Dominant Lethal Study in CD-1 Mice Following Inhalation Exposure to 1,3-Butadiene

P. L. Hackett	B. J. McClanahan
T. J. Mast	R. L. Buschbom
M. G. Brown	J. R. Decker
M. L. Clark	R. L. Rommereim
J. J. Evanoff	R. B. Westerberg
S. E. Rowe	

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DOMINANT LETHAL STUDY IN CD-1 MICE
FOLLOWING INHALATION EXPOSURE TO
1,3-BUTADIENE

FINAL TECHNICAL REPORT
NIH No. NIH-Y01-ES-70153

P.L. Hackett	B.J. McClanahan
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ABSTRACT

A series of studies conducted in this laboratory have evaluated the effects of whole-body inhalation exposures to 1,3-butadiene on the reproductive system. This report describes the results of a study of dominant lethality in CD-1 male mice that were exposed (6 hours/day for 5 consecutive days) to 0 (filtered air), 200, 1000 and 5000 ppm of 1,3-butadiene. Subsequent to exposure, each male was mated with two unexposed females for 1 week. Mating was continued for 8 weeks with replacement of two females each week. Females were euthanized 12 days after the last day of cohabitation to evaluate their reproductive status. Gravid uteri were removed, and the total number, position and status of implantations (classified as early and late resorptions and live and dead fetuses) were determined. The mice were weighed prior to exposure and at 0, 1, 2, 3, 4, 5, 6, 7, and 8 weeks after exposure and at sacrifice. The animals were observed for mortality, morbidity and signs of toxicity throughout the study.

No mortality was observed in any of the inhalation exposure groups. Transient toxic signs, including piloerection and dyspnea, were evident during a 20- to 30-minute period following exposure to 5000 ppm. Mean values for body weights and weight gains of the mice exposed to 1,3-butadiene were not significantly different from control values. Significant results from this study include a tendency toward increased numbers of dead implantations per pregnancy in females mated to 1,3-butadiene-exposed males during the first 2 postexposure weeks. These values and the percentage of dead implantations in litters sired by males exposed to 1000 ppm were significantly higher than control values for weeks 1 and 2; numbers of dead implantations per pregnancy in litters sired by males exposed to 200 ppm and mated during the second postexposure week were also significantly increased. The percentage of females with two or more dead implantations was significantly higher than the control value for the first mating of the 200-, 1000- and 5000-ppm exposure groups. Although this last parameter was the only significant indicator of a biological response in mice exposed to 5000 ppm of the test chemical, these data and the increased frequency of implantation deaths in groups of mice exposed to atmospheric concentrations of 200 and 1000 ppm during the first 2 postexposure weeks suggest that the more mature cells (spermatozoa and spermatids) may be altered by exposure to 1,3-butadiene.

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ABBREVIATIONS

ANOVA	= Analysis of variance
BNW	= Battelle, Pacific Northwest Laboratories; Battelle-Northwest
CDS	= Colorado Data Systems
CO ₂	= Carbon dioxide
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 two reported studies in which the reproductive toxicity of inhaled 1,3-butadiene was specifically evaluated (Carpenter et al., 1944; Hazelton, 1982), and only the former involved exposure of males. In this study, 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 per 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.

A review of the limited data available in the literature indicates a need for further investigations concerned with the reproductive toxicity of 1,3-butadiene, and specific evaluation of the potential of this chemical for producing genetic damage. A study (Tice et al., 1987) using male B6C3F1 mice exposed to 6.25, 62.5 and 625 ppm of 1,3-butadiene for 10 days, 6 hours/day, indicated that significant increases in the frequency of chromosomal aberrations and sister chromatid exchanges, lengthening of average generation time and a depression of the mitotic index were evident in bone marrow cells. The present study was performed to determine the mutagenic activity of 1,3-butadiene in exposed males, using the dominant lethal assay. The basis for this assay is the detection of genetic lesions in the germ cells that result in embryo lethality; however, recent evidence suggests that many mutagens produce both lethal and nonlethal chromosomal breakage, so that the dominant lethal assay should be regarded as a preliminary or confirmatory test for the more definitive assay of heritable translocation (Green et al., 1985). In contrast to the in vitro assays for chromosomal breakage and translocation, the in vivo dominant lethal assay yields information regarding the pharmacologic and metabolic characteristics of the test agent and is particularly valuable in assessing the effect of a chemical on the germ cells (Green et al., 1985).

The regimen for this dominant lethality study involved the subacute exposure of CD-1 male mice to sublethal concentrations of 1,3-butadiene, followed by eight sequential weekly matings of the exposed males with groups of unexposed females. According to studies by Bateman and Epstein (1971), results from the postexposure weekly matings provide information concerning chemical damage to specific stages of gametogenesis, thus indicating that embryonic mortality in Week 1 can be attributed to effects on mature spermatozoa. Effects of the chemical on spermatids, sper-

matocytes, differentiating spermatogonia and stem cells would be evident in results from matings during Weeks 2 and 3, 4 and 5, 6, and after Week 7, respectively.

In these series of studies, the potential genetic toxicity of 1,3-butadiene in male mice has been assessed using a dominant lethal study and the sperm morphology assay. Exposures of CD-1 mice for dominant lethal and B6C3F1 mice for sperm morphology assays (Hackett et al., 1988) used identical exposure regimens (atmospheric concentrations of 0, 200, 1000 and 5000 ppm for 6 hours/day on 5 successive days) during 2 consecutive weeks.

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 F858, 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 the study reported here, a single lot (F909) of 1,3-butadiene was packaged in three 28-gal steel cylinders and shipped directly from Phillips Chemical Company to Pacific Northwest Laboratory (PNL). The cylinders were fitted with double-entry valves, which permitted sampling of liquid 1,3-butadiene through an eductor tube or gaseous material through a valve from the cylinder headspace. As received, the test-material cylinders contained variable amounts of nitrogen, which had been used by the manufacturer to dispense the 1,3-butadiene from bulk storage into appropriate containers for off-site shipment. The nitrogen was released from the cylinders prior to the withdrawal of 1,3-butadiene for analyses or animal exposures. A single cylinder (BNW 50846-36-1) was used for the animal exposures of 5 days' duration in the study described in this report.

Procedures for reanalysis of bulk chemicals were provided by MRI, and the materials were analyzed in our laboratory prior to the initiation of the animal exposures. The infrared spectrum of Lot Number F909 of 1,3-butadiene (4000 to 600 cm^{-1} , using a gas cell with NaCl windows) confirmed its identity and did not detect major impurities (Appendix A). Although this IR spectrum was taken on material from BNW 50846-36-2, it is representative of the entire lot F909.

Gas chromatographic analysis (2 m x 2 mm Porapak QS 100/120, 100°C isothermal, flame ionization detector; FID) for area percent purity of this lot of 1,3-butadiene was determined on cylinder BNW 50846-36-2 and -3 to be 99.88% .

These analyses were considered representative of the entire lot F909 (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 the dimer, 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 Cylinder 1 was 171 ppm (Appendix A); analyses performed during exposures yielded a mean headspace dimer concentration of 215 ± 49 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. Mice were exposed in individual cages (60/cage unit) equipped with feed troughs and automatic watering. During exposure, feed was 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 ($75 \pm 3^\circ\text{F}$), which

was measured by means of resistance temperature devices, and relative humidity (RH; $55 \pm 15\%$), 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, the 1,3-butadiene was withdrawn directly from the gas cylinder through a solenoid valve and, subsequently, through a check-valve, filter-flow-limit switch and a flow meter, which accurately metered gas to a distribution manifold, where it was initially diluted with filtered air. An air-driven vacuum pump delivered the butadiene-air mixture to the exposure chamber inlet for final dilution to the desired concentration.

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

exceeded the control limits, the HP 85B computer transmitted the information to the executive computer, which initiated an appropriate action to correct the concentration. A summary of atmospheric concentrations of 1,3-butadiene for each of the three exposure chambers is shown in Table 1.

TABLE 1. Summary of Chamber Atmospheric Concentrations of 1,3-Butadiene During Exposure of Mice for the Dominant Lethal Study

Observation	Chamber Concentrations (ppm)		
	200	1000	5000
Mean chamber concentration $\pm$ standard deviation (ppm)	200 $\pm$ 5.73	1010 $\pm$ 13.9	5000 $\pm$ 85.4
Maximum-minimum (ppm)	210-161	1060-965	5190-4690
Relative standard deviation (%)	3	1	2
Mean of target concentrations (%)	100	101	100

Periodic measurements of the chamber atmosphere for the dimer of 1,3-butadiene, 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. Previous analyses for dimer concentrations in the atmosphere of the 1000-ppm chamber had shown that 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 concentration of 1,3-butadiene or chamber evacuation (0 ppm) and were obtained within 15 minutes, even when animals were in the chamber (Figure 1).

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 EXPERIMENTAL PROCEDURES

Salient features of the experimental design for this study are summarized in Table 2. For this study, three shipments of four lots of CD-1 mice were purchased from the Charles River Laboratory, Portage, MI Facility (Appendix F). Outbred CD-1 male and female mice were used in this study because of the availability of a large amount of useful information concerning the performance of dominant lethal studies using outbred animals (Epstein et al., 1972; Green et al., 1985). Proving of breeder males was initiated during quarantine, following 2 days of acclimation. At that time, one male was housed with two females for 17 days. The females were sacrificed after the last day of cohabitation to evaluate their reproductive status and the viability of their conceptus. After 6, 14, or 16 days of isolation (see Appendix F), 10 mice from each shipment 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 and heart were performed (Appendix D). At terminal sacrifice, serum from five females or from five males of the control group and five of the high dose group was tested for antibodies to selected pathogens; negative results were obtained.

TABLE 2. Experimental Design for the Dominant Lethal Study of Mice Exposed to 1,3-Butadiene

1,3-Butadiene Exposure Groups	Chamber concentrations (ppm): 0, 200, 1000 and 5000 Exposure regimen: 5 successive days; 6 hours/day Number of males/group: 20
Mating Schedule	Cohabitation of each male with two females for 1 week; matings continued for 8 weeks with replacement of two females each week.
Time of Sacrifice	Females: 12 days after the last day of cohabitation with the males Males: After the eighth week of mating
Observations	Females: Reproductive status; total number, position and status of uterine implants Males: Mortality and signs of toxicity--body weights prior to experimental treatment and at 0, 1, 2, 3, 4, 5, 6, 7 and 8 weeks after treatment; examination of gross tissue abnormalities

Animal facilities and the animal care and use program at PNL have been fully accredited by the American Association for the Accreditation of Laboratory Animal Care. During the isolation period, 10 female mice were housed in wire-mesh cages and provided (ad libitum) NIH-07 open formula diet; water was supplied by an automatic watering system. During the 8-week postexposure period, all animals were maintained on NIH-07 and automatic waterers ad libitum. 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 animals were individually identified by numbered eartags. The males 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.

During the 3 days prior to the initiation of exposure, the males were housed in the exposure chambers in the exposure room. Environmental data were collected during the entire interval that the animals were housed in the exposure chambers. Each animal was exposed to its assigned treatment (atmospheric concentrations of 0 [filtered air], 200, 1000 and 5000 ppm of 1,3-butadiene) for 6 hours/day for 5 consecutive days (01/13/86 through 01/17/86).

D. EXPERIMENTAL OBSERVATIONS

The animals were observed twice daily for mortality, morbidity and signs of toxicity; body weights of the males were determined at weekly intervals. Following the eighth week of cohabitation with the females, male mice were euthanized with CO₂, weighed and examined for lesions of the reproductive tract and for gross tissue abnormalities. Female mice were euthanized with CO₂ 12 days after the last day of cohabitation. The reproductive status was determined, and the gravid uterus was removed to ascertain the total number, position and status of implantations. The number of early and late resorptions, and live and dead fetuses were determined.

E. STATISTICAL METHODS

For body weight measurements, which were repeated over time, a randomization test (Zerbe, 1979) analyzed for differences among growth curves. The number of implantation sites and intrauterine deaths per litter for each week were analyzed by analysis of variance (ANOVA; Steel and Torrie, 1980). When appropriate, proportions of resorptions and dead or live fetuses per implant were subjected to an arcsin transformation and evaluated by ANOVA. If the ANOVA F statistic was significant, Duncan's multiple range test was used to delineate intergroup differences. Dose-response trends were determined by means of orthogonal contrasts (Winer, 1971).

III. RESULTS

No deaths attributable to 1,3-butadiene exposure occurred in any of the four experimental groups. When the mice were examined immediately after exposure to 1,3-butadiene, piloerection and dyspnea were observed in the mice exposed to 5000 ppm, but no toxic signs were evident in the animals exposed to the lower concentrations of the chemical. The appearance and behavior of the mice in the 5000-ppm group were normal within 20 to 30 minutes of the termination of the exposure.

Three of the 80 exposed males died or were excluded from the study. One mouse (#739) in the control group died from an accident after the fourth week of mating, and one male (#755), exposed to 1000 ppm, apparently died from dehydration, although no other instances of dehydration were observed in this study. Throughout the study, the mating rate for male mouse #717, exposed to 5000 ppm was excessively low; at necropsy, bladder stones were observed in this animal, and the decision was made to exclude all of the animal's data from the study summaries.

Mean values for body weights of 1,3-butadiene-treated male mice were not significantly different from those of the control mice (Table 3).

TABLE 3. Body Weights (g, $\bar{x} \pm$ Standard Error) of Male CD-1 Mice Exposed to 1,3-Butadiene

Weeks After Exposure	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
0	33.1 $\pm$ 0.6	32.7 $\pm$ 0.6	33.2 $\pm$ 0.6	33.3 $\pm$ 0.5
1	34.5 $\pm$ 0.6	34.3 $\pm$ 0.6	33.6 $\pm$ 0.9	34.2 $\pm$ 0.6
2	32.8 $\pm$ 0.6	32.4 $\pm$ 0.6	32.3 $\pm$ 0.7	32.5 $\pm$ 0.5
3	32.1 $\pm$ 0.6	32.2 $\pm$ 0.6	32.1 $\pm$ 0.7	32.5 $\pm$ 0.5
4	32.3 $\pm$ 0.6	32.4 $\pm$ 0.6	32.3 $\pm$ 0.6	33.1 $\pm$ 0.6
5	33.1 $\pm$ 0.8	32.8 $\pm$ 0.6	32.9 $\pm$ 0.6	33.6 $\pm$ 0.5
6	33.0 $\pm$ 0.7	32.9 $\pm$ 0.6	33.0 $\pm$ 0.6	33.7 $\pm$ 0.6
7	33.2 $\pm$ 0.7	33.2 $\pm$ 0.6	33.2 $\pm$ 0.6	33.9 $\pm$ 0.6
8	32.5 $\pm$ 0.6	32.4 $\pm$ 0.6	32.5 $\pm$ 0.7	33.1 $\pm$ 0.6

Data from eight of the 1,240 females cohabitating with the exposed males were lost or excluded: two died of unknown causes, two were housed in the wrong cage, and four lost their identifying eartags.

To evaluate the acceptability of the control data in this study, reproductive values from matings of control males with unexposed females during the 8-week postexposure interval are summarized in Table 4. The percentage of pregnant females during postexposure Weeks 1 through 8 varied from 90 to 98%. Ninety-five percent of the males were fertile during the second week, and 100% fertility was achieved in each of the remaining postexposure weeks of cohabitation. For mating Week 1, the total number of implantations per pregnancy was significantly lower than values for Weeks 7 and 8, and data for Weeks 4 and 6 were less than those for Weeks 5, 7 and 8. However, within lots of female mice per shipment (Shipments 1 and 2 contained lots of mice for Weeks 1 and 2 and 3 and 4, respectively, while Shipment 3 contained two lots of mice, one for Weeks 5 and 6 and one for Weeks 7 and 8), only one value, for postexposure Week 6, was significantly lower than values for the remaining females in the shipment (Appendix F). Differences among live implantations for the postexposure weeks are reflections of total implantations per pregnancy, except for the value on Week 6, which differs significantly only from the value for Week 7. In control matings, numbers of early deaths of implantations per pregnancy ranged from a low value of 0.30 to 0.72. The percentage of females with early resorptions varied from 24.3% on Week 6 to 48.7% for Week 1.

Reproductive measures in females mated with 1,3-butadiene-exposed males for each of the 8 postexposure weeks are shown in Table 5 (also see Appendix E). Data for matings during the first postexposure week show that the number of live implantations per pregnancy in the 1000-ppm exposure group is significantly lower than that of the 5000-ppm group, but is not different from the control value. During this interval, the number of early and total resorptions per pregnancy and the percentage of dead implantations tend to be larger in litters of males exposed to the test chemical and are significantly higher than control values in offspring of males exposed to 1000 ppm. In all females mated with the 1,3-butadiene-exposed males, the percentage of females with two or more dead implantations was significantly greater than that of the control mice.

TABLE 4. Reproductive Values from Matings of Control Males During the 8-Week Postexposure Interval

Observation	Postexposure Week							
	1	2	3	4	5	6	7	8
Number of females: pregnant/ mated	37/40	35/39	37/39	39/40	36/38	37/38	36/38	35/38
Number of males: fertile/mated	20/20	19/20	20/20	20/20	19/19	19/19	19/19	19/19
Number of implantations/preg- nancy ^a								
Live	10.70 ± 0.38 ^{cd}	11.09 ± 0.37 ^{bcd}	11.06 ± 0.39 ^{bcd}	9.94 ± 0.33 ^d	11.72 ± 0.46 ^{bc}	10.67 ± 0.37 ^{cd}	11.97 ± 0.30 ^b	11.83 ± 0.38 ^{bc}
Total	11.49 ± 0.35 ^{cd}	11.89 ± 0.32 ^{bcd}	11.68 ± 0.35 ^{bcd}	10.79 ± 0.28 ^d	12.22 ± 0.45 ^{bc}	11.08 ± 0.37 ^d	12.61 ± 0.28 ^b	12.74 ± 0.38 ^b
Number of dead implantations/ pregnancy ^a								
Early	0.65 ± 0.15	0.60 ± 0.15	0.49 ± 0.15	0.72 ± 0.18	0.42 ± 0.12	0.30 ± 0.09	0.42 ± 0.12	0.51 ± 0.12
Late	0.14 ± 0.06	0.20 ± 0.08	0.13 ± 0.06	0.13 ± 0.05	0.08 ± 0.05	0.11 ± 0.05	0.22 ± 0.08	0.40 ± 0.20
Total	0.79 ± 0.15	0.80 ± 0.17	0.62 ± 0.13	0.85 ± 0.18	0.50 ± 0.14	0.41 ± 0.10	0.64 ± 0.13	0.91 ± 0.22
Dead implantations/total implan- tations (%) ^a	6.87 ± 1.29	6.87 ± 1.46	5.91 ± 1.56	8.18 ± 1.77	3.97 ± 1.11	3.59 ± 0.90	5.09 ± 1.02	6.98 ± 1.60
Percentage of females with:								
Early deaths	48.7	40.0	37.8	41.0	27.8	24.3	30.6	40.0
≥ 1 intrauterine death	56.8	48.6	46.0	46.2	30.6	35.1	50.0	51.4
≥ 2 intrauterine deaths	13.5	22.9	13.5	28.2	16.7	5.4	11.1	20.0

^aMean ± standard error^{b-d}Values for the eight postexposure weeks that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.

During the second postexposure week, the number of implantations per pregnancy in females mated with males exposed to 5000 ppm of 1,3-butadiene was significantly lower than the value for litters of males exposed to 1000 ppm, although neither of these means differed significantly from the control mean. Values for the total number of dead implantations and early resorptions per pregnancy tended to be larger for offspring of all chemically exposed males and were significantly higher than control values in litters from males exposed to 200 and 1000 ppm of the test chemical.

Although no significant differences in mean numbers of dead implantations per pregnancy were observed in control and exposed groups at 4 weeks after exposure, the percentage of dead implantations was significantly increased in the control group, compared with the values from the mice exposed to 5000 ppm. During this time interval, the value for the percentage of females with two or more dead implantations was also high in females mated with control males, so that values for the 200- and 5000-ppm groups were significantly lower than those of the control group. No significant differences among treatment groups were observed for matings during postexposure Weeks 3, 5, 6, or 7. In litters from the eighth week of mating, the number of live implantations per pregnancy was significantly lower following exposure to 1000 ppm than to 200 ppm, although neither value differed significantly from the control value.

TABLE 5. Reproductive Measures of the Dominant Lethal Study of Male Mice Exposed to 1,3-Butadiene

Postexposure Week 1

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	37/40	40/40	38/38	37/38
Number of males: fertile/mated	20/20	20/20	19/19	19/19
Number of implantations/pregnancy ^a				
Live	10.70 ± 0.38 ^{bc}	10.25 ± 0.32 ^{bc}	10.03 ± 0.31 ^c	11.14 ± 0.32 ^b
Total	11.49 ± 0.35	11.45 ± 0.32	11.45 ± 0.30	12.08 ± 0.30
Number of dead implantations/pregnancy ^a				
Early	0.65 ± 0.15 ^b	1.00 ± 0.17 ^{bc}	1.26 ± 0.21 ^c	0.89 ± 0.16 ^{bc}
Late	0.14 ± 0.06	0.20 ± 0.08	0.16 ± 0.06	0.03 ± 0.03
Total	0.78 ± 0.15 ^b	1.20 ± 0.17 ^{bc}	1.42 ± 0.21 ^c	0.95 ± 0.16 ^{bc}
Dead implantations/total implantations (%) ^a	6.87 ± 1.29 ^b	10.31 ± 1.47 ^{bc}	12.27 ± 1.79 ^c	7.81 ± 1.35 ^{bc}
Percentage of females with: ≥ 1 intrauterine death ≥ 2 intrauterine deaths	56.8 13.5	67.5 38.5 ^d	73.7 42.11 ^d	54.1 37.1 ^d

Postexposure Week 2

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	35/39	39/40	36/38	38/38
Number of males: fertile/mated	19/20	20/20	19/19	19/19
Number of implantations/pregnancy ^a				
Live	11.09 ± 0.37	10.51 ± 0.37	11.42 ± 0.39	10.55 ± 0.35
Total	11.89 ± 0.32 ^{bc}	11.87 ± 0.36 ^{bc}	12.78 ± 0.32 ^b	11.45 ± 0.29 ^c
Number of dead implantations/pregnancy ^a				
Early	0.60 ± 0.15 ^b	1.23 ± 0.21 ^c	1.17 ± 0.20 ^c	0.82 ± 0.14 ^{bc}
Late	0.20 ± 0.08	0.13 ± 0.05	0.19 ± 0.08	0.08 ± 0.04
Total	0.80 ± 0.17 ^b	1.36 ± 0.22 ^c	1.36 ± 0.22 ^c	0.90 ± 0.14 ^{bc}
Dead implantations/total implantations (%) ^a	6.87 ± 1.46	11.40 ± 1.74	10.92 ± 1.89	8.34 ± 1.41
Percentage of females with: ≥ 1 intrauterine death ≥ 2 intrauterine deaths	48.6 22.9	71.8 43.6	66.7 41.7	63.2 21.1

^aMean ± standard error

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

^dSignificantly different ($P \leq 0.05$) from the control value

TABLE 5. Continued

Postexposure Week 3

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	37/39	35/39	36/38	35/37
Number of males: fertile/mated	20/20	20/20	19/19	19/19
Number of implantations/pregnancy ^a				
Live	11.05 ± 0.39	10.71 ± 0.47	10.22 ± 0.47	11.23 ± 0.34
Total	11.68 ± 0.35	11.71 ± 0.39	10.86 ± 0.42	11.80 ± 0.32
Number of dead implantations/pregnancy ^a				
Early	0.49 ± 0.11	0.80 ± 0.17	0.47 ± 0.13	0.51 ± 0.12
Late	0.14 ± 0.06	0.20 ± 0.08	0.14 ± 0.08	0.06 ± 0.04
Total	0.62 ± 0.13	1.00 ± 0.18	0.64 ± 0.14	0.57 ± 0.12
Dead implantations/total implantations (%) ^a	5.91 ± 1.56	9.52 ± 1.81	8.10 ± 2.91	4.87 ± 0.99
Percentage of females with: ≥ 1 intrauterine death	46.0	60.0	44.4	45.7
≥ 2 intrauterine deaths	13.5	31.4	16.7	11.4

Postexposure Week 4

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	39/40	39/40	36/38	37/38
Number of males: fertile/mated	20/20	20/20	19/19	19/19
Number of implantations/pregnancy ^a				
Live	9.95 ± 0.33	10.64 ± 0.26	10.19 ± 0.40	10.49 ± 0.33
Total	10.79 ± 0.28	11.21 ± 0.24	10.83 ± 0.40	10.95 ± 0.34
Number of dead implantations/pregnancy ^a				
Early	0.72 ± 0.18	0.44 ± 0.10	0.56 ± 0.15	0.32 ± 0.09
Late	0.13 ± 0.05	0.13 ± 0.05	0.08 ± 0.06	0.11 ± 0.06
Total	0.85 ± 0.18	0.56 ± 0.11	0.64 ± 0.17	0.46 ± 0.09
Dead implantations/total implantations (%) ^a	8.18 ± 1.77 ^b	5.09 ± 0.98 ^{bc}	5.73 ± 1.44 ^{bc}	4.04 ± 0.81 ^c
Percentage of females with: ≥ 1 intrauterine death	46.2	46.2	38.9	43.2
≥ 2 intrauterine deaths	28.2	10.3 ^d	16.7	2.7 ^d

^aMean ± standard error^{b-c}Values that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.^dSignificantly different ($P \leq 0.05$) from the control value

TABLE 5. Continued

Postexposure Week 5

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	36/38	38/40	37/38	35/36
Number of males: fertile/mated	19/19	20/20	19/19	19/19
Number of implantations/ pregnancy ^a				
Live	11.72 ± 0.46	11.47 ± 0.43	11.54 ± 0.30	11.29 ± 0.38
Total	12.22 ± 0.45	12.16 ± 0.43	12.08 ± 0.26	11.94 ± 0.40
Number of dead implantations/ pregnancy ^a				
Early	0.42 ± 0.12	0.55 ± 0.11	0.49 ± 0.13	0.54 ± 0.14
Late	0.08 ± 0.05	0.13 ± 0.06	0.05 ± 0.04	0.11 ± 0.07
Total	0.50 ± 0.14	0.68 ± 0.13	0.54 ± 0.13	0.66 ± 0.17
Dead implantations/total implantations (%) ^a	3.97 ± 1.11	5.47 ± 0.98	4.66 ± 0.13	5.30 ± 1.28
Percentage of females with: ≥ 1 intrauterine death	30.6	52.6	40.5	40.0
≥ 2 intrauterine deaths	16.7	13.2	10.8	17.1

Postexposure Week 6

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	37/38	39/40	38/38	37/38
Number of males: fertile/mated	19/19	20/20	19/19	19/19
Number of implantations/ pregnancy ^a				
Live	10.68 ± 0.37	10.56 ± 0.29	11.21 ± 0.28	11.14 ± 0.33
Total	11.08 ± 0.37	11.31 ± 0.24	11.82 ± 0.28	11.92 ± 0.31
Number of dead implantations/ pregnancy ^a				
Early	0.30 ± 0.09	0.67 ± 0.14	0.50 ± 0.13	0.68 ± 0.15
Late	0.11 ± 0.05	0.08 ± 0.04	0.11 ± 0.05	0.11 ± 0.05
Total	0.41 ± 0.10	0.74 ± 0.17	0.61 ± 0.14	0.78 ± 0.15
Dead implantations/total implantations (%) ^a	3.59 ± 0.90	6.68 ± 1.49	4.94 ± 1.08	6.64 ± 1.24
Percentage of females with: ≥ 1 intrauterine death	35.1	41.0	42.1	54.1
≥ 2 intrauterine deaths	5.4	25.6	13.2	18.9

^aMean ± standard error

TABLE 5. Continued

Postexposure Week 7

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	36/38	39/40	33/38	38/38
Number of males: fertile/mated	19/19	20/20	19/19	19/19
Number of implantations/ pregnancy ^a				
Live	11.97 ± 0.30	11.97 ± 0.39	11.61 ± 0.40	12.11 ± 0.25
Total	12.61 ± 0.28	12.69 ± 0.39	12.21 ± 0.40	12.66 ± 0.25
Number of dead implantations/ pregnancy ^a				
Early	0.42 ± 0.12	0.64 ± 0.17	0.39 ± 0.12	0.39 ± 0.09
Late	0.22 ± 0.08	0.08 ± 0.04	0.21 ± 0.08	0.16 ± 0.06
Total	0.64 ± 0.13	0.72 ± 0.17	0.60 ± 0.15	0.55 ± 0.11
Dead implantations/total implantations (%) ^a	5.09 ± 1.02	5.47 ± 1.22	4.85 ± 1.18	4.34 ± 0.87
Percentage of females with: ≥ 1 intrauterine death	50.0	46.2	42.4	44.7
≥ 2 intrauterine deaths	11.1	12.8	12.1	10.5

Postexposure Week 8

Observation	1,3-Butadiene Concentration (ppm)			
	0	200	1000	5000
Number of females: pregnant/mated	35/38	39/39	37/38	34/38
Number of males: fertile/mated	19/19	20/20	19/19	19/19
Number of implantations/ pregnancy ^a				
Live	11.83 ± 0.38 ^{bc}	12.18 ± 0.27 ^b	11.00 ± 0.35 ^c	11.74 ± 0.36 ^{bc}
Total	12.74 ± 0.38	12.85 ± 0.26	12.14 ± 0.32	12.79 ± 0.33
Number of dead implantations/ pregnancy ^a				
Early	0.51 ± 0.12	0.46 ± 0.09	0.78 ± 0.16	0.71 ± 0.16
Late	0.40 ± 0.20	0.21 ± 0.07	0.35 ± 0.11	0.35 ± 0.10
Total	0.91 ± 0.22	0.67 ± 0.11	1.14 ± 0.19	1.06 ± 0.17
Dead implantations/total implantations (%) ^a	6.98 ± 1.60	5.18 ± 0.85	9.40 ± 1.58	8.40 ± 1.39
Percentage of females with: ≥ 1 intrauterine death	51.4	53.9	67.6	64.7
≥ 2 intrauterine deaths	20.0	12.8	27.0	32.4

^aMean ± standard error^{b-c}Values that do not share a common superscript letter are significantly different ($P \leq 0.05$) from one another.

IV. DISCUSSION

Although transient signs of toxicity (piloerection and dyspnea) were observed immediately following exposure to 1,3-butadiene, overt symptoms of toxicity, as measured by mortality and changes in body weight, were not evident in this study. These results for CD-1 males are similar to those obtained with male B6C3F1 mice in a study performed under identical exposure conditions in this laboratory.

Recommendations of Epstein et al. (1972) and Green et al. (1985) for units of expression of the data and criteria for acceptability of control material were utilized for this report. In this study, the lowest value for the pregnancy rate of females mated to control males was 89%, a value which was almost three times that of the 30% minimum recommended in the literature. The maximum value for the number of early resorptions per pregnancy for our control groups was 0.72. The highest value for percentage of females with early resorptions was 48.7%. Both numbers are within the guidelines suggested by Epstein et al. (1972). The minimal mean value of 10.79 implantations per pregnancy was also larger than the expected minimum of nine implantations recommended by Epstein et al. (1972). The control data for this study were therefore considered acceptable for the interpretation of the experimental data and provided a basis for the assumption that each lot of females mated with chemically exposed males would have yielded results equivalent to control values if they had been mated with the control males.

Results from this study indicate that subacute inhalation exposure to 1,3-butadiene did not affect male fertility in CD-1 mice. Although significant effects of the test chemical on the number of early deaths of implantations per pregnancy were observed during the first 2 postexposure weeks, a strict atmospheric concentration-response relationship was not evident. Matings during these intervals resulted in early deaths in litters sired by males exposed to 200 and 1000 ppm but not in offspring of the 5000-ppm exposure group. However, during the first postexposure week, the percentage of females with two or more dead implantations was significantly elevated in all three chemical exposure groups. Since these effects occurred in animals mated soon after exposure, the results suggest that the more mature spermatozoa and spermatids were altered by exposure to 1,3-butadiene.

In addition to the lack of response in early deaths of implantations per pregnancy in the 5000-ppm group, other equivocal effects observed at this exposure level included low values for implantations per pregnancy during the second post-exposure week and for percentage of dead implantations and females with dead implantations during the fourth week. In each case, the significant differences may be attributed to unusually high values for other groups of animals (number of implantations in the 1000-ppm exposure group for Week 2 and control values for the parameters under consideration in postexposure Week 4). Under these circumstances, the significant values in the 5000-ppm group cannot be considered treatment-related.

To determine the potential mutagenic activity of 1,3-butadiene, sperm morphology (reported elsewhere; Hackett et al., 1988) and dominant lethal studies were performed in this laboratory, using identical exposure regimens but different strains of mice (B6C3F1 for the sperm morphology and CD-1 for dominant lethal studies). Although a concentration-related increase in the frequency of sperm-head abnormalities was observed following exposure to 1,3-butadiene, the relationship between chemical concentration and biological response was not consistent in the dominant lethal study. However, there were significant, pertinent effects, including the number of dead implantations per pregnancy and the percentage of females with two or more implantation deaths in litters from the first two post-exposure matings. These results indicate that the findings from the dominant lethal study should be confirmed and that these studies should be extended to include different atmospheric concentrations of the chemical, as well as additional assays for the potential mutagenic activity of 1,3-butadiene.

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

FIGURE A1. Infrared Spectrum of 1,3-Butadiene

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-Ø30SAØ3
 Notebook reference: BNW 50846-60 through 63

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

Results:

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

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

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

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

^aDifferences in values for dimer concentrations in individual cylinders reflect the thermal and usage history of each cylinder (see p. 7 of report).

HP RUN # 372
AREA %

NOV/14/85

TIME 12:46:23

RT	AREA	AREA %
0.25	74	0.000
0.32	1315	0.001
2.09	3876	0.004
2.33	2006	0.002
6.68	87700000	99.878
8.48	99500	0.113

DIL FACTOR: 1.0000 E+0

HP RUN # 373
AREA %

NOV/14/85

TIME 13:00:33

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

DIL FACTOR: 1.0000 E+0

FIGURE A2. Gas Chromatogram of 1,3-Butadiene

HEADSPACE DIMER CONTENT OF THE 1,3-BUTADIENE CYLINDER
(BNW 50846-36-1) PRIOR TO AND DURING ANIMAL EXPOSURES

Date	Exposure Day	Dimer Concentration (ppm v/v)
01/10/86	-3	171 ± 9
01/14/86	2	184 ± 72
01/15/86	3	222 ± 25
01/17/86	5	281 ± 8

APPENDIX B

**CONCENTRATION, TEMPERATURE AND RELATIVE
HUMIDITY MEASUREMENTS IN THE EXPOSURE CHAMBERS**

TABLE B1. Exposure Atmospheric Concentrations (Mean Daily Concentration $\pm$ Standard Deviation) of 1,3-Butadiene During the Dominant Lethal Study in Mice

Exposure Day	Exposure Chamber (ppm)		
	200	1000	5000
1	199 $\pm$ 4.1	1000 $\pm$ 13.6	4940 $\pm$ 94.7
2	199 $\pm$ 2.3	1010 $\pm$ 12.7	4990 $\pm$ 34.2
3	198 $\pm$ 9.5	1010 $\pm$ 15.8	5010 $\pm$ 95.8
4	203 $\pm$ 4.8	1010 $\pm$ 9.3	5030 $\pm$ 64.5
5	202 $\pm$ 4.1	1000 $\pm$ 18.0	5020 $\pm$ 98.6

TABLE B2. Exposure Chamber Temperatures ($^{\circ}$ F, Daily Mean $\pm$ Standard Deviation) During the Dominant Lethal Study of 1,3-Butadiene in Mice

Exposure Day	Exposure Chamber (ppm)			
	0	200	1000	5000
1	74.3 $\pm$ 0.27	73.5 $\pm$ 0.27	73.7 $\pm$ 0.28	74.5 $\pm$ 0.27
2	74.3 $\pm$ 0.36	73.5 $\pm$ 0.35	74.1 $\pm$ 0.34	74.7 $\pm$ 0.32
3	74.2 $\pm$ 0.43	73.3 $\pm$ 0.38	73.9 $\pm$ 0.41	74.4 $\pm$ 0.43
4	74.3 $\pm$ 0.48	73.4 $\pm$ 0.47	74.0 $\pm$ 0.59	74.4 $\pm$ 0.46
5	74.2 $\pm$ 0.43	73.0 $\pm$ 0.45	73.5 $\pm$ 0.65	74.1 $\pm$ 0.36

TABLE B3. Exposure Chamber Relative Humidity (RH; %, Daily Mean $\pm$ Standard Deviation) During the Dominant Lethal Study of 1,3-Butadiene in Mice

Exposure Day	Exposure Chamber (ppm)			
	0	200	1000	5000
1	44.4 $\pm$ 4.9	44.0 $\pm$ 3.6	46.6 $\pm$ 8.6	51.6 $\pm$ 8.5
2	43.1 $\pm$ 3.6	44.1 $\pm$ 3.2	44.3 $\pm$ 3.8	51.6 $\pm$ 4.7
3 ^a	39.2 $\pm$ 5.0	37.2 $\pm$ 5.2	38.2 $\pm$ 4.8	43.4 $\pm$ 5.7
4 ^a	53.2 $\pm$ 10.3	52.3 $\pm$ 17.0	50.0 $\pm$ 14.4	55.4 $\pm$ 14.0
5	57.9 $\pm$ 7.6	59.6 $\pm$ 3.2	62.6 $\pm$ 7.2	61.1 $\pm$ 7.3

^aValues for the mean daily RH were less than the lower operating limit (40%) specified in the protocol, as follows:

Exposure Day	Chamber (ppm)	Values	
		Number of Readings	Percent
3	0	2	34
	200	4	33
	1000	2	32
	5000	1	34
4	200	2	32
	1000	2	34

APPENDIX C
CHAMBER UNIFORMITY TESTS FOR 1,3-BUTADIENE CONCENTRATIONS

COMPOUND: IRT 1,3 BUTADIENE

EXPOSURE ROOM NUMBER: 436

TPV MEASUREMENTS

CHAMBER:		200 ppm		1000 ppm		5000 ppm			
DATE:		12/27/85		12/27/85		12/27/85			
SAMPLE PORT		MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD	MONITOR READING	%RSD
BACK:	1B	188	99.6%	938	100.2%	4995	99.9%		
	2B	190	100.7%	940	100.4%	4967	99.3%		
	3B	189	100.1%	939	100.3%	4997	99.9%		
	4B	190	100.7%	941	100.5%	4972	99.4%		
	5B	187	99.1%	933	99.9%	4967	99.3%		
	6B	190	100.7%	939	100.3%	5002	100.0%		
FRONT:	1F	189	100.1%	931	99.5%	4984	99.7%		
	2F	188	99.6%	932	99.6%	5003	100.0%		
	3F	189	100.1%	933	99.7%	5012	100.2%		
	4F	189	100.1%	934	99.8%	5035	100.7%		
	5F	188	99.6%	933	99.7%	5038	100.7%		
	6F	188	99.6%	936	100.0%	5036	100.7%		
MEAN:		188.8	100.0%	935.9	100.0%	5000.7	100.0%		
TPV:		0.97	0.5%	3.40	0.4%	25.88	0.5%		
BPV:		//////////	≤0%	//////////	0.2%	//////////	0.2%	//////////	//////////

WPV MEASUREMENTS

IN-LINE	1st	190	100.7%	940	100.2%	4967	100.0%		
	2nd	188	99.6%	940	100.2%	4994	100.5%		
	3rd	188	99.6%	933	99.6%	4945	99.5%		
MEAN:		188.7	100.0%	938.3	100.0%	4968.7	100.0%		
WPV:		1.15	0.6%	2.89	0.3%	24.54	0.5%		

MONITOR TYPE: GC 809569

SERIAL #: _____

MONITOR DATA LOCATION: _____

COMMENTS: Pre-exposure chamber balance without animals

ENTERED BY: ML Clark

DATE: 12/31/85

REVIEWED BY: MSCL

DATE: 1/3/86

FIGURE C1. Chamber Uniformity Data Sheet--Without Animals

COMPOUND: IRT 1,3 ButadieneEXPOSURE ROOM NUMBER: 436

TPV MEASUREMENTS

CHAMBER: #6 200 ppm		#7 1000 ppm		#8 5000 ppm			
DATE: 1/10/86		1/10/86		1/10/86			
SAMPLE PORT	MONITOR READING	%	MONITOR READING	%	MONITOR READING	%	MONITOR READING
BACK: 1B	177500	100.5%	886000	100.0%	4367000	100.0%	
2B							
3B			886200	100.0%	4363000	99.9%	
4B	176100	99.7%					
5B							
6B							
FRONT: 1F							
2F							
3F							
4F	176200	99.8%	886000	100.0%	4374000	100.1%	
5F							
6F							
MEAN:	176400.0	100.0%	886066.7	100.0%	4368000.0	100.0%	
TPV:	781.02	0.4%	115.47	0.0%	5567.76	0.1%	
RPV:	//////////	≤0%	//////////	≤0%	//////////	0.1%	//////////

WPV MEASUREMENTS

IN-LINE 1st	177500	100.5%	886000	100.1%	4367000	99.9%	
2nd	176400	99.9%	883200	100.0%	4374000	100.1%	
3rd	175700	99.5%	883600	99.8%	4368000	100.0%	
MEAN:	176533.3	100.0%	884933.3	100.0%	4369666.7	100.0%	
WPV:	907.38	0.5%	1222.02	0.1%	3785.94	0.1%	

MONITOR TYPE: GC type 5840SERIAL #: N809569

MONITOR DATA LOCATION: _____

COMMENTS: Chambers housing animalsENTERED BY: ML ClarkDATE: 1/11/86REVIEWED BY: MZCHLDATE: 1/31/86

FIGURE C2. Chamber Uniformity Data Sheet--With Animals

APPENDIX D
HEALTH EVALUATIONS OF EXPERIMENTAL ANIMALS

Battelle

Pacific Northwest Laboratories

Project Number _____

Internal Distribution

MG Brown
File/LB

Date January 10, 1986

To Pat Hackett

From S. E. Rowe *SEA*

Subject Health Evaluation, CD-1 Mice for
1,3 Butadiene Dominant Lethal Study

Mice for this study were received on 12/21/85 (ARC Shipment #850017). They were in remarkably good condition upon arrival considering they had been 5 days in transit due to prolonged closure of SEA-TAC Airport because of fog. They generally showed moderate dehydration but were active and alert when uncrated.

The health evaluation of this group was initiated on 1/6/86 and is documented in the attached lab report (ARC O-2). No significant pathogens or lesions were found. These animals were released from quarantine in the a.m. on 1/10/86.

MG Brown
File/LB

Date February 4, 1986

To Pat Hackett

From Steve Rowe *SR*

Subject Health Screen on CD-1 Female Mice for NTP/IRT
Dominant-Lethal Studies, Shipment Nos. 860018 and 860024

Confirming our conversation from February 2, we agreed to reject the CD-1 mice from shipment No. 860018 and substitute those from No. 860024. The release of the 860024 animals is with the provision that they remain on quarantine status.

One of the 10 mice examined in the initial health screen on 860018 had pneumonia and 2 other had focal pneumonitis (ARC report 0-9). In a follow-up, 3 mice culled from the group were examined. Two had traumatic injuries and one had a subcutaneous abscess. There was no evidence of infection in the first 2 but the mouse with the abscess had systemic lesions suggestive of septicemia. A coagulase positive Staphylococcus was isolated in pure culture from the abscess (ARC report 0-14).

There is no apparent relationship between the Staph. abscess and the lesions seen in the other mice. Serologic tests for antibodies to Sendai virus, PVM, GDVII, and MHV were negative in all 13 mice from this group. No significant bacterial pathogens were found in nasopharyngeal washes of the 13 mice. We collected additional serum and tissues from the 860018 group as they were killed on 2/4 and will continue to look for an etiologic agent.

The health evaluation of group 860024 was initiated earlier (6 days after arrival) than scheduled (14-21 days after arrival) because of a communication mix-up which resulted in their being delivered to the diagnostic lab rather than group 860018. One of these 10 mice was found to have significant focal inflammation in liver along with slight focal inflammation in lung (ARC report 0-S). An additional 3 randomly selected mice for this group were examined 10 days after arrival. No significant lesions were found in these (ARC report 0-15). No viral antibodies or significant bacterial pathogens were found in any of the 13 mice examined from this group but because of the liver and lung lesions seen in the one mouse, they will remain on quarantine status as will other mice with which they have contact.

Although there is some question as to the suitability of these mice for this study, failure to accept them would have resulted in the need to cancel this phase of the study which also involves several other animal shipments some of which have already been used. We will follow-up on this with serologic tests and histopathologic evaluation of these mice at terminal sacrifice.

MG Brown
File/lb

Date March 13, 1986
To Pat Hackett
From Steve Rowe *SR*
Subject Health Screen, Butadiene, Dominant-Lethal Studies, Shipment
Numbers 860027 and 860028

Five female mice randomly selected from each of two groups received for the study were examined beginning on 2/19/86. Both groups arrived together and, therefore, they were considered as one for health screening purposes. No significant pathogens were found in aerobic cultures of nasopharyngeal washes. In the serological tests, 1 of 10 was positive for Sendai virus antibodies and another of the 10 had a positive reaction for Mycoplasma and an equivocal reaction for reovirus 3. These positive sera have been sent to the University of Washington for testing (alternate method for Sendai and reovirus 3). There was no histopathological evidence of Sendai virus infection, and this is presumed to be a false positive reaction. The Mycoplasma reactivity is probably also a false positive (for M. pulmonis) and may be caused by reactivity to antibodies produced in response to some non-pathogenic Mycoplasma (other than M. pulmonis).

The reovirus 3 equivocal is of more concern since these mice have liver lesions similar but less severe than those produced in experimental reovirus 3 infections. The preceding shipment for this study, 860024, also had liver lesions like these. All affected groups have been from Charles River, Portage 8 area. Charles River was notified of our findings from the first group on 2/14.

Since we will be getting CD-1s for future studies from Raleigh, this should not be a continuing concern except that the B6C3F1 will be coming from Portage 2 (CD-1s were from P08). They don't have any at Raleigh. Charles River says they are not aware of any disease problems in P2, P8 or any Raleigh area. I'll send you another report when we get all the post-exposure data in on the butadiene dominant-lethal studies.

These animals were verbally released for study on 2/21 by call to Terry Mast. Although there are concerns about the liver lesions, these are similar to those seen in shipment 860024 which are being used in the same study. All these mice are being held in quarantine status and further investigation of the liver lesions are continuing. See 3/3/86

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APPENDIX E
REPRODUCTIVE MEASURES OF INDIVIDUAL FEMALE MICE
AND BODY WEIGHTS OF INDIVIDUAL MALE MICE

TABLE E1. Values for Reproductive Measures in Individual CD-1 Female Mice^a

^aColumn Headings:

OBS	= Sequential number of samples
MALENO	= Eartag number of male mouse
WEEK	= Postexposure week of mating
TMT	= Exposure concentration of 1,3-butadiene (ppm)

1	=	0
2	=	200
3	=	1000
4	=	5000

MATNO	= Eartag number of mated female
LIVE	= Live fetuses
EARLY	= Early resorptions
LATE	= Late resorptions
DEAD	= Dead fetuses
IMPLANT	= Number of implantation sites

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1	705	1	1	813	11	0	0	0	11
2	705	1	1	818	8	4	0	0	12
3	705	2	1	979	0	0	0	0	0
4	705	2	1	985	0	0	0	0	0
5	705	3	1	1707	14	0	0	0	14
6	705	3	1	1708	12	2	0	0	14
7	705	4	1	1868	9	0	0	0	9
8	705	4	1	1872	12	0	1	0	13
9	705	5	1	2207	13	0	0	0	13
10	705	5	1	2208	13	0	0	0	13
11	705	6	1	2388	0	1	0	0	9
12	705	6	1	2388	13	0	0	0	13
13	705	7	1	2541	9	0	2	0	11
14	705	7	1	2544	11	2	0	0	13
15	705	8	1	2823	10	1	0	0	11
16	705	8	1	2834	10	1	0	0	11
17	711	1	1	822	18	0	0	0	18
18	711	1	1	830	14	0	0	0	14
19	711	2	1	985	11	0	1	0	12
20	711	2	1	986	11	0	1	0	12
21	711	3	1	1715	9	1	1	0	11
22	711	3	1	1717	13	0	0	0	13
23	711	4	1	1875	11	0	0	0	11
24	711	4	1	1877	11	1	1	0	13
25	711	5	1	2215	12	1	0	0	13
26	711	5	1	2216	11	2	0	0	13
27	711	6	1	2361	12	0	1	0	13
28	711	6	1	2362	13	1	0	0	14
29	711	7	1	2549	11	1	0	0	12
30	711	7	1	2552	14	0	0	0	14
31	711	8	1	2827	15	0	0	0	15
32	711	8	1	2831	10	0	0	0	16
33	712	1	1	823	11	0	0	0	11
34	712	1	1	826	13	0	0	0	13
35	712	2	1	971	13	0	0	0	13
36	712	2	1	974	9	2	0	0	11
37	712	3	1	1718	11	0	0	0	11
38	712	3	1	1718	12	0	0	0	12
39	712	4	1	1876	12	0	0	0	12
40	712	4	1	1884	11	0	0	0	11
41	712	5	1	2217	11	0	0	0	11
42	712	5	1	2218	11	0	0	0	11
43	712	6	1	2360	11	0	0	0	11
44	712	6	1	2380	6	0	0	0	6
45	712	7	1	2547	10	0	1	0	11
46	712	7	1	2548	10	0	0	0	10
47	712	8	1	2828	12	0	0	0	12
48	712	8	1	2829	12	0	0	0	12
49	718	1	1	828	14	0	0	0	14
50	718	1	1	829	10	0	0	0	10
51	718	2	1	988	12	0	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
52	718	2	1	989	8	1	0	0	9
53	718	3	1	1723	12	1	0	0	13
54	718	3	1	1724	18	0	1	0	17
55	718	4	1	1886	4	2	0	0	6
56	718	4	1	1895	8	0	0	0	8
57	718	5	1	2223	1	0	0	0	1
58	718	5	1	2224	11	1	0	0	12
59	718	6	1	2377	12	0	1	0	13
60	718	6	1	2379	11	0	0	0	11
61	718	7	1	2553	9	0	1	0	10
62	718	7	1	2555	14	0	1	0	15
63	718	8	1	2818	14	1	0	0	15
64	718	8	1	2820	13	0	0	0	13
65	718	1	1	836	11	0	0	0	11
66	718	1	1	843	9	0	1	0	10
67	718	2	1	994	11	1	1	0	13
68	718	2	1	997	7	3	0	0	10
69	718	3	1	1727	11	2	0	0	13
70	718	3	1	1729	10	0	0	0	10
71	718	4	1	1893	7	5	0	0	12
72	718	4	1	1897	10	1	1	0	12
73	718	5	1	2227	10	1	0	0	11
74	718	5	1	2228	11	0	0	0	11
75	718	6	1	2378	14	0	0	0	14
76	718	6	1	2383	11	0	0	0	11
77	718	7	1	2561	13	0	0	0	13
78	718	7	1	2570	12	0	0	0	12
79	718	8	1	2811	12	0	0	0	12
80	718	8	1	2815	14	1	0	0	15
81	724	1	1	841	0	0	0	0	0
82	724	1	1	844	12	1	0	0	13
83	724	2	1	0	0	0	0	0	0
84	724	2	1	1006	12	0	0	0	12
85	724	3	1	1737	10	1	0	0	11
86	724	3	1	1738	12	0	0	0	12
87	724	4	1	1901	8	2	0	0	10
88	724	4	1	1902	8	2	0	0	10
89	724	5	1	2237	0	0	0	0	0
90	724	5	1	2238	17	0	0	0	17
91	724	6	1	2390	12	0	0	0	12
92	724	6	1	2398	13	0	0	0	13
93	724	7	1	2572	14	0	0	0	14
94	724	7	1	2591	12	0	0	0	12
95	724	8	1	2849	14	0	0	0	14
96	724	8	1	2859	8	0	0	0	8
97	729	1	1	847	12	0	0	0	12
98	729	1	1	857	10	1	0	0	11
99	729	2	1	1003	11	0	0	0	11
100	729	2	1	1010	12	1	0	0	13
101	729	3	1	1745	9	1	0	0	10
102	729	3	1	1746	9	0	0	0	9

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TWT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
103	729	4	1	1909	12	0	0	0	12
104	729	4	1	1917	14	0	0	0	14
105	729	5	1	2245	12	0	0	0	12
106	729	5	1	2246	12	0	0	0	12
107	729	6	1	2399	12	0	0	0	12
108	729	6	1	2400	11	1	0	0	12
109	729	7	1	2579	14	0	0	0	14
110	729	7	1	2582	13	1	0	0	14
111	729	8	1	2807	0	0	0	0	0
112	729	8	1	2856	8	2	0	0	10
113	739	1	1	868	12	1	0	0	13
114	739	1	1	871	10	0	0	0	10
115	739	2	1	1028	13	0	0	0	13
116	739	2	1	1035	10	0	2	0	12
117	739	3	1	1759	7	1	0	0	8
118	739	3	1	1760	8	0	0	0	8
119	739	4	1	1922	13	0	0	0	13
120	739	4	1	1933	5	2	0	0	7
121	739	5	1	0	0	0	0	0	0
122	741	1	1	869	9	0	1	0	10
123	741	1	1	863	12	0	0	0	12
124	741	2	1	1028	13	0	0	0	13
125	741	2	1	1030	9	1	0	0	10
126	741	3	1	1763	11	0	0	0	11
127	741	3	1	1764	14	1	0	0	15
128	741	4	1	0	0	0	0	0	0
129	741	4	1	1924	9	1	0	0	10
130	741	5	1	2263	13	1	1	0	15
131	741	5	1	2264	13	0	0	0	13
132	741	6	1	2422	11	0	0	0	11
133	741	6	1	2423	5	0	0	0	5
134	741	7	1	2597	14	0	0	0	14
135	741	7	1	2604	13	1	0	0	14
136	741	8	1	2789	11	0	1	0	12
137	741	8	1	2791	12	0	0	0	12
138	742	1	1	873	10	1	0	0	11
139	742	1	1	875	14	0	0	0	14
140	742	2	1	1033	11	0	0	0	11
141	742	2	1	1036	10	2	0	0	12
142	742	3	1	1785	12	0	0	0	12
143	742	3	1	1766	10	1	0	0	11
144	742	4	1	1929	12	0	0	0	12
145	742	4	1	1931	12	1	0	0	13
146	742	5	1	2265	15	0	0	0	15
147	742	5	1	2268	0	0	0	0	0
148	742	6	1	2428	0	0	0	0	0
149	742	6	1	2429	11	0	1	0	12
150	742	7	1	2600	10	0	0	0	10
151	742	7	1	2602	11	1	0	0	12
152	742	8	1	2786	10	2	0	0	12
153	742	8	1	2787	10	1	0	0	11

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
154	743	1	1	872	8	0	0	0	8
155	743	1	1	878	8	1	0	0	9
156	743	2	1	1031	8	0	0	0	8
157	743	2	1	1032	11	1	0	0	12
158	743	3	1	1767	13	0	0	0	13
159	743	3	1	1768	12	0	0	0	12
160	743	4	1	1923	11	0	1	0	12
161	743	4	1	1928	10	0	0	0	10
162	743	5	1	2267	14	0	0	0	14
163	743	5	1	2268	17	0	0	0	17
164	743	6	1	2424	11	0	0	0	11
165	743	6	1	2431	5	0	0	0	5
166	743	7	1	2605	12	1	0	0	13
167	743	7	1	2608	14	0	1	0	15
168	743	8	1	2788	8	1	3	0	12
169	743	8	1	2794	14	1	0	0	15
170	788	1	1	917	14	0	0	0	14
171	788	1	1	924	8	2	0	0	10
172	788	2	1	1083	11	0	0	0	11
173	788	2	1	1089	10	2	1	0	13
174	788	3	1	1804	11	0	1	0	12
175	788	3	1	1805	9	1	0	0	10
176	788	4	1	1962	13	0	0	0	13
177	788	4	1	1987	11	0	0	0	11
178	788	5	1	2303	10	0	0	0	10
179	788	5	1	2304	14	0	0	0	14
180	788	6	1	2467	7	2	0	0	9
181	788	6	1	2488	9	1	0	0	10
182	788	7	1	2631	15	0	0	0	15
183	788	7	1	2638	12	0	0	0	12
184	788	8	1	2751	10	0	1	0	11
185	788	8	1	2753	15	0	2	0	17
186	788	1	1	920	12	0	0	0	12
187	788	1	1	922	9	0	1	0	10
188	788	2	1	1077	8	3	0	0	11
189	788	2	1	1082	12	0	0	0	12
190	788	3	1	1816	11	1	0	0	12
191	788	3	1	1817	14	0	0	0	14
192	788	4	1	1970	10	1	0	0	11
193	788	4	1	1977	9	0	0	0	9
194	788	5	1	2315	12	2	0	0	14
195	788	5	1	2316	10	0	0	0	10
196	788	6	1	2471	11	2	0	0	13
197	788	6	1	2481	9	0	0	0	9
198	788	7	1	2649	10	0	0	0	10
199	788	7	1	2650	10	3	0	0	13
200	788	8	1	2740	8	2	0	0	10
201	788	8	1	2741	13	0	0	0	13
202	781	1	1	926	4	0	0	0	4
203	781	1	1	930	10	1	0	0	11
204	781	2	1	1084	13	0	0	0	13

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
206	781	2	1	1088	10	0	0	0	10
208	781	3	1	1819	9	0	0	0	9
207	781	3	1	1820	14	1	0	0	15
208	781	4	1	1974	11	0	0	0	11
209	781	4	1	1989	10	0	0	0	10
210	781	5	1	2317	13	1	0	0	14
211	781	5	1	2318	12	0	0	0	12
212	781	6	1	2473	9	0	0	0	9
213	781	6	1	2475	10	1	0	0	11
214	781	7	1	2653	14	0	0	0	14
215	781	7	1	2654	12	0	0	0	12
216	781	8	1	2738	11	1	0	0	12
217	781	8	1	2744	12	0	0	0	12
218	783	1	1	928	0	0	0	0	0
219	783	1	1	931	10	1	1	0	12
220	783	2	1	1081	0	0	0	0	0
221	783	2	1	1085	12	0	0	0	12
222	783	3	1	1821	9	2	0	0	11
223	783	3	1	1822	13	0	0	0	13
224	783	4	1	1983	12	0	0	0	12
225	783	4	1	1985	8	3	0	0	11
226	783	5	1	2319	12	0	0	0	12
227	783	5	1	2320	11	0	0	0	11
228	783	6	1	2472	9	0	0	0	9
229	783	6	1	2479	13	0	0	0	13
230	783	7	1	2646	15	0	0	0	15
231	783	7	1	2651	13	0	0	0	13
232	783	8	1	2739	10	1	0	0	11
233	783	8	1	2746	11	0	0	0	11
234	788	1	1	925	10	1	0	0	11
235	788	1	1	929	10	1	0	0	11
236	788	2	1	1089	12	1	0	0	13
237	788	2	1	1090	15	0	0	0	15
238	788	3	1	1829	0	0	0	0	0
239	788	3	1	1830	13	0	0	0	13
240	788	4	1	1984	10	1	1	0	12
241	788	4	1	1992	10	0	0	0	10
242	788	5	1	2327	8	2	0	0	10
243	788	5	1	2328	10	2	1	0	13
244	788	6	1	2483	11	0	0	0	11
245	788	6	1	2492	13	0	0	0	13
246	788	7	1	2663	9	0	0	0	9
247	788	7	1	2664	14	0	1	0	15
248	788	8	1	2725	0	0	0	0	0
249	788	8	1	2735	10	0	0	0	10
250	789	1	1	937	10	1	0	0	11
251	789	1	1	946	12	1	1	0	14
252	789	2	1	1096	13	0	0	0	13
253	789	2	1	1097	9	1	0	0	10
254	789	3	1	1831	12	0	0	0	12
255	789	3	1	1832	11	0	0	0	11

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
258	789	4	1	1987	8	2	0	0	10
257	789	4	1	2000	9	2	0	0	11
259	789	5	1	2329	11	0	0	0	11
259	789	5	1	2330	15	0	0	0	15
260	789	6	1	2482	11	1	0	0	12
261	789	6	1	2487	12	0	0	0	12
262	789	7	1	2657	12	1	0	0	13
263	789	7	1	2685	13	1	0	0	14
264	789	8	1	2727	15	2	1	0	18
265	789	8	1	2733	0	0	0	0	0
266	797	1	1	944	13	1	0	0	14
267	797	1	1	948	9	3	0	0	12
268	797	2	1	1106	17	0	0	0	17
269	797	2	1	1107	13	1	1	0	15
270	797	3	1	1841	3	2	1	0	6
271	797	3	1	1842	11	0	1	0	12
272	797	4	1	1999	11	1	0	0	12
273	797	4	1	2105	9	0	0	0	9
274	797	5	1	2339	15	0	0	0	15
275	797	5	1	2340	10	0	0	0	10
276	797	6	1	2496	11	0	0	0	11
277	797	6	1	2501	11	0	1	0	12
278	797	7	1	2688	0	0	0	0	0
279	797	7	1	2671	10	2	0	0	12
280	797	8	1	2704	12	0	0	0	12
281	797	8	1	2707	18	0	0	0	18
282	798	1	1	947	9	1	0	0	10
283	798	1	1	958	12	1	0	0	13
284	798	2	1	1110	11	1	0	0	12
285	798	2	1	1111	0	0	0	0	0
286	798	3	1	0	0	0	0	0	0
287	798	3	1	1844	11	0	0	0	11
288	798	4	1	2103	9	1	0	0	10
289	798	4	1	2106	8	0	0	0	8
290	798	5	1	2341	10	0	1	0	11
291	798	5	1	2342	11	0	0	0	11
292	798	6	1	2497	12	0	0	0	12
293	798	6	1	2504	10	1	0	0	11
294	798	7	1	2674	11	0	1	0	12
295	798	7	1	2677	0	0	0	0	0
296	798	8	1	2708	13	0	0	0	13
297	798	8	1	2713	15	1	0	0	16
298	805	1	1	952	10	1	0	0	11
299	805	1	1	954	0	0	0	0	0
300	805	2	1	1113	7	0	0	0	7
301	805	2	1	1131	13	0	0	0	13
302	805	3	1	1857	11	0	0	0	11
303	805	3	1	1858	0	0	0	0	0
304	805	4	1	2118	11	0	0	0	11
305	805	4	1	2124	10	0	0	0	10
306	805	5	1	2353	11	2	0	0	13

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
307	805	5	1	2354	10	0	0	0	10
308	805	6	1	2512	11	0	0	0	11
309	805	6	1	2516	14	0	0	0	14
310	805	7	1	2684	10	1	0	0	11
311	805	7	1	2690	11	0	0	0	11
312	805	8	1	2694	13	0	0	0	13
313	805	8	1	2698	13	0	0	0	13
314	701	1	2	809	9	1	0	0	10
315	701	1	2	818	10	1	0	0	11
316	701	2	2	978	9	1	0	0	10
317	701	2	2	978	14	2	0	0	16
318	701	3	2	1701	9	5	0	0	13
319	701	3	2	1702	10	2	0	0	12
320	701	4	2	1863	11	0	0	0	11
321	701	4	2	1868	12	0	1	0	13
322	701	5	2	2201	14	0	0	0	14
323	701	5	2	2202	0	0	0	0	0
324	701	6	2	2372	9	3	1	0	12
325	701	6	2	2373	8	2	0	0	10
326	701	7	2	2536	0	0	0	0	0
327	701	7	2	2537	13	4	0	0	17
328	701	8	2	2844	12	1	1	0	14
329	701	8	2	2845	9	1	0	0	10
330	703	1	2	812	10	1	1	0	12
331	703	1	2	819	8	2	0	0	10
332	703	2	2	977	13	1	1	0	15
333	703	2	2	988	9	0	1	0	10
334	703	3	2	1705	16	0	0	0	16
335	703	3	2	1706	14	0	0	0	14
336	703	4	2	1864	10	0	0	0	10
337	703	4	2	1867	9	2	0	0	10
338	703	5	2	2205	11	1	0	0	12
339	703	5	2	2206	1	0	0	0	1
340	703	6	2	2374	15	0	0	0	15
341	703	6	2	2375	8	2	1	0	11
342	703	7	2	2539	13	0	0	0	13
343	703	7	2	2543	13	1	0	0	14
344	703	8	2	2835	11	0	1	0	12
345	703	8	2	2837	13	0	1	0	14
346	708	1	2	811	13	2	0	0	15
347	708	1	2	815	10	1	0	0	11
348	708	2	2	987	11	0	0	0	11
349	708	2	2	972	8	2	0	0	10
350	708	3	2	1711	14	0	0	0	14
351	708	3	2	1712	3	2	0	0	5
352	708	4	2	1880	10	0	0	0	10
353	708	4	2	1882	10	1	0	0	11
354	708	5	2	2211	13	1	0	0	14
355	708	5	2	2212	14	1	0	0	15
356	708	6	2	2364	11	1	0	0	12
357	708	6	2	2365	10	0	0	0	10

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
358	708	7	2	2538	13	0	0	0	13
359	708	7	2	2542	9	0	0	0	9
360	708	8	2	2824	11	1	0	0	12
361	708	8	2	2830	13	2	0	0	15
362	710	1	2	831	10	1	0	0	11
363	710	1	2	833	9	2	0	0	11
364	710	2	2	964	10	0	0	0	10
365	710	2	2	973	13	0	0	0	13
368	710	3	2	1713	11	1	0	0	12
367	710	3	2	1714	0	0	0	0	0
368	710	4	2	1878	9	0	0	0	9
369	710	4	2	1881	15	0	0	0	15
370	710	5	2	2213	11	0	1	0	12
371	710	5	2	2214	10	0	0	0	10
372	710	6	2	2359	13	0	0	0	13
373	710	6	2	2363	10	0	0	0	10
374	710	7	2	2557	16	0	0	0	16
375	710	7	2	2558	13	0	0	0	13
376	710	8	2	2828	16	0	0	0	16
377	710	8	2	2833	12	0	0	0	12
378	713	1	2	821	15	0	0	0	15
379	713	1	2	825	11	1	0	0	12
380	713	2	2	968	11	0	0	0	11
381	713	2	2	975	14	1	0	0	15
382	713	3	2	1719	10	1	1	0	12
383	713	3	2	1720	12	2	0	0	14
384	713	4	2	1885	10	0	1	0	11
385	713	4	2	1886	10	0	0	0	10
386	713	5	2	2219	10	1	0	0	11
387	713	5	2	2220	14	0	0	0	14
388	713	6	2	2378	13	0	0	0	13
389	713	6	2	2382	8	1	0	0	9
390	713	7	2	2554	12	0	0	0	12
391	713	7	2	2556	14	0	0	0	14
392	713	8	2	2814	13	0	1	0	14
393	713	8	2	2821	12	1	0	0	13
394	714	1	2	824	8	1	2	0	11
395	714	1	2	827	9	4	0	0	13
396	714	2	2	969	11	1	1	0	13
397	714	2	2	990	10	0	0	0	10
398	714	3	2	1721	14	0	1	0	15
399	714	3	2	1722	9	0	0	0	9
400	714	4	2	1874	7	1	0	0	8
401	714	4	2	1883	10	1	0	0	11
402	714	5	2	2221	10	1	0	0	11
403	714	5	2	2222	13	0	1	0	14
404	714	6	2	2381	10	0	0	0	10
405	714	6	2	2385	12	1	0	0	13
406	714	7	2	2550	13	0	0	0	13
407	714	7	2	2551	9	0	0	0	9
408	714	8	2	2816	12	0	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
409	714	8	2	2819	18	0	0	0	18
410	730	1	2	850	10	3	0	0	13
411	730	1	2	855	10	0	0	0	10
412	730	2	2	1018	6	2	1	0	9
413	730	2	2	1019	11	0	0	0	11
414	730	3	2	1747	9	1	0	0	10
415	730	3	2	1748	13	1	0	0	14
416	730	4	2	1913	11	1	0	0	12
417	730	4	2	1918	12	0	1	0	13
418	730	5	2	2247	10	1	0	0	11
419	730	5	2	2248	10	3	0	0	13
420	730	6	2	2405	11	0	0	0	11
421	730	6	2	2408	11	0	0	0	11
422	730	7	2	2577	12	0	0	0	12
423	730	7	2	2580	14	0	0	0	14
424	730	8	2	2802	11	0	0	0	11
425	730	8	2	2803	12	1	0	0	13
426	735	1	2	863	11	0	0	0	11
427	735	1	2	865	13	2	0	0	15
428	735	2	2	1018	9	2	0	0	11
429	735	2	2	1021	10	1	0	0	11
430	735	3	2	1753	10	1	1	0	12
431	735	3	2	1754	13	0	0	0	13
432	735	4	2	1911	8	1	0	0	9
433	735	4	2	1914	12	0	0	0	12
434	735	5	2	2253	11	0	0	0	11
435	735	5	2	2254	11	1	1	0	13
436	735	6	2	2414	10	1	0	0	11
437	735	6	2	2415	13	0	0	0	13
438	735	7	2	2592	10	0	0	0	10
439	735	7	2	2594	14	0	0	0	14
440	735	8	2	2805	11	1	0	0	12
441	735	8	2	2808	11	1	0	0	12
442	748	1	2	892	12	1	0	0	13
443	748	1	2	885	8	0	1	0	9
444	748	2	2	1040	14	2	0	0	16
445	748	2	2	1048	10	1	0	0	11
446	748	3	2	1774	11	0	0	0	11
447	748	3	2	1775	0	0	0	0	0
448	748	4	2	1942	9	0	0	0	9
449	748	4	2	1944	11	1	0	0	12
450	748	5	2	2273	14	2	0	0	16
451	748	5	2	2274	7	1	0	0	8
452	748	6	2	2426	7	2	0	0	9
453	748	6	2	2437	0	0	0	0	0
454	748	7	2	2611	15	0	0	0	15
455	748	7	2	2617	10	1	0	0	11
456	748	8	2	2779	11	1	1	0	13
457	748	8	2	2782	11	0	0	0	11
458	748	1	2	874	12	0	0	0	12
459	748	1	2	884	6	2	0	0	8

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
460	748	2	2	1038	12	0	0	0	12
461	748	2	2	1041	11	4	0	0	15
462	748	3	2	1778	9	1	1	0	11
463	748	3	2	1777	12	0	0	0	12
464	748	4	2	1937	11	0	0	0	11
465	748	4	2	1939	15	0	0	0	15
466	748	6	2	2275	12	0	0	0	12
467	748	6	2	2276	15	0	0	0	15
468	748	6	2	2433	12	0	0	0	12
469	748	6	2	2435	12	0	0	0	12
470	748	7	2	2610	12	0	1	0	13
471	748	7	2	2614	14	0	1	0	15
472	748	8	2	2778	12	0	0	0	12
473	748	8	2	2778	12	0	0	0	12
474	756	1	2	889	11	3	0	0	14
475	756	1	2	893	11	0	1	0	12
476	756	2	2	1058	0	0	0	0	0
477	756	2	2	1059	13	1	1	0	15
478	756	3	2	1784	9	1	1	0	11
479	756	3	2	1785	10	1	0	0	11
480	756	4	2	1948	11	1	0	0	12
481	756	4	2	1954	9	0	0	0	9
482	756	5	2	2283	12	1	0	0	13
483	756	5	2	2284	13	0	0	0	13
484	756	6	2	2438	12	0	0	0	12
485	756	6	2	2443	10	0	0	0	10
486	756	7	2	2613	10	1	0	0	11
487	756	7	2	2618	13	1	0	0	14
488	756	8	2	2775	12	0	0	0	12
489	756	8	2	2780	12	1	0	0	13
490	760	1	2	886	10	0	0	0	10
491	760	1	2	890	11	1	1	0	13
492	760	2	2	1051	8	2	0	0	10
493	760	2	2	1054	14	2	0	0	16
494	760	3	2	1790	10	0	0	0	10
495	760	3	2	1791	10	1	0	0	11
496	760	4	2	1948	10	1	0	0	11
497	760	4	2	1949	11	0	0	0	11
498	760	5	2	2289	15	0	0	0	15
499	760	5	2	2290	10	0	0	0	10
500	760	6	2	2451	9	0	0	0	9
501	760	6	2	2454	11	1	1	0	13
502	760	7	2	2621	10	0	0	0	10
503	760	7	2	2624	13	0	0	0	13
504	760	8	2	2761	12	0	0	0	12
505	760	8	2	2766	11	1	0	0	12
506	765	1	2	899	10	0	0	0	10
507	765	1	2	904	11	0	0	0	11
508	765	2	2	1068	12	0	0	0	12
509	765	2	2	1073	7	1	0	0	8
510	765	3	2	1798	0	0	0	0	0

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
511	765	3	2	1799	11	1	0	0	12
512	765	4	2	1965	11	0	0	0	11
513	765	4	2	1986	11	0	0	0	11
514	765	5	2	2297	13	0	0	0	13
515	765	5	2	2298	18	0	0	0	16
516	765	6	2	2455	11	0	0	0	11
517	765	6	2	2462	9	0	0	0	9
518	765	7	2	2635	9	0	0	0	9
519	765	7	2	2642	13	1	0	0	14
520	765	8	2	2758	9	1	0	0	10
521	765	8	2	2780	11	1	0	0	12
522	766	1	2	909	11	0	0	0	11
523	766	1	2	911	13	0	0	0	13
524	766	2	2	1066	8	1	0	0	9
525	766	2	2	1074	10	1	0	0	11
526	766	3	2	1800	12	0	0	0	12
527	766	3	2	1801	12	1	0	0	13
528	766	4	2	1959	10	1	1	0	12
529	766	4	2	1961	10	2	0	0	12
530	766	5	2	2299	11	1	0	0	12
531	766	5	2	2300	9	1	0	0	10
532	766	6	2	2456	11	0	0	0	11
533	766	6	2	2463	13	0	0	0	13
534	766	7	2	2636	14	1	0	0	15
535	766	7	2	2639	8	3	0	0	11
536	766	8	2	2747	14	1	0	0	15
537	766	8	2	2756	10	0	0	0	10
538	776	1	2	901	8	1	0	0	9
539	776	1	2	921	11	1	0	0	12
540	776	2	2	1075	12	1	0	0	13
541	776	2	2	1083	14	2	0	0	16
542	776	3	2	1814	8	0	2	0	10
543	776	3	2	1815	15	0	0	0	16
544	776	4	2	1978	11	0	0	0	11
545	776	4	2	1979	12	0	0	0	12
546	776	5	2	2313	13	0	0	0	13
547	776	5	2	2314	0	0	0	0	0
548	776	6	2	2469	11	0	0	0	11
549	776	6	2	2470	10	1	0	0	11
550	776	7	2	2648	9	2	0	0	11
551	776	7	2	2652	9	1	0	0	10
552	776	8	2	2738	16	0	0	0	16
553	776	8	2	2737	13	0	0	0	13
554	786	1	2	927	4	0	0	0	4
555	786	1	2	934	11	1	0	0	12
556	786	2	2	1088	14	0	0	0	14
557	786	2	2	1095	10	1	0	0	11
558	786	3	2	1825	5	2	0	0	7
559	786	3	2	1828	13	0	0	0	13
560	786	4	2	1982	14	0	0	0	14
561	786	4	2	1988	11	0	0	0	11

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
562	786	5	2	2323	14	1	0	0	15
563	786	5	2	2324	9	0	0	0	9
564	786	6	2	2485	11	0	0	0	11
565	786	6	2	2491	9	2	0	0	11
566	786	7	2	2661	12	2	0	0	14
567	786	7	2	2668	10	1	0	0	11
568	786	8	2	2731	13	0	0	0	13
569	786	8	2	2734	14	0	1	0	15
570	792	1	2	939	12	0	0	0	12
571	792	1	2	945	9	2	0	0	11
572	792	2	2	1098	12	0	0	0	12
573	792	2	2	1099	8	2	0	0	10
574	792	3	2	1835	8	1	0	0	9
575	792	3	2	1836	12	0	0	0	12
576	792	4	2	1995	10	1	0	0	11
577	792	4	2	2104	10	1	0	0	11
578	792	5	2	2333	13	0	0	0	13
579	792	5	2	2334	12	1	0	0	13
580	792	6	2	2486	10	0	0	0	10
581	792	6	2	2490	13	0	0	0	13
582	792	7	2	2667	12	1	0	0	13
583	792	7	2	2676	12	1	0	0	13
584	792	8	2	2588	12	0	0	0	12
585	792	8	2	2593	11	1	0	0	12
586	799	1	2	958	12	0	2	0	14
587	799	1	2	962	11	0	0	0	11
588	799	2	2	1104	7	2	0	0	9
589	799	2	2	1112	9	2	0	0	11
590	799	3	2	0	0	0	0	0	0
591	799	3	2	1846	7	1	0	0	8
592	799	4	2	2115	10	1	1	0	12
593	799	4	2	2117	11	0	0	0	11
594	799	5	2	2343	11	1	1	0	13
595	799	5	2	2344	11	1	1	0	13
596	799	6	2	2494	8	1	0	0	9
597	799	6	2	2505	12	2	0	0	14
598	799	7	2	2673	14	0	0	0	14
599	799	7	2	2678	13	0	0	0	13
600	799	8	2	2709	12	0	0	0	12
601	799	8	2	2710	10	1	1	0	12
602	806	1	2	983	10	2	0	0	12
603	806	1	2	984	12	0	0	0	12
604	806	2	2	1110	8	7	0	0	13
605	806	2	2	1123	10	2	0	0	12
606	806	3	2	1859	0	0	0	0	0
607	806	3	2	1860	11	2	0	0	13
608	806	4	2	2125	12	0	0	0	12
609	806	4	2	2129	9	1	0	0	10
610	806	5	2	2355	11	0	0	0	11
611	806	5	2	2356	11	1	0	0	12
612	806	6	2	2510	10	2	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
813	806	6	2	2511	10	2	0	0	12
814	806	7	2	2679	15	0	0	0	15
815	806	7	2	2682	4	0	0	0	4
816	806	8	2	2692	13	1	1	0	15
817	806	8	2	2698	15	0	0	0	15
818	807	1	2	981	11	1	0	0	12
819	807	1	2	982	7	3	0	0	10
820	807	2	2	1120	10	0	0	0	10
821	807	2	2	1127	10	1	0	0	11
822	807	3	2	1861	10	0	0	0	10
823	807	3	2	1862	14	0	0	0	14
824	807	4	2	2128	0	0	0	0	0
825	807	4	2	2127	11	0	0	0	11
826	807	5	2	2357	9	0	0	0	9
827	807	5	2	2358	12	0	0	0	12
828	807	6	2	2517	8	2	0	0	10
829	807	6	2	2518	12	0	0	0	12
830	807	7	2	2691	11	0	1	0	12
831	807	7	2	2695	11	4	0	0	15
832	807	8	2	2697	14	0	0	0	14
833	807	8	2	2701	0	0	0	0	0
834	702	1	3	814	10	2	0	0	12
835	702	1	3	820	7	1	0	0	8
836	702	2	3	980	11	1	0	0	12
837	702	2	3	987	14	0	0	0	14
838	702	3	3	1703	10	1	0	0	11
839	702	3	3	1704	12	0	0	0	12
840	702	4	3	1871	8	0	0	0	8
841	702	4	3	1873	10	0	0	0	10
842	702	5	3	2203	12	0	0	0	12
843	702	5	3	2204	13	0	0	0	13
844	702	6	3	2389	10	1	0	0	11
845	702	6	3	2371	14	0	0	0	14
846	702	7	3	2535	10	1	0	0	11
847	702	7	3	2545	5	0	0	0	5
848	702	8	3	2840	12	1	0	0	13
849	702	8	3	2842	14	0	0	0	14
850	707	1	3	810	12	1	0	0	13
851	707	1	3	817	8	1	0	0	9
852	707	2	3	963	12	1	0	0	13
853	707	2	3	970	11	0	0	0	11
854	707	3	3	1709	11	1	0	0	12
855	707	3	3	1710	0	0	0	0	0
856	707	4	3	1865	10	0	0	0	10
857	707	4	3	1870	13	0	0	0	13
858	707	5	3	2209	18	0	0	0	18
859	707	5	3	2210	12	0	0	0	12
860	707	6	3	2367	9	2	0	0	11
861	707	6	3	2370	11	0	0	0	11
862	707	7	3	2540	12	1	0	0	13
863	707	7	3	2546	12	0	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
664	707	0	3	2825	13	0	0	0	13
665	707	0	3	2832	7	4	0	0	11
666	721	1	3	839	8	5	1	0	14
667	721	1	3	840	11	0	0	0	11
668	721	2	3	992	9	1	1	0	11
669	721	2	3	998	10	0	0	0	10
670	721	3	3	1733	0	0	0	0	0
671	721	3	3	1734	9	0	0	0	9
672	721	4	3	1890	3	0	0	0	3
673	721	4	3	1900	11	1	0	0	12
674	721	5	3	2233	11	0	0	0	11
675	721	5	3	2234	10	0	0	0	10
676	721	6	3	2393	13	0	0	0	13
677	721	6	3	2394	10	2	0	0	12
678	721	7	3	2565	13	3	0	0	16
679	721	7	3	2568	13	0	0	0	13
680	721	8	3	2817	12	1	1	0	14
681	721	8	3	2848	12	0	0	0	12
682	723	1	3	834	8	2	0	0	10
683	723	1	3	845	8	0	0	0	8
684	723	2	3	1001	8	2	1	0	11
685	723	2	3	1004	12	0	0	0	12
686	723	3	3	1735	12	0	0	0	12
687	723	3	3	1736	10	1	0	0	11
688	723	4	3	1898	9	1	0	0	10
689	723	4	3	1899	10	0	0	0	10
690	723	5	3	2235	9	1	0	0	10
691	723	5	3	2236	7	1	0	0	8
692	723	6	3	2392	12	0	0	0	12
693	723	6	3	2395	12	0	0	0	12
694	723	7	3	2560	14	0	1	0	15
695	723	7	3	2567	12	1	2	0	15
696	723	8	3	2855	10	1	3	0	14
697	723	8	3	2857	10	1	0	0	11
698	731	1	3	853	10	1	0	0	11
699	731	1	3	859	11	1	0	0	12
700	731	2	3	1015	10	2	0	0	12
701	731	2	3	1024	7	2	0	0	9
702	731	3	3	1749	11	0	0	0	11
703	731	3	3	1750	11	0	0	0	11
704	731	4	3	1915	13	0	0	0	13
705	731	4	3	1919	11	0	0	0	11
706	731	5	3	2249	0	0	0	0	0
707	731	5	3	2250	7	3	0	0	10
708	731	6	3	2402	10	0	0	0	10
709	731	6	3	2409	11	0	0	0	11
710	731	7	3	2587	9	2	0	0	11
711	731	7	3	2590	12	1	0	0	13
712	731	8	3	2798	8	1	0	0	7
713	731	8	3	2804	12	0	0	0	12
714	736	1	3	866	14	0	0	0	14

8:55 MONDAY, MAY 2, 1988 15

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
715	736	1	3	887	11	1	0	0	12
716	736	2	3	1013	11	0	0	0	11
717	736	2	3	1017	11	2	0	0	13
718	736	3	3	1755	8	1	0	0	9
719	736	3	3	1758	10	0	0	0	10
720	736	4	3	1920	8	0	0	0	8
721	736	4	3	1921	8	0	2	0	10
722	736	5	3	2255	11	1	0	0	12
723	736	5	3	2256	11	1	0	0	12
724	736	6	3	2413	11	3	0	0	14
725	736	6	3	2417	12	0	0	0	12
726	736	7	3	2588	0	0	0	0	0
727	736	7	3	2589	10	1	0	0	11
728	736	8	3	2797	10	2	0	0	12
729	736	8	3	2801	7	2	2	0	11
730	744	1	3	878	8	3	0	0	11
731	744	1	3	879	11	3	0	0	14
732	744	2	3	1027	12	3	0	0	15
733	744	2	3	1034	10	2	0	0	12
734	744	3	3	1769	11	1	0	0	12
735	744	3	3	1770	11	1	0	0	12
736	744	4	3	1928	9	1	0	0	10
737	744	4	3	1941	7	1	0	0	8
738	744	5	3	2269	11	1	0	0	12
739	744	5	3	2270	12	1	0	0	13
740	744	6	3	2421	7	0	0	0	7
741	744	6	3	2427	12	1	0	0	13
742	744	7	3	2595	10	0	0	0	10
743	744	7	3	2803	11	0	1	0	12
744	744	8	3	2785	11	1	0	0	12
745	744	8	3	2792	10	2	0	0	12
746	745	1	3	877	10	2	0	0	12
747	745	1	3	880	11	0	1	0	12
748	745	2	3	1037	8	4	1	0	13
749	745	2	3	1044	12	1	0	0	13
750	745	3	3	1771	10	0	0	0	10
751	745	3	3	1772	10	1	0	0	11
752	745	4	3	1934	10	0	0	0	10
753	745	4	3	1936	9	3	1	0	13
754	745	5	3	2271	12	0	0	0	12
755	745	5	3	2272	12	0	0	0	12
756	745	6	3	2425	7	1	0	0	8
757	745	6	3	2430	13	0	0	0	13
758	745	7	3	2596	10	0	0	0	10
759	745	7	3	2598	14	0	0	0	14
760	745	8	3	2790	15	0	0	0	15
761	745	8	3	2795	9	0	0	0	9
762	750	1	3	892	12	2	0	0	14
763	750	1	3	895	13	1	1	0	15
764	750	2	3	1045	0	0	0	0	0
765	750	2	3	1047	12	1	0	0	13

8:55 MONDAY, MAY 2, 1988 16

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
768	750	3	3	1780	10	0	0	1	11
767	750	3	3	1781	12	2	0	0	14
768	750	4	3	1938	9	0	0	0	9
769	750	4	3	1957	13	1	0	0	14
770	750	5	3	2279	13	0	0	0	13
771	750	5	3	2280	10	0	1	0	11
772	750	6	3	2434	9	0	1	0	10
773	750	6	3	2440	9	0	0	0	9
774	750	7	3	2609	0	0	0	0	0
775	750	7	3	2618	12	1	0	0	13
776	750	8	3	2772	13	2	0	0	15
777	750	8	3	2781	14	0	0	0	14
778	753	1	3	891	11	0	1	0	12
779	753	1	3	897	8	0	1	0	9
780	753	2	3	1043	12	1	0	0	13
781	753	2	3	1046	16	1	0	0	17
782	753	3	3	1782	13	0	0	0	13
783	753	3	3	1783	11	0	0	0	11
784	753	4	3	1935	0	0	0	0	0
785	753	4	3	1943	12	0	0	0	12
786	753	5	3	2261	15	0	0	0	15
787	753	5	3	2282	12	0	0	0	12
788	753	6	3	2441	15	0	0	0	15
789	753	6	3	2442	11	0	0	0	11
790	753	7	3	2612	10	1	0	0	11
791	753	7	3	2615	7	1	1	0	9
792	753	8	3	2783	11	0	1	0	12
793	753	8	3	2784	13	1	0	0	14
794	757	1	3	888	8	0	0	0	8
795	757	1	3	898	9	3	0	0	12
796	757	2	3	1050	10	4	0	0	14
797	757	2	3	1057	0	0	0	0	0
798	757	3	3	1786	11	0	1	0	12
799	757	3	3	1787	12	0	0	0	12
800	757	4	3	1952	8	1	0	0	9
801	757	4	3	1958	7	3	0	0	10
802	757	5	3	2285	13	1	0	0	14
803	757	5	3	2286	11	0	1	0	12
804	757	6	3	2438	10	1	0	0	11
805	757	6	3	2445	11	0	0	0	11
806	757	7	3	2625	15	0	0	0	15
807	757	7	3	2628	0	0	0	0	0
808	757	8	3	2768	10	0	1	0	11
809	757	8	3	2777	13	0	0	0	13
810	758	1	3	894	10	1	0	0	11
811	758	1	3	898	11	0	0	0	11
812	758	2	3	1055	14	2	0	0	16
813	758	2	3	1058	13	0	0	0	13
814	758	3	3	1789	16	0	0	0	16
815	758	3	3	1869	10	0	0	0	10
816	758	4	3	1953	9	1	0	0	10

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
817	758	4	3	1955	12	0	0	0	12
818	758	5	3	2287	13	0	0	0	13
819	758	5	3	2288	12	0	0	0	12
820	758	6	3	2444	12	1	0	0	13
821	758	6	3	2446	13	0	0	0	13
822	758	7	3	2622	11	0	1	0	12
823	758	7	3	2629	0	0	0	0	0
824	758	8	3	2767	11	0	0	0	11
825	758	8	3	2771	11	0	0	0	11
826	761	1	3	900	10	2	0	0	12
827	761	1	3	903	12	0	0	0	12
828	761	2	3	1049	15	0	0	0	15
829	761	2	3	1052	14	1	0	0	15
830	761	3	3	1792	10	0	0	0	10
831	761	3	3	1793	12	0	0	0	12
832	761	4	3	1950	13	0	0	0	13
833	761	4	3	1951	9	2	0	0	11
834	761	5	3	2291	11	2	0	0	13
835	761	5	3	2292	11	0	0	0	11
836	761	6	3	2450	10	0	0	0	10
837	761	6	3	2453	12	0	1	0	13
838	761	7	3	2623	0	0	0	0	0
839	761	7	3	2627	11	0	0	0	11
840	761	8	3	2763	7	0	0	0	7
841	761	8	3	2784	11	1	1	0	13
842	770	1	3	912	10	2	0	0	12
843	770	1	3	923	12	1	0	0	13
844	770	2	3	1064	13	0	1	0	14
845	770	2	3	1072	9	0	0	0	9
846	770	3	3	1808	8	0	2	0	10
847	770	3	3	1809	9	0	2	0	11
848	770	4	3	1969	0	0	0	0	0
849	770	4	3	1973	13	0	0	0	13
850	770	5	3	2307	11	0	0	0	11
851	770	5	3	2308	13	0	0	0	13
852	770	6	3	2461	12	1	0	0	13
853	770	6	3	2464	10	1	0	0	11
854	770	7	3	2632	10	0	0	0	10
855	770	7	3	2637	14	0	0	0	14
856	770	8	3	2750	13	0	0	0	13
857	770	8	3	2755	11	3	0	0	14
858	795	1	3	938	9	2	0	0	11
859	795	1	3	943	5	4	0	0	9
860	795	2	3	1101	14	0	0	0	14
861	795	2	3	1103	12	1	0	0	13
862	795	3	3	1838	9	2	0	0	11
863	795	3	3	1879	14	0	0	0	14
864	795	4	3	1994	10	0	0	0	10
865	795	4	3	2102	14	2	0	0	16
866	795	5	3	2335	11	0	0	0	11
867	795	5	3	2336	13	1	0	0	14

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
868	795	6	3	2499	13	0	0	0	13
869	795	6	3	2500	10	0	1	0	11
870	795	7	3	2670	15	0	0	0	15
871	795	7	3	2672	12	0	0	0	12
872	795	8	3	2718	11	0	1	0	12
873	795	8	3	2723	9	1	1	0	11
874	796	1	3	842	12	1	0	0	13
875	796	1	3	849	12	0	0	0	12
876	796	2	3	1105	12	0	0	0	12
877	796	2	3	1109	15	0	0	0	15
878	796	3	3	1839	3	0	0	0	3
879	796	3	3	1840	9	1	0	0	10
880	796	4	3	1996	11	0	0	0	11
881	796	4	3	1997	15	0	0	0	15
882	796	5	3	2237	12	2	0	0	14
883	796	5	3	2338	12	1	0	0	13
884	796	6	3	2495	12	1	1	0	14
885	796	6	3	2503	12	0	0	0	12
886	796	7	3	2669	11	0	0	0	11
887	796	7	3	2675	15	0	0	0	15
888	796	8	3	2718	13	0	1	0	14
889	796	8	3	2724	10	1	0	0	11
890	800	1	3	955	11	0	0	0	11
891	800	1	3	959	11	3	0	0	14
892	800	2	3	1102	11	2	0	0	13
893	800	2	3	1108	11	1	1	0	13
894	800	3	3	1848	13	0	0	0	13
895	800	3	3	1849	7	3	0	0	10
896	800	4	3	2111	10	1	0	0	11
897	800	4	3	2114	12	0	0	0	12
898	800	5	3	2345	12	0	0	0	12
899	800	5	3	2346	9	2	0	0	11
900	800	6	3	2498	12	1	0	0	13
901	800	6	3	2502	12	0	0	0	12
902	800	7	3	2687	9	0	0	0	9
903	800	7	3	2689	13	0	1	0	14
904	800	8	3	2703	0	0	0	0	0
905	800	8	3	2705	13	0	1	0	14
906	803	1	3	951	8	2	0	0	10
907	803	1	3	961	12	0	0	0	12
908	803	2	3	1116	12	1	2	0	15
909	803	2	3	1125	11	2	0	0	13
910	803	3	3	1853	13	0	0	0	13
911	803	3	3	1854	9	0	0	0	9
912	803	4	3	2107	10	2	0	0	12
913	803	4	3	2108	10	0	0	0	10
914	803	5	3	2349	11	0	0	0	11
915	803	5	3	2350	11	0	0	0	11
916	803	6	3	2508	12	0	0	0	12
917	803	6	3	2509	10	0	0	0	10
918	803	7	3	2680	11	0	0	0	11

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
919	803	7	3	2688	12	0	0	0	12
920	803	8	3	2699	8	1	0	0	9
921	803	8	3	2712	11	1	0	0	12
922	804	1	3	950	7	1	1	0	9
923	804	1	3	980	10	0	0	0	10
924	804	2	3	1114	5	4	0	0	9
925	804	2	3	1130	12	0	0	0	12
926	804	3	3	1855	0	2	0	0	2
927	804	3	3	1856	11	0	0	0	11
928	804	4	3	2110	8	0	0	0	8
929	804	4	3	2113	13	0	0	0	13
930	804	5	3	2351	15	0	0	0	15
931	804	5	3	2352	10	0	0	0	10
932	804	6	3	2514	13	0	0	0	13
933	804	6	3	2515	12	3	0	0	15
934	804	7	3	2681	15	0	0	0	15
935	804	7	3	2685	13	0	0	0	13
936	804	8	3	2693	11	1	0	0	12
937	804	8	3	2702	13	1	0	0	14
938	719	1	4	837	10	0	0	0	10
939	719	1	4	842	10	0	0	0	10
940	719	2	4	991	8	2	0	0	10
941	719	2	4	995	12	0	0	0	12
942	719	3	4	1729	11	0	0	0	11
943	719	3	4	1730	16	0	0	0	16
944	719	4	4	1887	8	0	0	0	8
945	719	4	4	1892	9	1	0	0	10
946	719	5	4	2229	15	1	0	0	16
947	719	5	4	2230	11	2	2	0	15
948	719	6	4	2387	12	2	0	0	14
949	719	6	4	2388	13	1	0	0	14
950	719	7	4	2563	10	1	0	0	11
951	719	7	4	2564	16	0	0	0	16
952	719	8	4	2812	15	0	0	0	15
953	719	8	4	2813	13	0	0	0	13
954	720	1	4	835	13	0	0	0	13
955	720	1	4	846	12	0	0	0	12
956	720	2	4	993	10	0	0	0	10
957	720	2	4	1000	10	1	0	0	11
958	720	3	4	1731	10	2	0	0	12
959	720	3	4	1732	11	1	0	0	12
960	720	4	4	1890	9	0	0	0	9
961	720	4	4	1891	10	0	0	0	10
962	720	5	4	2231	12	0	0	0	12
963	720	5	4	2232	8	1	0	0	9
964	720	6	4	2389	0	0	0	0	0
965	720	6	4	2391	12	0	0	0	12
966	720	7	4	2559	11	1	0	0	12
967	720	7	4	2562	12	1	0	0	13
968	720	8	4	2810	14	0	1	0	15
969	720	8	4	2822	12	2	0	0	14

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
970	728	1	4	858	11	0	0	0	11
971	728	1	4	858	13	0	0	0	13
972	728	2	4	1005	12	0	1	0	13
973	728	2	4	1009	10	1	0	0	11
974	728	3	4	1739	14	0	0	0	14
975	728	3	4	1740	11	0	0	0	11
976	728	4	4	1907	10	0	0	0	10
977	728	4	4	1908	9	0	0	0	9
978	728	5	4	2239	11	0	0	0	11
979	728	5	4	2240	9	0	0	0	9
980	728	6	4	2396	9	2	0	0	11
981	728	8	4	2397	11	2	0	0	13
982	728	7	4	2574	10	0	0	0	10
983	728	7	4	2575	11	0	0	0	11
984	728	8	4	2852	9	1	1	0	11
985	728	8	4	2854	13	0	1	0	14
986	727	1	4	849	12	0	0	0	12
987	727	1	4	854	12	2	0	0	14
988	727	2	4	1007	10	1	0	0	11
989	727	2	4	1011	13	0	0	0	13
990	727	3	4	1741	13	0	0	0	13
991	727	3	4	1742	15	0	0	0	15
992	727	4	4	1903	7	0	0	0	7
993	727	4	4	1904	10	0	0	0	10
994	727	5	4	2241	12	0	0	0	12
995	727	5	4	2242	11	0	0	0	11
996	727	6	4	2404	10	1	1	0	12
997	727	6	4	2407	14	0	0	0	14
998	727	7	4	2571	11	1	0	0	12
999	727	7	4	2578	12	0	0	0	12
1000	727	8	4	2851	14	0	1	0	15
1001	727	8	4	2853	11	0	0	0	11
1002	728	1	4	848	12	0	0	0	12
1003	728	1	4	851	13	0	0	0	13
1004	728	2	4	1002	14	0	0	0	14
1005	728	2	4	1012	11	0	0	0	11
1006	728	3	4	1743	11	0	0	0	11
1007	728	3	4	1744	10	0	0	0	10
1008	728	4	4	1905	9	0	0	0	9
1009	728	4	4	1906	10	2	0	0	12
1010	728	5	4	2243	14	0	0	0	14
1011	728	5	4	2244	11	3	0	0	14
1012	728	6	4	2401	12	1	0	0	13
1013	728	6	4	2403	8	1	0	0	9
1014	728	7	4	2573	12	0	0	0	12
1015	728	7	4	2578	10	1	0	0	11
1016	728	8	4	2850	12	1	0	0	13
1017	728	8	4	2856	13	2	0	0	15
1018	733	1	4	852	12	1	0	0	13
1019	733	1	4	864	8	3	0	0	11
1020	733	2	4	1014	10	1	1	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1021	733	2	4	1020	13	0	0	0	13
1022	733	3	4	1761	10	0	0	0	10
1023	733	3	4	1752	0	0	0	0	0
1024	733	4	4	1912	9	0	1	0	10
1025	733	4	4	1916	14	0	0	0	14
1026	733	5	4	2261	11	1	0	0	12
1027	733	5	4	2262	11	0	0	0	11
1028	733	6	4	2408	11	0	0	0	11
1029	733	6	4	2411	0	3	0	0	11
1030	733	7	4	2584	11	0	0	0	11
1031	733	7	4	2585	12	0	1	0	13
1032	733	8	4	2799	0	0	0	0	0
1033	733	8	4	2809	11	2	0	0	13
1034	737	1	4	861	15	1	0	1	17
1035	737	1	4	862	13	0	0	0	13
1036	737	2	4	1022	11	0	0	0	11
1037	737	2	4	1023	9	1	0	0	10
1038	737	3	4	1757	10	0	0	0	10
1039	737	3	4	1758	12	0	1	0	13
1040	737	4	4	0	0	0	0	0	0
1041	737	4	4	1910	14	1	0	0	15
1042	737	5	4	2257	10	2	0	0	12
1043	737	5	4	2258	0	0	0	0	0
1044	737	6	4	2416	7	0	1	0	8
1045	737	6	4	2418	12	0	1	0	13
1046	737	7	4	2583	12	0	0	0	12
1047	737	7	4	2591	13	0	0	0	13
1048	737	8	4	2800	10	0	0	0	10
1049	737	8	4	2806	14	0	0	0	14
1050	740	1	4	860	10	1	0	0	11
1051	740	1	4	870	11	1	0	0	12
1052	740	2	4	1025	13	0	0	0	13
1053	740	2	4	1029	6	3	0	0	8
1054	740	3	4	1781	8	1	0	0	9
1055	740	3	4	1782	12	0	0	0	12
1056	740	4	4	1926	10	0	0	0	10
1057	740	4	4	1930	13	1	0	0	14
1058	740	5	4	2261	15	0	0	0	15
1059	740	5	4	2262	14	0	0	0	14
1060	740	6	4	2412	16	1	0	0	17
1061	740	6	4	2420	12	0	0	0	12
1062	740	7	4	2599	13	2	0	0	15
1063	740	7	4	2601	15	0	0	0	15
1064	740	8	4	2793	10	4	0	0	14
1065	740	8	4	2798	12	1	0	0	13
1066	749	1	4	881	11	2	0	0	13
1067	749	1	4	887	13	0	0	0	13
1068	749	2	4	1039	12	1	0	0	13
1069	749	2	4	1042	6	2	0	0	8
1070	749	3	4	1778	9	1	0	0	10
1071	749	3	4	1779	12	0	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1072	749	4	4	1940	9	0	0	0	9
1073	749	4	4	1945	9	0	1	0	10
1074	749	5	4	2277	9	0	1	0	10
1075	749	5	4	2278	10	0	0	0	10
1076	749	6	4	2432	11	3	0	0	14
1077	749	6	4	2439	10	1	0	0	11
1078	749	7	4	2607	12	1	0	0	13
1079	749	7	4	2608	13	0	0	0	13
1080	749	8	4	2773	9	1	0	0	10
1081	749	8	4	2774	13	1	1	0	15
1082	762	1	4	908	0	0	0	0	0
1083	762	1	4	910	15	0	0	0	15
1084	762	2	4	1053	11	2	0	0	13
1085	762	2	4	1080	7	2	0	0	9
1086	762	3	4	1794	12	2	0	0	14
1087	762	3	4	1795	15	0	0	0	15
1088	762	4	4	1947	18	0	0	0	18
1089	762	4	4	1958	11	0	0	0	11
1090	762	5	4	2293	14	0	0	0	14
1091	762	5	4	2294	13	0	0	0	13
1092	762	6	4	2447	12	0	0	0	12
1093	762	6	4	2452	9	0	0	0	9
1094	762	7	4	2819	13	0	1	0	14
1095	762	7	4	2830	11	0	0	0	11
1096	762	8	4	2759	10	1	0	0	11
1097	762	8	4	2770	0	0	0	0	0
1098	763	1	4	902	11	2	0	0	13
1099	763	1	4	907	11	1	0	0	12
1100	763	2	4	1061	10	1	0	0	11
1101	763	2	4	1085	9	1	0	0	10
1102	763	3	4	1796	10	0	1	0	11
1103	763	3	4	1797	0	0	0	0	0
1104	763	4	4	1963	9	0	0	0	9
1105	763	4	4	1968	12	0	0	1	13
1106	763	5	4	2295	9	1	1	0	11
1107	763	5	4	2296	10	1	0	0	11
1108	763	6	4	2448	11	0	0	0	11
1109	763	6	4	2449	14	1	0	0	15
1110	763	7	4	2820	14	1	0	0	15
1111	763	7	4	2828	9	1	1	0	11
1112	763	8	4	2762	13	0	0	0	13
1113	763	8	4	2765	15	0	0	0	15
1114	767	1	4	905	8	0	0	0	8
1115	767	1	4	908	12	2	0	0	14
1116	767	2	4	1082	10	0	0	0	10
1117	767	2	4	1071	8	0	0	0	8
1118	767	3	4	1802	11	1	0	0	12
1119	767	3	4	1803	12	1	0	0	13
1120	767	4	4	1960	10	1	0	0	11
1121	767	4	4	1964	12	1	0	0	13
1122	767	5	4	2301	12	1	0	0	13

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1123	767	5	4	2302	13	2	0	0	15
1124	767	6	4	2457	8	1	0	0	9
1125	767	6	4	2465	8	2	0	0	10
1126	767	7	4	2634	12	0	0	0	12
1127	767	7	4	2640	12	0	0	0	12
1128	767	8	4	2748	12	0	2	0	14
1129	767	8	4	2749	13	0	0	0	13
1130	769	1	4	913	9	1	0	0	10
1131	769	1	4	918	8	2	0	0	10
1132	769	2	4	1067	12	1	0	0	13
1133	769	2	4	1070	10	1	0	0	11
1134	769	3	4	1806	10	2	0	0	12
1135	769	3	4	1807	8	0	0	0	8
1136	769	4	4	1972	9	1	0	0	10
1137	769	4	4	1975	10	0	1	0	11
1138	769	5	4	0	0	0	0	0	0
1139	769	5	4	2305	11	0	0	0	11
1140	769	6	4	2480	11	0	0	0	11
1141	769	8	4	2486	9	0	0	0	9
1142	769	7	4	2633	12	1	0	0	13
1143	769	7	4	2641	12	0	0	0	12
1144	769	8	4	2752	13	2	0	0	15
1145	769	8	4	2754	13	0	0	0	13
1146	773	1	4	914	10	1	1	0	12
1147	773	1	4	915	11	3	0	0	14
1148	773	2	4	1076	11	0	0	0	11
1149	773	2	4	1080	13	0	0	0	13
1150	773	3	4	1810	10	0	0	0	10
1151	773	3	4	1811	10	2	0	0	12
1152	773	4	4	1971	8	1	0	0	9
1153	773	4	4	1980	10	0	1	0	11
1154	773	5	4	2309	11	0	0	0	11
1155	773	5	4	2310	13	0	0	0	13
1156	773	6	4	2458	10	1	0	0	11
1157	773	6	4	2459	12	0	0	0	12
1158	773	7	4	2643	14	0	0	0	14
1159	773	7	4	2644	13	0	0	0	13
1160	773	8	4	2743	9	1	0	0	10
1161	773	8	4	2757	11	0	1	0	12
1162	774	1	4	916	9	2	0	0	11
1163	774	1	4	919	13	0	0	0	13
1164	774	2	4	1078	11	3	0	0	14
1165	774	2	4	1079	8	1	0	0	9
1166	774	3	4	1813	10	1	0	0	11
1167	774	3	4	1818	14	0	0	0	14
1168	774	4	4	1976	13	0	0	0	13
1169	774	4	4	1981	10	1	0	0	11
1170	774	5	4	0	0	0	0	0	0
1171	774	5	4	2312	9	0	0	0	9
1172	774	6	4	2474	15	0	0	0	15
1173	774	6	4	2478	12	0	0	0	12

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1174	774	7	4	2645	10	1	0	0	11
1175	774	7	4	2647	14	0	0	0	14
1176	774	8	4	2742	10	1	0	0	11
1177	774	8	4	2745	15	0	0	0	15
1178	785	1	4	933	9	1	0	0	10
1179	785	1	4	935	13	0	0	0	13
1180	785	2	4	1087	9	1	0	0	10
1181	785	2	4	1100	10	1	0	0	11
1182	785	3	4	1823	10	1	0	0	11
1183	785	3	4	1824	12	1	0	0	13
1184	785	4	4	1990	9	0	0	0	9
1185	785	4	4	1991	11	0	0	0	11
1186	785	5	4	2321	5	1	0	0	6
1187	785	5	4	2322	10	0	0	0	10
1188	785	6	4	2477	12	1	0	0	13
1189	785	6	4	2480	12	0	0	0	12
1190	785	7	4	2656	13	0	0	0	13
1191	785	7	4	2659	11	1	1	0	13
1192	785	8	4	2730	9	1	0	0	10
1193	785	8	4	2732	9	1	1	0	11
1194	787	1	4	932	14	0	0	0	14
1195	787	1	4	936	12	2	0	0	14
1196	787	2	4	1092	10	1	0	0	11
1197	787	2	4	1094	15	0	0	0	15
1198	787	3	4	1827	10	1	0	0	11
1199	787	3	4	1828	10	1	0	0	11
1200	787	4	4	1988	13	0	0	0	13
1201	787	4	4	1993	9	0	0	0	9
1202	787	5	4	2325	14	1	0	0	15
1203	787	5	4	2326	13	0	0	0	13
1204	787	6	4	2488	12	0	0	0	12
1205	787	6	4	2489	10	0	1	0	11
1206	787	7	4	2655	13	0	0	0	13
1207	787	7	4	2658	13	0	0	0	13
1208	787	8	4	2726	14	0	0	0	14
1209	787	8	4	2728	0	0	0	0	0
1210	791	1	4	940	10	2	0	0	12
1211	791	1	4	941	9	1	0	0	10
1212	791	2	4	1091	11	2	0	0	13
1213	791	2	4	1093	12	1	0	0	13
1214	791	3	4	0	0	0	0	0	0
1215	791	3	4	1833	8	0	0	0	8
1216	791	4	4	1998	13	0	0	0	13
1217	791	4	4	2101	10	1	0	0	11
1218	791	5	4	2331	13	2	0	0	15
1219	791	5	4	2332	7	0	0	0	7
1220	791	6	4	2484	11	0	0	0	11
1221	791	6	4	2493	13	0	0	0	13
1222	791	7	4	2680	14	1	1	0	16
1223	791	7	4	2682	13	1	0	0	14
1224	791	8	4	2720	0	0	0	0	0

8:55 MONDAY, MAY 2, 1988 25

1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	WEEK	TMT	MATNO	LIVE	EARLY	LATE	DEAD	IMPLANT
1225	791	8	4	2729	7	2	1	0	10
1226	802	1	4	953	9	0	0	0	9
1227	802	1	4	957	8	2	0	0	10
1228	802	2	4	1117	12	0	1	0	13
1229	802	2	4	1133	13	0	0	0	13
1230	802	3	4	1850	12	0	0	0	12
1231	802	3	4	1851	14	0	0	0	14
1232	802	4	4	2109	13	1	0	0	14
1233	802	4	4	2112	11	0	0	0	11
1234	802	5	4	2347	13	0	0	0	13
1235	802	5	4	2348	11	0	0	0	11
1236	802	6	4	2507	12	1	0	0	13
1237	802	6	4	2508	11	0	0	0	11
1238	802	7	4	2883	12	0	0	0	12
1239	802	7	4	2888	9	0	1	0	10
1240	802	8	4	2708	0	0	0	0	0
1241	802	8	4	2711	12	0	2	0	14

WEIGHTS (g) 1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	TMT	EXPOSURE DAY 1	POST-EXPOSURE WEEK 0	POST-EXPOSURE WEEK 1	POST-EXPOSURE WEEK 2	POST-EXPOSURE WEEK 3
1	705	1	28.8	28.8	28.8	27.6	28.4
2	711	1	33.8	35.0	33.0	33.0	34.0
3	712	1	33.8	34.8	32.2	31.4	31.8
4	718	1	34.0	35.8	33.4	33.0	33.4
5	718	1	35.4	35.8	35.8	34.6	35.0
6	724	1	29.4	30.2	29.0	28.8	28.8
7	729	1	31.2	35.4	32.4	31.8	31.8
8	739	1	34.4	35.4	33.2	31.0	31.0
9	741	1	31.8	33.4	30.0	29.2	29.2
10	742	1	34.8	36.0	33.4	33.0	32.2
11	743	1	34.4	36.4	34.2	34.4	33.8
12	768	1	34.2	35.6	34.0	33.0	33.2
13	780	1	32.0	33.8	32.4	31.2	31.2
14	781	1	29.8	31.0	29.6	29.0	29.4
15	783	1	31.0	32.4	31.2	31.2	31.2
16	788	1	34.8	36.2	35.0	34.0	33.4
17	789	1	35.8	37.8	37.2	35.8	36.4
18	797	1	34.8	35.6	35.0	33.6	33.4
19	798	1	39.2	40.6	38.2	37.8	38.8
20	805	1	28.4	30.4	28.6	28.4	28.6
21	701	2	25.4	27.8	25.6	25.0	26.6
22	703	2	31.4	32.2	31.2	31.2	32.2
23	708	2	32.4	35.2	32.2	31.4	33.2

OBS	POST-EXPOSURE WEEK 4	POST-EXPOSURE WEEK 5	POST-EXPOSURE WEEK 6	POST-EXPOSURE WEEK 7	POST-EXPOSURE WEEK 8
1	27.8	28.0	28.4	28.4	28.3
2	33.4	33.4	34.6	35.2	34.7
3	31.8	32.2	32.8	33.4	32.8
4	33.4	32.8	32.8	32.8	32.9
5	35.0	35.8	36.0	36.0	36.1
6	29.4	29.0	29.8	30.6	30.9
7	30.8	32.0	32.0	31.8	31.2
8	33.8	41.6	-1.0	-1.0	-1.0
9	30.4	29.6	30.2	31.4	29.2
10	33.0	34.4	34.0	33.8	34.1
11	34.4	35.6	36.2	35.6	33.9
12	33.4	34.8	34.2	34.6	33.7
13	30.4	30.8	31.4	32.0	31.1
14	29.2	29.8	29.6	29.8	29.4
15	31.2	31.8	32.6	32.4	31.1
16	33.8	33.8	34.0	34.2	32.8
17	35.2	36.2	37.4	37.2	35.5
18	33.8	34.8	34.2	35.4	34.2
19	38.0	38.4	39.0	38.8	38.0
20	28.2	28.4	28.8	27.8	27.9
21	26.4	26.8	27.0	27.2	26.7
22	32.2	32.8	32.4	34.6	34.3
23	32.0	32.8	33.4	33.2	33.1

WEIGHTS (g) 1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	TMT	EXPOSURE DAY 1	POST-EXPOSURE WEEK 0	POST-EXPOSURE WEEK 1	POST-EXPOSURE WEEK 2	POST-EXPOSURE WEEK 3
24	710	2	34.0	34.8	32.2	31.8	32.4
25	713	2	35.0	38.2	34.8	34.8	34.2
26	714	2	32.4	34.4	32.2	31.2	31.4
27	730	2	30.6	34.0	30.6	30.0	30.0
28	735	2	32.4	35.6	32.8	32.8	32.8
29	746	2	36.4	36.6	33.0	35.4	34.6
30	748	2	35.4	37.2	36.4	36.4	35.4
31	750	2	36.0	38.8	36.4	36.8	36.6
32	760	2	31.8	33.2	30.8	30.8	30.4
33	765	2	30.8	32.4	30.8	30.2	30.4
34	766	2	34.0	35.2	33.6	33.4	33.8
35	776	2	33.0	34.4	32.2	32.8	31.8
36	786	2	34.0	35.8	33.8	33.0	33.2
37	792	2	29.8	30.6	31.6	30.2	29.8
38	799	2	31.6	33.2	31.0	31.8	31.2
39	806	2	30.0	31.4	30.8	30.0	30.8
40	807	2	36.2	38.2	36.4	35.8	35.8
41	702	3	34.2	34.2	33.4	32.4	34.0
42	707	3	32.4	33.0	31.2	30.4	29.4
43	721	3	37.6	37.8	37.2	38.2	37.2
44	723	3	32.4	33.2	32.2	32.8	33.0
45	731	3	33.2	35.0	33.6	32.4	32.8
46	738	3	36.2	38.0	35.6	35.4	36.4

OBS	POST-EXPOSURE WEEK 4	POST-EXPOSURE WEEK 5	POST-EXPOSURE WEEK 6	POST-EXPOSURE WEEK 7	POST-EXPOSURE WEEK 8
24	32.6	33.2	32.4	32.4	32.4
25	35.2	34.2	34.6	36.4	37.1
26	31.0	31.0	31.2	31.4	31.6
27	30.0	30.0	29.8	30.2	30.6
28	33.2	34.4	32.8	33.6	31.8
29	35.0	34.8	35.2	35.8	34.4
30	36.4	35.4	36.8	36.4	35.0
31	37.8	37.8	39.4	38.8	35.8
32	30.2	30.8	31.2	32.0	31.1
33	30.2	30.8	31.0	31.2	30.6
34	33.8	35.0	35.2	35.4	34.8
35	31.6	31.4	31.6	30.8	29.8
36	32.4	33.4	33.8	33.2	32.2
37	29.4	30.4	29.8	30.6	28.7
38	32.0	33.2	33.6	34.2	33.8
39	29.4	30.2	30.2	31.2	30.1
40	36.8	37.6	36.8	36.8	34.8
41	33.0	33.2	34.0	34.6	35.1
42	30.2	30.8	30.8	31.0	31.4
43	36.8	37.0	37.0	37.8	37.2
44	33.2	34.2	31.2	32.8	31.8
45	33.2	34.8	34.6	33.8	32.7
46	35.4	35.8	36.0	36.8	36.8

WEIGHTS (g) 1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALENO	TMT	EXPOSURE DAY 1	POST-EXPOSURE WEEK 0	POST-EXPOSURE WEEK 1	POST-EXPOSURE WEEK 2	POST-EXPOSURE WEEK 3
47	744	3	28.8	30.6	27.8	29.0	29.4
48	745	3	33.6	33.8	30.4	31.2	30.8
49	750	3	33.0	34.8	31.4	32.2	30.4
50	753	3	35.2	36.6	34.6	34.2	34.0
51	755	3	30.8	18.8	-1.0	-1.0	-1.0
52	757	3	35.6	36.0	36.8	37.4	36.2
53	758	3	35.6	36.6	34.2	33.4	32.6
54	761	3	35.2	37.2	33.6	33.2	33.8
55	770	3	32.6	33.2	31.8	32.0	31.8
56	795	3	29.4	31.0	27.6	28.2	28.8
57	796	3	31.0	32.4	30.0	28.6	29.8
58	800	3	30.8	32.0	30.4	29.2	29.6
59	803	3	36.8	36.2	34.8	34.8	34.6
60	804	3	29.4	30.6	27.8	26.8	28.4
61	717	4	29.2	27.8	28.0	29.6	29.4
62	719	4	32.6	34.8	33.2	33.6	33.6
63	720	4	32.4	33.8	30.6	30.2	31.4
64	726	4	32.2	32.2	31.8	31.2	32.2
65	727	4	33.0	32.4	31.4	31.8	32.4
66	729	4	34.8	35.8	34.2	34.2	34.4
67	733	4	35.0	35.6	34.4	35.2	35.6
68	737	4	32.2	34.8	32.0	32.8	33.8
69	740	4	32.0	32.8	31.2	30.6	31.6
OBS	POST-EXPOSURE WEEK 4		POST-EXPOSURE WEEK 5	POST-EXPOSURE WEEK 6	POST-EXPOSURE WEEK 7	POST-EXPOSURE WEEK 8	
47	29.4		29.8	30.4	30.2	30.1	
48	30.2		30.8	32.0	33.8	31.5	
49	31.6		32.0	32.2	32.6	31.7	
50	35.0		35.4	35.4	35.4	34.7	
51	-1.0		-1.0	-1.0	-1.0	-1.0	
52	36.4		36.6	37.0	36.0	35.7	
53	34.0		34.0	34.4	33.8	34.3	
54	33.4		34.2	34.4	35.2	34.0	
55	31.8		33.4	34.2	33.8	32.9	
56	28.4		29.2	29.6	30.6	28.3	
57	29.4		30.2	30.6	30.2	29.3	
58	29.8		31.0	30.0	31.0	29.2	
59	34.2		35.6	35.6	35.0	33.6	
60	28.0		28.8	28.2	28.0	26.8	
61	28.0		29.2	30.0	-1.0	-1.0	
62	33.6		33.6	33.2	34.4	35.3	
63	30.6		31.6	31.8	32.4	31.7	
64	32.2		32.4	32.6	33.2	32.8	
65	31.2		32.2	32.6	32.2	31.4	
66	34.2		34.2	34.6	33.2	32.8	
67	35.6		36.6	36.6	36.2	35.7	
68	33.4		34.0	34.2	33.6	31.7	
69	32.0		30.8	31.0	31.4	31.5	

WEIGHTS (g) 1,3-BUTADIENE: DOMINANT LETHAL ASSAY IN B6C3F1 MICE

OBS	MALEND	TMT	EXPOSURE DAY 1	POST-EXPOSURE WEEK 0	POST-EXPOSURE WEEK 1	POST-EXPOSURE WEEK 2	POST-EXPOSURE WEEK 3
70	749	4	31.4	33.6	31.6	32.0	32.8
71	782	4	32.4	34.6	33.4	34.2	35.0
72	783	4	30.6	30.4	29.2	30.2	31.0
73	787	4	33.8	34.4	32.2	31.6	32.2
74	789	4	33.8	34.2	32.0	32.2	33.2
75	773	4	31.6	31.0	29.4	28.8	30.2
76	774	4	37.8	39.8	36.4	36.4	36.4
77	786	4	34.8	35.4	34.0	33.2	33.8
78	787	4	36.0	36.6	36.6	37.4	38.4
79	791	4	36.6	37.6	35.6	34.0	35.6
80	802	4	33.6	33.8	32.2	31.4	32.4
OBS	POST-EXPOSURE WEEK 4	POST-EXPOSURE WEEK 5	POST-EXPOSURE WEEK 6	POST-EXPOSURE WEEK 7	POST-EXPOSURE WEEK 8		
70	32.8	33.4	34.0	32.6	31.7		
71	35.8	37.0	36.6	36.4	37.0		
72	30.6	31.8	31.2	30.4	30.0		
73	31.8	33.0	32.2	33.0	30.9		
74	33.0	33.8	34.0	33.8	33.4		
75	29.4	30.0	29.4	30.2	28.9		
76	35.8	35.8	36.8	37.8	34.5		
77	34.4	34.2	35.4	34.6	34.0		
78	38.0	38.0	39.2	40.4	38.9		
79	38.8	36.8	36.4	36.2	34.5		
80	32.0	32.6	33.0	32.2	31.5		

APPENDIX F

QUALITY ASSURANCE STATEMENT, SAMPLE AND RECORD DISPOSITION, CALENDAR OF EVENTS FOR THE DOMINANT LETHAL STUDY, AND LIST OF PERSONNEL FOR THE DOMINANT LETHAL STUDY

DOMINANT LETHAL STUDY IN CD-1 MICE FOLLOWING EXPOSURE TO
1,3-BUTADIENE

QUALITY ASSURANCE STATEMENT

Listed below are the phases and/or procedures included in the study described in this report which were reviewed by the Quality Assurance Unit during the period, 12/1/86 - 4/1/86, specifically for this study and the dates the reviews were performed and findings reported to management. (All findings were reported to the study director or his designee at the time of the review.)

Phase/Procedure Reviewed	Review Date	Date Findings Submitted in Writing to Study Director/Management
Data	12/04/85	12/18/85
Health Screen	1/06/86	1/06/86
Animal Receipt	1/08/86	1/08/86
Necropsy	1/08/86	1/08/86
Randomization	1/09/86	1/09/86
Animal Identification	1/09/86	1/09/86
Body Weights	1/13/86	1/15/86
Dosing	1/13/86	1/15/86
Health Screen	1/27 & 28/86	1/28/86
Animal Receipt	2/05/86	2/05/86
Necropsy	2/07/86	2/07/86
Data	1/22, 25 & 26/88	1/26/88
Final Report	1/22 & 26/88 & 4/14/88	4/14/88

Quality Assurance Specialist

4/15/88

SAMPLE AND RECORD DISPOSITION

Upon completion of the 1,3-butadiene studies, all slides and tissue 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 THE DOMINANT LETHAL STUDY IN MICE

Animals ordered: 10/10/85 (CD-1 mice from Charles River Laboratories, Portage Facility, MI)

MALES

Receipt of animals: 12/21/85 (ARC #860017; 120 males; date of birth, 10/17/85)

Proving cohabitation 12/23/85 to 01/08/86

Health screen: 01/06/86

Exposure: 01/13/86 through 01/17/86 (6 hours/day)

Postexposure cohabitation: (Listed under females by week)

Body weight measurements: 01/08/86
01/13/86
01/20/86
01/27/86
02/03/86
02/10/86
02/17/86
02/24/86
03/03/86
03/10/86
03/17/86

Sacrifice: 03/17/86

FEMALES

Proving

Receipt of animals: 12/21/85 (ARC #860017; 208 females; date of birth, 10/17/85)

Health screen: 01/06/86

Cohabitation with males: 12/23/85 to 01/08/86

Sacrifice: 01/08/86

Postexposure Matings--Weeks 1 and 2

Receipt of animals: 12/21/85 (ARC #860017; 337 females; date of birth, 10/24/85)

Health screen: 01/06/86

Cohabitation with males

Week 1: 01/20/86 through 01/26/86

Week 2: 01/27/86 through 02/02/86

Sacrifice

Week 1: 02/07/86

Week 2: 02/14/86

Postexposure Matings--Weeks 3 and 4

Receipt of animals:	01/21/86 (ARC #860024; 336 females; date of birth, 11/21/85)
Health screen:	01/27/86
Cohabitation with males	
Week 3:	02/03/86 through 02/09/86
Week 4:	02/10/86 through 02/16/86
Sacrifice	
Week 3:	02/21/86
Week 4:	02/28/86

Postexposure Matings--Weeks 5 and 6

Receipt of animals:	02/05/86 (ARC #860027; 341 females; date of birth, 12/05/85)
Health screen:	02/19/86
Cohabitation with males	
Week 5:	02/17/86 through 02/23/86
Week 6:	02/24/86 through 03/02/86
Sacrifice	
Week 5:	03/07/86
Week 6:	03/14/86

Postexposure Matings--Weeks 7 and 8

Receipt of animals:	02/05/86 (ARC #860028; 365 females; date of birth, 12/26/85)
Health screen:	02/19/86
Cohabitation with males	
Week 7:	03/03/86 through 03/09/86
Week 8:	03/10/86 through 03/16/86
Sacrifice	
Week 7:	03/21/86
Week 8:	03/28/86

Completion of data and statistical evaluations:	05/13/86
Submission of Draft Report:	January 1988

LIST OF PERSONNEL FOR DOMINANT
LETHAL STUDY OF 1,3-BUTADIENE

Responsibility	Name
Principal Investigators	P.L. Hackett
	B.J. McClanahan
	T.J. Mast
Exposure System	M.L. Clark
	J.R. Decker
	G.R. Eli
	L.G. Florek
	D.K. Hammerberg
	E.M. Milliman
	E.J. Rossignol
	R.D. Swanneck
Monitoring/Analytical Chemistry	M. McCulloch
	N.S. Stamps
	K.H. Stoney
	R.B. Westerberg
Animal Resources Center	M.G. Brown
	S.E. Rowe
	A.E. Jarrell
Morphologic Evaluations	B.J. McClanahan
	J.J. Evanoff
	R.L. Rommereim
	M.L. Sours
Statistical Analyses	R.L. Buschbom

P.L. Hackett 4/29/88

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