055
337	7	1	1	1.070	0.067
337	8	1	1	1.207	0.079
337	9	1	2	1.048	0.059
337	10	1	1	1.173	0.088
337	11	1	2	0.945	0.058
337	12	1	1	1.141	0.072
339	1	1	1	1.183	0.095
339	2	1	1	1.207	0.082
339	3	1	2	1.072	0.071
339	4	1	1	1.090	0.094
339	5	1	1	0.993	0.074
339	6	1	2	1.049	0.065
339	7	1	2	1.073	0.084
339	8	1	1	1.110	0.072
339	9	1	2	1.034	0.078
339	10	1	1	1.058	0.086
339	11	1	1	0.730	0.069
342	1	1	2	0.979	0.094
342	2	1	1	1.148	0.094
342	3	1	1	1.028	0.070
342	4	1	1	1.116	0.086
342	5	1	1	1.162	0.083

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
342	6	1	1	1.135	0.098
342	7	1	2	1.028	0.066
342	8	1	2	1.071	0.087
342	9	1	1	1.119	0.073
342	10	1	1	1.116	0.098
342	11	1	1	1.134	0.076
343	1	2	.	.	.
343	2	1	2	1.097	0.068
343	3	1	2	1.118	0.066
343	4	1	1	1.052	0.063
343	5	1	1	1.133	0.068
343	6	1	2	1.087	0.056
343	7	1	2	0.981	0.059
343	8	1	1	1.049	0.079
343	9	1	1	1.077	0.061
343	10	1	2	1.038	0.063
343	11	1	2	1.159	0.079
343	12	1	2	0.940	0.044
343	13	1	1	1.101	0.064
343	14	1	2	1.057	0.061
348	1	1	2	1.257	0.102
348	2	1	2	1.162	0.073
348	3	1	1	1.255	0.100
348	4	1	2	1.181	0.096
348	5	1	2	1.154	0.080
348	6	1	1	1.161	0.090
348	7	1	2	1.167	0.084
348	8	1	2	1.177	0.095
348	9	1	2	1.142	0.085
348	10	1	1	1.186	0.094
348	11	1	1	1.107	0.075
348	12	1	2	1.149	0.078
348	13	1	1	1.242	0.106
348	14	1	1	1.209	0.115
353	1	1	1	1.198	0.080
353	2	4	.	.	.
353	3	1	1	1.181	0.074
353	4	1	1	1.236	0.084
353	5	1	1	1.167	0.080
353	6	1	1	1.104	0.079
353	7	1	2	1.182	0.088
353	8	1	2	1.187	0.076
353	9	1	2	1.158	0.074
353	10	1	1	1.167	0.064
353	11	1	2	1.151	0.071
353	12	1	1	1.182	0.074
353	13	1	1	1.226	0.069
366	1	1	2	1.212	0.077
366	2	1	1	1.263	0.068
366	3	1	1	1.378	0.076

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
366	4	1	2	1.178	0.087
366	5	1	2	1.270	0.083
366	6	1	1	1.210	0.083
366	7	1	1	1.192	0.080
366	8	1	1	1.226	0.080
366	9	1	2	1.133	0.089
366	10	2	.	.	.
366	11	1	1	1.232	0.075
366	12	1	1	1.144	0.082
366	13	2	.	.	.
366	14	1	2	1.189	0.077
371	1	1	1	1.091	0.097
371	2	1	1	1.093	0.093
371	3	1	2	0.902	0.059
371	4	1	2	0.976	0.071
371	5	1	1	1.012	0.080
371	6	1	2	0.935	0.049
371	7	1	2	0.987	0.059
371	8	1	2	1.002	0.070
371	9	1	1	1.022	0.068
371	10	1	2	0.984	0.068
371	11	1	2	1.001	0.068
371	12	1	1	1.055	0.069
371	13	1	1	0.973	0.082
371	14	1	1	1.068	0.075
371	15	1	2	0.897	0.055
382	1	1	2	1.548	0.123
382	2	1	2	1.325	0.131
392	1	1	1	1.206	0.084
392	2	1	1	1.253	0.085
392	3	1	2	1.214	0.072
392	4	1	1	1.295	0.074
392	5	1	2	1.087	0.060
392	6	1	2	1.052	0.062
392	7	1	1	1.114	0.078
392	8	1	2	1.135	0.055
392	9	1	2	1.123	0.083
392	10	1	1	1.252	0.089
392	11	1	1	1.134	.
392	12	1	2	1.132	0.056
392	13	1	1	1.168	0.068
392	14	1	2	1.178	0.089
392	15	1	1	1.240	0.065
392	16	1	2	1.198	0.081
402	1	1	2	0.903	0.071
402	2	1	1	1.208	0.092
402	3	1	1	1.093	0.041
402	4	1	2	1.078	0.073
402	5	1	1	1.052	0.066
402	6	1	2	1.098	0.083

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
402	7	1	2	0.941	0.056
402	8	1	1	1.109	0.080
402	9	1	2	1.051	0.060
402	10	1	2	1.164	0.066
402	11	1	1	1.135	0.073
402	12	1	2	0.933	0.071
402	13	2	.	.	.
402	14	1	2	1.061	0.072
402	15	1	1	1.071	0.068
402	16	1	1	1.072	0.089
420	1	1	1	1.294	0.065
420	2	1	1	1.289	0.091
420	3	2	.	.	.
420	4	1	1	1.284	0.080
420	5	2	.	.	.
420	6	1	2	1.160	0.081
420	7	1	1	1.144	0.032
420	8	1	1	1.263	0.090
420	9	1	1	1.239	0.072
420	10	1	1	1.130	0.075
420	11	1	2	1.143	0.082
420	12	1	1	1.192	0.065
420	13	1	1	1.306	0.083

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
231	1	2	.	.	.
231	2	1	1	1.112	0.073
231	3	1	2	0.932	0.080
231	4	1	2	1.063	0.099
231	5	1	2	1.026	0.092
231	6	1	2	0.955	0.094
231	7	1	1	1.051	0.089
231	8	1	2	1.036	0.079
231	9	1	1	1.038	0.093
231	10	1	1	1.046	0.079
243	1	1	2	0.982	0.062
243	2	1	2	0.980	0.075
243	3	1	2	1.016	0.060
243	4	1	1	1.130	0.076
243	5	1	2	0.949	0.051
243	6	1	2	1.046	0.071
243	7	1	1	1.003	0.064
243	8	1	1	0.998	0.054
243	9	1	1	1.001	0.064
243	10	1	2	1.077	0.073
243	11	1	2	1.028	0.070
243	12	1	2	1.041	0.098
243	13	1	2	1.018	0.076
243	14	1	1	1.037	0.080
244	1	1	1	0.934	0.075
244	2	1	2	0.537	0.059
244	3	1	2	0.882	0.060
244	4	1	2	0.746	0.060
244	5	1	2	0.889	0.069
244	6	1	1	0.942	0.057
244	7	1	2	0.948	0.063
244	8	1	1	0.885	0.069
244	9	1	2	1.000	0.055
244	10	1	1	0.925	0.062
244	11	1	1	1.080	0.059
244	12	2	.	.	.
255	1	1	2	1.067	0.062
255	2	1	2	1.130	0.094
255	3	1	1	1.081	0.093
255	4	1	1	1.073	0.098
255	5	1	1	1.056	0.084
255	6	1	2	1.034	0.050
255	7	1	1	1.087	0.073
255	8	1	2	1.078	0.089
255	9	1	2	1.058	0.090
255	10	1	1	1.087	0.080
255	11	1	1	1.133	0.077
255	12	1	1	1.131	0.070
264	1	1	1	1.067	0.074
264	2	1	1	0.901	0.060

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
264	3	1	2	1.057	0.070
264	4	1	2	0.980	0.063
264	5	1	2	1.038	0.060
264	6	1	2	0.856	0.054
264	7	1	2	0.937	0.069
264	8	1	1	0.950	0.078
264	9	1	2	1.090	0.071
264	10	1	1	1.162	0.075
264	11	1	2	1.074	0.069
264	12	1	1	1.004	0.074
264	13	1	1	1.083	0.079
264	14	1	2	1.001	0.059
276	1	1	1	0.862	0.061
276	2	1	2	0.930	0.053
276	3	1	2	0.786	0.058
276	4	1	2	0.783	0.058
276	5	4	.	.	.
276	6	1	2	0.809	0.050
276	7	1	1	0.737	0.061
276	8	1	1	0.984	0.069
276	9	1	1	1.000	0.067
276	10	1	1	0.840	0.060
276	11	1	1	0.850	0.058
276	12	1	1	0.695	0.049
276	13	1	1	0.934	0.059
276	14	1	2	0.790	0.050
276	15	1	1	0.915	0.063
294	1	1	1	1.047	0.080
294	2	1	1	1.184	0.101
294	3	1	1	1.091	0.101
294	4	1	2	0.917	0.082
294	5	1	1	1.065	0.084
294	6	1	1	1.059	0.077
294	7	1	2	0.934	0.061
294	8	1	1	1.042	0.085
294	9	1	2	0.958	0.061
294	10	1	2	1.029	0.065
294	11	1	1	0.958	0.065
294	12	1	2	0.894	0.077
294	13	1	2	1.032	0.065
294	14	1	2	0.951	0.068
294	15	1	2	1.020	0.068
305	1	1	1	1.197	0.080
305	2	1	1	1.021	0.071
305	3	1	2	1.031	0.078
305	4	1	2	0.924	0.077
305	5	1	2	1.106	0.083
305	6	1	1	1.029	0.071
305	7	1	1	1.127	0.089
305	8	1	1	1.230	0.103

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
305	9	1	1	1.054	0.091
305	10	1	2	0.998	0.074
305	11	1	2	0.952	0.064
305	12	1	1	0.991	0.078
309	1	1	2	1.045	0.068
309	2	1	2	1.082	0.070
309	3	1	1	1.165	0.076
309	4	1	1	1.076	0.048
309	5	1	1	1.106	0.063
309	6	1	2	1.054	0.063
309	7	1	2	1.097	0.085
309	8	1	2	1.090	0.073
309	9	1	1	1.088	0.064
309	10	1	1	1.097	0.050
309	11	1	1	1.153	0.076
309	12	1	2	1.183	0.070
309	13	1	2	1.019	0.062
309	14	1	1	1.072	0.060
309	15	1	1	1.017	0.059
309	16	1	1	1.105	0.068
317	1	1	1	1.046	0.084
317	2	1	1	1.071	0.094
317	3	1	1	.	0.083
317	4	1	1	1.055	0.098
317	5	1	1	1.054	0.093
317	6	1	1	1.080	0.077
317	7	1	2	0.902	0.081
317	8	1	1	0.806	0.087
317	9	1	2	0.982	0.078
317	10	1	2	1.034	0.083
317	11	1	1	.	0.071
317	12	1	1	1.018	0.078
317	13	1	2	1.031	0.090
317	14	1	1	1.008	0.074
325	1	1	1	1.076	0.065
325	2	2	.	.	.
325	3	1	2	1.156	0.075
325	4	1	1	1.128	0.085
325	5	1	2	1.129	0.063
325	6	1	2	1.082	0.078
325	7	1	2	1.176	0.069
325	8	1	1	1.037	0.054
325	9	1	1	1.187	0.092
325	10	1	1	1.080	0.078
325	11	1	1	1.134	0.085
325	12	1	1	1.068	0.066
325	13	1	1	1.003	0.062
325	14	1	1	0.936	0.070
325	15	1	2	0.965	0.065
340	1	1	1	1.071	0.076

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
340	2	1	1	1.106	0.088
340	3	1	2	1.078	0.076
340	4	1	1	1.112	0.070
340	5	1	2	1.045	0.079
340	6	1	1	1.017	0.087
340	7	2	.	.	.
340	8	1	1	1.090	0.097
340	9	2	.	.	.
340	10	1	2	1.143	0.074
340	11	1	1	1.138	0.083
340	12	1	2	1.069	0.073
340	13	1	1	1.056	0.075
365	1	1	1	0.848	0.085
365	2	1	2	0.829	0.081
365	3	1	2	0.937	0.145
365	4	1	2	0.888	0.102
365	5	1	2	0.868	0.104
365	6	1	2	0.570	0.083
365	7	1	1	0.839	0.082
365	8	1	2	0.945	0.075
365	9	1	1	0.902	0.078
365	10	1	1	0.818	0.068
365	11	2	.	.	.
374	1	2	.	.	.
374	2	1	2	1.022	0.064
374	3	1	2	1.048	0.069
374	4	1	1	1.091	0.079
374	5	1	1	1.048	0.062
374	6	1	1	1.150	0.078
374	7	1	1	1.201	0.082
374	8	1	1	1.068	0.055
374	9	1	1	1.092	0.079
374	10	1	1	1.077	0.064
377	1	1	2	1.189	0.081
377	2	1	1	1.129	0.092
377	3	1	2	1.049	0.078
377	4	1	2	1.127	0.072
377	5	1	1	0.985	0.079
377	6	2	.	.	.
377	7	1	1	1.056	0.079
377	8	1	1	1.248	0.081
377	9	1	1	1.020	0.071
377	10	1	2	1.188	0.062
377	11	1	2	1.082	0.078
377	12	1	2	1.025	0.083
377	13	1	2	1.155	0.084
389	1	1	1	1.087	0.074
389	2	1	2	1.025	0.087
389	3	1	2	1.074	0.067
389	4	1	2	1.140	0.070

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
389	5	2	.	.	.
389	6	1	2	1.015	0.071
389	7	1	2	0.945	0.057
389	8	1	1	1.191	0.078
389	9	1	1	1.182	0.090
389	10	4	.	.	.
389	11	2	.	.	.
400	1	1	2	1.278	0.075
400	2	1	2	1.375	0.053
400	3	1	1	1.341	0.075
400	4	1	1	1.468	0.074
400	5	1	2	1.349	0.085
400	6	2	.	.	.
400	7	1	1	1.249	0.085
400	8	2	.	.	.
400	9	1	1	1.358	0.080
400	10	1	1	1.368	0.080
400	11	1	1	1.415	0.085
400	12	1	2	1.300	0.056
427	1	1	2	1.119	0.063
427	2	1	1	1.235	0.072
427	3	1	1	1.222	0.069
427	4	1	1	1.153	0.084
427	5	1	1	1.078	0.062
427	6	1	2	1.032	0.066
427	7	1	1	0.975	0.068
427	8	1	1	1.092	0.075
427	9	1	1	1.217	0.079
427	10	1	2	1.121	0.058
427	11	1	2	1.105	0.058
427	12	1	1	1.172	0.086
427	13	2	.	.	.
427	14	1	1	1.188	0.065
428	1	1	2	1.017	0.065
428	2	1	1	0.965	0.068
428	3	1	2	1.044	0.081
428	4	1	2	0.993	0.070
428	5	1	2	0.971	0.054
428	6	1	1	1.011	0.072
428	7	1	2	0.928	0.060
428	8	1	2	0.956	0.070
428	9	2	.	.	.
428	10	1	2	1.069	0.061
428	11	1	2	0.935	0.047
428	12	1	2	0.982	0.064
445	1	1	1	0.889	0.056
445	2	4	.	.	.
445	3	1	2	0.928	0.054
445	4	1	1	1.105	0.069
445	5	1	1	1.058	0.064

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
445	6	1	2	.	0.071
445	7	1	2	1.039	0.068
445	8	1	1	1.067	0.069
445	9	1	2	0.983	0.067
445	10	1	1	1.058	0.058
445	11	1	2	0.977	0.061
445	12	1	2	0.975	0.057
445	13	1	2	0.993	0.062
445	14	2	2	.	.
445	15	1	2	1.021	0.060
445	16	1	2	0.530	0.055
445	17	1	1	1.030	0.082

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption; 5 = Live
Sex: Male = 1; Female = 2

APPENDIX F

INDIVIDUAL BODY WEIGHT DATA FOR PLUG-POSITIVE FEMALE MICE

FILE=MICE.MAT 15-JUL-87 PAGE= 1

CASE	DAM ID	TMT GRP	GES GRP	PREG?	PREWT	DG0 WT	DG8 WT	DG11 WT	DG18 WT	DG20 WT	UTERUSWT
1	228.	1.	A	1.	27.4	26.8	31.6	38.4	49.8	56.0	17.2
2	266.	1.	B	1.	30.2	30.0	30.4	37.8	48.8	53.9	16.7
3	270.	1.	D	1.	28.4	26.4	30.6	32.8	39.4	41.6	6.3
4	273.	1.	B	1.	27.8	26.6	29.6	35.8	48.8	54.9	19.8
5	304.	1.	D	1.	31.2	29.4	30.6	34.4	48.2	52.9	18.1
6	320.	1.	B	1.	27.6	26.8	30.0	36.0	51.2	57.7	21.3
7	321.	1.	A	1.	28.8	29.4	30.0	36.4	53.0	60.4	24.4
8	341.	1.	E	1.	28.2	27.8	30.2	35.8	50.2	58.5	22.4
9	351.	1.	D	1.	26.8	28.2	30.0	35.2	49.8	53.8	19.6
10	372.	1.	C	1.	28.6	28.2	30.0	34.6	48.4	54.7	21.9
11	378.	1.	D	1.	29.8	27.0	30.0	35.0	50.4	55.9	20.5
12	380.	1.	E	1.	27.2	27.4	30.6	36.2	50.4	56.1	21.1
13	388.	1.	C	1.	27.0	26.8	27.8	33.4	43.8	48.2	15.6
14	391.	1.	D	1.	27.6	26.4	31.0	35.6	50.2	55.0	20.9
15	415.	1.	E	1.	27.8	27.6	31.2	33.8	44.2	48.1	14.9
16	418.	1.	E	1.	28.6	28.2	31.4	36.4	50.6	55.4	20.5
17	422.	1.	E	1.	29.6	28.6	32.2	41.6	57.4	64.6	24.5
18	444.	1.	D	1.	28.8	28.8	34.4	40.6	54.2	59.6	22.4
19	234.	1.	A	0.	28.0	29.0	28.6	29.8	30.0	29.0	0.1
20	240.	1.	D	0.	29.2	29.4	32.0	30.8	32.2	32.4	0.2
21	268.	1.	B	0.	28.2	28.0	31.6	32.0	33.0	31.7	0.3
22	282.	1.	C	0.	28.0	28.6	30.6	31.4	30.4	29.7	0.1
23	283.	1.	C	0.	27.6	26.4	29.2	28.4	28.6	28.3	0.3
24	293.	1.	D	0.	31.2	30.4	30.4	29.8	30.4	30.0	0.1
25	301.	1.	A	0.	28.8	24.8	29.2	30.8	30.0	29.9	0.2
26	323.	1.	B	0.	28.0	27.2	28.6	29.6	29.0	28.4	0.1
27	338.	1.	C	0.	29.0	28.6	28.2	28.4	30.2	28.6	0.1
28	352.	1.	C	0.	26.4	27.0	30.0	29.4	29.6	28.3	0.1
29	355.	1.	C	0.	27.8	27.6	30.4	28.8	29.2	28.6	0.3
30	387.	1.	C	0.	29.8	29.2	32.6	31.2	30.2	28.5	0.1
31	399.	1.	E	0.	28.6	28.6	31.2	30.0	29.2	28.6	0.1
32	409.	1.	E	0.	29.8	28.8	29.8	31.2	32.0	30.9	0.2
33	242.	2.	C	1.	26.2	26.6	29.2	33.0	44.2	50.1	19.0
34	246.	2.	E	1.	29.0	28.6	30.8	37.2	48.6	54.0	18.0
35	263.	2.	C	1.	27.0	28.8	32.2	38.2	50.8	58.7	20.6
36	286.	2.	D	1.	28.4	29.4	32.8	37.0	50.4	58.5	22.7
37	295.	2.	C	1.	29.6	28.0	32.8	38.8	51.2	57.3	21.9
38	302.	2.	B	1.	29.2	28.2	31.4	36.8	50.8	57.1	23.0
39	307.	2.	B	1.	27.0	26.4	29.6	36.0	49.6	56.3	21.6
40	311.	2.	C	1.	30.6	29.0	31.2	37.2	48.4	52.7	19.4
41	312.	2.	D	1.	26.8	28.8	32.0	38.0	54.4	61.8	25.5
42	314.	2.	B	1.	27.2	27.0	31.8	38.8	50.2	54.3	18.7
43	318.	2.	C	1.	27.0	26.8	30.2	37.0	49.8	55.0	20.7
44	346.	2.	C	1.	27.6	28.2	26.8	30.2	39.6	42.0	9.4
45	349.	2.	D	1.	28.4	28.0	31.8	38.0	50.4	56.6	21.8

CASE	DAM ID	TMT GRP	GES GRP	PREG?	PREWT	DG0 WT	DG8 WT	DG11 WT	DG16 WT	DG20 WT	UTERUSWT
46	350.	2.	D	0.	28.6	28.4	28.6	29.8	29.6	28.0	0.2
47	368.	2.	D	1.	27.6	26.8	28.6	34.2	45.8	51.4	18.5
48	369.	2.	E	1.	27.0	27.6	30.8	36.4	49.2	52.4	16.3
49	373.	2.	D	1.	31.0	29.2	34.8	41.0	57.6	64.7	24.8
50	381.	2.	E	1.	29.6	28.8	31.2	38.8	51.8	59.2	22.0
51	390.	2.	D	1.	29.4	30.2	33.0	37.8	49.8	58.2	20.8
52	433.	2.	E	1.	28.2	27.4	30.6	37.4	51.0	58.8	20.9
53	229.	2.	A	0.	28.4	29.0	30.4	30.0	30.8	28.1	0.2
54	237.	2.	A	0.	27.8	26.6	28.4	30.0	30.0	28.3	0.1
55	269.	2.	C	0.	28.4	27.8	30.6	31.6	30.4	29.2	0.1
56	279.	2.	E	0.	31.0	29.0	30.8	31.6	31.8	31.5	0.2
57	289.	2.	A	0.	27.6	29.4	31.2	30.6	30.8	30.1	0.3
58	291.	2.	B	0.	28.4	27.4	28.2	29.6	29.8	28.5	0.1
59	315.	2.	B	0.	27.2	27.8	32.0	31.8	31.4	29.1	0.1
60	326.	2.	A	0.	25.4	25.4	27.0	27.4	27.0	27.2	0.2
61	329.	2.	C	0.	27.6	27.6	29.2	28.8	27.6	27.0	0.3
62	376.	2.	D	0.	27.2	26.4	29.6	30.4	28.8	26.9	0.2
63	379.	2.	E	0.	29.0	28.0	30.8	31.0	30.8	29.5	0.1
64	395.	2.	E	0.	30.0	28.8	28.6	29.4	30.2	28.1	0.2
65	401.	2.	E	0.	28.8	28.0	28.6	29.6	29.8	27.8	0.1
66	251.	3.	D	1.	25.8	25.8	28.6	32.6	43.0	49.4	18.5
67	258.	3.	C	1.	30.8	29.4	31.4	37.0	47.2	51.3	17.3
68	260.	3.	C	1.	30.0	29.0	32.2	37.4	49.6	55.5	20.2
69	265.	3.	A	1.	27.2	25.8	30.0	36.8	48.8	52.9	23.6
70	272.	3.	D	1.	30.0	27.6	30.8	35.4	47.8	54.8	18.9
71	274.	3.	A	1.	29.8	30.4	32.2	39.4	52.8	58.4	20.9
72	296.	3.	D	1.	27.8	29.6	32.6	38.0	46.8	52.8	15.9
73	319.	3.	A	1.	27.4	28.0	30.8	37.0	50.0	54.8	19.6
74	328.	3.	B	1.	27.6	27.0	30.0	35.0	47.8	50.6	15.3
75	337.	3.	C	1.	27.2	28.0	30.8	35.2	45.8	49.4	17.0
76	339.	3.	E	1.	26.4	27.2	29.2	35.0	46.2	51.2	16.0
77	342.	3.	D	1.	27.2	28.6	30.8	35.0	44.8	49.0	15.7
78	343.	3.	B	1.	31.0	31.2	33.2	38.4	51.2	52.9	17.9
79	348.	3.	D	1.	28.0	28.0	31.2	38.2	51.8	56.9	21.2
80	353.	3.	E	1.	27.4	27.6	28.8	34.8	46.8	52.2	17.6
81	366.	3.	E	1.	26.8	29.0	31.8	39.0	49.8	56.5	18.3
82	371.	3.	D	1.	27.4	29.2	30.6	34.8	46.8	52.0	19.7
83	382.	3.	C	1.	28.6	27.8	28.6	32.4	36.8	36.5	4.1
84	392.	3.	E	1.	28.0	28.2	31.2	38.0	52.6	58.0	23.6
85	402.	3.	E	1.	27.8	28.8	31.0	38.6	51.0	56.4	20.6
86	420.	3.	D	1.	29.4	28.6	31.0	35.8	46.6	51.5	16.6
87	238.	3.	C	0.	28.8	28.2	28.0	28.4	28.0	27.3	0.2
88	241.	3.	C	0.	29.4	26.4	27.6	28.8	29.6	28.7	0.2
89	275.	3.	A	0.	31.2	28.2	29.2	31.4	30.2	28.3	0.1
90	284.	3.	A	0.	28.6	28.0	30.0	28.8	29.2	27.3	0.2

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CASE	DAM ID	TMT GRP	GES GRP	PREG?	PREWT	DG0 WT	DG8 WT	DG11 WT	DG18 WT	DG20 WT	UTERUSWT
91	287.	3.	B	0.	28.2	28.0	28.4	28.8	28.2	27.2	0.1
92	290.	3.	B	0.	28.4	28.4	28.0	29.8	29.6	27.7	0.2
93	384.	3.	E	0.	28.8	28.2	28.6	28.8	29.4	28.2	0.1
94	384.	3.	E	0.	29.4	28.0	30.4	31.0	31.6	28.8	0.1
95	386.	3.	C	0.	30.8	29.0	31.4	30.8	31.6	28.3	0.1
96	398.	3.	E	0.	25.4	27.4	28.6	28.8	27.8	28.8	0.1
97	231.	4.	D	1.	27.0	26.6	28.6	33.2	41.6	46.2	12.5
98	243.	4.	A	1.	28.2	28.2	31.2	38.6	51.0	55.7	19.5
99	244.	4.	C	1.	26.8	28.0	29.8	32.8	41.4	47.3	14.2
100	255.	4.	C	1.	29.0	28.8	30.8	36.0	46.4	51.4	17.4
101	264.	4.	B	1.	28.6	27.0	30.0	35.0	46.8	51.8	18.5
102	278.	4.	B	1.	30.6	29.6	31.0	34.8	46.2	51.0	15.9
103	294.	4.	B	1.	27.2	26.6	31.4	36.6	49.2	53.5	19.7
104	305.	4.	C	1.	28.0	26.8	29.4	33.4	43.0	49.0	16.3
105	309.	4.	D	1.	30.0	30.0	32.2	36.4	50.8	58.0	22.5
106	317.	4.	D	1.	26.2	27.8	30.6	34.2	44.6	51.9	18.5
107	325.	4.	D	1.	28.6	28.8	30.6	35.6	49.0	55.2	19.9
108	340.	4.	B	1.	28.2	27.6	31.0	38.8	46.4	49.8	16.8
109	365.	4.	C	1.	28.0	29.2	31.0	34.6	42.4	46.0	12.4
110	374.	4.	E	1.	29.4	29.2	30.0	34.6	44.2	47.3	12.8
111	377.	4.	D	1.	30.4	28.6	31.0	37.2	48.8	53.6	17.3
112	389.	4.	E	1.	29.0	28.4	30.6	35.2	43.8	46.1	11.2
113	400.	4.	D	1.	29.6	29.4	31.8	35.8	46.8	49.6	16.8
114	427.	4.	D	1.	31.0	30.8	33.2	39.8	51.8	57.3	19.0
115	428.	4.	D	1.	27.0	26.8	28.0	32.8	41.8	46.0	14.5
116	445.	4.	C	1.	28.4	27.2	29.8	35.2	46.4	51.2	19.0
117	281.	4.	B	0.	28.4	28.2	27.8	28.4	28.2	28.2	0.3
118	280.	4.	C	0.	29.4	27.6	29.8	30.8	31.8	28.9	0.2
119	298.	4.	C	0.	26.0	26.6	27.2	27.2	27.2	25.7	0.2
120	330.	4.	C	0.	28.0	28.4	30.2	30.8	29.4	28.6	0.1
121	360.	4.	E	0.	28.8	28.8	29.0	30.8	30.6	29.6	0.1
122	375.	4.	E	0.	28.6	28.6	29.0	29.2	30.0	29.6	0.2
123	383.	4.	E	0.	28.4	28.0	28.2	28.0	28.6	28.6	0.1
124	397.	4.	E	0.	29.6	27.4	27.8	29.4	29.2	27.0	0.1
125	408.	4.	E	0.	30.0	27.8	28.8	30.4	30.8	28.9	0.2
126	440.	4.	E	0.	28.2	27.8	28.2	29.8	27.8	28.8	0.2
127	292.	4.	A	-1.	28.2	29.4	31.6	27.0	-1.0	-1.0	-1.0
128	332.	4.	A	-1.	27.2	27.8	28.8	22.2	-1.0	-1.0	-1.0

APPENDIX G

MALFORMATIONS AND VARIATIONS IN INDIVIDUAL MOUSE FETUSES EXPOSED TO 1,3-BUTADIENE

0 ppm

Mat ID	228	256	270	273	304	320	321
Number examined:							
Fetuses	9	10	3	13	12	13	15
Heads	4	5	2	5	6	7	7
Thoracogastroschiisis				13			
Pale						7	
Hydroureter	10						
Misaligned Sternebrae				8			
Supernumerary Ribs							
Normal Length		6			2,9		
Rudimentary	4	4					6,9
Ossif. Site Lumbar #1				7,10			3
Reduced Ossification:							
Sternebrae	1,2,4	3,4,7,8	5	13	3,7,10	2,7,8	

Mat ID	341	351	372	378	380	388	391
Number examined:							
Fetuses	13	13	13	12	13	9	13
Heads	6	8	6	6	6	5	7
Exencephaly, open eye		10					
Hydroureter			11				
Misaligned Sternebrae		7				2	1,7,10
Supernumerary Ribs							
Normal Length		4		5			
Rudimentary		2,3,6,7,10					12,13
Ossif. Site Lumbar #1		1,9,11			9,14		
Reduced Ossification:							
Sternebrae		2,9	9				9

	0 ppm			
Mat ID	**415**	**418**	**422**	**444**
Number examined:				
Fetuses	9	13	14	14
Heads	5	6	7	7
Limb Flexure		8,13		
Misaligned Sternebrae		6,8		10,11
Supernumerary Ribs				
Normal Length				14
Rudimentary	4,6			
Ossif. Site Lumbar	8,9,11			
Reduced Ossification:				
Sternebrae	7	1,2,6,7,11,13	8	4,8,10,13

40 ppm

Mat ID	242	246	263	286	295	302	307
Number examined:							
Fetuses	11	11	13	14	13	15	13
Heads	5	6	6	7	6	8	7
Hydroureter				3	9		
Misaligned Sternebrae			14				
Fused Rib			13				
Supernumerary Ribs							
Normal Length							
Rudimentary	1,12			2	1	12,13,16	
Ossif. Site Lumbar #1				5,14			
Reduced Ossification:							
Sternebrae			2,5,8,13,14	12	2,4,7,9		
Lumbar Vertebrae (centra)				12			

Mat ID	311	312	314	318	346	349	368
Number examined:							
Fetuses	12	16	11	12	6	13	11
Heads	6	8	5	6	3	7	6
Hydroureter	2,3,7,12						
Misaligned Sternebrae		8					
Oss. Site btwn Stern 5 & 6		2					
Fused Rib			3				
Supernumerary Ribs							
Normal Length	3,4,7,9,11						
Rudimentary			1-4,8,9		5,6		
Ossif. Site Lumbar #1			6		8,9		
Reduced Ossification:							
Sternebrae					7		2
Lumbar Vertebrae (centra)							

40 ppm

Mat ID	369	373	381	390	433
Number examined:					
Fetuses	10	15	14	14	13
Heads	6	8	7	7	6
Cleft Palate			4		
Misaligned Sternebrae		3		8	
Supernumerary Ribs					
Normal Length					
Rudimentary	2		7,9,11		
Ossif. Site Lumbar #1			2		
Reduced Ossification:					
Sternebrae		8,13	3,6,14	8	4,8
Lumbar Vertebrae (centra)					

200 ppm Butadiene

Mat ID	251	258	260	265	272	274	296
Number examined:							
Fetuses	13	12	12	13	14	15	11
Heads	6	6	6	6	7	7	6
Misaligned Sternebrae	1			7	6		
Supernumerary Ribs							
Normal Length	3,6			9,11,12	1-4,6,8-12,14	5,8,15	
Rudimentary	1,5,7,9-13	5,12	1,3,5,8,9-14	5,8,10	7	9,12,14	1,2,8-11
Oss Site Lumbar #1	4		4,7			13	
Reduced Ossification:							
Sternebrae			1,5,10,14	4	1,2,8,11,13,14	2,3,6	1,2,4,5
Lumbar Vertebrae (centra)							
Skull			1				

Mat ID	319	328	337	339	342	343	348
Number examined:							
Fetuses	14	11	12	11	11	13	14
Heads	7	6	6	5	6	7	7
Misaligned Sternebrae					7		9
Supernumerary Ribs							
Normal Length		2,3,7,13		3,6			
Rudimentary	1	8,9	6,7,9-11	8	1,3,4	4-7,9,10	2,3,6,7
Ossif. Site Lumbar #1			2,4,5		5	2,8,11,13,14	5
Reduced Ossification:							
Sternebrae	2,6,9,13,15	2,3	4,7	10,11	7		3,6,7,9
Lumbar Vertebrae (centra)							
Skull				11			

200 ppm

Mat ID	353	366	371	382	392	402	420
Number examined:							
Fetuses	12	12	15	2	16	15	11
Heads	6	6	7	1	8	8	6
Misaligned Sternebrae		12				1	1,11
Oss. Site btwn Stern 5 & 6							12
Supernumerary Ribs							
Normal Length		12			6		1,4
Rudimentary	1,3,5,12	1-4,11	6,11,13		8	1,2,5,8,9	2,6-12
Ossif. Site Lumbar	8	6	15				
Reduced Ossification:							
Sternebrae	8,10,13	12	2,3-5,8-11,13,15		12,14	2,3,6,7,9,12,14	
Lumbar Vertebrae (centra)							

				1000 ppm		
Mat ID	**231**	**243**	**244**	**255**	**264**	**276**
Number examined:						
Fetuses	9	14	11	12	14	14
Heads	4	7	5	6	7	7
Hydroureter			10		1,7-11	
Misaligned Sternebrae					1,13	
Fused Sternebrae					1	
Supernumerary Ribs						
Normal Length		1-8,11-14	2-5,8-11	1-6,8-12		1,3,4,10,12,14
Rudimentary	2,4,6-10	9,10	6,7		2,4,6,7,11	2,6-9,13,15
Ossif. Site Lumbar #1					8	
Reduced Ossification:						
Sternebrae	3,9	2,3,7,8,11,12	1-8,10	6,8	3,5,8,14	7,15
Lumbar Vertebrae (centra)						
Skull					5,7,9	

Mat ID	**294**	**305**	**309**	**317**	**325**	**340**	**365**
Number examined:							
Fetuses	15	12	16	14	14	11	10
Heads	8	6	8	7	7	5	5
Exencephaly, open eye					14		10
External hydrocephaly	9						
Missing left atrium							2
Hydroureter	1,8						
Fused Sternebrae		4	9	12			4
Fused Rib							
Supernumerary Ribs							
Normal Length						1,2,5	4,6-10
Rudimentary	1,4,5,7-15	1-7,9-12	1,2,5,7,9,13,14	1-14	1,5,8,14,15	3,4,6,7,11	
Ossif. Site Lumbar #1		8	10			10,13	
Reduced Ossification:							
Sternebrae	5,12,14,15	2,4-6,8,10	8,14	8,12	4,6,10,13	5,8,11	1,10
Lumbar Vertebrae (centra)							
Skull							
Phalanges							6,9

1000 ppm

Mat ID	374	377	389	400	427	428	445
Number examined:							
Fetuses	9	12	8	10	13	11	15
Heads	4	6	4	5	7	5	7
Misaligned Sternebrae		10			5,7		5
Oss. Site btwn Stern 5 & 6		2			4		10
Supernumerary Ribs							
Normal Length	2,10		1	1-3,5,7,9-12		1-6,8,10-12	
Rudimentary	3-7,9	3-5,7-13	2-4		1-11,14		1,3-8,11-13,15,17
Ossif. Site Lumbar #1			6,7,9		12		9
Reduced Ossification:							
Sternebrae	5,6,8-10	5,7-10		1,5,9	7	7,11	5,13,15,17
Lumbar Vertebrae (centra)							

APPENDIX H

QUALITY ASSURANCE STATEMENT, SAMPLE AND RECORD DISPOSITION, AND CALENDAR OF EVENTS

TERATOLOGY STUDY OF 1,3-BUTADIENE IN MICE

Quality Assurance Statement

Listed below are the phases and/or procedures included in the study described in this report which were reviewed by the Quality Assurance Unit during the period, 11/1/85 - 3/1/86, specifically for this study and the dates the reviews were performed and findings reported to management. (All findings were reported to the study director or his designee at the time of the review.)

Phase/Procedure Reviewed	Review Date	Date Findings Submitted in Writing to Study Director/Management
Test Chemical Analysis	11/13/85	12/02/85
Animal Receipt	11/13/85	11/13/85
Health Screen	11/25/85	11/26/85
Body Weights	11/26/85	12/02/85
Animal Identification	11/26/85	12/02/85
Mating	12/03/85	12/05/85
Data	12/04/85	12/18/85
Dosing	12/06/85	12/06/85
Teratology Examinations	12/19/85	12/06/85
Data	2/05-07/86	2/11/86
Report	4/27&28, 5/8,11/30/87	11/30/87

R A Gelman
Quality Assurance Officer

11/30/87
Date

SAMPLE AND RECORD DISPOSITION

Upon completion of the 1,3-butadiene studies, all tissue and fetal specimens will be shipped to the National Toxicology Program (NTP) Archives. Records generated in the conduct of the study will be microfiched. Computer tapes of biological data, the original and two copies of the microfiche, and the microfiche index will be sent to Dr. Schwetz (National Institute of Environmental Health Sciences) for storage in NTP Archives.

The Quality Assurance Unit at Pacific Northwest Laboratory (PNL) will retain all documents and records associated with the conduct of the study for a period of at least 2 years following completion of the study. These materials will be placed in Room 1433 of the Life Sciences Laboratory-II building at PNL according to 21 CFR 58.195. NTP will be notified of the completion of the storage period so that they may specify the terms of the disposition of these records.

CALENDAR OF EVENTS FOR TERATOLOGY STUDY OF 1,3-BUTADIENE IN THE MOUSE

Completion of exposure/monitoring system:	10/24/85
Approval of protocol:	10/11/85
Animal order:	10/02/85 (CD-1 mice from Charles River Laboratories, Kingston Facility, NY)
Receipt of animals:	11/12/85 (ARC #860011; 108 males and 226 females; date of birth, 09/19/85)
Initial health screen:	11/25/85
Overnight cohabitation:	11/29/85 to 12/03/85
Detection of copulation (0 dg)	(A) 11/30/85 (B) 12/01/85 (C) 12/02/85 (D) 12/03/85 (E) 12/04/85
Exposure (6 hours/day; 6-15 dg)	(A) 12/06/85-12/15/85 (B) 12/07/85-12/16/85 (C) 12/08/85-12/17/85 (D) 12/09/85-12/18/85 (E) 12/10/85-12/19/85
Sacrifice (18 dg)	(A) 12/18/85 (B) 12/19/85 (C) 12/20/85 (D) 12/21/85 (E) 12/22/85
Completion of fetal examinations:	02/14/86
Completion of statistical evaluations:	03/01/86
Submission of Draft Report:	April 1987
Submission of Final Report:	November 1987

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