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Inhalation Developmental Toxicology Studies of 1,3-Butadiene in the Rat

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INHALATION DEVELOPMENTAL TOXICOLOGY STUDIES OF 1,3-BUTADIENE IN THE RAT

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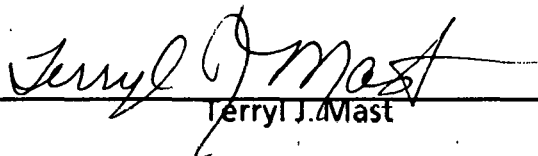
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ABSTRACT

Maternal toxicity, reproductive performance and developmental toxicology were evaluated in Sprague-Dawley-derived rats during and following 6 hours/day, whole-body, inhalation exposures to 0 (filtered air), 40, 200 and 1000 ppm of 1,3-butadiene. The female rats (Ns = 24 to 28), which had mated with unexposed males (day of sperm detection = 0 days of gestation; dg), were exposed to the chemical from 6 through 15 dg and sacrificed on 20 dg.

Maternal animals were weighed prior to mating and on 0, 6, 11, 16 and 20 dg; the rats were observed for mortality, morbidity and signs of toxicity during exposure and examined for gross tissue abnormalities at necropsy. Reproductive measures included the determination of 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.

There were no significant differences among treatment groups in maternal body weights or extragestational weights of rats exposed to 1,3-butadiene concentrations of 40 or 200 ppm, but, in animals exposed to 1000 ppm, significantly depressed body weight gains were observed during the first 5 days of exposure and extragestational weight gains tended to be lower than control values. These results, and the absence of clinical signs of toxicity, were considered to indicate that there was no maternal toxicity at exposure levels of 200 ppm or lower. The percentage of pregnant animals and the number of litters with live fetuses were unaffected by treatment.

Placental weights, fetal body weights and sex ratios were unaffected by treatment. There were no significant differences among groups in incidences of fetal malformations. However, in the 200-ppm exposure group, a significant increase in the incidence of reduced sternebral ossification was detected when the analyses were based on the number of affected fetuses but not on the number of affected litters. This difference could not be correlated with fetal body weights or exposure regimens and was not considered to be treatment-related. There were also irregularities in the thoracic vertebrae, but the incidence of reduced ossification in fetuses

of the control group was significantly higher than in fetuses of the 200- and 1000-ppm exposure groups.

Under the conditions of this exposure regimen, there was no evidence for a teratogenic response to 1,3-butadiene exposure.

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ABBREVIATIONS

ANOVA	= Analysis of variance
BNW	= Battelle, Pacific Northwest Laboratories; Battelle-Northwest
CDS	= Colorado Data Systems
CO₂	= 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

I. 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 reviews 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 other study, female rats were exposed to 0, 200, 1000 and 8000 ppm of butadiene from 6 through 15 days of gestation (dg; Hazelton, 1982). 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. The purpose of the study described in this report was to determine the reproductive and teratologic effects of inhalation exposure to 1,3-butadiene in outbred rats of

Sprague-Dawley derivation. Because it was important to confirm and extend the findings reported by Hazelton (1982), this study used the same strain of rats, but from a different source. The exposure regimen included two of the atmospheric concentrations (200 and 1000 ppm) that were used in the Hazelton study; in addition, a lower concentration (40 ppm) was used in an attempt to determine a level that was not overtly toxic. Furthermore, it was desirable that the results from this study be compared with data from another rodent, the mouse, in which 1,3-butadiene has been reported to be more toxic than in the rat (BNW, 1984). Accordingly, a separate teratology study in CD-1 mice has also been performed in this laboratory, using an identical exposure regimen, and will be described in a separate report.

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). The chemical composition of Lot Number F-858, Batch 06, which was analyzed by Phillips Chemical Company, was reported by MRI on July 23, 1985 to be 99.84% 1,3-butadiene, 0.13% cis(butene)₂, 0.03% heavies (residues remaining following evaporation of 1,3-butadiene at room temperature), and 13 ppm of the peroxide inhibitor, t-butyl catechol.

For this study, a single lot (F-909) 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. A single cylinder (BNW 50846-36-2) was 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 F-909 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 the spectrum of Lot Number F-858 and 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. Prior to the study, the headspace dimer concentration of BNW 50846-36-2 was 332 ppm (Appendix A); periodic analyses performed during animal exposures yielded a mean headspace dimer concentration of 197 ± 6 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 m³, and the active mixing volume was 1.7 m³. 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. Rats were exposed in individual cages (24/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 85B 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 con-

centration. 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 in the Rat

Observation	Chamber Concentrations (ppm)		
	40	200	1000
Mean chamber concentration \pm standard deviation (ppm)	40.1 \pm 0.62	199.8 \pm 2.61	1005 \pm 11.9
Range (ppm)	42.6 to 31.1	212 to 165	1070 to 926
Relative standard deviation (%)	1.6	1.3	1.2
Mean of target concentrations (%)	100	100	101

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 an 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 Rats

Exposure Day	Dimer Concentration (ppm, v/v)
11/26/85	0.15
12/03/85	0.17
12/05/85	0.19

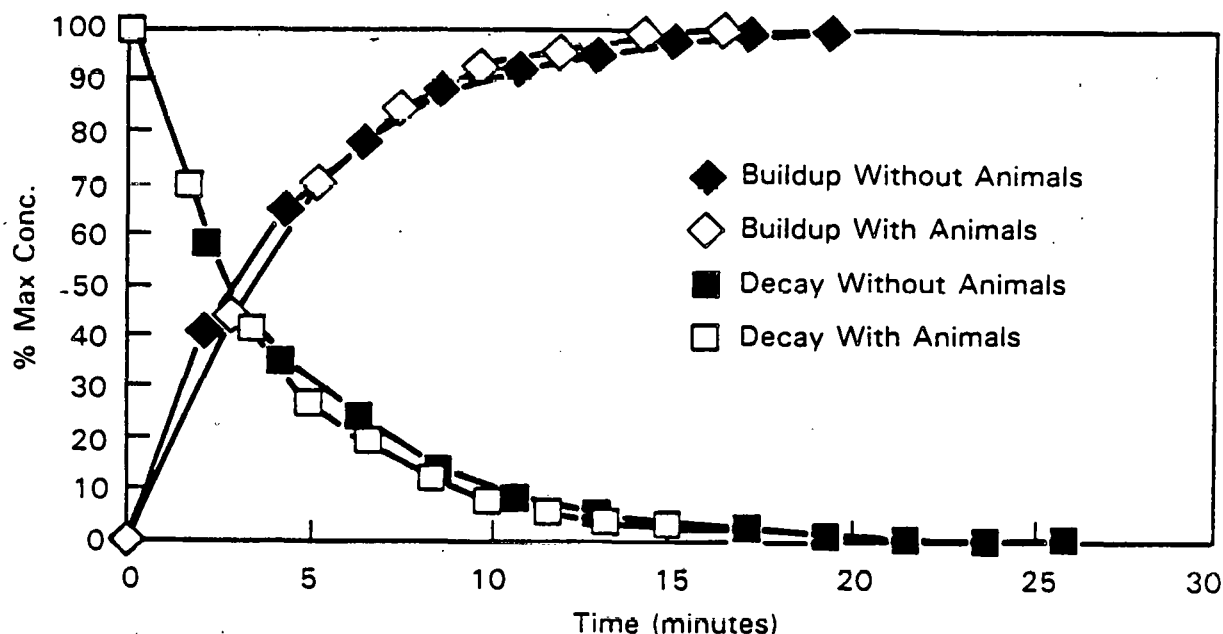


FIGURE 1. Buildup and Decay of the Atmosphere of the 1000-ppm 1,3-Butadiene Exposure Chamber in the Presence and Absence of Animals

C. ANIMAL HUSBANDRY AND EXPOSURE PROCEDURES

Salient features of the experimental design for this study are summarized in Table 3. For the study, 208 young-adult, Sprague-Dawley CD female (7 to 8 weeks old; 170 to 175 g) and 108 male (7 to 8 weeks old; 200 to 225 g) rats were purchased from Charles River Laboratory, Portage, MI Facility. The animals were isolated for 19 days, at which time five females and five males were killed and examined 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 sac-

rifice, 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 Rats Exposed to 1,3-Butadiene

Chamber concentrations (ppm): 0, 40, 200, and 1000
Number of sperm-positive females/exposure group: 30
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: 20 dg
Maternal observations: Mortality and signs of toxicity; body weights on 0, 6, 11, 16 and 20 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, five rats 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 $72 \pm 3^{\circ}\text{F}$ and $50 \pm 15\%$, 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 number of sperm-positive females. Copulation was established by a microscopic examination for sperm in a drop of normal saline delivered into, then recovered from, the vagina with a pipette. The morning of observation of sperm was designated as 0 dg. At this time, the sperm-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/day from 6 through 15 dg. From 16 dg until sacrifice at 20 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 rats were weighed during the week prior to mating, and on 0, 6, 11 and 16 dg. On 20 dg, the animals were euthanized with CO₂, 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. Because of the findings reported by Hazelton (1982), 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, Duncan's multiple-range test (Duncan, 1955; Kramer, 1956) was used for further statistical analyses. Response proportions, such as the number of resorptions, implants, live, dead, or

affected fetuses/litter, were also analyzed by ANOVA 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). These variables included numbers of pregnant females/number inseminated.

III. RESULTS

No deaths occurred in any of the four exposure groups during the study interval. No significant effects of treatment were observed for maternal body weight gains of rats exposed to 1,3-butadiene levels of 40 or 200 ppm, but weight gains of animals of the 1000-ppm group were significantly decreased for the period from 6 through 11 dg, the first 5 days of exposure (Table 4). Extragestational weight gains in the rats exposed to this highest concentration tended to be lower than values for control and 40-ppm groups and were significantly less than gains of animals exposed to 200 ppm (Table 5). Weights of gravid uteri and values for extragestational body weights for exposed animals were not significantly different from control values.

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

Time Interval (Day of Gestation)	1,3-Butadiene Concentration (ppm)			
	0 (N = 28) ^a	40 (N = 24)	200 (N = 26)	1000 (N = 28)
0 to 6	21.4 \pm 1.6	21.1 \pm 1.6	22.9 \pm 1.3	20.1 \pm 1.5
6 to 11	25.5 \pm 1.3 ^b	23.6 \pm 1.3 ^b	26.6 \pm 1.5 ^b	17.5 \pm 1.9 ^c
11 to 16	29.2 \pm 1.4	30.9 \pm 1.7	31.7 \pm 1.9	31.2 \pm 2.1
16 to 20	44.5 \pm 1.8	36.7 \pm 2.5	43.6 \pm 2.3	43.2 \pm 2.9

^aNumber of animals

^{b,c}Values that do not share a common letter are significantly different ($P \leq 0.05$) from one another.

The overall pregnancy rate among the rats of the study was 88% and ranged from 80% in those exposed to 40 ppm to 93% in the 0- and 1000-ppm groups (Table 6). Differences in pregnancy rates among groups were not statistically significant. Numbers and percentages of implantations, resorptions and live or dead fetuses per litter were not affected by treatment.

TABLE 5. Maternal Measures (g, Mean \pm Standard Error) for Rats Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Body weight on 0 day of gestation (dg)	242 \pm 3.7	239 \pm 3.2	244 \pm 3.0	242 \pm 4.0
Body weight on 20 dg	362 \pm 7.1	351 \pm 5.9	369 \pm 6.6	354 \pm 6.1
Weight of gravid uterus	73.0 \pm 2.9	69.5 \pm 3.5	73.9 \pm 2.8	71.2 \pm 4.1
Extragestational weight ^a	289 \pm 5.7	282 \pm 3.9	295 \pm 5.8	283 \pm 5.7
Extragestational weight gain ^b	47.6 \pm 2.8	42.7 \pm 2.2	50.9 \pm 3.0	39.9 \pm 3.5 ^c

^aExtragestational weight = body weight on 20 dg - weight of gravid uterus

^bExtragestational weight gain = extragestational weight - body weight on 0 dg

^cSignificantly less than control at P < 0.05

Exposure to 1,3-butadiene during development had no significant effect on fetal body weights, placental weights, or fetal sex ratios (Table 7). Individual data are presented in Appendix E.

One fetus in each of three litters in the 40-ppm exposure group was hydrocephalic. Two fetuses from one litter in the 1000-ppm group each had a meningoencephalocele; in addition, one of these fetuses also had microphthalmia accompanied by aphakia and retinal dysgenesis. Another litter in the 1000-ppm group had one fetus with a dilation between the meninges and the skull. No major malformations of the head were found in fetuses from the control or the 200-ppm exposure groups. No significant treatment-related differences or trends were noted in the incidence of malformations (Table 8; Appendix F).

The incidence of reduced ossification of sternebrae numbers 1 through 4 was higher in fetuses of the 200-ppm treatment group than in control fetuses, but values for fetuses from the 40- and 1000-ppm groups were not different from control values (Table 9; Appendix F). In contrast, the number of fetuses with

TABLE 6. Reproductive Measures (Mean \pm Standard Error) for Rats Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number of:				
Rats exposed	30	30	30	30
Pregnant rats (%)	28 (93)	24 (80)	26 (87)	28 (93)
Litters with live fetuses	28	24	26	27 ^a
Implantations/dam	14.4 \pm 0.55	14.0 \pm 0.71	15.3 \pm 0.45	14.8 \pm 0.63
Resorptions/litter	0.46 \pm 0.17	0.58 \pm 0.17	0.96 \pm 0.26	0.67 \pm 0.14
Early	0.39 \pm 0.15	0.54 \pm 0.16	0.88 \pm 0.25	0.63 \pm 0.14
Late	0.07 \pm 0.05	0.04 \pm 0.04	0.08 \pm 0.08	0.04 \pm 0.04
Dead fetuses/litter	0	0	0	0
Live fetuses/litter	13.9 \pm 0.56	13.4 \pm 0.66	14.3 \pm 0.52	14.2 \pm 0.60
Percentage of:				
Resorptions/litter	3.24 \pm 1.20	3.80 \pm 1.05	6.37 \pm 1.86	4.29 \pm 0.86
Early	2.79 \pm 1.12	3.50 \pm 0.96	5.85 \pm 1.78	4.06 \pm 0.87
Late	0.45 \pm 0.31	0.30 \pm 0.30	0.51 \pm 0.51	0.23 \pm 0.22
Live fetuses/litter	96.8 \pm 1.20	96.2 \pm 1.05	93.6 \pm 1.86	95.7 \pm 0.86

^aStatistical analyses were performed after dam #94 was excluded from the 1000-ppm group. This dam, which had only one implant, was considered to be an outlier and not representative of the population. The following numbers were obtained when results from this dam remained in the data set: Implantations/dam, 14.4 \pm 0.78; Resorptions/litter, 0.68 \pm 0.14; Early/litter, 0.64 \pm 0.14; Live fetuses/litter, 13.7 \pm 0.77; Percentage of resorptions/litter, 7.71 \pm 3.52; Early, 7.49 \pm 3.53; and Live fetuses/litter, 92.3 \pm 3.52.

TABLE 7. Fetal and Placental Measures (Mean \pm Standard Error) for Rat Litters Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number of:				
Litters examined	28	24	26	27
Fetuses examined	389	321	372	382
Body weight (g)				
Females	3.49 \pm 0.04	3.44 \pm 0.05	3.40 \pm 0.05	3.50 \pm 0.06
Males	3.40 \pm 0.05	3.36 \pm 0.05	3.29 \pm 0.05	3.38 \pm 0.06
Sex ratio (% males)	50.2 \pm 2.28	52.5 \pm 2.95	50.5 \pm 2.77	52.5 \pm 2.58
Placental weight (mg)				
Females	429 \pm 9.0	423 \pm 9.6	437 \pm 12.4	421 \pm 9.3
Males	421 \pm 9.3	414 \pm 9.8	431 \pm 13.4	414 \pm 10.3
	435 \pm 9.7	429 \pm 9.7	443 \pm 11.8	428 \pm 9.3

reduced ossification of thoracic vertebrae in the 200- and in the 1000-ppm groups was significantly lower than the number with this variation in the control group. When reduced ossifications at all anatomical sites were combined and the incidences compared on a litter basis, there were no effect of treatment on the mean percent of litters affected (Table 10).

TABLE 8. Malformations in Fetuses of Rats Exposed to 1,3-Butadiene^a

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number Examined				
Litters	28	24	26	27
Fetuses	389	321	372	382
Fetal heads	196	161	185	191
Malformations				
Generalized edema	1/1	3/1	1/1 ^b	3/1 ^c
Hydrocephalus	---	3/3	---	---
Meningoencephalocele	---	---	---	2/1 ^c
Dilatation between meninges and skull	---	---	---	1/1
Aphakia/retinal dysgenesis	---	---	---	1/1 ^c
Microphthalmia	---	---	---	1/1 ^c
Retroesophageal right subclavian artery	1/1	---	---	---
Aortic stenosis	---	---	1/1 ^b	---
Undescended testes	---	---	1/1 ^b	---
Fused sternebrae	---	---	1/1	---
Missing ribs	---	---	2/2 ^d	---
Bent tibia	---	---	1/1 ^b	---
TOTAL MALFORMED	2/2	6/4	3/3	4/2

^aExpressed as number of fetuses/number of litters

^bFetus #6 in litter #187

^cLitter #188: fetus #9, edema, meningoencephalocele; #14, edema, meningoencephalocele, aphakia/retinal dysgenesis; #16, edema, microphthalmia

^dIncludes fetus #6 in litter #187

Lens opacities were not observed when fetal eye examinations were conducted in situ immediately after death. It was noted, however, that lens opacities could be detected in fetuses from both exposed and control groups when the examination was delayed, or when the eye was removed prior to examination. When water or saline was added to the eyes during examination, the lens no longer appeared opaque. Although a formal study of this phenomenon was not con-

TABLE 9. Fetal Variations^a in Rats Exposed to 1,3-Butadiene

Observation	1,3 Butadiene Concentration (ppm)			
	0	40	200	1000
Number Examined				
Litters	28	24	26	27
Fetuses	389	321	372	382
Fetal heads	196	161	185	191
Variations				
Pale	1/1	---	---	---
Low ear set	---	---	1/1 ^c	---
Missing innominate artery	---	---	2/1	---
Hydroureter	36/17	35/15	39/14	31/12
Misaligned sternebrae	---	---	1/1	1/1
Extra ribs	---	1/1	4/2	---
Reduced Ossification				
Skull	27/13	22/13	18/10	29/11
Sternebrae #1-4	60/15	48/13	95/21	66/15
Ribs	1/1	2/2	5/3	2/2
Vertebrae (Centra)				
Thoracic	109/23	97/21	75/20	81/25
Lumbar	---	---	1/1 ^b	---
Pelvis	9/7	---	6/5	5/5
Phalanges	1/1	6/1	2/1	---
Tibia	---	---	1/1 ^b	---
Fibula	---	---	1/1 ^b	---

^aExpressed as number of fetuses/number of litters^bFetus #13 in litter #92TABLE 10. Mean Percent of Reduced Ossification or Hydroureter per Litter Following Exposure to 1,3-Butadiene (Mean \pm Standard Deviation)

Observation	1,3 Butadiene Exposure Concentration (ppm)			
	0%	40%	200%	1000%
Reduced ossification	41 \pm 27 ^a	48 \pm 24	45 \pm 28	43 \pm 29
Hydroureter	9 \pm 11	14 \pm 22	10 \pm 16	8 \pm 13

^aMean percent \pm standard deviation of the litter affected

ducted, these results suggest that the opacities were artifactual, most probably resulting from postmortem dehydration of the fetal eye.

IV. DISCUSSION

In this study, no significant effects on maternal body weight gains were found in rats exposed to concentrations of 1,3-butadiene as high as 200 ppm. Body weight gains of animals exposed to 1000 ppm were significantly decreased during the first 5 days of exposure. Extragestational gains in these rats were also depressed, although they were not significantly lower than those of the control animals. Results from the Hazelton study (1982) showed that a significant depression in body weight gains occurred in rats during exposure to 200 and 1000 ppm and that a significant decrease in adjusted body weight gain from 0 to 20 dg (analogous to extragestational weight gain) was evident in the rats exposed to 1000 ppm. Although the findings in this study and the Hazelton study are not in complete agreement, the overall results show that higher concentrations (≥ 1000 ppm) of 1,3-butadiene have a detectable effect on various measures of maternal weight gain. However, our results from exposure to 200 ppm were not consistent with the Hazelton study which indicated that weight gains, depressed during exposure, recovered to control values by the time the animals were sacrificed. Our study showed that the lower concentrations, 40 and 200 ppm, did not have detectable effects on various measures of weight gain, nor did they produce clinical signs of toxicity, suggesting that these concentrations were not maternally toxic.

None of the reproductive indices (e.g., number of litters with live fetuses, number of live fetuses per litter, number of resorptions per litter) were significantly affected by exposure to 1,3-butadiene vapors during gestation. Although the percentages of early resorptions per litter for all butadiene exposure groups were slightly elevated above controls, these differences were not statistically significant. Results from the Hazelton study (1982) also indicated that postimplantation losses, primarily early resorptions, were slightly, but not significantly, higher in all butadiene-exposed groups (200, 1000 and 8000 ppm).

For interpretation of the results of examinations for fetal variations, such as those obtained for reduced ossification, it is considered more appropriate to use the litter, rather than the fetus, as the experimental unit (Kalter, 1974; Haseman and Hogan, 1975). Moreover, irregular rates of ossification, particularly in fetal vertebrae and sternebrae, is a common observation in stocks of animals that have been

used in this laboratory as well as in other laboratories. Previous studies (Aliverti et al., 1979) have demonstrated that there are within-litter variations in skeletal ossification at 20 dg, a result that would tend to indicate that the use of the litter as the experimental unit would provide the most conservative interpretation. The foregoing considerations, together with our inability to correlate these findings with reductions in fetal body weight or exposure level, strongly indicate that these changes are not biologically significant. Under the conditions of this exposure regimen, there was no evidence for a teratogenic response to 1,3-butadiene exposure.

All facets of these studies were conducted in compliance with the Food and Drug Administration's Good Laboratory Practices, 21 CFR 58. During the performance of these studies, no problems were encountered that we consider would affect the integrity of the results.

V. REFERENCES

Aliverti, V., L. Bonanomi, E. Giavini, V. G. Leone, and L. Mariani. 1979. The extent of fetal ossification as an index of delayed development in teratogenic studies on the rat. Teratology 20: 237-242.

Battelle, Pacific Northwest Laboratories; Battelle-Northwest (BNW). 1984. *Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-00-0) in B6C3F₁ Mice (Inhalation Studies)*, National Toxicology Program Technical Report Series No. 288, August, NIH Publication No. 84-2544. National Institutes of Health, Washington, DC.

Brown, M. G. and O. R. Moss. 1981. An inhalation exposure chamber designed for animal handling. Lab. Anim. Sci. 31: 717-720.

Carpenter, C. P., C. B. Shaffer, C. S. Weil, and H. F. Smyth, Jr. 1944. Studies on the inhalation of 1,3-butadiene; with a comparison of its narcotic effect with benzol, toluol, and styrene, and a note on the elimination of styrene by the human. J. Ind. Hyg. Toxicol. 26: 69-78.

Duncan, D. B. 1955. Multiple range and multiple F tests. Biometrics 11: 1-42.

Erley, D. S. and B. H. Blake. Infrared spectra of gases and vapors, Part No. 001-3994. In: *Grating Spectra*, Volume II. The Dow Chemical Company, Midland, MI.

Griffis, L. C., R. K. Wolfe, R. L. Beethe, C. H. Hobbs, and R. O. McClellan. 1981. Evaluation of a multitiered inhalation exposure chamber. Fundam. Appl. Toxicol. 1: 8-12.

Haseman, J. K. and M. D. Hogan. 1975. Selection of the experimental unit in teratology studies. Teratology 12: 165-172.

Hazelton Laboratories, Europe, Ltd. 1981. *The Toxicity and Carcinogenicity of Butadiene Gas Administered to Rats by Inhalation for Approximately 24 Months*, Report No. 2653-522/2. International Institute of Synthetic Rubber Producers.

Hazelton Laboratories, Europe, Ltd. 1982. *1,3-Butadiene: Inhalation Teratogenicity Study in the Rat*, Report No. 2653-522/2; HSE-81-0040/3, November 1; HSE-81-0040, Addendum 1, March 1982. International Institute of Synthetic Rubber Producers.

Kalter, H. 1974. Choice of the number of sampling units in teratology. Teratology 9: 257-258.

Kimmel, C. A. and G. Trammell. 1981. A rapid procedure for routine double staining of cartilage and bone in fetal and adult animals. Stain Technol. 56: 271-273.

Kopf, R., D. Lorenz, and E. Salewski. 1964. Der Einfluss von Thalidomid auf die Fertilität van Ratten in Generations versuch über Zwei Generationen. Naunyn-Schmiedeberg's Arch. Exp. Pathol. Pharmacol. 247: 127-135.

Kramer, C. Y. 1956. Extension of multiple range tests to group means with unequal numbers of replications. Biometrics 12: 307-310.

Moss, O. R., J. R. Decker, and W. C. Cannon. 1982. Aerosol mixing in an animal exposure chamber having three levels of caging with excreta pans. Am. Ind. Hyg. Assoc. J. 43: 244-249.

National Institute of Occupational Safety and Health (NIOSH). 1980. *Projected Number of Occupational Exposures to Chemical and Physical Hazards*. NIOSH, Cincinnati, OH.

Siegel, S. 1956. *Non-Parametric Statistics for the Behavioral Sciences*. McGraw-Hill, New York, NY.

SRI International. 1979. *Chemical Economics Handbook*. SRI International, Menlo Park, CA.

SRI International. 1981. *Chemical Hazard Information Profile, 1,3-Butadiene, CAS No. 106-99-0*, Draft Report. SRI International, Menlo Park, CA.

Staples, R. E. 1977. Detection of visceral alterations in mammalian fetuses. Teratology 9: A37-A38.

Steel, R. D. G. and J. H. Torrie. 1980. *Principles and Procedures of Statistics*. McGraw-Hill, New York, NY.

Wilson, J. G. 1965. Methods for administering agents and detecting malformations in experimental animals, pp. 262-277. In: *Teratology Principles and Techniques*, J. G. Wilson and J. Warkany (eds.). University of Chicago Press, Chicago, IL.

Winer, B. J. 1971. *Statistical Principles in Experimental Design*. McGraw-Hill, New York, NY.

Zerbe, G. O. 1979. Randomization analysis of a completely randomized design extended to growth and response curves. J. Am. Stat. Assoc. 79: 215-221.

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

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

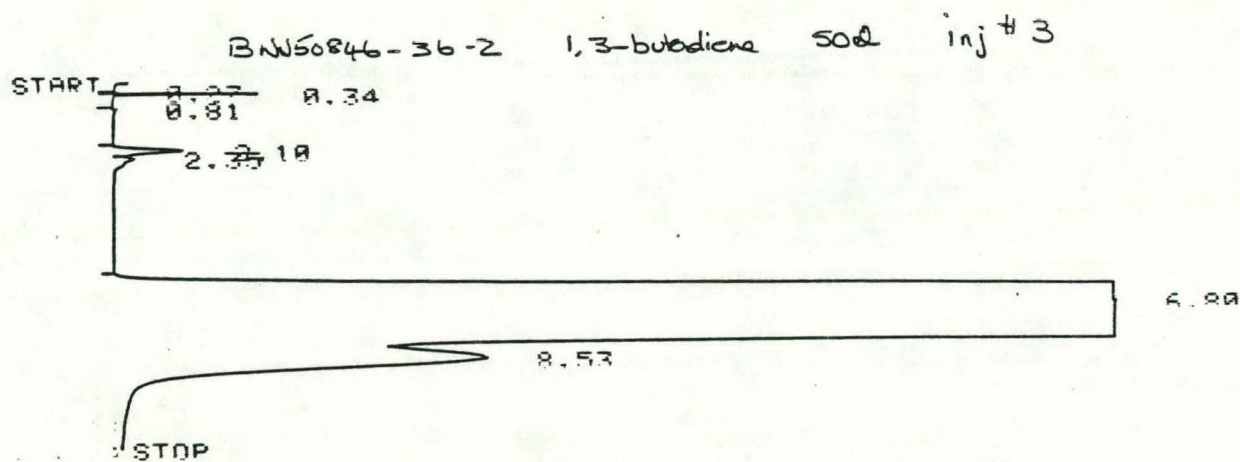
1,3-Butadiene eluted at ~0.4 minutes, the dimer at ~4.7 minutes. The dimer retention time was confirmed by running a dimer standard.

^aDifferences 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 RAT EXPOSURES

Cylinder Number BNW 50846-36-	Date	Dimer Concentration (ppm v/v)
2	11/26/85	190
2	12/02/85	200
2	12/06/85	202

Purity Analysis of 1,3-butadiene
 Lot# BNW50846-36-2+3.
 BNW50846-60 → 63 M.M. Culloch
 GC: HP5840 WA10706
 Column: 2mm x 6 ft glass packed:
 Porapak QS 100/120.



HP RUN # 371
 AREA %

NOV/14/85

TIME 12:33:35

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. Gas Chromatogram of 1,3-Butadiene

Dimer Analysis of 1,3-butadiene.

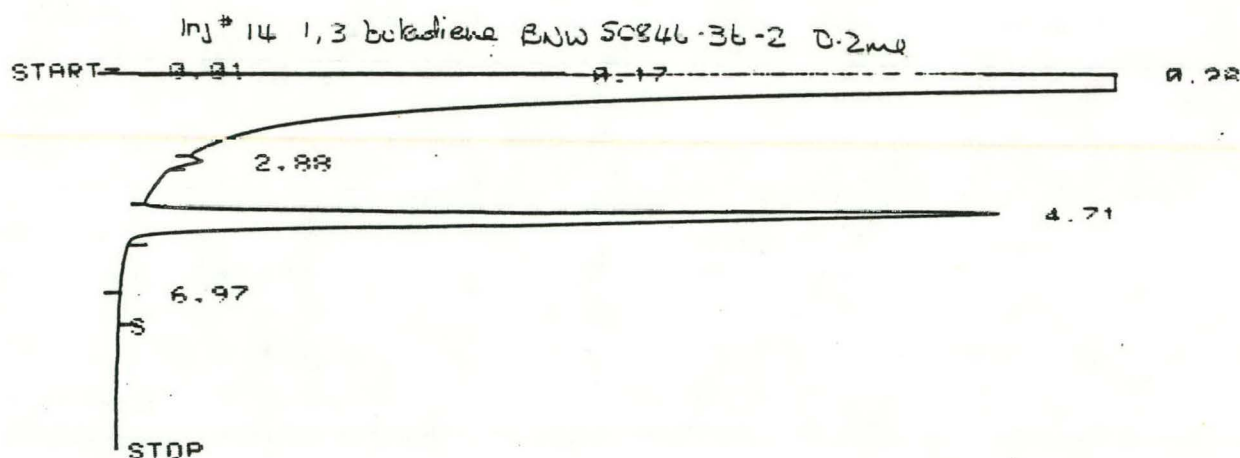
Lor# Bnw 50846-36-2+3.

Bnw 50846-60763

M.M. Celloch 11/13/85

GC HP5840 WA#10706

Column: 2mmx 3ft glass packed ~~capat~~ PS
80/100



HP RUN # 364
AREA %

NOV/13/85

TIME 14:15:10

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. Gas Chromatogram of 1,3-Butadiene Dimer

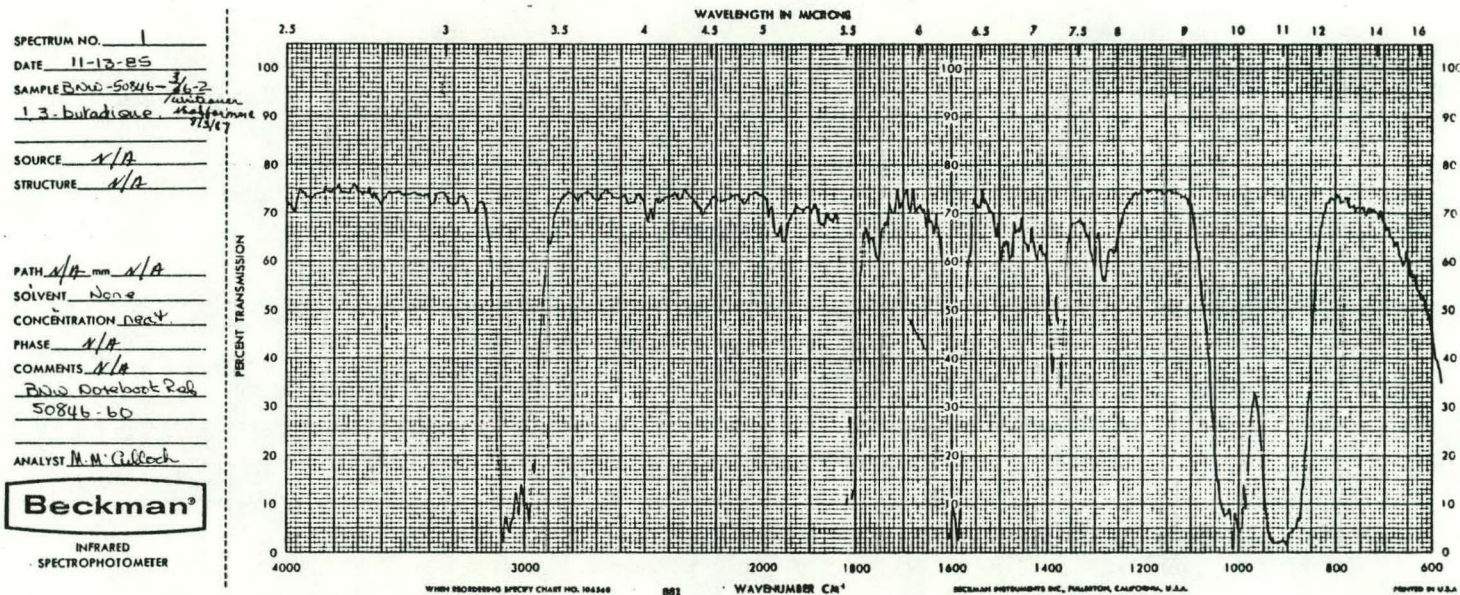


FIGURE A3. Infrared Spectrum of 1,3-Butadiene (Beckman Acculab 8, 10-cm Gas Cell)

APPENDIX B

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

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

Exposure Day	Chamber Concentrations (ppm)		
	40	200	1000
11/25/85	38.5 \pm 0.55	195 \pm 3.94	981 \pm 18.8
11/26/85	40.0 \pm 0.15	199 \pm 1.55	1010 \pm 6.39
11/27/85	40.2 \pm 0.59	199 \pm 4.89	1000 \pm 19.2
11/28/85	40.7 \pm 0.70	205 \pm 2.72	1030 \pm 12.0
11/29/85	40.2 \pm 0.42	201 \pm 1.31	1010 \pm 7.77
11/30/85	40.5 \pm 0.29	200 \pm 1.44	1000 \pm 7.31
12/01/85	40.3 \pm 0.42	201 \pm 1.58	1000 \pm 9.52
12/02/85	40.3 \pm 0.80	202 \pm 3.92	1010 \pm 27.6
12/03/85	38.9 \pm 2.70 ^a	195 \pm 9.63	992 \pm 17.8
12/04/85	40.3 \pm 0.34	200 \pm 1.70	1000 \pm 8.40
12/05/85	40.4 \pm 0.61	200 \pm 1.84	1000 \pm 7.48
12/06/85	40.6 \pm 0.71	202 \pm 3.30	1020 \pm 15.0
12/07/85	40.0 \pm 0.75	199 \pm 3.19	1010 \pm 23.8
12/08/85	40.0 \pm 0.61	199 \pm 2.66	1010 \pm 8.80

^aThe computer terminated the exposure prematurely (cause unknown). Only one individual chamber concentration measurement (31.11 ppm) was less than the lower critical operating limit of 32 ppm

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

Exposure Day	Exposure Chamber (ppm)			
	0	40	200	1000
11/22/85	71.0 \pm 0.51 ^a	71.8 \pm 0.27 ^a	72.0 \pm 0.34	72.0 \pm 0.21
11/23/85	70.9 \pm 0.24 ^a	72.0 \pm 0.36	72.3 \pm 0.35	72.2 \pm 0.28
11/24/85	71.2 \pm 0.44 ^a	72.3 \pm 0.24	72.8 \pm 0.34	72.5 \pm 0.23
11/25/85	73.0 \pm 0.89	73.3 \pm 0.63	73.3 \pm 0.57	73.9 \pm 0.86
11/26/85	73.0 \pm 0.61	73.4 \pm 0.37	73.3 \pm 0.52	74.0 \pm 0.51
11/27/85	73.1 \pm 0.29	73.4 \pm 0.37	73.5 \pm 0.48	74.2 \pm 0.50
11/28/85	73.2 \pm 0.31	73.9 \pm 0.52	74.2 \pm 0.84	74.2 \pm 0.54
11/29/85	72.5 \pm 0.80	73.5 \pm 0.66	73.9 \pm 0.86	73.9 \pm 0.60
11/30/85	72.6 \pm 0.51	73.0 \pm 0.73	73.5 \pm 0.67	73.9 \pm 0.51
12/01/85	72.6 \pm 0.53	73.0 \pm 0.39	73.4 \pm 0.56	74.0 \pm 0.59
12/02/85	72.8 \pm 0.63	73.2 \pm 0.38	73.3 \pm 0.59	73.5 \pm 0.58
12/03/85	73.4 \pm 0.47	74.0 \pm 0.62	73.4 \pm 0.49	73.5 \pm 0.61
12/04/85	73.2 \pm 0.66	73.8 \pm 0.51	73.4 \pm 0.61	73.6 \pm 0.77
12/05/85	73.6 \pm 0.33	73.6 \pm 0.43	73.4 \pm 0.53	73.5 \pm 0.62
12/06/85	74.7 \pm 0.78	74.2 \pm 0.55	74.1 \pm 0.71	74.0 \pm 0.75
12/07/85	75.5 \pm 0.47	74.7 \pm 0.42	74.4 \pm 0.60	73.7 \pm 0.79
12/08/85	74.8 \pm 0.59	74.6 \pm 0.53	74.2 \pm 0.75	73.3 \pm 0.74

^aDaily mean temperatures were below the minimum specified in the Protocol (72°F), but remained above the critical minimum temperature (70°F)

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

Exposure Day	Exposure Chamber (ppm)			
	0	40	200	1000
11/22/85	52.2 \pm 6.7	56.0 \pm 5.7	48.8 \pm 8.4	58.2 \pm 4.6
11/23/85	54.2 \pm 4.6	57.5 \pm 5.5	45.3 \pm 3.5	59.9 \pm 5.0
11/24/85	57.4 \pm 5.9	59.0 \pm 3.8	44.9 \pm 2.6	57.4 \pm 5.9
11/25/85	52.1 \pm 6.1	55.4 \pm 2.5	44.0 \pm 2.2	56.1 \pm 2.3
11/26/85	53.9 \pm 4.7	55.2 \pm 2.6	43.4 \pm 2.6	52.2 \pm 6.5
11/27/85	53.6 \pm 3.7	54.0 \pm 5.6	43.0 \pm 2.9	54.7 \pm 3.3
11/28/85	55.7 \pm 1.5	61.8 \pm 12.3	53.5 \pm 12.5	56.1 \pm 10.0
11/29/85	53.7 \pm 4.8	68.7 \pm 6.9	65.7 \pm 6.8	62.3 \pm 4.9
11/30/85	51.6 \pm 11.8	54.9 \pm 15.6	56.0 \pm 14.3	61.4 \pm 6.7
12/01/85	46.1 \pm 2.2	44.0 \pm 2.0	46.1 \pm 1.7	65.0 \pm 2.7
12/02/85	47.4 \pm 2.2	45.3 \pm 2.9	47.7 \pm 3.1	63.0 \pm 3.7
12/03/85	50.7 \pm 2.0	60.4 \pm 13.0	49.4 \pm 3.4	59.7 \pm 6.9
12/04/85	53.7 \pm 2.4	60.3 \pm 5.0	51.4 \pm 2.3	64.6 \pm 3.3
12/05/85	53.4 \pm 4.6	57.2 \pm 4.8	48.8 \pm 3.5	63.0 \pm 5.3
12/06/85	58.4 \pm 3.4	59.3 \pm 3.3	51.6 \pm 3.5	59.1 \pm 5.1
12/07/85	57.7 \pm 4.3	57.0 \pm 5.9	51.9 \pm 4.5	56.6 \pm 8.9
12/08/85	57.7 \pm 5.3	61.7 \pm 5.4	53.4 \pm 3.8	49.4 \pm 2.9

APPENDIX C

CHAMBER UNIFORMITY TESTS FOR 1,3-BUTADIENE CONCENTRATIONS

TABLE C1. 1,3-Butadiene Gas Concentration Uniformity Test^a

Sample Location	Chamber (ppm)		
	40	200	1000
1B	100.3	99.6	99.8
1F	99.5	100.0	100.2
2B	100.3	99.6	100.1
2F	99.2	100.1	99.7
3B	100.5	100.0	100.0
3F	99.7	100.0	100.1
4B	100.8	100.2	100.3
4F	100.0	100.3	100.3
5B	100.5	100.3	99.6
5F	99.0	99.7	100.1
6B	100.5	100.5	99.5
6F	100.5	99.8	100.4
Mean \pm Standard Deviation	100 \pm 0.6	100 \pm 0.3	100 \pm 0.3

^aResults expressed as percent normalized average concentration at 12 sample locations in each chamber.

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%	999.5	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: *MXCL*

DATE: 1/3/86

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

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
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%	197.3	101.0%	1007.9	100.6%	
5B							
6B							
FRONT: 1F							
2F							
3F	39.3	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%	
RPV:	////////	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: MSCL

DATE: 1/3/86

FIGURE C2. Chamber Uniformity Data Sheet--Chamber Balance

APPENDIX D
HEALTH EVALUATIONS OF EXPERIMENTAL ANIMALS



Pacific Northwest Laboratories

Project Number _____

Internal Distribution

MG Brown
File/Lb

Date November 22, 1985
To P. L. Hackett
From S. E. Rowe *SE*
Subject Pre-Exposure Health Evaluation, Butadiene Teratology Rats

Ten CD(SD) rats (5 M, 5 F) randomly selected from the group received for the study were submitted on 11-13-85 for health evaluation. The rats were received on 10-30-85 from Charles River, Portage Area 6. Two shipment numbers were assigned (860009 for the males, 860010 for the females) although both sexes were shipped together and received at the same time. Health evaluation findings are recorded on the attached lab report (N-114).

There was some evidence of very slight irritation to the eyes and respiratory tract based on clinical signs and pathologic findings. No significant pathogens were found in aerobic cultures of nasopharyngeal washes and serologic tests for antibodies to viral pathogens were negative. I observed the remaining rats in the quarantine room on 11/15 and found them clinically normal. I could not find any evidence of a possible cause for eye and respiratory irritation. Perhaps this was a residual effect from something which happened in transit.

On 11-18-85, a dead rat from the group was submitted for examination. He had been killed when found to have a nasal and ocular discharge. No significant bacterial pathogens were found from nasopharyngeal cultures. No serologic testing was possible since the rat was submitted dead. The method of euthanasia resulted in hemorrhage in the nasopharyngeal area as well as in the CNS area and this interfered with the pathologic evaluation. There was some pathologic evidence of mild upper respiratory tract inflammation.

The investigation of the mild upper respiratory signs and lesions seen in some rats could have been continued with microscopic examination of nasal turbinates but this could not have been completed until the study was well underway. I don't believe these effects were caused by infection and feel reasonably confident that whatever the cause, it will not influence the results of this study. The remaining population is not noticeably affected at this point.

This group was verbally released from quarantine on 11-21-85.

APPENDIX E

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

BUTADIENE RAT FETAL DATA

1

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
3	1	1	1	2.88	0.343
3	2	1	1	3.34	0.417
3	3	1	2	2.92	0.367
3	4	1	2	3.17	0.378
3	5	1	1	3.21	0.435
3	6	1	2	3.00	0.423
3	7	1	1	3.38	0.425
3	8	1	1	3.59	0.479
22	1	1	2	3.59	0.450
22	2	1	1	3.92	0.503
22	3	1	2	3.79	0.518
22	4	1	1	4.10	0.483
22	5	1	1	3.58	0.478
22	6	1	1	3.47	0.377
22	7	1	2	3.40	0.468
22	8	1	2	3.58	0.514
22	9	1	2	3.48	0.423
22	10	1	1	3.45	0.472
22	11	1	2	3.70	0.414
22	12	1	2	3.57	0.437
28	1	1	1	3.38	0.357
28	2	1	1	3.34	0.442
28	3	1	1	3.70	0.379
28	4	1	2	3.66	0.397
28	5	1	2	3.22	0.349
28	6	1	1	3.67	0.451
28	7	1	2	3.48	0.380
28	8	1	1	3.56	0.457
28	9	1	1	3.43	0.365
28	10	1	1	3.45	0.447
28	11	1	2	2.94	0.340
28	12	1	2	3.25	0.350
28	13	1	2	3.43	0.370
28	14	1	2	3.31	0.374
28	15	1	2	3.54	0.469
30	1	1	1	3.09	0.431
30	2	1	1	3.59	0.355
30	3	1	1	3.33	0.357
30	4	1	2	3.30	0.311
30	5	1	1	3.51	0.389
30	6	1	2	3.56	0.400
30	7	1	1	3.77	0.373
30	8	1	2	2.96	0.341
30	9	1	1	3.22	0.394
30	10	1	2	3.29	0.327
30	11	1	1	3.37	0.361
30	12	1	1	3.28	0.419
30	13	1	2	3.17	0.317
30	14	1	2	3.14	0.411
51	1	1	1	3.63	0.426

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

TJM-482A

E-1

BUTADIENE RAT FETAL DATA

2

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
51	2	2	-1	-1.00	-1.000
51	3	1	2	3.39	0.507
51	4	1	2	3.58	0.484
51	5	1	2	3.53	0.495
51	6	1	1	3.84	0.492
51	7	1	1	3.33	0.412
51	8	1	1	3.85	0.518
51	9	1	2	3.39	0.471
51	10	1	1	3.83	0.443
51	11	1	1	3.71	0.468
51	12	1	1	3.83	0.512
51	13	1	1	3.78	0.431
51	14	1	2	3.31	0.397
51	15	1	2	2.99	0.351
61	1	1	1	3.97	0.382
61	2	1	1	4.03	0.388
61	3	1	2	3.72	0.368
61	4	1	2	3.55	0.324
61	5	1	2	3.58	0.340
61	6	1	1	4.02	0.477
61	7	1	2	3.42	0.403
61	8	1	1	3.41	0.338
61	9	1	1	3.53	0.348
61	10	1	2	3.44	0.377
61	11	1	1	3.79	0.490
61	12	1	1	3.76	0.368
61	13	1	1	4.18	0.488
61	14	1	1	3.78	0.404
68	1	2	-1	-1.00	-1.000
68	2	1	2	3.51	0.463
68	3	1	1	3.81	0.500
68	4	1	2	3.40	0.429
68	5	1	2	3.38	0.437
68	6	1	1	3.49	0.423
68	7	1	1	3.01	0.352
68	8	2	-1	-1.00	-1.000
68	9	1	2	2.91	0.462
68	10	1	1	3.37	0.333
68	11	2	-1	-1.00	-1.000
68	12	1	2	3.44	0.438
68	1	1	2	2.75	0.368
68	2	1	2	2.91	0.390
68	3	1	1	3.15	0.405
68	4	1	1	3.39	0.424
68	5	1	2	2.97	0.382
68	6	1	1	3.18	0.368
68	7	1	2	3.12	0.351
68	8	1	1	3.04	0.369
68	9	1	1	3.27	0.436
68	10	1	1	2.71	0.360

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

TJM-482A

E-2

BUTADIENE RAT FETAL DATA

3

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
88	11	1	1	3.13	0.370
88	12	1	2	3.10	0.397
88	13	1	1	3.25	0.397
88	14	1	1	3.38	0.389
88	15	1	2	2.82	0.308
88	16	1	1	3.37	0.398
85	1	1	2	3.80	0.483
85	2	1	2	1.24	0.405
85	3	1	2	3.78	0.435
85	4	1	2	4.08	0.512
85	5	1	1	4.24	0.550
85	6	1	2	3.89	0.530
85	7	1	1	3.93	0.526
85	8	1	2	3.91	0.411
85	9	1	2	4.05	0.465
85	10	2	-1	-1.00	-1.000
85	11	1	2	4.04	0.515
85	12	1	1	4.28	0.518
85	13	1	2	2.48	0.491
92	1	1	1	3.77	0.417
92	2	1	2	3.58	0.367
92	3	1	1	3.73	0.414
92	4	1	2	3.72	0.412
92	5	1	2	3.69	0.438
92	6	1	1	3.81	0.425
92	7	1	2	3.41	0.387
92	8	1	2	3.32	0.403
92	9	1	2	3.38	0.325
92	10	1	2	3.48	0.363
92	11	1	2	3.81	0.446
92	12	1	2	3.82	0.410
92	13	1	1	2.37	0.374
92	14	1	2	3.87	0.432
92	15	1	1	4.01	0.460
92	16	1	1	3.90	-1.000
95	1	1	1	3.88	0.427
95	2	1	1	3.82	0.498
95	3	1	1	3.90	0.410
95	4	1	2	3.81	0.477
95	5	1	1	3.98	0.484
95	6	1	2	4.14	0.446
95	7	1	2	3.85	0.457
95	8	1	2	3.60	0.391
95	9	1	1	4.12	0.431
95	10	1	2	3.21	0.421
95	11	1	1	3.60	0.417
95	12	1	2	3.67	0.450
95	13	1	2	3.68	0.398
95	14	1	2	3.67	0.555
95	15	1	1	3.67	0.495

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

TMT-482A

E-3

BUTADIENE RAT FETAL DATA

4

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
95	16	1	1	3.93	0.417
95	17	1	2	3.58	0.388
98	1	1	1	3.83	0.415
98	2	1	2	3.82	0.506
98	3	1	2	3.88	0.483
98	4	1	1	3.88	0.595
98	5	1	2	3.84	0.510
98	6	1	2	3.91	0.450
98	7	1	1	2.83	0.482
98	8	4	-1	-1.00	-1.000
98	9	1	1	3.31	0.493
98	10	1	1	3.81	0.477
98	11	1	2	3.75	0.537
98	12	1	2	3.78	0.485
98	13	1	2	3.57	0.531
98	14	1	2	3.78	0.439
98	15	1	2	3.13	0.390
104	1	1	1	3.82	0.437
104	2	1	1	3.94	0.527
104	3	1	1	3.77	0.435
104	4	1	2	3.37	0.398
104	5	1	2	3.49	0.451
104	6	1	2	3.11	0.467
104	7	1	2	3.48	0.579
104	8	1	1	3.45	0.458
104	9	1	2	3.39	0.530
104	10	1	1	3.78	0.501
104	11	1	2	3.43	0.476
104	12	1	1	3.83	0.383
104	13	1	1	3.55	0.415
115	1	4	-1	-1.00	-1.000
115	2	1	2	3.24	0.419
115	3	1	2	3.34	0.337
115	4	1	2	3.33	0.383
115	5	1	1	3.70	0.418
115	6	1	2	3.35	0.445
115	7	2	-1	-1.00	-1.000
115	8	1	1	3.42	0.358
115	9	2	-1	-1.00	-1.000
115	10	1	2	3.49	0.384
115	11	1	1	3.74	0.466
115	12	1	2	3.23	0.394
115	13	1	1	3.34	0.332
115	14	1	2	3.21	0.392
115	15	1	2	3.31	0.382
115	16	1	2	3.30	0.342
115	17	1	2	3.58	0.336
121	1	1	1	3.55	0.458
121	2	1	1	3.78	0.480
121	3	1	1	3.84	0.499

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

TJM-482A

E-4

BUTADIENE RAT FETAL DATA

5

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
121	4	1	2	3.40	0.512
121	5	1	2	3.10	0.375
121	6	1	2	3.81	0.477
121	7	1	1	3.69	0.483
121	8	1	1	3.74	0.420
121	9	1	1	3.78	0.535
121	10	1	2	3.46	0.432
121	11	1	1	3.58	0.471
121	12	1	2	3.52	0.428
121	13	1	1	3.83	0.418
121	14	1	1	3.92	0.441
121	15	1	1	3.88	0.488
121	16	1	2	3.61	0.444
121	17	1	1	3.57	0.370
122	1	1	2	3.20	0.385
122	2	1	2	3.57	0.435
122	3	1	2	3.53	0.475
122	4	1	1	3.51	0.360
122	5	1	1	3.62	0.422
122	6	1	1	3.59	0.395
122	7	1	2	3.61	0.420
122	8	1	2	3.50	0.352
122	9	1	2	3.84	0.460
122	10	1	1	3.89	0.454
122	11	1	1	3.87	0.437
122	12	1	1	3.68	0.435
122	13	1	1	3.54	0.387
122	14	1	1	3.72	0.509
122	15	1	1	3.63	0.416
122	16	1	1	3.55	0.445
123	1	1	1	3.57	0.503
123	2	1	2	3.75	0.510
123	3	1	1	3.63	0.858
123	4	1	2	3.57	0.541
123	5	1	2	3.77	0.675
123	6	1	2	3.82	0.593
123	7	1	1	3.99	0.571
123	8	1	2	3.79	0.574
123	9	1	1	4.11	0.652
124	1	1	2	3.14	0.306
124	2	1	1	3.27	0.348
124	3	1	2	2.94	0.321
124	4	1	2	3.28	0.449
124	5	1	1	3.60	0.319
124	6	1	1	3.50	0.342
124	7	1	1	3.57	0.435
124	8	1	1	3.57	0.359
124	9	1	2	2.78	0.447
124	10	1	1	3.16	0.426
124	11	1	2	3.15	0.348

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

TJM-482A

E-5

BUTADIENE RAT FETAL DATA

6

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placental Wt (g)
124	12	1	2	3.28	0.434
124	13	2	-1	-1.00	-1.000
124	14	1	1	3.40	0.383
124	15	1	2	3.39	0.379
124	16	1	1	3.66	0.430
124	17	1	1	3.42	0.392
128	1	1	2	2.00	0.424
128	2	1	2	3.20	0.422
128	3	1	1	3.26	0.397
128	4	1	2	3.01	0.379
128	5	1	2	-1.00	0.368
128	6	1	2	3.05	0.379
128	7	1	1	2.73	0.260
128	8	1	1	3.38	0.355
128	9	1	2	3.23	0.334
128	10	1	1	3.32	0.334
128	11	1	2	3.18	0.373
128	12	1	1	3.17	0.387
128	13	1	2	3.30	0.445
128	14	1	2	3.22	0.435
128	15	1	2	3.26	0.370
151	1	1	1	3.41	0.327
151	2	1	1	3.80	0.333
151	3	1	1	3.88	0.447
151	4	1	2	3.42	0.479
151	5	1	2	3.52	0.347
151	6	1	2	3.72	0.400
151	7	1	2	3.58	0.436
151	8	1	1	3.80	0.476
151	9	1	1	3.87	0.375
151	10	1	1	3.55	0.464
151	11	1	1	3.79	0.520
151	12	1	1	4.15	0.466
151	13	1	1	3.87	0.512
151	14	1	1	4.15	0.420
151	15	1	2	3.66	0.403
156	1	1	1	3.41	0.404
156	2	1	1	3.51	0.357
156	3	1	1	3.64	0.411
156	4	1	2	3.32	0.343
156	5	1	2	3.47	0.366
156	6	1	2	3.38	0.303
156	7	1	2	3.44	0.429
156	8	1	2	3.14	0.434
156	9	1	1	3.40	0.364
156	10	1	1	3.39	0.388
156	11	1	1	3.62	0.355
156	12	1	2	3.47	0.460
156	13	1	2	3.57	0.393
156	14	1	2	3.52	0.402

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

TJM-482A

E-6

BUTADIENE RAT FETAL DATA

7

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
162	1	1	2	3.63	0.467
162	2	1	1	4.00	0.459
162	3	1	1	3.80	0.538
162	4	1	1	3.78	0.484
162	5	1	2	3.58	0.415
162	6	1	1	3.95	0.425
162	7	1	2	3.68	0.455
165	1	1	1	3.27	0.391
165	2	1	2	3.08	0.398
165	3	1	2	3.37	0.336
165	4	1	1	3.24	0.383
165	5	1	1	3.16	0.454
165	6	1	2	3.47	0.389
165	7	2	-1	-1.00	-1.000
165	8	1	2	3.39	0.467
165	9	1	1	3.58	0.489
165	10	2	-1	-1.00	-1.000
165	11	1	1	3.12	0.467
165	12	1	2	2.67	0.369
165	13	1	2	2.90	0.363
170	1	1	1	2.87	0.366
170	2	1	2	2.96	0.339
170	3	1	2	3.10	0.449
170	4	1	2	3.09	0.466
170	5	1	2	2.93	0.441
170	6	1	2	3.17	0.506
170	7	1	1	3.22	0.398
170	8	1	2	2.75	0.379
170	9	1	2	3.13	0.425
170	10	1	1	3.22	0.480
170	11	1	2	2.95	0.437
170	12	1	1	3.28	0.443
170	13	1	1	3.14	0.412
170	14	1	2	3.02	0.411
170	15	1	1	3.53	0.513
170	16	1	1	3.05	0.401
170	17	1	1	3.30	0.453
170	18	1	2	3.05	0.390
170	19	1	1	3.22	0.400
170	20	1	2	3.15	-1.000
173	1	1	2	3.08	0.495
173	2	1	1	3.45	0.528
173	3	1	2	3.30	0.533
173	4	1	2	3.37	0.458
173	5	1	1	3.67	0.547
173	6	1	2	2.56	0.462
173	7	1	1	3.44	0.449
173	8	1	2	3.40	0.419
173	9	1	1	3.53	0.512
173	10	1	1	3.36	0.454

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

BUTADIENE RAT FETAL DATA

8

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
173	11	1	1	3.08	0.412
173	12	1	2	3.08	0.391
173	13	1	2	3.52	0.522
180	1	1	2	2.71	0.368
180	2	1	1	3.44	0.407
180	3	1	2	3.00	0.338
180	4	1	2	3.38	0.421
180	5	1	1	3.66	0.377
180	6	1	2	3.48	0.389
180	7	1	1	3.62	0.406
180	8	1	1	3.21	0.399
180	9	1	1	3.41	0.323
180	10	1	1	3.71	0.380
180	11	1	1	3.45	0.346
180	12	1	2	3.15	0.367
180	13	1	2	3.26	0.368
180	14	1	1	3.59	0.395
180	15	1	1	3.58	0.384
181	1	1	2	3.85	0.435
181	2	2	-1	-1.00	-1.000
181	3	1	1	4.22	0.479
181	4	1	1	4.20	0.531
181	5	1	1	4.56	0.608
181	6	1	1	4.30	0.412
181	7	1	1	4.14	0.534
181	8	1	2	3.79	0.494
181	9	1	2	3.62	0.349
181	10	1	1	3.54	0.320
181	11	1	1	3.68	0.530
181	12	1	1	4.11	0.443
181	13	1	1	4.00	0.401
181	14	1	2	3.75	0.411
181	15	1	1	3.89	0.446
181	16	1	1	1.10	0.370
181	17	1	2	3.77	0.442
190	1	1	1	3.89	0.419
190	2	1	2	3.77	0.313
190	3	1	1	3.93	0.380
190	4	1	1	3.90	0.399
190	5	1	2	3.80	0.420
190	6	1	2	3.51	0.368
190	7	1	2	3.81	0.379
190	8	1	2	3.66	0.370
190	9	1	2	3.71	0.431
190	10	1	2	4.09	0.412
190	11	1	1	4.20	0.463
190	12	1	2	3.91	0.384
190	13	1	2	3.78	0.351
190	14	1	1	4.01	0.452
190	15	1	2	4.03	0.394

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

Sex: Male = 1; Female = 2

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E-8

BUTADIENE RAT FETAL DATA

9

TMT=0 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
190	18	1	1	3.81	0.431
190	17	1	1	3.54	0.392

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E-9

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

BUTADIENE RAT FETAL DATA

10

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
8	1	1	2	3.22	0.388
8	2	1	2	3.16	0.391
8	3	1	2	3.31	0.384
8	4	1	2	3.33	0.423
8	5	1	2	3.01	0.313
8	6	2	-1	-1.00	-1.000
8	7	1	2	3.27	0.374
8	8	1	1	3.33	0.427
8	9	1	1	3.47	0.421
8	10	1	1	3.52	0.383
8	11	1	2	3.35	0.413
8	12	1	2	-1.00	0.390
8	13	1	1	3.48	0.394
14	1	1	2	3.24	0.459
14	2	1	1	3.03	0.492
14	3	1	2	3.62	0.603
14	4	1	1	3.72	0.477
14	5	1	1	3.76	0.489
14	6	1	2	3.37	0.487
14	7	1	2	3.43	0.585
14	8	1	2	3.61	0.402
14	9	1	1	3.74	0.487
14	10	1	2	3.69	0.452
14	11	1	2	3.51	0.477
14	12	1	1	3.93	0.408
26	1	1	2	3.11	0.380
26	2	1	1	3.55	0.603
26	3	2	-1	-1.00	-1.000
26	4	1	2	3.51	0.534
26	5	1	2	3.33	0.528
26	6	1	2	3.45	0.432
26	7	1	2	3.11	0.608
26	8	1	1	3.52	0.472
26	9	1	1	3.28	0.443
26	10	1	2	2.78	0.528
26	11	1	1	3.32	0.513
26	12	1	1	3.80	0.492
26	13	1	2	3.63	0.582
26	14	1	2	3.33	0.446
31	1	1	2	3.08	0.410
31	2	1	2	3.53	0.395
31	3	1	2	3.39	0.376
31	4	1	2	3.73	0.395
31	5	1	2	3.61	0.424
31	6	1	2	3.62	-1.000
31	7	1	1	3.86	0.362
31	8	1	1	3.89	0.375
31	9	1	1	3.20	0.372
31	10	1	1	3.51	0.365
31	11	1	2	3.58	0.440

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

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E-10

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
31	12	1	1	3.19	0.410
31	13	1	1	3.66	0.407
31	14	1	1	3.87	0.362
31	15	1	2	3.46	0.388
31	16	1	1	3.58	0.337
31	17	1	2	3.42	0.349
37	1	1	2	3.18	0.311
37	2	1	1	3.28	0.352
37	3	1	2	3.42	0.417
37	4	1	2	3.35	0.298
37	5	1	2	2.92	0.335
37	6	1	1	3.38	0.365
37	7	1	1	3.23	0.341
37	8	1	2	3.08	0.368
37	9	1	1	3.50	0.382
37	10	1	2	3.25	0.337
37	11	1	2	3.57	0.402
37	12	1	2	3.26	0.370
37	13	1	1	3.25	0.361
37	14	1	1	3.37	0.373
37	15	1	1	3.51	0.346
50	1	1	1	3.80	0.493
50	2	1	2	3.55	0.439
50	3	1	2	3.45	0.387
50	4	1	1	3.87	0.428
50	5	1	2	3.55	0.396
50	6	1	2	3.51	0.454
50	7	1	1	3.66	0.383
50	8	1	2	3.11	0.342
50	9	1	2	3.31	0.358
50	10	1	2	3.72	0.425
50	11	1	1	3.60	0.384
50	12	1	1	3.75	0.482
50	13	1	1	3.56	0.383
50	14	1	1	3.51	0.348
50	15	1	2	3.60	0.447
50	16	1	1	3.94	0.449
60	1	1	2	3.19	0.397
60	2	1	1	3.30	0.457
60	3	1	1	3.66	0.507
60	4	1	1	3.70	0.453
60	5	1	1	3.70	0.464
60	6	1	2	3.47	0.441
60	7	1	1	3.50	0.439
60	8	1	1	3.47	0.433
60	9	1	2	2.63	0.369
60	10	1	1	3.28	0.397
60	11	1	1	3.45	0.484
60	12	1	1	3.33	0.487
60	13	1	1	3.53	0.432

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

BUTADIENE RAT FETAL DATA

12

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
60	14	1	1	3.51	0.487
60	15	1	2	3.21	0.427
60	16	1	2	3.36	0.385
62	1	1	2	3.47	0.359
62	2	1	1	3.84	0.481
62	3	1	1	3.47	0.391
62	4	1	2	3.55	0.486
62	5	1	1	3.51	0.513
62	6	2	-1	-1.00	-1.000
62	7	1	2	3.27	0.377
62	8	1	2	3.38	0.389
62	9	2	-1	-1.00	-1.000
62	10	1	2	3.38	0.418
62	11	1	2	3.48	0.339
62	12	1	1	3.47	0.496
62	13	2	-1	-1.00	-1.000
62	14	1	1	3.76	0.428
62	15	1	1	3.66	0.436
62	16	1	2	3.64	0.388
62	17	1	1	3.55	0.464
62	18	1	1	-1.00	0.442
69	1	1	2	3.64	0.372
69	2	1	1	4.08	0.510
69	3	1	2	3.61	0.461
69	4	1	2	3.59	0.364
69	5	1	1	3.72	0.438
69	6	1	2	3.53	0.383
69	7	1	1	3.67	0.402
69	8	1	1	3.77	0.434
69	9	1	1	3.78	0.432
69	10	1	1	3.63	0.393
69	11	2	-1	-1.00	-1.000
69	12	1	2	3.65	0.423
101	1	1	1	3.06	0.337
101	2	1	2	3.34	0.389
101	3	1	1	3.17	0.342
101	4	1	2	3.29	0.319
101	5	1	1	3.71	0.460
101	6	1	2	2.94	0.320
101	7	1	1	3.32	0.296
101	8	1	2	3.29	0.349
101	9	1	2	2.94	0.272
101	10	1	2	3.09	0.333
101	11	1	2	3.19	0.393
101	12	1	1	3.31	0.365
101	13	1	1	3.36	0.336
101	14	1	1	3.52	0.419
101	15	2	-1	-1.00	-1.000
101	16	1	2	3.40	0.401
101	17	1	1	3.47	0.370

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

Sex: Male = 1; Female = 2

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E-12

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
102	1	1	2	3.31	0.410
102	2	1	1	3.37	0.365
102	3	1	2	3.39	0.393
102	4	1	2	3.36	0.398
102	5	1	1	3.45	0.416
102	6	1	2	3.31	0.321
102	7	1	1	3.39	0.408
102	8	1	1	3.16	0.349
102	9	1	2	3.32	0.351
102	10	1	1	3.56	0.399
102	11	1	1	3.43	0.379
102	12	1	1	3.71	0.507
102	13	1	2	3.73	0.377
102	14	1	1	3.65	0.381
102	15	1	1	3.62	0.354
106	1	1	1	3.31	0.526
106	2	1	2	3.49	0.515
113	1	1	1	3.10	0.381
113	2	1	2	3.08	0.355
113	3	1	2	2.87	0.420
113	4	1	1	3.13	0.420
113	5	1	1	3.25	0.382
113	6	1	1	2.93	0.402
113	7	1	1	2.90	0.401
113	8	1	1	3.17	0.361
113	9	1	2	2.25	0.373
113	10	4	-1	-1.00	-1.000
113	11	1	2	3.10	0.465
113	12	2	-1	-1.00	-1.000
113	13	1	1	3.24	0.370
113	14	1	2	2.98	0.344
116	1	1	2	2.64	0.367
116	2	1	2	2.40	0.302
116	3	1	2	3.12	0.521
116	4	1	2	3.42	0.397
116	5	1	2	3.41	0.394
116	6	1	1	3.53	0.478
116	7	1	2	3.39	0.406
116	8	1	2	3.15	0.421
116	9	1	1	3.48	0.399
116	10	1	2	2.97	0.424
116	11	1	2	3.09	0.456
116	12	2	-1	-1.00	-1.000
116	13	1	2	3.63	0.532
116	14	1	2	3.51	0.485
116	15	1	1	3.04	0.464
138	1	1	1	3.67	0.433
138	2	1	1	3.93	0.404
138	3	1	1	3.67	0.438
138	4	1	1	3.53	0.387

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

BUTADIENE RAT FETAL DATA

14

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
138	5	1	2	3.59	0.422
138	6	1	1	3.60	0.397
138	7	1	1	3.61	0.392
138	8	1	1	3.58	0.407
138	9	1	1	3.84	0.442
138	10	1	2	3.35	0.353
138	11	1	2	3.71	0.422
145	1	1	1	4.13	0.428
145	2	1	2	3.77	0.403
145	3	1	1	4.11	0.500
145	4	1	1	4.19	0.574
145	5	1	2	3.98	0.455
145	6	1	1	4.51	0.485
145	7	1	1	3.81	0.422
145	8	1	2	4.03	0.477
145	9	1	2	4.18	0.502
145	10	1	1	4.38	0.491
145	11	1	2	4.00	0.463
145	12	1	1	4.42	0.443
145	13	1	2	4.10	0.587
145	14	1	1	4.15	0.485
148	1	1	1	3.40	0.420
148	2	1	2	3.22	0.418
148	3	1	1	3.45	0.479
148	4	1	1	3.25	0.488
148	5	1	1	3.29	0.673
148	6	1	1	3.27	0.424
148	7	1	1	3.04	0.418
148	8	1	2	3.50	0.432
148	9	1	1	3.21	0.428
148	10	1	1	3.43	0.482
148	11	1	1	3.44	0.403
148	12	1	2	3.18	0.409
148	13	1	1	3.22	0.495
148	14	1	2	3.31	0.507
148	15	1	1	3.48	0.413
155	1	1	2	3.08	0.412
155	2	1	1	3.51	0.503
155	3	1	2	3.20	0.439
155	4	1	2	3.39	0.475
155	5	1	1	3.38	0.461
155	6	1	1	3.33	0.431
155	7	1	1	3.31	0.448
155	8	1	1	3.30	0.371
155	9	1	1	3.28	0.438
155	10	1	2	2.98	0.411
155	11	1	1	3.31	0.487
155	12	1	2	3.37	0.440
155	13	1	1	3.24	0.440
155	14	1	2	3.20	0.421

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

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E-14

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
155	15	1	1	3.07	0.421
155	16	1	2	3.20	0.406
166	1	1	1	3.49	0.374
166	2	1	2	3.09	0.398
166	3	2	-1	-1.00	-1.000
166	4	1	1	3.90	0.379
166	5	1	2	3.29	0.298
166	6	1	1	3.81	0.401
166	7	1	1	3.48	0.344
166	8	1	1	3.60	0.350
166	9	1	1	3.48	0.411
166	10	1	1	3.51	0.394
166	11	1	1	3.68	0.402
166	12	1	1	3.67	0.331
166	13	1	2	2.75	0.343
166	14	1	1	3.43	0.340
166	15	1	1	3.68	0.401
171	1	1	2	3.38	0.403
171	2	1	1	3.77	0.435
171	3	1	2	3.34	0.424
171	4	1	2	3.69	0.494
171	5	1	2	3.27	0.381
171	6	1	1	3.53	0.418
171	7	1	1	3.89	0.378
171	8	1	2	3.29	0.329
171	9	2	-1	-1.00	-1.000
171	10	1	2	3.23	0.377
171	11	1	2	3.58	0.363
171	12	1	2	3.46	0.455
171	13	1	2	3.09	0.378
171	14	1	2	3.85	0.345
171	15	1	1	3.64	0.376
188	1	1	2	3.11	0.391
188	2	1	2	3.11	0.396
188	3	1	2	3.39	0.402
188	4	1	1	3.40	0.410
188	5	1	1	3.20	0.493
188	6	1	2	2.94	0.395
188	7	1	1	2.43	0.303
188	8	1	1	3.39	0.471
188	9	1	1	3.37	0.448
194	1	1	1	3.38	0.390
194	2	1	1	3.52	0.396
194	3	1	2	3.63	0.444
194	4	1	2	3.62	0.403
194	5	1	1	3.12	0.409
194	6	1	2	3.16	0.386
194	7	1	1	3.47	0.391
194	8	1	1	3.19	0.373
194	9	1	1	3.32	0.405

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

BUTADIENE RAT FETAL DATA

18

TMT=40 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
194	10	1	1	3.04	0.478
201	1	1	2	2.81	0.318
201	2	1	2	2.88	0.372
201	3	1	1	3.07	0.424
201	4	1	2	2.66	0.338
201	5	1	1	3.21	0.407
201	6	2	-1	-1.00	-1.000
201	7	1	2	3.26	0.399
201	8	1	2	3.20	0.342
201	9	1	2	3.05	0.440
201	10	1	2	2.87	0.413
201	11	2	-1	-1.00	-1.000
201	12	1	1	3.58	0.375
201	13	1	2	3.12	0.373
201	14	1	2	2.84	0.319
201	15	1	1	3.08	0.368
201	16	1	1	3.51	0.367
201	17	1	2	3.38	0.401
201	18	1	1	3.28	0.353
202	1	1	2	3.98	0.450
202	2	1	1	4.24	0.462
202	3	1	1	4.23	0.463
202	4	1	2	3.82	0.484
202	5	1	1	4.30	0.580
202	6	1	1	3.98	0.486
202	7	1	2	3.97	0.481
202	8	1	1	4.09	0.519
202	9	1	2	3.97	0.456
202	10	1	2	4.05	0.523
202	11	1	1	4.06	0.525
202	12	1	1	4.32	0.645
202	13	1	2	3.97	0.469
202	14	1	2	3.74	0.468
202	15	1	1	3.80	0.484
202	16	1	1	4.38	0.501

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

TJM-482A

E-16

BUTADIENE RAT FETAL DATA

17

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
5	1	1	2	3.39	0.343
5	2	1	1	3.18	0.409
5	3	1	1	3.11	0.473
5	4	1	1	3.35	0.412
5	5	1	1	3.42	0.449
5	6	1	1	3.32	0.374
5	7	1	1	3.37	0.466
5	8	1	2	2.91	0.379
5	9	1	1	3.22	0.356
5	10	1	2	2.78	0.407
5	11	1	1	3.65	0.448
5	12	1	2	3.17	0.482
17	1	1	2	3.29	0.470
17	2	1	2	3.28	0.454
17	3	1	1	3.50	0.444
17	4	1	1	3.52	0.464
17	5	1	2	3.45	0.439
17	6	2	-1	-1.00	-1.000
17	7	1	2	2.88	0.432
17	8	2	-1	-1.00	-1.000
17	9	1	1	3.51	0.461
17	10	1	2	2.97	0.537
17	11	1	2	2.97	0.435
17	12	1	1	3.44	0.453
17	13	1	1	3.44	0.490
17	14	1	1	3.58	0.460
17	15	1	2	3.03	0.381
17	16	2	-1	-1.00	-1.000
17	17	1	2	3.47	0.414
24	1	2	-1	-1.00	-1.000
24	2	1	1	3.15	0.320
24	3	1	1	2.91	0.405
24	4	1	1	3.23	0.416
24	5	1	2	3.01	0.368
24	6	1	2	3.09	0.346
24	7	1	1	3.15	0.376
24	8	1	1	3.25	0.519
24	9	1	1	3.30	0.345
24	10	1	1	3.36	0.552
24	11	1	2	2.35	0.319
24	12	1	1	2.99	0.432
24	13	1	1	3.58	0.435
24	14	1	1	3.42	0.508
24	15	1	1	3.26	0.412
24	16	1	2	3.16	0.388
29	1	1	1	3.73	0.507
29	2	1	1	3.66	0.482
29	3	1	1	3.73	0.476
29	4	1	1	3.72	0.596
29	5	1	1	3.78	0.437

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

BUTADIENE RAT FETAL DATA

18

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
29	6	1	1	3.91	0.548
29	7	1	2	3.37	0.511
29	8	1	2	3.29	0.412
29	9	1	1	3.15	0.393
29	10	1	2	3.09	0.629
29	11	1	2	3.17	0.400
29	12	1	1	3.52	0.422
29	13	1	1	3.61	0.600
29	14	1	2	3.61	0.457
29	15	1	1	3.82	0.481
33	1	2	-1	-1.00	-1.000
33	2	1	2	3.51	0.410
33	3	2	-1	-1.00	-1.000
33	4	1	2	3.55	0.470
33	5	1	2	3.63	0.500
33	6	1	1	3.50	0.516
33	7	1	2	3.81	0.457
33	8	1	1	3.94	0.512
33	9	1	2	3.46	0.543
33	10	1	1	3.68	0.481
33	11	1	1	3.46	0.389
33	12	1	1	3.39	0.534
33	13	1	2	3.62	0.483
35	1	1	2	3.46	0.452
35	2	1	1	3.44	0.364
35	3	1	1	3.55	0.515
35	4	1	2	3.45	0.419
35	5	1	2	3.28	0.408
35	6	1	1	3.56	0.511
35	7	1	1	3.51	0.421
35	8	1	2	3.38	0.449
35	9	1	1	3.53	0.395
35	10	1	1	3.39	0.382
35	11	1	2	2.99	0.374
35	12	1	1	3.22	0.423
35	13	1	1	3.52	0.504
35	14	1	1	3.40	0.464
35	15	1	2	3.23	0.570
35	16	1	1	3.43	0.419
35	17	1	2	3.45	0.404
36	1	1	1	2.99	0.394
36	2	1	2	2.82	0.484
36	3	1	1	3.07	0.439
36	4	1	2	2.99	0.435
36	5	1	2	2.94	0.338
36	6	1	2	2.92	0.444
36	7	1	2	2.83	0.310
36	8	1	1	3.22	0.398
36	9	1	1	3.49	0.482
36	10	1	2	3.14	0.424

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

TJM-482A

E-18

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
38	11	1	2	3.28	0.420
38	12	1	2	2.48	0.459
38	13	1	1	3.07	0.368
38	14	1	1	3.34	0.425
38	15	1	1	3.34	0.551
38	18	1	1	3.24	0.384
38	17	2	-1	-1.00	-1.000
40	1	1	2	3.31	0.368
40	2	1	1	4.14	0.408
40	3	1	1	3.52	0.375
40	4	1	2	3.35	0.363
40	5	1	1	3.80	0.374
40	8	1	2	3.30	0.313
40	7	1	2	3.82	0.363
40	8	1	2	3.24	0.266
40	9	1	2	3.29	0.318
40	10	1	1	3.68	0.352
40	11	1	2	3.48	0.304
40	12	1	2	3.21	0.322
40	13	1	2	3.33	0.347
40	14	1	2	3.43	0.352
40	15	1	2	3.51	0.341
41	1	1	2	3.58	0.618
41	2	2	-1	-1.00	-1.000
41	3	2	-1	-1.00	-1.000
41	4	1	1	3.85	0.558
41	5	1	2	3.55	0.630
41	6	1	2	2.94	0.857
41	7	2	-1	-1.00	-1.000
41	8	1	2	3.24	0.748
41	9	1	1	3.51	0.817
41	10	2	-1	-1.00	-1.000
41	11	2	-1	-1.00	-1.000
41	12	1	2	2.71	0.671
41	13	1	2	2.63	0.606
48	1	1	1	4.08	0.478
48	2	1	2	3.20	0.547
48	3	1	2	3.91	0.399
48	4	1	2	3.78	0.571
48	5	1	1	3.78	0.471
48	6	1	2	3.94	0.377
48	7	1	2	4.09	0.454
48	8	1	2	3.91	0.441
48	9	1	1	4.23	0.517
48	10	1	1	4.12	0.398
48	11	1	1	3.95	0.525
48	12	1	1	4.01	0.406
48	13	1	1	3.67	0.358
48	14	2	-1	-1.00	-1.000
48	15	1	2	3.68	0.421

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

BUTADIENE RAT.FETAL DATA

20

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
48	18	1	2	3.91	0.407
57	1	1	2	2.90	0.328
57	2	1	2	3.28	0.381
57	3	1	1	3.58	0.455
57	4	1	1	3.85	0.402
57	5	1	2	3.47	0.321
57	6	1	1	3.51	0.293
57	7	1	1	3.35	0.408
57	8	1	1	3.68	0.342
57	9	1	1	3.71	0.382
57	10	1	2	3.50	0.370
57	11	1	2	3.19	0.294
57	12	1	2	3.39	0.380
57	13	1	1	3.48	0.359
57	14	1	1	3.75	0.361
70	1	1	2	2.91	0.482
70	2	1	2	2.98	0.476
70	3	1	2	2.87	0.403
70	4	1	1	3.38	0.530
70	5	1	2	3.31	0.436
70	6	1	2	3.11	0.493
70	7	1	1	3.35	0.454
82	1	1	2	3.07	0.421
82	2	1	2	3.48	0.478
82	3	1	2	3.49	0.602
82	4	1	1	3.85	0.485
82	5	1	2	3.59	0.514
82	6	1	2	3.37	0.416
82	7	1	1	3.73	0.458
82	8	1	2	3.23	0.486
82	9	1	1	3.11	0.421
82	10	1	1	3.53	0.419
82	11	1	2	3.48	0.491
82	12	1	1	3.56	0.449
82	13	1	2	3.25	0.451
82	14	1	2	3.41	0.527
82	15	1	2	3.40	0.564
82	16	1	1	3.71	0.416
83	1	1	2	2.11	0.289
83	2	1	1	3.58	0.550
83	3	2	-1	-1.00	-1.000
83	4	1	2	3.17	0.363
83	5	1	2	3.44	0.389
83	6	1	1	3.21	0.432
83	7	1	1	3.34	0.320
83	8	2	-1	-1.00	-1.000
83	9	1	2	3.58	0.449
83	10	1	2	3.51	0.375
83	11	1	2	3.17	0.362
83	12	1	1	3.64	0.365

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

TJM-482A

E-20

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
83	13	2	-1	-1.00	-1.000
83	14	1	1	3.80	0.378
83	15	1	1	3.74	0.455
110	1	1	1	4.24	0.495
110	2	1	2	3.77	0.537
110	3	1	2	3.74	0.426
110	4	1	2	3.59	0.448
110	5	1	2	3.80	0.426
110	6	1	1	3.85	0.387
110	7	1	2	3.84	0.446
110	8	1	1	3.95	0.483
110	9	1	1	3.79	0.357
110	10	1	1	4.07	0.531
110	11	1	1	3.88	0.518
110	12	1	2	3.84	0.446
110	13	1	1	4.01	0.486
118	1	1	2	3.38	0.472
118	2	1	1	3.72	0.407
118	3	1	1	3.58	0.470
118	4	1	2	3.57	0.442
118	5	1	1	3.90	0.493
118	6	1	2	3.92	0.534
118	7	1	2	4.12	0.514
118	8	1	1	3.92	0.544
118	9	1	2	3.58	0.522
118	10	1	1	2.93	0.383
118	11	1	2	3.20	0.447
118	12	1	1	3.62	0.491
118	13	1	2	3.72	0.476
118	14	2	-1	-1.00	-1.000
118	15	1	1	3.93	0.490
118	16	1	1	3.88	0.502
118	17	1	1	4.01	0.509
118	18	1	1	4.11	0.496
119	1	1	1	2.58	0.436
119	2	1	2	2.57	0.330
119	3	1	1	2.51	0.344
119	4	1	2	2.80	0.334
119	5	1	1	2.70	0.441
119	6	1	1	2.67	-1.000
119	7	1	2	2.81	0.377
119	8	2	-1	-1.00	-1.000
119	9	1	2	2.88	0.429
119	10	1	1	2.92	0.377
119	11	1	1	2.70	0.384
119	12	1	1	2.71	0.444
119	13	1	2	2.78	0.348
119	14	1	2	3.10	0.448
119	15	2	-1	-1.00	-1.000
119	16	1	2	2.89	-1.000

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

BUTADIENE RAT. FETAL DATA

22

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
127	1	1	2	3.24	0.381
127	2	1	2	3.24	0.449
127	3	1	1	3.33	0.408
127	4	1	2	3.15	0.405
127	5	1	1	3.42	0.438
127	6	1	2	3.22	0.384
127	7	1	2	2.87	0.377
127	8	1	2	2.81	0.401
127	9	1	2	3.11	0.384
127	10	1	2	3.19	0.360
127	11	1	1	3.51	0.400
127	12	1	2	3.34	0.513
127	13	1	2	3.10	0.415
127	14	1	2	3.34	0.376
127	15	1	2	3.27	0.390
127	16	1	1	3.67	0.388
127	17	1	1	3.42	0.433
130	1	1	1	3.74	0.440
130	2	1	1	3.87	0.428
130	3	1	1	3.94	0.414
130	4	1	1	3.92	0.449
130	5	1	1	4.09	0.427
130	6	1	1	4.29	0.480
130	7	1	1	4.07	0.447
130	8	1	2	3.60	0.378
130	9	1	2	3.63	0.444
130	10	1	2	3.63	0.407
130	11	1	1	4.01	0.479
130	12	1	2	3.86	0.431
130	13	1	1	4.22	0.426
130	14	1	1	4.29	0.425
130	15	1	2	3.58	0.391
131	1	1	1	2.85	0.407
131	2	1	2	3.05	0.376
131	3	1	2	3.28	0.458
131	4	1	2	2.68	0.373
131	5	1	2	2.88	0.375
131	6	1	1	3.37	0.415
131	7	1	1	3.07	0.523
131	8	1	1	2.94	0.356
131	9	1	2	2.83	0.421
131	10	1	1	2.87	0.389
131	11	1	2	2.85	0.471
131	12	1	2	2.72	0.420
131	13	1	1	3.36	0.451
131	14	1	2	3.05	0.400
131	15	1	2	2.74	0.356
131	16	1	1	2.86	0.405
133	1	1	2	3.03	0.458
133	2	1	2	3.09	0.430

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

Sex: Male = 1; Female = 2

TJM-482A

E-22

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
133	3	1	1	3.47	0.509
133	4	1	2	3.26	0.441
133	5	1	2	3.23	0.570
133	6	1	1	3.37	0.477
133	7	1	1	3.28	0.424
133	8	1	1	3.18	0.422
133	9	1	1	3.41	0.459
133	10	1	1	3.29	0.403
133	11	1	2	3.22	0.500
133	12	1	2	3.09	0.424
133	13	1	1	3.24	0.420
133	14	2	-1	-1.00	-1.000
133	15	1	2	3.23	0.452
133	16	1	2	3.11	-1.000
133	17	1	2	3.12	0.450
140	1	1	2	3.53	0.358
140	2	1	1	3.64	0.392
140	3	1	1	3.54	0.443
140	4	1	1	3.50	0.372
140	5	1	1	3.58	0.425
140	6	1	1	3.74	0.488
140	7	1	1	3.45	0.425
140	8	1	2	3.39	0.438
140	9	1	1	3.50	0.417
140	10	2	-1	-1.00	-1.000
140	11	1	1	3.68	0.558
140	12	2	-1	-1.00	-1.000
140	13	1	2	3.61	0.599
140	14	1	1	3.48	0.514
140	15	1	2	3.41	0.484
140	16	1	2	3.00	0.333
140	17	1	2	3.47	0.372
163	1	1	1	3.47	0.332
163	2	4	-1	-1.00	-1.000
163	3	1	2	3.42	0.397
163	4	1	2	3.57	0.440
163	5	1	2	3.60	0.373
163	6	4	-1	-1.00	-1.000
163	7	1	2	3.39	0.399
163	8	1	1	3.38	0.417
163	9	1	2	3.56	0.374
163	10	1	2	3.84	0.417
163	11	1	1	3.60	0.414
163	12	2	-1	-1.00	-1.000
163	13	1	2	3.53	0.288
163	14	1	1	3.67	0.353
163	15	1	1	3.81	0.487
184	1	1	2	3.36	0.414
184	2	1	1	3.49	0.402
184	3	1	1	3.64	0.433

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

BUTADIENE RAT FETAL DATA

24

TMT=200 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
184	4	1	1	3.44	0.369
184	5	1	1	3.89	0.366
184	6	1	2	3.27	0.398
184	7	1	2	3.47	0.419
184	8	1	1	3.68	0.416
184	9	1	1	3.72	0.414
184	10	1	2	3.34	0.398
184	11	1	1	3.65	0.420
184	12	1	2	3.40	0.431
184	13	1	2	3.66	0.438
184	14	1	1	3.75	0.434
184	15	1	1	3.65	0.429
184	16	1	2	3.59	0.436
184	17	1	2	3.54	0.392
184	18	1	1	3.88	0.482
187	1	1	2	3.36	0.494
187	2	1	2	3.54	0.418
187	3	1	2	3.37	0.471
187	4	1	1	3.70	0.390
187	5	1	1	3.53	0.431
187	6	1	1	1.74	0.209
187	7	1	1	3.62	0.427
187	8	1	1	3.21	0.370
187	9	1	1	3.08	0.400
187	10	1	2	3.16	0.365
187	11	1	1	3.34	0.484
187	12	1	1	3.72	0.470
187	13	1	1	3.16	0.424
187	14	1	1	3.22	0.406
187	15	1	1	3.74	0.430
187	16	1	1	3.79	0.498
197	1	1	2	3.23	0.376
197	2	1	1	3.64	0.354
197	3	1	1	2.96	0.344
197	4	1	1	3.68	0.360
197	5	1	2	3.21	0.332
197	6	1	1	2.89	0.370
197	7	1	1	3.50	0.338
197	8	1	1	3.64	0.382
197	9	1	1	3.52	0.363
197	10	1	1	3.85	0.373
197	11	1	2	3.71	0.397
197	12	1	2	3.42	0.443
197	13	1	2	3.17	0.420
197	14	1	1	3.20	0.442
197	15	1	1	3.60	0.376
197	16	1	2	3.47	0.396

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

TJM-482A

E-24

BUTADIENE RAT FETAL DATA

25

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
1	1	1	2	3.25	0.333
1	2	1	1	3.38	0.346
1	3	1	1	3.58	0.410
1	4	1	1	3.22	0.396
1	5	1	2	3.48	0.411
1	6	1	2	3.37	0.408
1	7	1	1	3.45	0.359
1	8	1	2	3.11	0.393
1	9	1	1	3.21	0.385
1	10	1	1	3.19	0.399
1	11	1	2	2.94	0.424
1	12	1	2	3.46	0.335
1	13	1	1	3.49	0.405
1	14	1	2	3.04	0.420
1	15	1	1	3.34	0.380
1	16	1	1	3.64	0.402
15	1	1	2	3.08	0.293
15	2	2	1	-1.00	-1.000
15	3	1	2	3.16	0.287
15	4	1	2	3.47	0.342
15	5	1	1	3.32	0.367
15	6	1	1	3.27	0.402
15	7	1	2	2.86	0.347
15	8	1	2	3.04	0.386
15	9	1	2	3.07	0.325
15	10	1	1	3.26	0.399
15	11	1	2	3.05	0.381
15	12	1	2	2.88	0.308
15	13	1	2	2.75	0.333
15	14	1	2	3.00	0.312
15	15	1	1	3.15	0.391
16	1	1	1	3.94	0.455
16	2	1	2	3.47	0.525
16	3	1	1	3.79	0.433
16	4	1	1	4.45	-1.000
21	1	1	2	3.21	0.328
21	2	1	1	3.80	0.363
21	3	1	1	3.94	0.425
21	4	1	1	3.74	0.338
21	5	1	2	3.63	0.363
21	6	1	2	3.77	0.424
21	7	1	2	3.36	0.347
21	8	1	2	3.51	0.385
21	9	1	1	3.46	0.325
21	10	1	1	3.61	0.350
21	11	1	1	3.55	0.362
21	12	1	1	3.55	0.328
21	13	1	2	3.44	0.411
21	14	1	2	3.96	0.371
21	15	1	1	3.84	0.347

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

TJM-482A

- E-25

BUTADIENE RAT FETAL DATA

26

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
21	16	1	2	3.22	0.358
21	17	1	1	3.91	0.412
32	1	1	1	3.70	0.398
32	2	1	2	3.22	0.318
32	3	1	2	3.39	0.334
32	4	1	2	3.45	0.358
32	5	1	1	3.58	0.331
32	6	1	1	3.65	0.430
32	7	1	1	3.76	0.420
32	8	1	1	3.70	0.429
32	9	1	2	3.58	0.380
32	10	1	1	1.98	0.205
32	11	1	2	3.69	0.415
32	12	1	2	3.49	0.341
32	13	1	2	3.47	0.354
32	14	1	2	3.88	0.517
46	1	1	2	3.98	0.433
46	2	1	1	3.88	0.439
46	3	1	1	4.39	0.435
46	4	1	1	4.02	0.532
46	5	1	1	4.16	0.425
46	6	1	1	4.21	0.414
46	7	1	1	4.21	0.521
46	8	1	2	4.07	0.494
46	9	1	2	3.82	0.488
46	10	1	2	3.61	0.418
46	11	1	2	3.86	0.421
46	12	1	1	4.03	0.405
46	13	1	1	4.68	0.500
46	14	1	2	4.05	0.380
46	15	1	1	4.20	0.405
46	16	1	1	4.14	0.450
47	1	1	1	4.44	0.550
47	2	1	2	4.12	0.451
47	3	1	1	4.04	0.481
47	4	1	1	4.22	0.478
47	5	1	1	3.93	0.395
47	6	1	2	4.10	0.430
47	7	1	1	4.33	0.575
47	8	2	-1	-1.00	-1.000
47	9	1	1	4.32	0.522
47	10	1	1	4.32	0.440
47	11	1	1	4.17	0.378
47	12	1	1	4.24	0.532
47	13	1	1	4.23	0.385
47	14	1	2	3.98	0.435
52	1	1	1	3.49	0.613
52	2	1	2	3.45	0.518
52	3	1	2	3.46	0.572
52	4	1	2	3.44	0.529

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

TJM-482A

E-26

BUTADIENE RAT FETAL DATA

27

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
52	5	1	1	3.58	0.558
52	6	1	2	3.36	0.574
52	7	1	2	3.35	0.482
52	8	1	1	3.85	0.608
52	9	1	1	3.56	0.559
52	10	1	1	3.32	0.496
52	11	1	1	3.57	0.536
52	12	2	-1	-1.00	-1.000
52	13	1	1	3.65	0.478
52	14	1	2	3.36	0.468
52	15	1	1	3.74	0.454
59	1	1	2	3.83	0.423
59	2	1	1	4.02	0.520
59	3	1	1	4.20	0.554
59	4	1	2	4.23	0.517
59	5	1	2	3.80	0.615
59	6	1	1	4.01	0.557
59	7	1	2	4.24	0.661
59	8	1	2	4.17	0.600
75	1	1	2	2.91	0.456
75	2	1	2	2.82	0.384
75	3	1	2	3.14	0.394
75	4	1	1	3.15	0.489
75	5	1	2	3.20	0.389
75	6	2	-1	-1.00	-1.000
75	7	1	1	3.09	0.383
75	8	1	1	3.22	0.498
75	9	1	1	3.04	-1.000
75	10	1	2	3.28	0.426
75	11	1	2	2.91	0.371
75	12	1	1	2.93	0.378
75	13	1	1	3.09	0.424
75	14	1	2	3.00	0.396
75	15	1	2	2.91	0.485
79	1	1	2	3.12	0.393
79	2	1	1	3.66	0.448
79	3	1	1	3.28	0.487
79	4	1	2	3.35	0.339
79	5	1	2	3.20	0.330
79	6	1	1	4.07	0.430
79	7	1	2	3.12	0.430
79	8	1	1	3.64	0.410
79	9	1	2	2.39	0.407
79	10	1	1	3.81	0.420
79	11	1	1	3.36	0.492
79	12	1	2	3.20	0.332
79	13	1	1	3.41	0.389
79	14	1	2	3.37	0.378
79	15	1	1	3.20	0.394
80	1	1	1	3.79	0.356

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

TJM-482A

E-27

BUTADIENE RAT FETAL DATA

28

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
80	2	1	1	3.48	0.432
80	3	1	1	3.75	0.357
80	4	1	1	3.78	0.444
80	5	1	2	3.91	0.406
80	6	1	2	3.61	0.364
80	7	1	2	3.52	0.419
80	8	1	1	3.83	0.454
80	9	1	2	3.81	0.410
80	10	1	1	3.32	0.318
80	11	1	2	3.95	0.428
80	12	2	-1	-1.00	-1.000
80	13	1	1	4.08	0.342
80	14	1	2	3.76	0.462
80	15	1	1	3.80	0.398
81	1	1	2	2.99	0.386
81	2	1	1	3.32	0.489
81	3	1	1	3.28	0.429
81	4	1	2	3.26	0.401
81	5	1	2	3.19	0.385
81	6	1	2	3.10	0.449
81	7	2	-1	-1.00	-1.000
81	8	1	1	2.90	0.435
81	9	1	2	3.24	0.439
94	1	2	-1	-1.00	-1.000
105	1	1	2	3.15	0.465
105	2	1	2	3.32	0.418
105	3	1	1	3.39	0.409
105	4	1	2	3.70	0.448
105	5	1	1	3.71	0.473
105	6	1	1	3.57	0.471
105	7	1	1	3.65	0.469
105	8	2	-1	-1.00	-1.000
105	9	1	2	3.48	0.443
105	10	1	2	3.31	0.417
105	11	1	2	3.46	0.431
105	12	1	2	3.64	0.423
105	13	1	2	2.95	0.496
105	14	1	1	3.45	0.537
105	15	1	2	3.79	0.442
109	1	2	-1	-1.00	-1.000
109	2	2	-1	-1.00	-1.000
109	3	2	-1	-1.00	-1.000
109	4	1	1	3.00	0.418
109	5	1	1	3.12	0.311
109	6	1	1	2.73	0.443
109	7	1	1	3.76	0.463
109	8	1	2	3.16	0.369
109	9	1	1	3.54	0.499
109	10	1	1	3.53	0.364
109	11	1	1	3.59	0.304

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

Sex: Male = 1; Female = 2

TJM-482A

E-28

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
109	12	1	2	3.19	0.374
109	13	1	2	3.13	0.368
109	14	1	2	3.68	0.350
109	15	1	2	3.05	0.352
109	16	1	1	3.41	0.393
109	17	1	1	3.29	0.467
109	18	1	1	3.28	0.465
109	19	1	1	3.55	0.472
109	20	1	1	3.34	0.481
128	1	1	1	2.97	0.339
128	2	1	1	3.35	0.358
128	3	1	1	3.72	0.373
128	4	1	1	3.27	0.347
128	5	2	-1	-1.00	-1.000
128	6	1	2	3.15	0.333
128	7	1	1	3.57	0.352
128	8	1	2	3.08	0.361
128	9	1	1	3.23	0.332
128	10	1	1	3.43	0.347
128	11	1	1	3.33	0.305
128	12	1	2	3.40	0.360
128	13	1	2	3.17	0.382
128	14	1	2	3.27	0.399
128	15	1	2	3.42	0.373
128	16	1	2	3.25	0.398
128	17	1	1	3.32	0.361
138	1	1	1	3.63	0.489
138	2	1	2	3.27	0.376
138	3	1	1	3.70	0.442
138	4	1	1	3.63	0.474
138	5	1	2	3.39	0.398
138	6	1	1	3.77	0.411
138	7	1	1	3.62	0.449
138	8	1	1	3.38	0.417
138	9	1	1	3.52	0.437
138	10	1	2	3.34	0.398
138	11	1	1	3.49	0.434
138	12	1	1	3.58	0.605
138	13	1	2	3.55	0.431
138	14	1	1	3.77	0.484
138	15	1	1	3.92	0.455
148	1	1	2	3.08	0.300
148	2	1	1	3.48	0.441
148	3	1	1	3.75	0.420
148	4	1	2	3.24	0.358
148	5	1	1	3.94	0.457
148	6	1	2	3.44	0.382
148	7	1	1	3.30	0.338
148	8	1	1	3.37	0.451
148	9	1	1	3.59	0.468

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

TJM-482A

E-29

BUTADIENE RAT FETAL DATA

30

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
146	10	1	2	3.24	0.452
146	11	1	2	3.02	0.407
146	12	1	2	3.12	0.395
146	13	1	1	3.07	0.503
146	14	2	-1	-1.00	-1.000
146	15	2	-1	-1.00	-1.000
153	1	2	-1	-1.00	-1.000
153	2	1	2	3.33	0.408
153	3	1	1	3.44	0.491
153	4	1	2	3.23	0.473
153	5	1	1	3.07	0.697
153	6	1	1	3.56	0.450
153	7	1	2	3.00	0.429
153	8	1	2	3.47	0.427
153	9	1	2	3.26	0.516
153	10	1	2	3.21	0.501
153	11	1	2	3.26	0.447
153	12	1	1	3.26	0.480
153	13	1	2	3.08	0.463
153	14	1	1	3.49	0.452
153	15	1	1	3.65	0.511
153	16	1	1	3.49	-0.002
153	17	1	1	4.04	0.545
153	18	1	1	3.78	0.703
157	1	1	1	3.44	0.406
157	2	1	1	4.04	0.426
157	3	1	1	4.12	0.420
157	4	1	2	3.41	0.398
157	5	1	1	4.16	0.455
157	6	1	2	3.80	0.392
157	7	1	2	3.65	0.393
157	8	1	1	3.84	0.416
157	9	1	2	3.95	0.487
157	10	1	1	3.86	0.379
157	11	1	2	3.46	0.439
157	12	1	2	3.64	0.505
157	13	1	1	3.97	0.450
157	14	1	2	3.44	0.422
157	15	1	1	3.72	0.405
157	16	1	2	3.36	0.472
157	17	1	2	3.32	0.431
158	1	1	2	3.07	0.382
158	2	1	2	3.55	0.401
158	3	2	-1	-1.00	-1.000
158	4	1	2	3.31	0.374
158	5	1	2	3.60	0.371
158	6	1	2	3.35	0.360
158	7	1	1	3.88	0.379
158	8	1	1	3.03	0.404
158	9	1	1	3.55	0.393

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

TJM-482A

E-30

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
158	10	1	2	3.08	0.381
158	11	1	1	3.33	0.463
158	12	1	2	0.00	0.484
158	13	1	2	3.83	0.457
158	14	4	-1	-1.00	-1.000
158	15	1	2	3.43	0.321
158	16	1	2	3.41	0.404
158	17	1	1	3.35	0.403
160	1	1	1	4.03	0.359
160	2	1	2	3.77	0.400
160	3	1	2	3.44	0.394
160	4	1	2	3.40	0.330
160	5	1	2	4.05	0.403
160	6	1	1	3.57	0.442
160	7	1	2	3.66	0.400
160	8	1	2	3.81	0.433
160	9	1	1	4.14	0.455
160	10	1	2	3.77	0.365
160	11	1	2	3.88	0.428
160	12	1	2	3.69	0.363
160	13	1	1	3.98	0.362
160	14	1	1	3.74	0.391
160	15	1	2	3.77	0.397
161	1	1	2	3.58	0.453
161	2	1	1	3.71	0.471
161	3	1	1	3.56	0.474
161	4	1	1	3.67	0.415
161	5	1	2	3.35	0.430
161	6	1	1	3.65	0.446
161	7	1	1	3.56	0.374
161	8	1	1	3.59	0.431
161	9	1	1	3.84	0.367
161	10	1	1	3.66	0.401
161	11	2	-1	-1.00	-1.000
161	12	1	2	3.49	0.369
161	13	1	1	3.46	0.350
161	14	1	1	3.88	0.399
161	15	1	1	3.80	0.477
161	16	1	2	3.23	0.512
161	17	1	2	3.62	0.428
161	18	1	2	3.91	0.441
161	19	1	1	4.17	0.472
177	1	1	2	3.09	0.299
177	2	1	1	3.34	0.437
177	3	1	1	3.55	0.398
177	4	1	1	3.44	0.403
177	5	1	2	2.98	0.343
177	6	1	1	3.51	0.381
177	7	1	1	3.31	0.313
177	8	1	1	3.78	0.459

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

BUTADIENE RAT FETAL DATA

32

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
177	9	1	2	3.08	0.309
177	10	1	1	3.17	0.373
177	11	1	2	3.24	0.349
177	12	1	2	3.17	0.460
177	13	1	1	3.37	0.463
177	14	1	1	3.60	0.476
179	1	1	1	3.49	0.393
179	2	1	2	3.67	0.361
179	3	1	2	3.40	0.441
179	4	2	-1	-1.00	-1.000
179	5	1	1	3.54	0.381
179	6	1	2	3.48	0.370
179	7	1	1	4.02	0.434
179	8	1	2	3.48	0.391
179	9	1	2	3.63	0.416
179	10	1	2	3.52	0.399
179	11	1	1	3.66	0.453
179	12	1	1	3.80	0.373
179	13	1	2	3.53	0.430
179	14	1	1	3.98	0.496
188	1	1	1	3.09	0.357
188	2	1	1	3.25	0.321
188	3	1	2	3.19	0.301
188	4	1	1	3.65	0.383
188	5	1	1	3.34	0.330
188	6	1	2	3.52	0.363
188	7	1	2	3.12	0.336
188	8	1	2	3.51	0.291
188	9	1	2	2.80	0.912
188	10	1	1	2.71	0.641
188	11	1	1	3.36	0.416
188	12	4	-1	-1.00	-1.000
188	13	1	1	3.38	0.352
188	14	1	2	3.05	0.382
188	15	1	2	3.25	0.333
188	16	1	2	1.91	0.325
196	1	1	2	3.01	0.428
196	2	1	1	3.39	0.386
196	3	1	1	2.80	0.321
196	4	1	2	3.20	0.462
196	5	1	1	3.23	0.405
196	6	1	1	2.87	0.351
196	7	1	1	3.01	0.333
196	8	1	2	2.82	0.384
196	9	1	2	2.96	0.312
196	10	1	1	3.48	0.370
196	11	1	2	2.30	0.391
196	12	1	2	3.02	0.373
196	13	1	1	2.97	0.308
196	14	1	2	2.90	0.372

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

Sex: Male = 1; Female = 2

TJM-482A

E-32

BUTADIENE RAT FETAL DATA

33

TMT=1000 ppm Butadiene

Dam ID	SITE	Status	Sex	Fetal Wt (g)	Placenta Wt (g)
196	15	1	1	3.64	0.465
196	16	1	1	3.55	0.399

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

APPENDIX F
INDIVIDUAL MATERNAL BODY AND UTERINE WEIGHTS

TMT=0 ppm

TJM-482A

F-1

MATID	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	11 dg Wt (g)	16 dg Wt (g)	20 dg Wt (g)	UTERWT	PREG	XGESWT	XGESGN	IMPLANT	LIVE	EARLY	LATE	DEAD
3	257.6	277.0	290.2	307.8	326.2	354.8	40.6	1	314.3	37.3	8	8	0	0	0
11	224.8	233.8	250.0	247.4	246.4	243.0	0.4	0	242.6	8.8
22	221.4	221.0	232.2	248.0	275.4	320.1	64.8	1	255.3	34.3	12	12	0	0	0
28	254.2	255.0	286.4	312.2	347.8	396.2	79.0	1	317.2	62.2	15	15	0	0	0
30	212.2	211.2	222.8	240.6	262.2	300.9	70.2	1	230.7	19.5	14	14	0	0	0
51	218.4	221.4	237.2	257.6	287.6	339.7	73.7	1	266.0	44.6	15	14	1	0	0
61	230.0	235.2	261.6	283.2	308.8	350.4	74.2	1	276.1	40.9	14	14	0	0	0
66	214.8	222.8	248.2	271.0	291.4	321.1	46.5	1	274.6	51.8	12	9	3	0	0
68	217.8	239.2	252.4	285.0	318.0	364.2	76.6	1	287.6	48.4	16	16	0	0	0
85	266.4	266.4	289.6	323.6	348.8	387.1	69.8	1	317.3	50.9	13	12	1	0	0
92	266.6	271.8	291.0	321.8	358.6	413.0	84.1	1	328.8	57.0	16	16	0	0	0
95	246.0	246.2	280.0	302.4	332.0	370.8	92.3	1	278.5	32.3	17	17	0	0	0
98	234.0	231.8	252.8	281.0	322.0	371.8	82.2	1	289.5	57.7	15	14	0	1	0
104	228.8	243.4	275.2	311.6	337.0	377.1	71.2	1	305.9	62.5	13	13	0	0	0
115	236.0	257.2	288.2	321.4	352.2	406.1	72.1	1	334.0	76.8	17	14	2	1	0
121	242.0	252.0	272.8	302.2	336.8	390.4	90.5	1	299.9	47.9	17	17	0	0	0
122	261.2	272.2	302.4	334.4	362.8	413.9	88.1	1	325.7	53.5	16	16	0	0	0
123	252.4	261.0	283.6	305.0	332.4	366.3	52.4	1	313.9	52.9	9	9	0	0	0
124	222.2	227.0	238.0	271.6	290.2	328.3	76.2	1	252.2	25.2	17	16	1	0	0
128	235.8	247.4	281.4	301.4	335.2	383.6	72.9	1	310.8	63.4	15	15	0	0	0
151	246.4	250.4	275.2	315.6	347.4	403.2	82.3	1	320.9	70.5	15	15	0	0	0
156	248.6	241.6	276.6	305.2	345.0	388.3	71.1	1	317.2	75.6	14	14	0	0	0
162	224.8	226.6	238.4	255.6	270.0	295.9	38.6	1	257.3	30.7	7	7	0	0	0
165	197.4	201.4	213.8	231.6	255.8	288.6	54.3	1	234.3	32.9	13	11	2	0	0
170	244.4	253.4	269.8	290.0	333.8	386.7	92.8	1	293.9	40.5	20	20	0	0	0
173	213.4	213.4	227.8	243.6	270.4	309.5	64.7	1	244.7	31.3	13	13	0	0	0
176	220.4	224.4	245.6	255.6	242.2	239.2	0.9	0	238.2	13.8
180	229.6	231.4	243.2	262.0	286.0	333.8	74.0	1	259.8	28.4	15	15	0	0	0
181	234.8	242.6	261.0	292.0	324.6	381.9	93.7	1	288.2	45.6	17	16	1	0	0
190	236.0	248.2	276.6	304.0	340.2	401.0	94.4	1	306.6	58.4	17	17	0	0	0

REPRO INDICES FROM RAT BUTA DATA

Page 2

TMT=40 ppm

MATID	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	11 dg Wt (g)	16 dg Wt (g)	20 dg Wt (g)	UTERWT	PREG	XGESWT	XGESGN	IMPLANT	LIVE	EARLY	LATE	DEAD
8	235.0	233.2	256.2	281.2	308.0	347.2	61.6	1	285.6	52.4	13	12	1	0	0
14	244.8	254.8	265.6	278.2	304.8	359.3	63.7	1	295.7	40.9	12	12	0	0	0
25	250.8	245.0	273.4	286.6	277.2	269.3	.	0
26	212.0	217.4	235.4	251.8	282.6	322.3	67.8	1	254.4	37.0	14	13	1	0	0
31	245.6	254.6	271.8	290.2	341.8	383.0	88.3	1	294.6	40.0	17	17	0	0	0
37	232.4	228.6	252.2	271.4	305.6	344.6	71.5	1	273.1	44.5	15	15	0	0	0
50	236.2	234.0	249.4	284.4	321.2	350.4	82.7	1	267.8	33.8	16	16	0	0	0
60	213.8	219.6	248.0	268.2	297.4	352.2	81.6	1	270.6	51.0	16	16	0	0	0
62	254.8	253.4	273.0	302.4	325.8	379.1	80.1	1	299.0	45.6	18	15	3	0	0
69	221.4	220.2	230.0	252.0	278.6	309.2	58.9	1	250.3	30.1	12	11	1	0	0
73	277.6	269.4	288.4	304.4	293.6	286.1	1.2	0	284.9	15.5
101	248.4	250.6	270.2	286.6	329.0	372.1	78.7	1	293.4	42.8	17	16	1	0	0
102	232.6	235.6	268.2	285.2	324.4	364.1	76.5	1	287.6	52.0	15	15	0	0	0
106	209.4	230.0	256.8	271.6	297.2	304.6	11.5	1	293.1	63.1	2	2	0	0	0
108	206.8	216.6	224.6	231.0	229.4	227.7	0.6	0	227.2	10.6
111	207.2	223.2	251.2	280.6	279.2	274.0	0.4	0	273.5	50.3
113	215.4	244.4	262.2	292.2	309.6	339.0	58.8	1	280.3	35.9	14	12	1	1	0
116	220.0	249.0	273.4	300.8	331.8	350.8	68.5	1	282.3	33.3	15	14	1	0	0
138	225.8	238.8	258.0	287.8	316.2	354.0	61.7	1	292.3	53.5	11	11	0	0	0
144	235.6	251.8	280.4	294.4	287.4	275.9	0.5	0	275.4	23.6
145	220.8	232.8	251.6	285.8	332.0	361.2	83.6	1	277.6	44.8	14	14	0	0	0
148	233.6	240.6	261.6	282.4	312.6	353.8	76.5	1	277.3	36.7	15	15	0	0	0
155	241.6	242.4	268.0	287.4	322.0	372.2	82.3	1	289.9	47.5	16	16	0	0	0
166	223.8	235.0	251.6	276.2	299.8	335.2	72.3	1	282.9	27.9	15	14	1	0	0
171	239.0	251.4	272.4	297.4	319.6	359.0	73.1	1	285.8	34.4	15	14	1	0	0
186	206.6	207.4	233.8	260.4	283.6	308.2	44.1	1	264.1	56.7	9	9	0	0	0
194	222.8	230.6	230.8	254.2	274.0	298.5	50.5	1	248.0	17.4	10	10	0	0	0
200	236.6	246.0	240.6	254.6	243.6	246.7	0.8	0	245.9	-0.1
201	263.2	277.8	316.8	345.4	378.8	404.0	78.3	1	325.8	48.0	18	16	2	0	0
202	241.6	259.6	290.6	320.0	358.2	412.3	96.3	1	316.0	56.4	16	16	0	0	0

TJM-482A

F-2

TMT=200 ppm

TJM-482A

F-3

MATID	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	11 dg Wt (g)	16 dg Wt (g)	20 dg Wt (g)	UTERWT	PREG	XGESWT	XGESGN	IMPLANT	LIVE	EARLY	LATE	DEAD
5	238.2	245.0	271.0	302.0	325.4	353.9	56.3	1	297.7	52.7	12	12	0	0	0
17	247.4	241.6	264.6	304.6	341.6	393.3	71.1	1	322.1	80.5	17	14	3	0	0
24	242.4	247.0	268.0	285.6	319.6	363.0	73.8	1	289.2	42.2	16	15	1	0	0
29	240.4	245.2	254.4	291.6	338.6	407.7	86.4	1	321.2	76.0	15	15	0	0	0
33	261.8	260.6	275.0	300.0	333.0	367.5	61.3	1	306.2	45.6	13	11	2	0	0
35	245.4	252.0	277.6	303.8	347.6	393.5	83.4	1	310.1	58.1	17	17	0	0	0
36	257.8	259.6	285.0	307.8	314.6	352.2	74.4	1	277.8	18.2	17	16	1	0	0
40	219.4	217.8	250.2	272.4	306.0	346.2	76.3	1	270.0	52.2	15	15	0	0	0
41	262.4	289.2	311.2	339.8	379.8	432.0	45.0	1	387.0	97.8	13	8	5	0	0
48	214.4	239.6	268.0	305.8	340.8	393.3	87.6	1	305.8	66.2	16	15	1	0	0
57	212.4	219.6	236.8	258.0	284.8	324.9	72.2	1	252.6	33.0	14	14	0	0	0
70	220.8	232.4	253.0	267.8	285.0	309.4	36.0	1	273.3	40.9	7	7	0	0	0
82	222.8	234.4	265.6	288.6	325.6	380.8	82.9	1	298.0	63.6	16	16	0	0	0
83	231.6	229.8	249.0	268.8	291.0	322.7	62.1	1	260.6	30.8	15	12	3	0	0
107	204.6	217.4	248.8	262.8	255.0	247.1	0.8	0	246.3	28.9
110	211.6	227.0	251.6	267.4	297.4	344.9	72.5	1	272.4	45.4	13	13	0	0	0
118	240.0	259.6	285.6	318.2	365.0	410.3	93.9	1	316.4	56.8	18	17	1	0	0
119	225.8	227.0	242.6	269.2	301.6	349.1	61.3	1	287.8	60.8	16	14	2	0	0
127	261.4	269.4	293.2	322.0	360.8	409.1	87.2	1	321.9	52.5	17	17	0	0	0
130	222.6	239.8	271.6	306.0	346.0	400.8	86.7	1	314.1	74.3	15	15	0	0	0
131	228.8	227.6	233.8	253.8	277.8	328.2	75.4	1	252.8	25.2	16	16	0	0	0
133	219.8	224.0	253.0	278.2	307.4	353.0	79.3	1	273.8	49.8	17	16	1	0	0
140	251.6	259.2	273.8	295.0	319.8	361.6	78.2	1	283.4	24.2	17	15	2	0	0
163	237.8	252.0	277.4	305.2	336.2	357.5	62.5	1	295.0	43.0	15	12	1	2	0
164	245.8	248.6	271.2	278.4	268.8	265.0	0.4	0	264.6	16.0
168	247.4	261.4	264.0	278.4	283.8	277.4	0.3	0	277.1	15.7
174	225.4	222.2	243.8	262.0	252.8	250.4	0.6	0	249.8	27.6
184	259.0	262.0	286.0	331.4	371.2	433.1	97.0	1	336.1	74.1	18	18	0	0	0
187	231.6	238.2	271.2	293.2	329.0	365.7	79.7	1	286.0	47.8	16	16	0	0	0
197	244.4	250.0	275.2	299.2	315.2	340.8	78.5	1	262.3	12.3	16	16	0	0	0

REPRO INDICES FROM RAT BUTA DATA

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TMT=1000 ppm

TJM-482A

F-4

MATID	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	11 dg Wt (g)	16 dg Wt (g)	20 dg Wt (g)	UTERWT	PREG	XGESWT	XGESGN	IMPLANT	LIVE	EARLY	LATE	DEAD
1	262.4	263.0	282.0	308.0	325.0	375.8	77.1	1	298.7	35.7	16	16	0	0	0
15	238.6	229.0	238.2	257.2	276.4	322.9	68.2	1	254.7	25.7	15	14	1	0	0
16	242.8	252.8	267.0	267.4	306.4	319.1	22.9	1	296.2	43.4	4	4	0	0	0
21	236.6	234.4	256.2	276.6	307.2	369.2	89.1	1	280.1	45.7	17	17	0	0	0
32	212.2	239.8	265.4	293.8	324.8	362.7	70.9	1	291.8	52.0	14	14	0	0	0
46	211.1	231.0	264.8	281.4	322.6	377.5	93.8	1	283.6	52.6	16	16	0	0	0
47	187.4	220.2	234.8	272.2	308.0	356.5	.	1	.	.	14	13	1	0	0
52	211.4	206.2	218.6	243.4	288.0	347.9	75.1	1	272.9	66.7	15	14	1	0	0
59	235.6	241.6	265.6	281.6	308.2	339.0	47.4	1	291.6	50.0	8	8	0	0	0
75	243.0	242.8	258.4	263.2	284.6	328.1	66.9	1	261.2	18.4	15	14	1	0	0
79	262.8	262.0	280.2	284.2	330.8	376.9	75.2	1	301.6	39.6	15	15	0	0	0
80	258.0	260.4	275.4	308.6	336.8	377.4	75.6	1	301.8	41.4	15	14	1	0	0
81	233.4	246.4	265.2	272.0	293.8	325.1	40.1	1	285.0	38.6	9	8	1	0	0
94	306.6	306.2	336.4	346.4	345.8	331.5	1.1	1	330.3	24.1	1	0	1	0	0
105	230.2	231.4	261.0	295.4	338.4	379.8	73.5	1	306.3	74.9	15	14	1	0	0
109	202.0	215.6	227.8	237.8	272.0	315.0	85.2	1	229.9	14.3	20	17	3	0	0
114	240.2	255.2	284.0	298.2	285.0	284.0	0.5	0	283.5	28.3
126	248.4	257.0	267.2	284.2	321.2	366.1	78.9	1	287.1	30.1	17	16	1	0	0
136	223.6	222.4	243.2	258.6	287.6	340.2	81.6	1	258.6	36.2	15	15	0	0	0
146	224.6	222.0	222.2	237.4	261.8	303.5	67.2	1	236.3	14.3	15	13	2	0	0
149	219.4	211.0	232.8	248.2	238.0	231.8	0.4	0	231.4	20.4
153	256.0	272.8	309.0	330.6	384.0	439.2	89.5	1	349.7	76.9	18	17	1	0	0
157	242.0	244.8	273.4	298.0	333.4	390.0	92.8	1	297.1	52.3	17	17	0	0	0
158	256.8	270.6	297.4	327.8	367.0	421.0	78.4	1	342.6	72.0	17	16	1	0	0
160	225.4	237.6	254.8	274.6	308.8	359.5	84.2	1	275.4	37.8	15	15	0	0	0
161	235.0	252.8	278.8	284.0	315.4	367.6	96.0	1	271.6	18.8	19	18	1	0	0
177	219.2	225.0	250.2	266.4	294.8	335.9	70.5	1	265.4	40.4	14	14	0	0	0
179	218.4	223.6	246.2	250.6	268.6	307.2	73.2	1	234.0	10.4	14	13	1	0	0
188	223.2	235.8	255.8	265.8	299.6	339.4	73.0	1	266.4	30.6	16	15	0	1	0
196	236.0	240.4	256.2	274.2	304.4	350.9	75.6	1	275.4	35.0	16	16	0	0	0

APPENDIX G

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

1M-482A

0 ppm

Mat ID	3	22	28	30	51
Number examined:					
Fetuses	8	12	15	14	14
Heads	4	6	8	7	7

Hydroureter	6	3	7	1,11,13
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Reduced Ossification:

Sternebrae 1-6	1-8	1-12	1-15	1-14	1,3-15
Sternebrae 1-4		2,8,10,12	9,10,11,13	12	5-9,11,12,14,15
Ribs			8		
Skull			4,6,10,12	4,6,10	13,15
Thoracic vertebra (centra)	3,8		1,2,4-7,9-13	2,3,5,6,8,9,10,12	1,7,11,12
Pelvis			8		

Mat ID	61	66	68	85	92
Number examined:					
Fetuses	14	9	16	12	16
Heads	7	4	8	6	8

Vessel Defect

Hydroureter	1,4,5,10,14	3,5	11		13
Pale					3,16
					13

Reduced Ossification:

Sternebrae 1-6	1-14	2-7,9,10,12	1-16	1-3,6,8,12,13	1-16
Sternebrae 1-4	1,3,5-10,12,14		1,2		13
Ribs					
Skull		2,4	9,11,15		
Thoracic vertebra (centra)	6-8,12,13	2,7	1-3,8,10-13,15,16		1,3-5,8,11,12,14
Pelvis					

Butadiene Fetal Abnormalities: Rat

TJM-482A

0 ppm

Mat ID	95	98	104	115	121
Number examined:					
Fetuses	17	14	13	14	17
Heads	9	7	7	7	8
Edema					
Hydrourter		3,5			9
Reduced Ossification:					
Sternebrae 1-6	1-17	1-7,9-15	1-13	2-6,8,10-17	1-17
Sternebrae 1-4	1,10,15	2,3,5-7,9,10,14		3	6,7,11-13
Skull		14		11	3
Thoracic vertebra (centra)		2,3,13	5,10,12,13		5-10,13,16,17
Pelvis				8	1,8

G-2

Mat ID	122	123	124	128	151
Number examined:					
Fetuses	16	9	16	15	15
Heads	8	5	8	7	8
Hydrourter	5,6,10,12-14,16				7
Reduced Ossification:					
Sternebrae 1-6	1-3,5-7,11,14,16	1-9	1-12,14-17	1-15	13,14
Sternebrae 1-4			1	1	
Skull		6		1	4,6,10,12,14
Thoracic vertebra (centra)		2	1,7-11,16	4	5,13-15
Pelvis				1	1
Phalanges		6			

Butadiene Fetal Abnormalities: Rat

TJM-482A

0 ppm

Mat ID	156	162	165	170	173
Number examined:					
Fetuses	14	7	11	20	13
Heads	7	4	5	10	7
Edema					6
Hydroureter	2,13,14		9,11	7	
Reduced Ossification:					
Sternebrae 1-6	1-14	1-7	1-6,8,9,11-13	1-20	1-13
Sternebrae 1-4				4,7,9-14,18,19	6,13
Ribs			12		
Skull					12
Thoracic vertebra (centra)	5,9	3		3,8	1-5,8,10-13
Pelvis		4			2,10

G-3

Mat ID	180	181	190
Number examined:			
Fetuses	15	16	17
Heads	8	8	8
Hydroureter		11,12	3
Reduced Ossification:			
Sternebrae 1-6	1-15	1,3-11,13,16,17	1-17
Sternebrae 1-4		1	
Skull	2		
Thoracic vertebra (centra)	2	1,3,8,15,16	1,2,5,7,10,11

Butadiene Fetal Abnormalities: Rat

40 ppm

Mat ID	8	14	26	31	37
Number examined:					
Fetuses	12	12	13	17	15
Heads	6	6	6	9	7
Hydrocephaly			13		8
Hydrourter		8,12		3,4,12	15
Reduced Ossification:					
Sternebrae 1-6	1-5,7-13	1-12	1,2,4,5,9,11,13	1-3,5-17	1,3,4,9-13,15
Sternebrae 1-4	3,5,8			16	3
Skull	11		1,6,14	12,16	3
Thoracic vertebra (centra)	1,2,4,5,7,12	2,4	2	6,13-15	2-5,8,11

Mat ID	50	60	62	69	101
Number examined:					
Fetuses	16	16	15	11	16
Heads	8	8	8	5	8
Hydrourter	1-3,11,12		8		4
Reduced Ossification:					
Sternebrae 1-6	1,2,4-16	1-16	1-5,7,8,10-12,14-18	1-10,12	1-14,16,17
Sternebrae 1-4			3,5,7,11	1,6,7,10	
Skull	4		2		
Thoracic vertebra (centra)	2,5,7,15	1-3,5,6,12,14	3,11	1,4	2,3,5,7-9,12,14,16

Butadiene Fetal Abnormalities: Rat

40 ppm

Mat ID	102	106	113	116	138
Number examined:					
Fetuses	15	2	12	14	11
Heads	8	1	6	7	6
Hydroureter	1,11,12	1,2	2	5,9	3,10
Reduced Ossification:					
Sternebrae 1-6	1-14	1,2	1-9,11,13,14	1-11,13-15	1-11
Sternebrae 1-4			9	1,2,11	
Ribs				14	2
Skull			9	2,6,10,13	
Thoracic vertebra (centra)	5,11	1	2,3,5,6,8,9,11,13,14	3,5-9,11,13,15	

Mat ID	145	148	155	166	171
Number examined:					
Fetuses	14	15	16	14	14
Heads	7	7	8	7	7
Hydrocephaly					1
Hydroureter	4,6,10,12	8	6	4,5,8-11	
Reduced Ossification:					
Sternebrae 1-6	1-14	1-12,14	1-16	1,2,4-14	1-8,10-15
Sternebrae 1-4			1,3-5,9,10,12-16	6,11	12,14
Skull				2,5,15	6
Thoracic vertebra (centra)	1,7,10,12,13,	2,8,10-13	2,3,12,16	10,14	1,2,4,5,7,8,11-15
Phalanges				4-9	

Butadiene Fetal Abnormalities: Rat

TJM-482A

40 ppm

Mat ID	186	194	201	202
Number examined:				
Fetuses	9	10	16	16
Heads	5	5	8	8
Edema			1,2,4	
Extra ribs			10	
Reduced Ossification:				
Sternebrae 1-6	1-9	1-10	1-5,7-10,12-18	1,3-16
Sternebrae 1-4	1,4-8	3,4	1-3,7,10,15	1-14
Skull	2	6,8		6
Thoracic vertebra (centra)	1,4,7			

G-6

Butadiene Fetal Abnormalities: Rat

TJM-482A

200 ppm

Mat ID	5	17	24	29	33
Number examined:					
Fetuses	12	14	15	15	11
Heads	6	7	8	7	6
Hydroureter	5,11		4,6,7,9-14,16	7	5,8
Misaligned Sternebrae				5	
Reduced Ossification:					
Sternebrae 1-6	1-12	1-5,9,11,12,14,15,17	2-6,9-16	1,3-15	2,4-13
Sternebrae 1-4	2,3,6,8,10,12			1,4-6,8-10,12,14,15	5
Skull		10	11	11,15	4
Thoracic vertebra (centra)	4	9,11,14,15	2,3,8,14,15	3,4,8,9,12	2,4-6,9,12
Pelvis		9,12			

G-7

Mat ID	35	36	40	41	48
Number examined:					
Fetuses	17	16	15	8	15
Heads	8	8	7	4	7
Hydroureter	4,7	16			4,5,13
Misaligned Sternebrae					
Reduced Ossification:					
Sternebrae 1-6	1-16	1-16	1,2,4-15	1,5,6,8,12,13	2-13,15,16
Sternebrae 1-4	5	12	6,8-10,14	13	
Skull			1,3,5		1,3,5,9,11,16
Thoracic vertebra (centra)		14		5,13	4,10,13
Pelvis			6		13

Butadiene Fetal Abnormalities: Rat

200 ppm

Mat ID	57	70	82	83	110
Number examined:					
Fetuses	14	7	16	12	13
Heads	7	3	8	6	6
Hydroureter					3,5,8,13
Missing ribs				7	
Reduced Ossification:					
Sternebrae 1-6	1-14	1-7	1-16	1,2,4-7,9-12,14,15	1-13
Sternebrae 1-4	1,2,6,12	1-6	3,8,10	1	5,7,8,11
Ribs	10			1,7,12	
Thoracic vertebra (centra)	3,10	1-3,5-7	12,13	9,11	3
Mat ID	118	119	127	130	131
Number examined:					
Fetuses	17	14	17	15	16
Heads	9	7	8	8	8
Hydroureter	13		13	1,2,4,8-11	
Missing Ribs	11,16,17				
Missing Innominate Artery			1-11		
Reduced Ossification:					
Sternebrae 1-6	1-13,15-18	1-7,9-14,16	1-17	1-9,11-15	1-16
Sternebrae 1-4	1,10,11	1-6,9-14,16	7,8,10	15	1,2,4,5,7-12,14,15
Ribs			7		
Skull	4		7		5
Thoracic vertebra (centra)	1-3,5,7,11	1,6,7,9,10,13,14	5,6,8-10,16		1,3-5,7,13,16
Pelvis	10		7		

Butadiene Fetal Abnormalities: Rat

11M-482A

	200 ppm			200 ppm	
Mat ID	133	140	163	184	187
<hr/>					
Number examined:					
Fetuses	16	15	12	18	16
Heads	8	8	6	9	8
Edema					6*
Hydroureter			1,5		7,16
Missing ribs					6
Reduced Ossification:					
Sternebrae 1-6	1-13,15-17	1-9,11,13-17	1,3-5,7-11,13,15	1-18	1-7,9-16
Sternebrae 1-4	2-8,10-13,16	3,5,15	7,8,11		
Skull		11			
Thoracic vertebrae					
(centra)	16		11,14		5,6,9,10,11,15
Lumbar vertebrae					6

*This fetus also had aortic stenosis, undescended testes, bent tibia, low ear set and reduced ossification of tibia and fi

	Mat ID	197
Number examined:		
Fetuses		16
Heads		8
Hydrourter		8
Extra rib		6
Reduced Ossification:		
Sternebrae 1-6		1-16
Sternebrae 1-4		3,6
Phalanges		3,6

G-9

Butadiene Fetal Abnormalities: Rat

1000 ppm

Mat ID	1	15	16	21	32
Number examined:					
Fetuses	16	14	4	17	14
Heads	8	8	2	8	7
Hydroureter	9			11,17	
Reduced Ossification:					
Sternebrae 1-6	1-16	1,3-15	1-4	1-17	1-14
Sternebrae 1-4	6,8	1,4,5,13	1,2	8,9	
Ribs					10
Skull				3	2,8,14
Thoracic vertebra					
(centra)	1,6,12,15	3,9-12	3,4	2,8,9	8
Pelvis				2	

Mat ID	46	47	52	59	75
Number examined:					
Fetuses	16	13	14	8	14
Heads	8	6	7	4	7
Cystic dilation*		4			
Hydroureter	2,5,6,8,12,14,16	3,4,7,11-13		3	
Misaligned Sternebrae					
Reduced Ossification:					
Sternebrae 1-6	1-12,14-16	1-6,9-14	1-7,9-11,13-15	1-8	1-5,7-15
Sternebrae 1-4			9		
Skull			3,14	3,5,7	10,12,14,
Thoracic vertebra	2,3,5,6,8,10,11,15	1,4-6,9-11			
(centra)				3,4,6,8	1,11
Pelvis			3		

*Between meninges and skull.

1M-482A

G-10

TJM-482A

1000 ppm

Mat ID	79	80	81	105	109
Number examined:					
Fetuses	15	14	8	14	17
Heads	7	7	4	7	8
Hydrourerter		4,11			8,9,10
Reduced Ossification:					
Sternebrae 1-6	1-15	2-6,13-15	1-6,8,9	1-7,9-15	4-20
Sternebrae 1-4				6,7,9-13,15	13
Ribs	13				
Skull				2,4,9,11	4,14,16,18,20
Thoracic vertebra (centra)	5	3,4,8	4	10,12	12,18

Mat ID	126	136	146	153	157
Number examined:					
Fetuses	16	15	13	17	17
Heads	8	8	7	9	8
Hydrourerter		10		17	
Reduced Ossification:					
Sternebrae 1-6	1-4,6-17	1-15	1-13	2-16,18	1-17
Sternebrae 1-4	1,3,4,6-8,11-14,17	1,2,4,5,8,9,11-15	1-3,6,10-12		11
Skull			2		
Thoracic vertebra (centra)	3,8,1,16,17	14	1,4,5,7,9,10,12,13	4,5,9,12,15,16,18	
Pelvis			13		

G-11

Butadiene Fetal Abnormalities: Rat

1M-482A

1000 ppm

Mat ID	158	160	161	177	179
Number examined:					
Fetuses	15	15	18	14	13
Heads	7	7	9	7	7
Hydrourter			7	3, 6, 7, 11, 13	
Reduced Ossification:					
Sternebrae 1-6	1, 2, 4, 6, 10-12, 15-17	1-15	1-10, 12-14, 16-18	1, 4-9, 11-14	1-13
Sternebrae 1-4					1, 3, 7, 10
Ribs				13	
Skull		5, 15			2
Thoracic vertebra (centra)	8, 17	6	10	2, 3	1, 3, 5, 9, 14
Pelvis			6		

G-12

Mat ID	188	196
Number examined:		
Fetuses	15	16
Heads	8	8
Edema	9, 14, 16	
Meningoencephalocele	9, 14	
Aphakia/retinal dysgen	14	
Microphthalmia	16	
Hydrourter		7
Misaligned Sternebrae		6
Reduced Ossification:		
Sternebrae 1-6	1-7, 9-11, 13-16	1-16
Sternebrae 1-4	16	1, 6-11, 13, 14, 16
Skull		3, 5, 11, 15
Thoracic vertebra (centra)	8	4, 7, 12
Pelvis		15

APPENDIX H

QUALITY ASSURANCE STATEMENT, SAMPLE AND RECORD
DISPOSITION, SCHEDULE OF EVENTS, AND
REPRODUCTIVE INDICES FROM RAT
1,3-BUTADIENE DATA

TERATOLOGY STUDY OF 1,3-BUTADIENE
IN RATS
(Final Report)

Quality Assurance Statement

Listed below are phases and/or procedures included in the study described in this report which were reviewed by the Quality Assurance Unit during the period 10/01/85 - 03/01/86 or 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.)

PHASES/PROCEDURES REVIEWED	REVIEW DATES	DATE FINDINGS SUBMITTED IN WRITING TO STUDY DIRECTOR/MANAGEMENT
Animal Receipt	10/30/85*	11/01/85
Test Chemical Analysis	11/13/85*	12/02/85
Health Screen	11/13/85*	11/15/85
Mating	11/21/85*	11/26/85
Body Weights	11/26/85*	12/02/85
Animal Identification	11/26/85*	12/02/85
Dosing	12/06/85*	12/06/85
Teratology Examinations	12/10/85*	12/16/85
Necropsy	1/08/86	1/08/86
Randomization	1/09/86	1/09/86
Data	2/05-07/86*	2/11/86
Final Report	4/27-29/87 & 11/09,20/87*	11/20/87

* Reviewed specifically for this study.

R. A. Gelman

Quality Assurance Specialist

11/20/87

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 RAT

Completion of exposure/monitoring system:	9/15/85
Approval of protocol:	10/22/85
Animal order:	10/02/85 (CD Sprague-Dawley-derived rats from Charles River Laboratories, Portage Facility, MI)
Receipt of animals:	10/30/85 (ARC #860010; 205 females; ARC #860009; 105 males; date of birth, 09/05/85)
Initial health screen:	11/13/85
Overnight cohabitation:	11/18/85 to 11/22/85
Detection of copulation (0 dg)	(A) 11/19/85 (B) 11/20/85 (C) 11/21/85 (D) 11/22/85 (E) 11/23/85
Exposure period (6-19 dg)	(A) 11/25/85 to 12/04/85 (B) 11/26/85 to 12/05/85 (C) 11/27/85 to 12/06/85 (D) 11/28/85 to 12/07/85 (E) 11/29/85 to 12/08/85
Sacrifice (20 dg)	(A) 12/09/85 (B) 12/10/85 (C) 12/11/85 (D) 12/12/85 (E) 12/13/85
Completion of fetal examinations:	01/15/86
Completion of statistical evaluations:	03/03/86
Submission of Draft Report:	(1) June 1986 (2) April 1987
Submission of Final Report	November 1987

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