**Inhalation Developmental
Toxicology Studies: Teratology
Study of Isoprene in Mice and Rats
Final Report**

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INHALATION DEVELOPMENTAL TOXICOLOGY STUDIES:
TERATOLOGY STUDY OF ISOPRENE
IN MICE AND RATS

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No. NIH-Y01-ES-70153

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Richland, Washington 99352

SUMMARY

Isoprene, a reactive, branched diene, is used in large quantities in the manufacture of polyisoprene and as a copolymer in the synthesis of butyl rubber. The potential for isoprene to cause developmental toxicity was assessed in rodents, by exposing four groups each of Sprague-Dawley rats and Swiss (CD-1) mice to 0, 280, 1400, or 7000 ppm isoprene vapors, 6 h/day, 7 day/wk. Each treatment group consisted of 10 virgin females (for comparison), and ~30 positively mated rats or mice. Positively mated mice were exposed on days 6-17 of gestation (dg), and rats on 6-19 dg. The day of plug or sperm detection was designated as 0 dg. Body weights were obtained throughout the study period, and uterine and fetal body weights were obtained at sacrifice (rats, 20 dg; mice, 18 dg). Implants were enumerated and their status recorded. Live fetuses were sexed and examined for gross, visceral, skeletal, and soft-tissue craniofacial defects.

Exposure of pregnant rats to these concentrations of isoprene did not result in apparent maternal toxicity or in developmental toxicity. There were no treatment-related effects upon body weights or reproductive indices at any exposure level, nor was there a significant increase in the incidence of fetal malformations or variations. The only effect observed in the dams was an increased kidney to body weight ratio, and in the fetuses there was a slight, but not statistically significant, exposure-correlated increase in the incidence of reduced vertebral ossifications (centra) which suggests that the 7000-ppm exposure level may be at or near a developmental toxicity threshold.

Exposure of Swiss (CD-1) mice to isoprene resulted in (from 12 dg onward) significant reductions in maternal body weight, body weight gain during treatment and in uterine weight for the 7000-ppm group. Since neither the extra-gestational weight gain of the pregnant dams, nor the body weight gain of the virgin animals was affected, there was an indication of selective developmental toxicity at the 7000-ppm exposure level. Liver to body weight ratios for pregnant dams were significantly greater than the 0-ppm group for both the 1400- and 7000-ppm groups. Kidney to body weight ratios were

significantly greater than the 0-ppm group for the 7000-ppm group . Developmental toxicity was further evident as an exposure-correlated reduction in fetal body weights which was statistically significant at the 280-ppm level (the lowest isoprene level) for female fetuses and at the 1400-ppm level for male fetuses. However, no embryotoxicity in the form of increased intrauterine death was present at any exposure level.

Fetuses of mice exposed to isoprene had an increased incidence of supernumerary ribs which was significantly correlated to increasing exposure concentration and was statistically significant for the 7000-ppm group. Although there was no significant increase in the incidence of malformations, two fetuses with cleft palate were found, one in each of the two highest exposure groups. Cleft palates were not detected in the 0-ppm group.

In summary, pregnant Sprague-Dawley rats and their offspring appeared to be relatively resistant to the toxic effects of isoprene at the exposure levels employed in this study. Swiss (CD-1) mouse dams exhibited significant toxic effects at the 7000-ppm level; however, the offspring of the mice exhibited significant signs of toxicity, including reductions in fetal body weight and ossification, at all the exposure concentrations employed. In light of the above results, the 7000-ppm isoprene level could be set as a no observable effect level (NOEL) in the Sprague-Dawley (CD) rat for both maternal and developmental toxicity. In the Swiss (CD-1) mouse, a NOEL of 1400 ppm could be set for maternal toxicity; however, a NOEL based on the results of this study cannot be assigned to the Swiss (CD-1) mouse for developmental toxicity.

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Principal Investigator

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INTRODUCTION

Isoprene was originally isolated as a pyrolysis product of natural rubber and is now used in large quantities for the manufacture of polyisoprene, and in smaller amounts as a copolymer with isobutylene for the synthesis of butyl rubber (Saltman, 1981). In 1982, the U.S. production level of isoprene was 187 million pounds (USITC, 1983). Isoprene is also the basic building block in many natural products (e.g. terpenes, camphors, and vitamin A), is a normal constituent of human breath, and is naturally present in the atmosphere as a result of volatilization from plant surfaces and combustion processes.

Isoprene is a branched diene that is structurally related to another diene, 1,3-butadiene, which is also widely used in the synthetic rubber industry. Their close structural relationship and similar chemical properties, the fact that 1,3-butadiene causes some developmental toxicity in mice (Hackett et al., 1987a), and the significant potential for human exposure to isoprene have raised concern over the potential for isoprene exposure during pregnancy to result in developmental toxicity. Isoprene undergoes metabolic reactions similar to those of butadiene (compare Figures 1 and 2). Acting as both a diene and a dienophile in a Diels-Alder addition reaction, isoprene readily forms dimers in the atmosphere; limonene is the predominant product. In the presence of oxygen, isoprene may undergo peroxidation to form peroxides which, if present in sufficient amounts, may present an explosion hazard. In order to prevent the production of high levels of peroxides in the exposure generator an inhibitor, 40-48 ppm *t*-butylcatechol, is added to the test material (MRI, 1986). Significant levels of either peroxides or the limonene dimer are prevented from reaching animal exposure chambers by isoprene vapor generation methodology (Battelle, 1986).

METABOLISM AND PHARMACOKINETICS

Isoprene may be metabolized *in vitro* to either of two epoxides (compounds II and III, Figure 1) which may then be hydrolyzed to the respective diols, or in the case of compound III, further metabolized to the

diepoxide, compound IV. As can be seen in Figure 2, the metabolism of isoprene closely corresponds to that of 1,3-butadiene. Epoxide II is the major metabolic oxidation product for isoprene; however, since it rapidly undergoes hydrolysis to the corresponding diol (Gervasi et al., 1985) and does not form the mutagenic diepoxide (Del Monte, Citti and Gervasi, 1985) it is probably of little toxicological significance. Formation of both epoxides I and II and the diepoxide have been shown to occur in the presence of liver microsomes prepared from rats, mice, rabbits, or hamsters, and to be catalyzed via the P₄₅₀-monooxygenase complex (Longo, Citti and Gervasi, 1985).

Pre-treatment of the animals with phenobarbital, a cytochrome P₄₅₀-monooxygenase inducer, resulted in an increased V_{max} for the microsomal oxidation of isoprene to compound III in all of these species (Del Monte, Citti and Gervasi, 1985). Epoxide III, 3,4-epoxy-2-methyl-1-butene, can then be further oxidized to the diepoxide, which like its counterpart in the metabolism of 1,3-butadiene (Figure 2), is highly mutagenic (Gervasi et al., 1985).

Inhalation studies in male Wistar rats and B6C3F1 mice (Peter et al. 1987) have shown that the rate of isoprene metabolism ($\mu\text{mol/h}\cdot\text{kg}$) was directly proportional to exposure chamber concentrations up to about 300 ppm. In these studies animals were subjected to a single exposure to the test material in a closed system. The stated exposure concentrations were the initial concentrations of the test material which declined as the material was absorbed and metabolized. At isoprene exposure concentrations >300 ppm saturation kinetics applied, and the maximal metabolic rate was about 130 and 400 $\mu\text{mol/h}\cdot\text{kg}$ for rats and mice, respectively. Thus, the half-life ($t_{1/2}$) of the parent compound, isoprene, for exposure concentrations >300 ppm was approximately 44 min for rats and 18 min for mice. The $t_{1/2}$ for isoprene at exposure concentrations <300 ppm was much shorter, 6.8 min in rats and 4.4 min in mice. The kinetic characteristics of isoprene metabolism were very similar to those of butadiene which also exhibited saturation kinetics; however, metabolic saturation for butadiene was not attained until chamber concentrations reached approximately 1,000 ppm (Kreiling et al. 1986).

Another recent study on the fate of inhaled isoprene in rats (Dahl et al. 1987) provided further insight into the toxicokinetics of isoprene during, and following, a single inhalation exposure of male F344 rats to 8, 266, 1480, or 8200 ppm ^{14}C -isoprene for up to 6 h. Dahl et al. (1987) found that:

1) 75% of the metabolites associated with isoprene exposure were excreted in the urine within a 66-h post-exposure period, 2) 3 to 20% of the metabolites were excreted in the feces or exhaled as CO_2 , and 3) 8-18% remained in the body after 66 h. The concentration of circulating metabolites generally increased with increasing exposure concentration, as well as with the duration of exposure. The percent of original material present as the isoprene diepoxide and/or as the diols remained relatively constant as a function of time for the two lower concentrations, but increased as the exposure concentration increased. The percent of inhaled ^{14}C -isoprene retained by the animal immediately after an exposure period of ≤ 6 h decreased with increasing dose (e.g., from 19% at 8 ppm to 4.5% at 8200 ppm). The $t_{1/2}$ for urinary excretion of ^{14}C in the rat was 10.2 ± 1 h (mean $\pm$ SE). Since it is the metabolites of isoprene that are suspected of causing genotoxicity (see below), the $t_{1/2}$ for urinary excretion of metabolites is of toxicological significance.

Saturation of metabolic capabilities was also indicated when Dahl et al. (1987) found that the diepoxide/diol metabolite levels in blood plateaued following exposure to 1480 ppm isoprene, and did not increase when animals were exposed 8200 ppm. Furthermore, blood levels of the parent compound, isoprene, appeared to be maximal immediately following a 2-h exposure to 8200 ppm, and did not increase with a longer exposure period. Tissue distribution studies showed that subcutaneous fat, followed by blood, had the highest diepoxide/diol metabolite concentrations immediately following a 6-h exposure to 1480 ppm isoprene. However, diepoxide/diol levels in tissue samples obtained at earlier time points were highest in the fat followed by the nose, liver and lung. These results indicated that substantial metabolism occurred in the respiratory tract as well as in the liver. Tissue levels of both isoprene and its metabolites decreased substantially after an 18-h recovery period.

Isoprene, which has a high octanol to water partition coefficient, should be readily absorbed via the lung (Peter et al., 1987). This was shown to be the case in dogs by Egle and Gochberg (1975) who found that: 1) the retention of inhaled isoprene in the dog was 74-76%, and 2) that the amount retained was not affected by the ventilatory rate. The amount of isoprene retained remained in the range of 74-76% up to an exposure concentration of approximately 0.72 µg/ml (≈264 ppm) and then declined. At a concentration of 0.96 µg/ml (≈367 ppm) the amount of isoprene retained dropped to ≈40 percent. Considerably lower values were reported by Dahl et al. (1987) for the rat where 19% was retained following exposure to 8 ppm, 9% at 266 ppm, and <5% at an exposure level of 8200 ppm.

TOXICOLOGY

In vitro

Isoprene was negative for mutagenic activity in *Salmonella* mutagenicity assays in strains TA1530, TA1535, TA100, TA98, or TA1538, in the presence or absence of liver microsomes from Aroclor-induced rats (deMeester et al., 1981; Gervasi, 1985). Isoprene was also negative in Ames/*Salmonella* assays conducted by the NTP (unpublished results).

Although isoprene itself was not found to be mutagenic (Gervasi, et al., 1985), the diepoxide metabolite of isoprene, 2-methyl-1,2,3,4-diepoxybutane (produced in mouse hepatic microsomes [Del Monte, Citti, and Gervasi, 1985] and in hepatic microsomes of other rodent species [Longo, Citti and Gervasi, 1985]), was highly mutagenic to *Salmonella* strain TA100 (Figure 1). Gervasi et al. (1985) further showed that this diepoxide had a half-life in water and mutagenic and alkylating activities similar to those of the mutagenic, clastogenic, and carcinogenic metabolite of 1,3-butadiene, 1,2,3,4-diepoxybutane.

Recent studies in B6C3F1 male mice conducted by the NTP assessed the cytogenetic toxicity of isoprene (Tice et al. 1987). Using bone marrow and peripheral red blood cells the following endpoints were measured: 1) the average generation time (AGT), 2) the mitotic index (MI), 3) the number of

chromosomal aberrations (CA), 4) the number of sister-chromatid exchanges (SCE), 5) the percent polychromatic erythrocytes (%PCE), 6) the percent micronucleated PCE (MN-PCE), and 7) micronucleated normochromatic erythrocytes (MN-NCE). Multiple exposures of 4-5 week old male mice (exposed 12 out of 16 days) to 0, 438, 1750, or 7000 ppm isoprene for 6 h/day caused an increase in the AGT, MN-PCE and MN-NCE relative to controls; the increases were positively correlated to increasing exposure concentration. The mean frequencies for SCE and CA were also elevated above controls, but the values plateaued at an exposure concentration of 438 ppm isoprene. Increases in frequencies for CA, SCE, and/or MN-PCE or MN-NCE were indicative of the induction of genotoxic damage, while alterations in AGT, MI, and %PCE reflected cytotoxicity. The cytotoxicity may have been caused by genotoxic damage or by independent mechanisms. Results from these studies indicate that isoprene exposure induces somatic genotoxicity in these mice. The increase in micronucleated erythrocytes is consistent with the induction of DNA damage observed in the presence of an S-phase dependent clastogen. The plateau effect observed in the elevation of micronucleated erythrocytes and SCE frequencies suggests a saturation of the capacity of the mice to metabolize isoprene which is consistent with the results reported by Dahl et al. (1987) and Peter et al. (1987), mentioned above.

Animal Studies

Acute

Isoprene is more acutely toxic than 1,3-butadiene. The 2-h LC₅₀ value for isoprene exposure in mice was approximately 50,000 ppm and the 4-h LC₅₀ value for rats was approximately 64,500 ppm (Shugaev, 1969; Sandmeyer, 1981). Corresponding values for butadiene were 122,000 and 130,000 ppm, respectively (Shugaev, 1969).

Repeated Dose

A repeated dose study designed to characterize the toxicity, to identify target organs, to determine the "no-effect" level, to establish the differences in sensitivity between species and sexes, and to determine the slope of the dose-response curve associated with short-term exposure to

isoprene has been conducted in mice and rats (Battelle, 1987a and 1987b). Male and female F344/N rats and B6C3F1 mice were exposed to 0, 438, 875, 1750, 3500 and 7000 ppm isoprene, 6 h/day, 5 day/wk, for a total of 12 exposure days.

Results from the rat study indicated that exposure to isoprene concentrations ranging from 438 to 7000 ppm caused no deaths and no clinical signs of toxicity. There were no significant differences in body weight gain or in the organ to body weight ratios between the exposed groups and the control group. When examined after 4 days of exposure, hematology parameters, clinical chemistry measures, and urinalysis values were not altered with respect to controls. Neither gross lesions nor histopathological changes attributable to isoprene exposure were observed at necropsy.

In the mouse study, isoprene exposure did not result in deaths or cause obvious clinical signs of toxicity. However, body weight gain with respect to controls, as well as the mean testes to body weight ratios, were decreased in male mice in an exposure concentration-related fashion. Body weights of female mice were not significantly affected. At all exposure levels, and in both sexes, liver to body weight ratios were increased while thymus and spleen to body weight ratios were decreased with respect to controls. Changes in these ratios were directly proportional to exposure concentrations in all cases. The increase in the liver to body weight ratio as compared to controls was statistically significant for all exposure levels for both sexes.

Clinical pathology results in mice exposed for 5 days indicated a slight non-regenerative anemia in all exposure groups, but there were no observable effects on hepatic or renal function. Focal, raised or thickened areas in the pole of the forestomach were observed at all exposure concentrations for both sexes at necropsy. Subsequent histopathological evaluations demonstrated the presence of forestomach epithelial hyperplasia. Histopathological evaluations also showed olfactory epithelial degeneration at 7000, 3500, and 1750 ppm in male mice, and testicular atrophy at 7000 ppm. Male mice also had vacuolized hepatocellular cytoplasm at all exposure concentrations.

Subchronic

No effect on weight gain in mice, rabbits, or rats with respect to controls was observed following 4 to 5 months of 4 h/day exposures to 790-1750 ppm isoprene (Sandmeyer, 1981). However, prolonged exposure to isoprene has been suggested to affect the function of the central and autonomic nervous system of mice, rabbits, and rats (CRCS, 1984).

Chronic

No information was found addressing the chronic toxicity of isoprene.

Reproductive and Developmental

Isoprene administered orally to pregnant female Wistar rats at 0, 22, 379, or 1895 mg/kg from 9-12 days of gestation (dg) had no effect on maternal weight gain, but caused increased fetal death and retarded ossification of the sternebrae with respect to controls (Komatsu, 1971 cited in CRCS, 1984). These effects were not correlated to dose.

Human

No studies addressing chronic effects of human exposure to isoprene were found in the literature. Threshold limit values for occupational exposure to isoprene vapors have not been established (ACGIH, 1987).

SUMMARY

Repeated exposure of F344 rats or B6C3F1 mice to isoprene concentrations as high as 7000 ppm did not result in clinical signs of toxicity. However, there was considerable evidence that isoprene, or one or more of its metabolites, caused either cyto- or genotoxicity. The capacity of rodents to metabolize isoprene apparently becomes saturated at exposure concentrations greater than $\approx$ 400 ppm. Studies on the retention of inhaled isoprene indicate that retention appears to decline with increasing exposure concentrations.

Although oral administration of isoprene did not appear to cause dose-related developmental effects, the close structural relationship of

isoprene to 1,3-butadiene and their similar metabolic pathways are cause for concern. Furthermore, circulating concentrations of the mutagenic diepoxide have been found in rats following a single inhalation exposure to isoprene (Dahl et al. 1987), and *in vivo* results indicated that exposure to isoprene may induce the P₄₅₀-monooxygenase system (as indicated by significant and exposure-correlated increase in liver to body weight ratios following repeated exposures to isoprene [Battelle, 1987a]). Thus, the metabolic capacity of the animals may increase with repeated exposures.

A two-species (mice and rats) inhalation developmental toxicology study was conducted on isoprene due to concern over the close structural relationship and similar metabolic pathways between isoprene and 1,3-butadiene, the widespread use of isoprene, and the lack of adequate knowledge to judge the potential for isoprene to cause developmental toxicity. Pregnant Swiss (CD-1) mice and Sprague-Dawley rats were exposed to 0, 280, 1400, and 7000 ppm isoprene for a duration of 6 h/day on 6-17 days of gestation (dg) for mice, and on 6-19 dg in rats. In order to better assess the potential for isoprene to produce effects late in gestation, exposures were continued through the fetal period rather than just through organogenesis. Since there was some indication that isoprene exposure induces the P₄₅₀-monooxygenase system, maternal liver and kidney weights were also obtained.

MATERIALS AND METHODS

Four groups each of Sprague-Dawley rats (13 wk; Charles River, Portage, MI) and Swiss (CD-1) mice (12 wk; Charles River, Portage, MI), were exposed to 0 (filtered air), 280, 1400, or 7000-ppm isoprene vapors in whole body inhalation chambers, 6 h/day, 7 days/week. Virgin and mated female mice were exposed concurrently for 12 consecutive days (6-17 dg for mated mice), and the rats for 14 consecutive days (6-19 dg for mated rats). Each of the four exposure groups consisted of 10 virgin females per species, 28-29 sperm-positive rats, and 33 plug-positive mice; all of the groups were randomly selected using body weight as the blocking variable. The day of plug or sperm detection was designated as 0 dg. Developmental evaluations were

conducted on pregnant mice killed on 18 dg, and on pregnant rats killed on 20 dg. Virgin females were killed on the day after the last day of exposure.

The highest exposure chamber concentration was limited to 50% of the lower explosion limit, approximately 15,000 ppm for isoprene, and was therefore set at 7000 ppm. The two lower concentrations were chosen to study the possibility of a dose-response relationship following isoprene inhalation, and to be below the exposure level at which metabolic saturation occurs from a single dose.

EXPOSURE SYSTEM

Inhalation exposures were conducted in Battelle-designed inhalation exposure chambers (Harford System; Lab Products, Inc., Aberdeen, MD). The 2.3-m³ stainless-steel chamber (1.7-m³ active mixing volume) contained three levels of caging, each of which was split into two offset tiers. The drawer-like stainless-steel cage units accommodated individual animal cages, feed troughs and automatic waterers. Stainless-steel catch pans designed to aid in maintaining a uniform concentration of vapor throughout the chamber, as well as for the collection of urine and feces, were suspended below each cage unit. Air (HEPA- and charcoal-filtered) containing a uniform mixture of the test article flowed through the chamber at approximately 15 ft³/min (CFM) which was equivalent to approximately 15 air changes per hour. The uniform mixture was diverted along the inner surfaces of the chamber and a portion of the flow was "peeled off" by each catch pan, thus creating mixing eddies. Exhaust from each tier was cleared through the space between the tiers (Appendix B).

The isoprene exposures were conducted using an automated data acquisition and control system in an exposure suite. This system monitored and controlled the basic inhalation test system functions including chamber air flow, vacuum, temperature, relative humidity, and test chemical concentrations at approximately 4-h intervals. Conditions which may have been a threat to the health of the animals or constituted an explosion hazard triggered alarms to personnel who were on call 24 h/day. All data acquisition and exposure control originated from an executive computer which contained the exposure protocols and controlled a multiplexing-interface system.

Isoprene vapor was generated by a rotary evaporation system (Büchi Rotavapor, Model EL-131S) which produced high purity isoprene vapor (Figure 3). Low pressure nitrogen (4 - 6 psi) was introduced into the vapor inlet of an isoprene cylinder, forcing liquid isoprene out at a steady, controlled rate which was adjusted with a metering valve and monitored with a flowmeter. The liquid was delivered to a rotating flask immersed in a hot water bath, 50°C. The resulting vapor was forced out of the mouth of the flask into a chilled water condenser where much of the vapor was recondensed and returned to the evaporator flask. Nitrogen was metered into the bottom of the condenser and flowed out the top saturated with isoprene vapor. The temperature of the isoprene-saturated nitrogen was monitored using a sensor at the top of the condenser. The vapor entered a short distribution manifold where individual delivery lines carried a metered amount of vapor to the exposure chambers. Injection of the nitrogen/vapor mix into the conditioned airstream entering the chamber occurred at a point sufficiently removed from the chamber to allow for proper mixing. This assured uniformity of chemical-laden atmosphere within the chamber.

Normal operation called for approximately 20% excess vapor to be exhausted from the manifold through a flowmeter. This caused a slight positive pressure in the manifold and allowed independent adjustment of the chamber flow rates.

Generation proceeded in stages: warmup, generation and shutdown. During warmup, filling of the evaporator flask and heating of the water bath proceeded together. During this time, some evaporation occurred but all vapor was exhausted from the distribution manifold through the excess flowmeter and at each chamber through pneumatic 3-way valves. When the bath temperature and fluid level reached the correct values, computer-controlled startup of the exposure was initiated by rotation of the pneumatic 3-way valves to the chamber position.

Shutdown at the end of the generation stage was normally initiated by the computer which closed the valves at the chambers, stopped flask rotation, and turned off the bath heater. The operator then dumped additional cooling water into the bath. The remaining isoprene in the evaporating flask was

removed to a waste bottle. Nitrogen continuously purged the generation system until preparation for the next day's generation.

In order to determine the persistence of the chemical in the chamber following exposure, the concentration of isoprene in the 7000-ppm chamber was monitored overnight following shutoff of the chemical flow to the chamber. Monitoring was performed once during the prestart activities without animals, and again during the study when animals were present. Concentration of isoprene in the chamber without animals was below 1% of the initial concentration in less than 28 minutes following shutdown of the vapor generation system compared with approximately 21 minutes with animals in the chambers (Figure 4).

Exposure chambers without animals, and the exposure room, were monitored for particles during one day of test generation with a particle detector (Gardner Associates, Type CN, Schnectedy, NY). Particle monitoring was also conducted once during the exposure with animals in the chambers. No particles were detected in the control chamber or in any of the exposure chambers during any of the tests. A count of approximately 200 particles/cm³ was found in the room during generation; however, these particles were not considered to result from test material generation.

The time for the concentration to build up to 90% of the final, stable concentration following the start of generation (T_{90}), and the time for the vapor concentration to decay to 10% of the stable concentration following the cessation of generation (T_{10}), were determined before and after animals were placed in the chambers (Figure 4). The experimental value for T_{90} without animals was found to range from 9 to 11 min; with animals present, the range was 10 to 13 min. At a chamber air flow rate of 15 air changes per hour, the theoretical value for T_{90} is ≈ 12.5 min. Since there could have been variability in experimental buildup times due to fluctuations in chamber flow rates and sampling accuracy, a T_{90} of 12 min was chosen for this study. The value of T_{10} ranged from 8 to 10 min without animals present, and was 10 to 13 min with animals present.

Uniformity of vapor concentration in the exposure chambers was measured prior to the start of, and once during, the study. The vapor concentrations for these determinations were measured using the on-line gas chromatograph with the automatic sampling valve disabled to allow continuous monitoring from a single input line. Prior to animal loading, 12 chamber positions were measured. The second set of isoprene concentration measurements was taken from the front and back positions of the chamber only where cage units contained animals. Uniformity in all chambers was acceptable $\leq 5\%$ relative standard deviation (RSD) for between and within port variability (Appendix B).

Chamber and room temperatures ($\pm 0.5^\circ\text{F}$) were measured with calibrated resistance temperature detectors (RTD) which were located at the measurement site, and were multiplexed to a digital thermometer interfaced to the computer. Chamber temperature was controlled primarily by adjusting the temperature of the exposure room. Percent relative humidity (%RH) was calculated by the executive computer from temperature and dew point measurements ($\pm 6\%$ RH). The dew point was determined by pulling an air sample through a Teflon[®] tube into a dew point hygrometer located in the control center. Measurements were taken from different chambers using a valving system which multiplexed the sampling tubes to the hygrometer.

Chamber air flow (± 15 l/min) was calculated by measuring the pressure drop across calibrated orifices located at the inlet and exhaust of each chamber. Leaks in the chambers could be detected by comparison of the inlet flow rate with exhaust flow rate. Flow was established by a gate valve in the exhaust line of each chamber. Chamber vacuum, relative to the control center, (± 0.2 cm H₂O) was measured using the same pressure transducer system which measured chamber air flows. Chamber vacuum was maintained at approximately (-1) cm H₂O primarily by inlet resistance provided by the HEPA and charcoal filters.

ANALYTICAL CHEMISTRY

Test Material Bulk Analysis

Isoprene (Goodyear Tire and Rubber Co., Beaumont Chemical Plant, Beaumont, TX) was received in cylinders containing ~45 kg of test material. The identity of the bulk material was confirmed by infrared spectroscopy, and the initial percent purity was found to be >99% (cumulative total for all cylinders) by determining the percent of the total peak area that was represented by the isoprene peak. Purity analyses were performed by gas chromatography (GC) on a Hewlett Packard (HP) 5890 equipped with a 6 ft x 4 mm glass column packed with Porapak QS 80/100. Cylinders were also analyzed for dimer (limonene) content by gas chromatography using a 6 ft x 2 mm glass column packed with 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport. Quantitation of limonene (dimer) was made against a gravimetrically prepared limonene standard. Cylinders with a limonene content >1% were considered unusable as exposure material. (See Appendix A for further detail.)

Isoprene was stored at room temperature prior to use. The teratology studies consumed approximately 4.5 kg/day, a total of 115 kg.

Exposure Chamber Monitoring

The concentrations of isoprene vapor in the chambers were monitored at 20-30 min intervals with an HP5840 GC system. This instrument was equipped with an 8-port stream select valve, and measured isoprene vapor levels in the three exposure chambers, the control chamber, the holding chamber, the exposure room, the on-line standard, and the nitrogen blank. In order to confirm values generated by the on-line monitor, bubbler grab samples were collected from the chamber and analyzed on an HP5840 GC. An on-line, certified gas standard, 2000 ppm isoprene in nitrogen, was used to check instrument drift throughout the exposure day.

Precision of the on-line GC was estimated by taking 8 consecutive measurements of the on-line standard, one from every sampling port. A 0.13% coefficient of variation was observed. Accuracy of the on-line GC was assured

by calibrating it against a gravimetrically calibrated GC. (See Appendix A.) The minimum detectable limit of the GC was estimated from the decay profile for the 7000-ppm chamber and was found to be 0.04 ppm isoprene.

Degradation and Stability Studies

The chemical stability of isoprene vapor in occupied and unoccupied chambers was determined for the 280- and 7000-ppm chambers as well as for the distribution line and the evaporator flask. Grab samples collected onto charcoal sampling tubes were desorbed with 1.0 ml dodecane and analyzed by gas chromatography. Concentrations of impurities found in the distribution line and chamber grab samples were similar to those observed in the pre-exposure cylinder sample, <0.2%. Thus, no detectable degradation of test material was observed during the generation of isoprene vapor. Analysis of evaporator flask residues at the end of the exposure day demonstrated the accumulation of the thermally catalyzed dimer, limonene; however this compound was not detected in the exposure chambers due to its lower volatility. The evaporator residue was also analyzed for isoprene peroxide content and was found to contain <0.1 meq/kg.

ANIMAL HUSBANDRY

Upon receipt, all animals were housed in quarantine rooms for 3-4 weeks prior to the start of exposure. Males and females were housed separately on stainless steel wire racks equipped with automatic waterers (10 mice per cage, 3-6 rats per cage). During the quarantine period five males and five females of each species were killed and examined for gross and microscopic lesions. Nasopharyngeal washes from these animals were cultured for bacterial pathogens. Serum from each animal was tested for antibodies to selected pathogens (Appendix D). Another check for antibodies to selected pathogens was performed on serum obtained at the final sacrifice from five females in the 0-ppm group and from five females in the highest exposure group for each species. All results were negative for significant pathogens and lesions. Study animals were observed daily for mortality, morbidity, and overt signs of toxicity.

Food, pelleted NIH-07 diet (Ziegler Bros., Inc., Gardner, PA), was provided *ad libitum* during the entire time the animals were in the test facility except during the 6-h exposure period when it was removed to prevent contamination and oral ingestion of the test material. Water was provided *ad libitum* with automatic waterers throughout the study. Room lighting was maintained on a 12-h on-off cycle (0600-1800 h for the light phase). During the quarantine period animal room temperature was maintained at $75\pm 3^{\circ}\text{F}$ and the percent relative humidity was maintained at $50\pm 15\%$.

Average chamber temperatures during the exposure periods were within the limits of $75\pm 3^{\circ}\text{F}$. Daily chamber temperature means for all exposure days were within the specified limits. Mean percent relative humidity in all exposure chambers was within the specified limits of $55\pm 15\%$. The average air flow in all chambers for the study was within the specified limits of 12 to 18 CFM. A complete summary of the daily chamber environmental data can be found in Appendix B.

DEVELOPMENTAL TOXICOLOGY

Female mice and rats were weighed and individually identified by eartags 1-2 weeks prior to mating. At this time forty virgin females of each species were randomly selected using body weight as the blocking variable. The remaining females were available for breeding by caging two to three females overnight with each male. A positive mating was established on the following morning by the presence of a vaginal plug in the case of the mice; or for rats, by a sperm-positive vaginal lavage. If mating was detected, this day was designated as 0 days of gestation (dg) and positively mated females were weighed and randomly assigned to exposure groups using body weight as the blocking variable. Mating was conducted for four consecutive nights for each species to obtain 132 positively mated female mice (33/group), and 114 positively mated rats (28-29/group). The positively mated females were individually caged on 0 dg (virgins were individually caged eight days prior to exposure) in an open exposure chamber for the purposes of acclimation. The virgin females were assigned to the four exposure groups based on weights obtained 3 and 6 days before exposure, mice and rats respectively.

Mice were exposed from 6-17 dg and sacrificed on 18 dg. Rats were exposed from 6-19 dg and sacrificed on 20 dg. Virgin mice were exposed for 12 consecutive days and rats for 14 consecutive days, concurrently with mated animals, and were sacrificed 1 day after their last exposure day. Mated female mice were weighed on 0, 6, 9, 12, 15 and 18 dg, and rats on 0, 6, 10, 14, 17 and 20 dg. Virgin mice and rats were weighed 3 and 6 days prior to the start of exposure, respectively, and on exposure days 1, 5, and 10, and at sacrifice.

At the time of sacrifice, rats and mice were killed with CO₂, weighed and examined grossly for signs of maternal toxicity. Maternal liver and kidney weights were obtained, and both ovaries were saved for sectioning and quantitative follicle counts (performed by another laboratory designated by the sponsor; data will not be presented in this report). Apparently nongravid uteri from mated females were stained with 10% ammonium sulfide to detect possible implantation sites. The number, position and status of implants were recorded for each gravid uterus. Placentas were examined and discarded unless abnormal.

Live fetuses were weighed, examined for gross defects, and their sex was determined by internal examination of the gonads after a lethal injection of Nembutal® (sodium pentobarbital). Fifty percent of the live fetuses (randomly selected) from each litter and any fetuses with gross external abnormalities were examined for visceral defects by dissection of fresh tissue (modified from the method of Staples 1977). The heads of fifty percent of the live fetuses were removed and placed in Bouin's fixative. After fixation the heads were serially sectioned with a razor blade and examined for soft-tissue craniofacial abnormalities. All fetal carcasses, with and without heads, were prepared for skeletal staining. Cartilage as well as ossified bone was visualized by double-staining with alcian blue and alizarin red S. The individual identity of each skeletal and head specimen was maintained throughout the study.

STATISTICAL ANALYSES

All means and standard deviations for animal data were calculated with SAS statistical software on a VAX 11/780 computer. Mean body weights (as a mean of litter means for fetal data) were analyzed using the SAS General Linear Models (GLM) Procedure (SAS, 1985) with an analysis of variance (ANOVA) model for unbalanced data. Response variables, either body weight or the arc-sin transformations of proportional incidence data, were analyzed against the class variable, "treatment", in a one-way ANOVA model. A Tukey's t-test (two-tailed) was used to assess statistically significant differences between control and exposed groups. If appropriate, the dose-response relationship was determined by means of an orthogonal trend test (Winer, 1971). In the case of proportional data the t-tests and trend analyses were performed on transformed variables. The litter was used as the basis for analysis of fetal variables.

RESULTS

EXPOSURE AND CHEMISTRY

Test material stability studies indicated that the materials and techniques used to generate isoprene vapor for inhalation exposures did not affect its stability. The chemical stability of isoprene was evaluated in the exposure chambers (with and without animals) by direct measurements of chamber atmospheres for potential isoprene degradation products. Results of these analyses demonstrated that degradation products were not produced in significant amounts. (Appendix A).

The test material concentration uniformity data for each chamber during prestart testing, and after animals were in place was acceptable in all chambers according to the limits defined in Table 1. To provide easier interpretation of the uniformity measurement results, the concentration readings for each port are expressed as a percentage of the mean value at all ports measured. The table includes analysis of Total Port Variability (TPV), Within Port Variability (WPV) and Between Port Variability (BPV): all are expressed as % Relative Standard Deviation (%RSD). The possible variation of

test chemical concentration measured from one sample port to another during the measurement procedure is termed the Total Port Variability and consists of both spatial and temporal variations. Two factors contribute to the TPV, 1) the Between Port Variability (BPV) which is the factor of interest as it represents the spatial variation of test chemical distribution within the chamber, and 2) the Within Port Variability (WPV) which represents the temporal fluctuation of the average chemical concentration within the chamber during the time the measurements were taken. This temporal factor includes variations in vapor generation as well as variation of the measurement instrument itself.

Summaries of the isoprene concentration data for the mouse study showed that the grand mean of the isoprene concentration in each chamber was between 99% and 100% of the target, with the overall RSDs in the range of 2 to 7% (Table 2). More than 99% of all individual concentration measurements were within $\pm 10\%$ of the specified operating limits for the target levels. The maximum concentration observed in the control chamber, the holding chamber, and in the room were 0.2, 0 and 0.6 ppm, respectively.

The grand means of chamber concentrations for all exposure levels for the rat study were 100% of the target with relative standard deviations in the range of 2 to 6% (Table 3). At least 99% of all individual concentration measurements were within $\pm 10\%$ of the specified operating limits for the exposure target level. There was no measurable concentration in the control and holding chambers. The maximum concentration observed in the room was 0.8 ppm.

Chamber air flow, temperature and relative humidity data for both mouse and rat exposures were all within specified limits (Appendix B).

DEVELOPMENTAL TOXICOLOGY: RAT

The mean pregnancy rate of the sperm-positive females was 87.7%. There were no deaths or overt symptoms of toxicity for virgin or pregnant rats. Mean body weights of virgin female rats were not significantly affected at any time during the 14-day exposure period or at sacrifice (Table 4). Similarly

there were no significant reductions in maternal body weight (Figure 5), uterine weight or extra-gestational weight gain (Table 5). However, dams in the 7000-ppm group had a lower weight gain between 6 and 10 dg than the other groups, but the rate of gain for this group was comparable to the other groups from 10-20 dg. The mean liver and kidney weights of pregnant dams were not affected by exposure to isoprene (Table 6). However, there was a slight, but statistically significant increase in the percent kidney to body weight (on 20 dg) ratio for the 7000-ppm group (Table 6). The increase of this ratio was significantly correlated to increasing exposure concentration.

Gestational exposure of rats to isoprene vapors on 6-19 dg had no statistically significant effect on the number of implants per dam, the number or percent of live fetuses per litter or on the number or percent of total intrauterine deaths (Table 7). There was an exposure-correlated increase in the mean percent of early resorptions, but since values for the 7000-ppm group were approximately equivalent to those found in the contemporary control data¹, 5.5 ± 6.1 and 5.3 ± 7.9 , respectively, the increase may not be biologically significant. (Contemporary control data are tabulated in Appendix C.) Neither fetal weights (as means of litter means) nor the fetal sex ratio were affected by gestational exposure to isoprene vapor (Table 8).

The incidence of fetal malformations was not significantly increased by gestational exposure of rats to isoprene vapors, nor was the percent of live fetuses with malformations per litter² affected (Tables 9 and 10). There were no malformations observed in exposed groups that were not present in the 0-ppm group. Gestational exposure to isoprene did not significantly increase the incidence of total fetal variations or reduced ossifications, although there was a treatment-correlated increase in the incidence of reduced vertebral

¹Concurrent control data is data from the 0-ppm exposure groups of several studies. All studies employed the same strain, very nearly the same age, and the same environmental conditions.

²The mean percent incidence per litter was calculated based on the number of live fetuses examined for a given malformation or variation per litter, i.e. the incidence of visceral defects was based on the number of fetuses in each litter that received a visceral exam.

ossifications per litter² (Tables 10 and 11). There was also a low incidence of reduced ossification of the ribs in the 7000-ppm group which was not observed in the 0-ppm group.

DEVELOPMENTAL TOXICOLOGY: MICE

The mean pregnancy rate of plug-positive female mice was 87.9%. A total of 4 mated mice were removed from the study; 3 because of premature delivery and one other due to its small litter size (≤ 2 implants). There were no deaths and no overt symptoms of toxicity evident in the plug-positive or virgin mice.

Mean body weights of virgin female mice were not affected by exposure to isoprene at any time during the 12-day exposure period or at sacrifice (Table 12); however, there was a significant reduction in body weights of pregnant mice for the 7000-ppm group at 15 dg and at sacrifice (18 dg) when compared to the 0-ppm group (Table 13). Cumulative body weight gains of dams in the 7000-ppm exposure group were significantly less than controls on 12, 15 and 18 dg (Figure 6). The mean uterine weight for the 7000-ppm group was also significantly reduced, but the extragestational weight gain was not affected. These reductions in weight were significantly correlated to increasing exposure concentrations. Mouse maternal liver and kidney weights were not significantly affected by this exposure regimen (Table 14), however, there were significant increases in both the liver and kidney to body weight ratios which were significantly correlated to increasing exposure concentrations.

Exposure of pregnant mice to isoprene vapors on 6-17 dg did not affect the number of implants, the number or percent of live pups per litter, or the number or percent of resorptions per litter (Table 15). However, female fetal body weights were significantly less than the 0-ppm group for all exposure levels, and male fetal weights were significantly reduced for the 1400- and 7000-ppm groups (Table 16). The decreases in fetal weights were significantly correlated with exposure concentrations. The relative fetal weight reduction (approximately 14% relative to control values) was equivalent for both male and female fetuses in the 7000-ppm group. The ratios of male to female fetuses in the litters were not affected.

The only malformation observed in fetal mice exposed to isoprene was cleft palate which was present in one fetus in each of the two highest exposure levels, 1400- and 7000-ppm (Tables 17 and 18). Gestational exposure to isoprene caused a treatment-correlated increase in the mean percent per litter of supernumerary ribs which was statistically significant for the 7000-ppm group (Tables 18 and 19). There was also a significant increase in the mean percent per litter of total variations and reduced ossifications, mostly as a result of the increase in the incidence of supernumerary ribs. Other sites examined for reduced ossifications included the skull, pelvis, phalanges, sternabrae and vertebrae; however, there were no reductions in the ossification of these areas.¹

DISCUSSION

Exposure of pregnant rats to 0, 280, 1400 or 7000 ppm isoprene did not result in apparent maternal toxicity (other than an increase in the kidney to body weight ratio of the dam at 7000 ppm) or in developmental toxicity. There were no treatment-related effects upon body weights or reproductive indices at any exposure level, nor was there a significant increase in the incidence of fetal malformations or variations. The only developmentally toxic effect observed was a slight, but exposure-correlated increase in the incidence of reduced vertebral ossifications (centra) which indicates that the 7000-ppm exposure level may be at or near a developmental toxicity threshold.

Exposure of Swiss (CD-1) mice to 0, 280, 1400 or 7000 ppm isoprene resulted in significant reductions in maternal body weight and uterine weight for dams in the 7000-ppm group. Since neither the extra-gestational weight gain of the pregnant dams, nor the body weight gain of the virgin animals was affected there was an indication of selective developmental toxicity at the 7000-ppm exposure level. Developmental toxicity was further evident as an exposure-correlated reduction in fetal body weights which became statistically

¹ The mean percent incidence per litter was calculated based on the number of live fetuses examined for a given malformation or variation per litter, i.e. the incidence of visceral defects was based on the number of fetuses in each litter that received a visceral exam.

significant at the lowest exposure level (280 ppm) for female fetuses and at the middle exposure level (1400 ppm) for male fetuses. Fetuses of dams exposed to isoprene had an increased incidence of supernumerary ribs which was significantly correlated to increasing exposure concentration and was statistically significant for the 7000-ppm group. There was no significant increase in the incidence of malformations; however, two fetuses with cleft palate were found, one in each of the two highest exposure groups. Although an occasional cleft palate is not unusual, cleft palates were not detected in the control group for this study or in the control groups from other recently completed studies and may be indicative of developmental toxicity.

The differences in species sensitivity with regard to developmental toxicity were comparable between isoprene and 1,3-butadiene. Although the 1,3-butadiene exposure concentrations were lower (Hackett et al. 1987a and 1987b), Swiss (CD-1) mice exposed to 0, 40, 200 or 1000 ppm 1,3-butadiene, under the same exposure conditions as isoprene, exhibited developmental toxicity in the absence of maternal toxicity at 40 ppm. Fetal body weights of female fetuses in the 40-ppm group were significantly less than those for the control group and the male body weights were significantly reduced at 200 ppm. There was a significant reduction in maternal body weight and in extra-gestational weight gain in both the 200- and 1000-ppm groups, but not for the 40-ppm group. In the 200- and 1000-ppm groups, this maternal toxicity was accompanied by a significant increase in the incidence of supernumerary ribs in the offspring; and, in the 1000-ppm group, by significant increases in the incidences of reduced ossifications and abnormal sternebrae.

Sprague-Dawley rats gestationally exposed to 1,3-butadiene, like those exposed to isoprene, did not exhibit developmental toxicity in the absence of maternal toxicity at any of the 1,3-butadiene exposure concentrations.

In summary, pregnant Sprague-Dawley rats and their offspring, appear to be relatively resistant to the toxic effects of isoprene at the exposure concentrations employed in this study. Swiss (CD-1) mice on the other hand, exhibited significant signs of developmental toxicity in the absence of reductions in extra-gestational weight gain at all the exposure concentrations employed. In light of these results the 7000-ppm isoprene level could be set

as a no observable effect level (NOEL) in the Sprague-Dawley (CD) rat for both developmental and maternal toxicity; however, a NOEL based on the results of this study cannot be assigned to the Swiss (CD-1) mouse for developmental toxicity but for maternal toxicity a NOEL of 1400 ppm could probably be assigned.

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FIGURE 2. Metabolism Scheme for 1,3-Butadiene.

FIGURE 3. Isoprene Generation and Delivery System

ISOPRENE IRT: 280 ppm Chamber

ISOPRENE IRT: 1400 ppm Chamber

ISOPRENE IRT: 7000 ppm Chamber

FIGURE 4. Buildup and Decay of Isoprene Concentrations in 280, 1400, and 7000 ppm Exposure Chambers (With and Without Animals Present).

FIGURE 5. Isoprene Rat Teratology: Cumulative Weight Gain

FIGURE 6. Isoprene Mouse Teratology: Cumulative Weight Gain

TABLE 1. Isoprene Teratology Study: Summary of Chamber Uniformity Data
Obtained Before and During Exposure of Mice and Rats.

Chamber	TPV (%RSD)		WPV (%RSD)		BPV (%RSD)	
	<u>Pre</u>	<u>Post</u>	<u>Pre</u>	<u>Post</u>	<u>Pre</u>	<u>Post</u>
280 ppm	1.0	0.3	1.6	0.5	*	*
1400 ppm	0.4	0.1	0.7	0.1	*	*
7000 ppm	0.5	0.2	1.0	0.2	*	*

*Indistinguishable from WPV

Chamber Uniformity Limits

WPV $\leq$ 5% RSD

BPV $\leq$ 5% RSD

TPV $\leq$ 7% RSD

TPV: Total Port Variability

WPV: Within Port variability

BPV: Between Port Variability

TABLE 2. Isoprene Teratology Study: Average Daily Exposure Chamber Concentrations for Mouse Exposures.

0 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (b)	Percent in Range
1	<MDL (a)	<MDL	<MDL	20	20	100
2	<MDL	0.21	<MDL	18	18	100
3	<MDL	<MDL	<MDL	19	19	100
4	<MDL	<MDL	<MDL	19	19	100
5	<MDL	<MDL	<MDL	20	20	100
6	<MDL	<MDL	<MDL	18	18	100
7	<MDL	<MDL	<MDL	19	19	100
8	<MDL	<MDL	<MDL	20	20	100
9	<MDL	<MDL	<MDL	19	19	100
10	<MDL	<MDL	<MDL	15	15	100
11	<MDL	<MDL	<MDL	8	8	100
12	<MDL	<MDL	<MDL	15	15	100
13	<MDL	<MDL	<MDL	20	20	100
14	<MDL	<MDL	<MDL	19	19	100
15	<MDL	<MDL	<MDL	20	20	100
Summary	<MDL	0.21	<MDL	269	269	100

(a) Minimum Detectable Limit (MDL)=0.04 ppm Isoprene.

(b) Range=0-1 ppm Isoprene.

280 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	277 $\pm$ 6	289	267	17	17	100
2	277 $\pm$ 6	289	265	16	16	100
3	279 $\pm$ 4	288	273	16	16	100
4	281 $\pm$ 3	287	278	17	17	100
5	283 $\pm$ 4	293	278	17	17	100
6	276 $\pm$ 17	295	223	15	14	93
7	279 $\pm$ 6	289	272	16	16	100
8	276 $\pm$ 5	285	267	16	16	100
9	279 $\pm$ 5	289	272	16	16	100
10	275 $\pm$ 6	288	261	15	15	100
11	281 $\pm$ 8	292	267	8	8	100
12	277 $\pm$ 3	284	272	15	15	100
13	278 $\pm$ 4	289	271	16	16	100
14	279 $\pm$ 3	286	275	16	16	100
15	280 $\pm$ 5	295	271	16	16	100
Summary	278 $\pm$ 7	295	223	232	231	100

(a) Range = $\pm$ 10% target.

TABLE 2. (contd)

1400 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	1400 $\pm$ 42	1530	1340	17	17	100
2	1390 $\pm$ 38	1420	1310	15	15	100
3	1400 $\pm$ 17	1440	1370	16	16	100
4	1440 $\pm$ 15	1480	1420	18	18	100
5	1440 $\pm$ 23	1490	1410	17	17	100
6	1360 $\pm$ 187	1470	695	15	14	93
7	1410 $\pm$ 30	1470	1370	16	16	100
8	1390 $\pm$ 19	1430	1370	17	17	100
9	1400 $\pm$ 24	1440	1360	16	16	100
10	1390 $\pm$ 51	1510	1270	14	14	100
11	1390 $\pm$ 32	1440	1330	8	8	100
12	1410 $\pm$ 15	1440	1380	15	15	100
13	1390 $\pm$ 29	1450	1320	16	16	100
14	1400 $\pm$ 14	1440	1390	16	16	100
15	1400 $\pm$ 22	1450	1370	16	16	100
Summary	1400 $\pm$ 56	1530	695	232	231	100

(a) Range = $\pm 10\%$ target.

7000 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	7030 $\pm$ 140	7300	6800	17	17	100
2	6970 $\pm$ 116	7290	6740	16	16	100
3	7010 $\pm$ 68	7140	6890	17	17	100
4	7110 $\pm$ 51	7210	7040	17	17	100
5	7130 $\pm$ 105	7380	7020	17	17	100
6	6560 $\pm$ 1812	7290	31	15	14	93
7	6970 $\pm$ 145	7290	6750	16	16	100
8	6930 $\pm$ 100	7100	6790	17	17	100
9	6980 $\pm$ 79	7170	6840	16	16	100
10	7000 $\pm$ 158	7460	6780	13	13	100
11	6990 $\pm$ 119	7120	6760	7	7	100
12	7080 $\pm$ 91	7240	6850	15	15	100
13	6980 $\pm$ 111	7350	6870	17	17	100
14	7000 $\pm$ 56	7140	6930	16	16	100
15	7000 $\pm$ 109	7250	6780	17	17	100
Summary	6980 $\pm$ 473	7460	31	233	232	100

(a) Range = $\pm 10\%$ target.

TABLE 3. Isoprene Teratology Study: Average Daily Exposure Chamber Concentrations for Rat Exposures.

0 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (b)	Percent in Range
1	<MDL (a)	<MDL	<MDL	20	20	100
2	<MDL	<MDL	<MDL	18	18	100
3	<MDL	<MDL	<MDL	19	19	100
4	<MDL	<MDL	<MDL	20	20	100
5	<MDL	<MDL	<MDL	19	19	100
6	<MDL	<MDL	<MDL	15	15	100
7	<MDL	<MDL	<MDL	8	8	100
8	<MDL	<MDL	<MDL	15	15	100
9	<MDL	<MDL	<MDL	20	20	100
10	<MDL	<MDL	<MDL	19	19	100
11	<MDL	<MDL	<MDL	20	20	100
12	<MDL	<MDL	<MDL	19	19	100
13	<MDL	<MDL	<MDL	19	19	100
14	<MDL	<MDL	<MDL	17	17	100
15	<MDL	<MDL	<MDL	19	19	100
16	<MDL	<MDL	<MDL	19	19	100
17	<MDL	<MDL	<MDL	20	20	100
18	<MDL	<MDL	<MDL	18	18	100
Summary	<MDL	<MDL	<MDL	324	324	100

(a) Minimum Detectable Limit (MDL)=0.04 ppm Isoprene.

(b) Range=0-1 ppm Isoprene

280 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	276 $\pm$ 17	295	223	15	14	93
2	279 $\pm$ 6	289	272	16	16	100
3	276 $\pm$ 5	285	267	16	16	100
4	279 $\pm$ 5	289	272	16	16	100
5	275 $\pm$ 6	288	261	15	15	100
6	281 $\pm$ 8	292	267	8	8	100
7	277 $\pm$ 3	284	272	15	15	100
8	278 $\pm$ 4	289	271	16	16	100
9	279 $\pm$ 3	286	275	16	16	100
10	280 $\pm$ 5	295	271	16	16	100
11	284 $\pm$ 6	295	278	17	17	100
12	281 $\pm$ 7	305	268	16	16	100
13	284 $\pm$ 6	297	279	16	16	100
14	286 $\pm$ 4	290	279	16	16	100
15	279 $\pm$ 1	282	277	16	16	100
16	275 $\pm$ 6	284	265	16	16	100
17	280 $\pm$ 3	286	276	16	16	100
Summary	279 $\pm$ 7	305	223	262	261	100

(a) Range = $\pm$ 10% target.

TABLE 3. (contd)

1400 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	1360 $\pm$ 187	1470	695	15	14	93
2	1410 $\pm$ 30	1470	1370	16	16	100
3	1390 $\pm$ 19	1430	1370	17	17	100
4	1400 $\pm$ 24	1440	1360	16	16	100
5	1390 $\pm$ 51	1510	1270	14	14	100
6	1390 $\pm$ 32	1440	1330	8	8	100
7	1410 $\pm$ 15	1440	1380	15	15	100
8	1390 $\pm$ 29	1450	1320	16	16	100
9	1400 $\pm$ 14	1440	1390	16	16	100
10	1400 $\pm$ 22	1450	1370	16	16	100
11	1410 $\pm$ 43	1490	1350	16	16	100
12	1400 $\pm$ 34	1480	1330	16	16	100
13	1400 $\pm$ 18	1450	1380	16	16	100
14	1400 $\pm$ 16	1420	1370	16	16	100
15	1390 $\pm$ 29	1430	1350	16	16	100
16	1410 $\pm$ 23	1440	1370	16	16	100
17	1410 $\pm$ 15	1440	1390	16	16	100
Summary	1400 $\pm$ 52	1510	695	261	260	100

(a) Range = $\pm$ 10% target.

7000 ppm Isoprene Vapor						
Exposure Day	Mean $\pm$ SD (ppm)	Max (ppm)	Min (ppm)	Number Samples	Number in Range (a)	Percent in Range
1	6560 $\pm$ 1812	7290	31	15	14	93
2	6970 $\pm$ 145	7290	6750	16	16	100
3	6930 $\pm$ 100	7100	6790	17	17	100
4	6980 $\pm$ 79	7170	6840	16	16	100
5	7000 $\pm$ 158	7460	6780	13	13	100
6	6990 $\pm$ 119	7120	6760	7	7	100
7	7080 $\pm$ 91	7240	6850	15	15	100
8	6980 $\pm$ 111	7350	6870	17	17	100
9	7000 $\pm$ 56	7140	6930	16	16	100
10	7000 $\pm$ 109	7250	6780	17	17	100
11	7070 $\pm$ 148	7320	6850	16	16	100
12	7050 $\pm$ 169	7650	6830	16	16	100
13	7020 $\pm$ 86	7230	6910	16	16	100
14	7050 $\pm$ 77	7140	6850	16	16	100
15	6920 $\pm$ 87	7070	6820	17	17	100
16	6980 $\pm$ 114	7140	6790	17	17	100
17	7040 $\pm$ 47	7150	6980	16	16	100
Summary	6980 $\pm$ 446	7650	31	263	262	100

(a) Range = $\pm$ 10% target.

TABLE 4. Isoprene Teratology Study: Mean Body Weights for Virgin Rats (g $\pm$ SD).

Exposure Concentration	N	Exposure Day 1	Exposure Day 5	Exposure Day 10	Sacrifice
0 ppm	10	252.9 $\pm$ 23.0	260.5 $\pm$ 24.0	265.4 $\pm$ 24.0	264.3 $\pm$ 24.0
280 ppm	10	250.9 $\pm$ 26.2	263.9 $\pm$ 26.3	272.6 $\pm$ 28.4	269.4 $\pm$ 25.1
1400 ppm	10	250.8 $\pm$ 21.5	261.4 $\pm$ 22.9	265.9 $\pm$ 21.4	269.1 $\pm$ 24.4
7000 ppm	10	250.8 $\pm$ 25.9	255.9 $\pm$ 25.6	257.1 $\pm$ 23.2	259.6 $\pm$ 26.7

TABLE 5. Isoprene Teratology Study: Mean Body, Uterine, and Extra-gestational Weights of Pregnant Rats (g $\pm$ SD).

Exposure Concentration	N	DG0	DG6	DG10	DG14	DG17	DG20	Uterine	Extra-gestational Weight gain
0 ppm	26	247.7 $\pm$ 22.6	270.1 $\pm$ 23.8	282.0 $\pm$ 30.6	301.8 $\pm$ 29.0	326.0 $\pm$ 30.8	359.2 $\pm$ 32.9	70.0 $\pm$ 11.8	41.6 $\pm$ 12.3
280 ppm	25	246.1 $\pm$ 21.7	266.4 $\pm$ 22.6	282.0 $\pm$ 24.0	301.7 $\pm$ 25.7	324.2 $\pm$ 28.9	356.3 $\pm$ 33.1	71.3 $\pm$ 9.0	39.0 $\pm$ 27.3
1400 ppm	25	248.3 $\pm$ 22.9	272.8 $\pm$ 25.6	287.2 $\pm$ 28.2	307.6 $\pm$ 29.2	334.2 $\pm$ 32.5	367.5 $\pm$ 37.9	72.0 $\pm$ 11.5	47.2 $\pm$ 14.4
7000 ppm	24	249.7 $\pm$ 19.7	270.8 $\pm$ 19.5	276.3 $\pm$ 18.4	297.2 $\pm$ 18.9	322.4 $\pm$ 19.9	352.1 $\pm$ 24.8	65.0 $\pm$ 12.4	37.4 $\pm$ 12.7

TABLE 6. Isoprene Teratology Study: Mean Organ Weights of Pregnant Rats (g $\pm$ SD).

Exposure Concen- tration	N	Liver	Percent LBWR (a)	Kidney	Percent KBWR (b,c)
0 ppm	26	14.58 $\pm$ 1.30	4.07 $\pm$ 0.24	1.90 $\pm$ 0.18	0.53 $\pm$ 0.04
280 ppm	25	14.53 $\pm$ 2.01	4.07 $\pm$ 0.35	1.92 $\pm$ 0.22	0.54 $\pm$ 0.04
1400 ppm	25	14.85 $\pm$ 1.85	4.04 $\pm$ 0.32	1.99 $\pm$ 0.22	0.54 $\pm$ 0.05
7000 ppm	24	14.97 $\pm$ 1.72	4.25 $\pm$ 0.35	1.99 $\pm$ 0.21	0.57 $\pm$ 0.05 (d)

(a) Percent LBWR=Percent Liver to Body Weight Ratio.

(b) Percent KBWR=Percent Kidney to Body Weight Ratio.

(c) Significantly correlated with exposure concentration, $p < 0.05$.

(d) Significantly different than control, $p < 0.05$.

TABLE 7. Isoprene Teratology Study: Reproductive Measures for Rats (mean $\pm$ SD).

	Isoprene Chamber Concentration (ppm)			
	0	280	1400	7000
Sperm-positive Females	29	28	29	28
Number Pregnant	26	25	25	24
Pregnant (%)	89.7	89.3	86.2	85.7
Pregnancies Examined	26	25	25	24
Implantations/Dam	14.2 $\pm$ 2.2	14.6 $\pm$ 1.5	14.9 $\pm$ 1.9	13.8 $\pm$ 2.6
Live Fetuses/Litter	13.8 $\pm$ 2.4	13.9 $\pm$ 1.7	14.1 $\pm$ 2.1	13.1 $\pm$ 2.6
Resorptions/Litter: Total	0.4 $\pm$ 0.6	0.6 $\pm$ 0.9	0.8 $\pm$ 0.8	0.7 $\pm$ 0.8
Early	0.2 $\pm$ 0.4	0.6 $\pm$ 0.9	0.6 $\pm$ 0.8	0.7 $\pm$ 0.8
Late	0.2 $\pm$ 0.4	0.1 $\pm$ 0.4	0.2 $\pm$ 0.4	0
Dead Fetuses/Litter	0	0	0	0
Litters with Resorptions	9	10	14	13
PERCENTAGE OF:				
Live Fetuses/Litter	97.2 $\pm$ 4.3	95.6 $\pm$ 6.3	94.4 $\pm$ 5.9	94.5 $\pm$ 6.1
Resorptions/Litter: Total	2.8 $\pm$ 4.3	4.4 $\pm$ 6.3	5.6 $\pm$ 5.9	5.5 $\pm$ 6.1
Early (a)	1.7 $\pm$ 3.1	3.7 $\pm$ 5.9	4.5 $\pm$ 5.9	5.5 $\pm$ 6.1
Late	1.2 $\pm$ 2.8	0.6 $\pm$ 3.1	1.1 $\pm$ 2.5	0
Dead Fetuses/Litter	0	0	0	0
Litters with Resorptions	34.6	40.0	56.0	54.2

(a) Significantly correlated with exposure concentration after arcsine transformation, $p < 0.05$.

TABLE 8. Isoprene Teratology Study: Average Rat Fetal Weights (Means of Litter Means; $g \pm$ SD), and Percent Male Fetuses.

	Isoprene Chamber Concentration (ppm)			
	0	280	1400	7000
Litter Examined	26	25	25	24
Live Fetuses Examined	359	348	352	315
Fetal Weight	3.33 $\pm$ 0.23	3.37 $\pm$ 0.28	3.37 $\pm$ 0.21	3.31 $\pm$ 0.23
Male	3.38 $\pm$ 0.23	3.45 $\pm$ 0.28	3.47 $\pm$ 0.24	3.40 $\pm$ 0.24
Female	3.27 $\pm$ 0.24	3.30 $\pm$ 0.28	3.29 $\pm$ 0.22	3.21 $\pm$ 0.22
Percent Male Fetuses	54.5 $\pm$ 14.9	48.0 $\pm$ 16.4	45.6 $\pm$ 12.1	52.4 $\pm$ 13.0

TABLE 9. Isoprene Teratology Study: Malformations Observed in Live Rat Fetuses.

		Fetuses (a)				Litters (a)			
Isoprene (ppm)		0	280	1400	7000	0	280	1400	7000
Total Examined (b)		359	348	352	315	26	25	25	24
Heads examined (c)		183	175	181	157	26	25	25	24
Skulls examined (d)		176	173	171	158	26	25	25	24
Viscera examined (e)		178	173	173	158	26	25	25	24
Malformations:									
Exencephaly	NO. (%)	1 (0.3)	0	0	0	1 (3.9)	0	0	0
Anophthalmia	NO. (%)	1 (0.5)	0	1 (0.6)	0	1 (3.9)	0	1 (4.0)	0
Rachischisis	NO. (%)	1 (0.3)	0	0	0	1 (3.9)	0	0	0
Umbilical Hernia	NO. (%)	1 (0.3)	1 (0.3)	1 (0.3)	0	1 (3.9)	1 (4.0)	1 (4.0)	0
Total Malformations	NO.	4	1	2	0	---	---	---	---
Total Fetuses (Litters) with Malformations	NO. (%)	2 (0.6)	1 (0.3)	2 (0.6)	0	2 (7.7)	1 (4.0)	2 (8.0)	0

(a) A single fetus or litter may be represented more than once in this table.

(b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.

(c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.

(d) Heads remaining on the fetuses for skeletal examination; see (b).

(e) Viscerals performed on approx. 50% of live fetuses and all fetuses with external defects.

TABLE 10. Isoprene Teratology Study: Mean Percent of Live Rat Fetuses Affected per Litter (Mean $\pm$ SD).

	Isoprene Concentration (ppm)			
	0	280	1400	7000
Number Litters	26	25	25	24
Live Fetuses/Litter	13.8 $\pm$ 2.4	13.9 $\pm$ 1.7	14.1 $\pm$ 2.1	13.1 $\pm$ 2.6
Malformations:				
Exencephaly	0.3 $\pm$ 1.5	0	0	0
Anophthalmia	0.5 $\pm$ 2.8	0	0.4 $\pm$ 2.2	0
Rachischisis	0.3 $\pm$ 1.5	0	0	0
Umbilical Hernia	0.2 $\pm$ 1.2	0.3 $\pm$ 1.7	0.3 $\pm$ 1.5	0
Total Malformations	1.1 $\pm$ 4.6	0.3 $\pm$ 1.7	0.6 $\pm$ 2.0	0
Variations:				
Misaligned Sternebrae	0.6 $\pm$ 2.0	0.3 $\pm$ 1.3	0.6 $\pm$ 3.1	0
Rudimentary Rib	0	0.4 $\pm$ 1.8	0.9 $\pm$ 3.2	1.4 $\pm$ 6.8
Renal Pelvic Cavitation	0	0	1.7 $\pm$ 6.3	0
Dilated Ureter	2.3 $\pm$ 7.2	3.6 $\pm$ 7.9	3.4 $\pm$ 7.4	1.2 $\pm$ 4.2
Missing Innominate	0.5 $\pm$ 2.8	0	0.5 $\pm$ 2.5	0
Reduced Ossifications:				
Sternebrae	9.6 $\pm$ 12.6	6.3 $\pm$ 17.5	5.8 $\pm$ 10.0	7.8 $\pm$ 12.2
Vertebrae, centra (a)	1.6 $\pm$ 4.9	4.2 $\pm$ 11.6	3.3 $\pm$ 7.3	7.1 $\pm$ 11.8
Phalanges	1.1 $\pm$ 3.5	2.0 $\pm$ 6.0	0.9 $\pm$ 3.3	0
Pelvis	1.7 $\pm$ 4.3	4.0 $\pm$ 15.9	1.8 $\pm$ 4.1	1.3 $\pm$ 3.9
Skull	2.7 $\pm$ 14.0	1.1 $\pm$ 3.7	0	1.7 $\pm$ 4.6
Ribs	0	0	0.4 $\pm$ 2.0	0.3 $\pm$ 1.7
Total Variations and Reduced Ossifications	17.4 $\pm$ 24.8	19.7 $\pm$ 49.5	16.5 $\pm$ 17.7	19.5 $\pm$ 24.0

(a) Significantly correlated with exposure concentration, $p < 0.05$.

TABLE 11. Isoprene Teratology Study: Variations Observed in Live Rat Fetuses.

		Fetuses (a)				Litters (a)			
Isoprene (ppm)		0	280	1400	7000	0	280	1400	7000
Total Examined (b)		359	348	352	315	26	25	25	24
Heads examined (c)		183	175	181	157	26	25	25	24
Skulls examined (d)		176	173	171	158	26	25	25	24
Viscera examined (e)		178	173	173	158	26	25	25	24
Variations:									
Misaligned Sternebrae	NO. (%)	2 (0.6)	1 (0.3)	2 (0.6)	0	2 (7.7)	1 (4.0)	1 (4.0)	0
Rudimentary Rib	NO. (%)	0	1 (0.3)	4 (1.1)	4 (1.3)	0	1 (4.0)	2 (8.0)	1 (4.2)
Renal Pelvic Cavitation	NO. (%)	0	0	3 (1.7)	0	0	0	2 (8.0)	0
Dilated Ureter	NO. (%)	4 (2.3)	7 (4.1)	6 (3.5)	2 (1.3)	3 (11.5)	6 (24.0)	5 (20.0)	2 (8.3)
Missing Innominate	NO. (%)	1 (0.6)	0	1 (0.6)	0	1 (3.9)	0	1 (4.0)	0
Reduced Ossifications:									
Sternebrae	NO. (%)	35 (9.8)	22 (6.3)	21 (6.0)	26 (8.3)	14 (53.9)	8 (32.0)	11 (44.0)	10 (41.7)
Vertebrae, centra	NO. (%)	6 (1.7)	15 (4.3)	12 (3.4)	24 (7.6)	3 (11.5)	7 (28.0)	7 (28.0)	10 (41.7)
Phalanges	NO. (%)	4 (1.1)	7 (2.0)	3 (0.9)	0	3 (11.5)	4 (16.0)	2 (8.0)	0
Pelvis	NO. (%)	6 (1.7)	14 (4.0)	6 (1.7)	5 (1.6)	4 (15.4)	3 (12.0)	5 (20.0)	3 (12.5)
Skull	NO. (%)	5 (2.8)	2 (1.2)	0	3 (1.9)	1 (3.9)	2 (8.0)	0	3 (12.5)
Ribs	NO. (%)	0	0	2 (0.6)	1 (0.3)	0	0	1 (4.0)	1 (4.2)
Total Variations and Reduced Ossifications (f)	NO.	63	69	60	65	—	—	—	—
Total Fetuses (Litters) with Variations or Reduced Ossifications	NO. (%)	48 (13.4)	40 (11.5)	46 (13.1)	55 (17.5)	16 (61.5)	16 (64.0)	16 (64.0)	17 (70.8)

(a) A single fetus or litter may be represented more than once in this table.

(b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.

(c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.

(d) Heads remaining on the fetuses for skeletal examination; see (b).

(e) Viscerals performed on approx. 50% of live fetuses and all fetuses with external defects.

(f) There may be >1 variation or reduced ossification per fetus.

TABLE 12. Isoprene Teratology Study: Mean Body Weights for Virgin Mice(g $\pm$ SD).

Exposure Concentration	N	Exposure Day -2	Exposure Day 1	Exposure Day 5	Exposure Day 10	Sacrifice 1 day post-exp
0 ppm	10	28.7 $\pm$ 1.9	27.9 $\pm$ 1.5	28.4 $\pm$ 1.3	28.3 $\pm$ 1.3	27.8 $\pm$ 2.4
280 ppm	10	27.9 $\pm$ 2.4	28.1 $\pm$ 1.9	27.9 $\pm$ 1.9	28.3 $\pm$ 1.8	28.6 $\pm$ 2.0
1400 ppm	10	28.3 $\pm$ 1.2	28.1 $\pm$ 1.5	28.0 $\pm$ 1.6	28.9 $\pm$ 1.3	29.5 $\pm$ 1.9
7000 ppm	10	28.8 $\pm$ 2.3	28.1 $\pm$ 1.6	27.2 $\pm$ 1.5	27.7 $\pm$ 1.3	28.5 $\pm$ 1.7

TABLE 13. Isoprene Teratology Study: Mean Body, Uterine, and Extra-gestational Weights of Pregnant Mice (g $\pm$ SD).

Exposure Concentration	N	DG 0	DG 6	DG 9	DG 12 (a)	DG 15 (a)	Sacrifice DG 18 (a)	Uterine (a)	Extra-gestational Weight gain
0 ppm	28	28.4 $\pm$ 2.4	30.7 $\pm$ 2.0	32.4 $\pm$ 1.9	37.9 $\pm$ 2.4	45.5 $\pm$ 3.4	53.5 $\pm$ 4.9	19.1 $\pm$ 4.4	5.9 $\pm$ 1.9
280 ppm	29	28.4 $\pm$ 1.9	30.5 $\pm$ 2.2	32.3 $\pm$ 2.3	37.5 $\pm$ 3.3	45.4 $\pm$ 3.7	53.1 $\pm$ 5.0	19.3 $\pm$ 2.8	5.4 $\pm$ 2.0
1400 ppm	28	28.2 $\pm$ 2.1	30.4 $\pm$ 2.2	31.9 $\pm$ 2.5	37.3 $\pm$ 2.9	44.7 $\pm$ 3.3	52.5 $\pm$ 4.2	18.1 $\pm$ 3.0	6.2 $\pm$ 1.5
7000 ppm	27	28.2 $\pm$ 2.1	30.3 $\pm$ 1.9	32.2 $\pm$ 2.4	36.4 $\pm$ 2.6	43.2 $\pm$ 2.4 (b)	49.8 $\pm$ 4.3 (b)	15.9 $\pm$ 2.2 (b)	5.7 $\pm$ 2.8

(a) Significantly correlated with exposure concentration, $p < 0.05$.(b) Significantly different than control, $p < 0.05$.

TABLE 14. Isoprene Mouse Teratology Study: Mean Organ Weights of Pregnant Dams (g $\pm$ SD).

Exposure Concentration	N	Liver	Percent LBWR (c)	Kidney (a)	Percent KBWR (a,d)
0 ppm	28	2.96 $\pm$ 0.25	5.56 $\pm$ 0.47	0.47 $\pm$ 0.04	0.88 $\pm$ 0.09
280 ppm	29	3.01 $\pm$ 0.32	5.68 $\pm$ 0.41	0.46 $\pm$ 0.05	0.88 $\pm$ 0.08
1400 ppm	28	3.10 $\pm$ 0.29	5.91 $\pm$ 0.52(b)	0.48 $\pm$ 0.05	0.91 $\pm$ 0.09
7000 ppm	27	3.03 $\pm$ 0.23	6.11 $\pm$ 0.53(b)	0.50 $\pm$ 0.07	1.01 $\pm$ 0.11(b)

(a) Significantly correlated with exposure concentration, $p < 0.05$.

(b) Significantly different than controls $p < 0.05$.

(c) Percent LBWR=Percent Liver to Body Weight Ratio.

(d) Percent KBWR=Percent Kidney to Body Weight Ratio.

TABLE 15. Isoprene Teratology Study: Reproductive Measures for Mice (Mean $\pm$ SD).

	Isoprene Chamber Concentration (ppm)			
	0	280	1400	7000
Plug-positive Females	33	33	33	33
Number Pregnant	30	30	28	28
Pregnant (%)	90.9	90.9	84.8	84.8
Pregnancies Examined	28 (a,b)	29 (a)	28	27 (a)
Implantations/Dam	12.3 $\pm$ 2.9	12.8 $\pm$ 1.5	12.4 $\pm$ 2.1	12.0 $\pm$ 1.5
Live Fetuses/Litter	11.5 $\pm$ 3.0	12.0 $\pm$ 1.9	11.9 $\pm$ 2.2	10.9 $\pm$ 1.8
Resorptions/Litter	0.7 $\pm$ 0.8	0.7 $\pm$ 0.8	0.5 $\pm$ 0.8	1.0 $\pm$ 1.1
Early	0.5 $\pm$ 0.7	0.5 $\pm$ 0.7	0.4 $\pm$ 0.6	0.7 $\pm$ 1.0
Late	0.3 $\pm$ 0.5	0.2 $\pm$ 0.4	0.2 $\pm$ 0.4	0.3 $\pm$ 0.6
Dead Fetuses/Litter	0	0.1 $\pm$ 0.3	0	0
Litters with Resorptions	15	15	11	16
PERCENTAGE OF:				
Live Fetuses/Litter	94.1 $\pm$ 7.1	94.0 $\pm$ 7.3	95.7 $\pm$ 6.7	91.4 $\pm$ 9.2
Resorptions/Litter	5.9 $\pm$ 7.1	5.3 $\pm$ 6.5	4.3 $\pm$ 6.7	8.6 $\pm$ 9.2
Early	3.8 $\pm$ 6.1	4.0 $\pm$ 6.4	2.9 $\pm$ 4.7	6.2 $\pm$ 8.2
Late	2.0 $\pm$ 4.3	1.3 $\pm$ 3.0	1.4 $\pm$ 3.1	2.5 $\pm$ 5.2
Dead Fetuses/Litter	0	0.7 $\pm$ 2.5	0	0
Litters with Resorptions	53.6	51.7	39.3	59.3

(a) One dam removed from study, premature delivery.

(b) One dam removed from study, $\leq$ 2 implants.

TABLE 16. Isoprene Teratology Study: Average Fetal Mouse Weights (Mean of Litter Means; g $\pm$ SD) and Fetal Sex Ratio.

	Isoprene Chamber Concentration (ppm)			
	0	280	1400	7000
Litters Examined	28	29	28	27
Live Fetuses Examined	323	349	333	295
Fetal Weight(a)	1.34 $\pm$ 0.10	1.28 $\pm$ 0.10	1.22 $\pm$ 0.10 (b)	1.15 $\pm$ 0.12 (b)
Male (a)	1.37 $\pm$ 0.11	1.30 $\pm$ 0.10	1.23 $\pm$ 0.10 (b)	1.16 $\pm$ 0.12 (b)
Female (a)	1.32 $\pm$ 0.10	1.25 $\pm$ 0.10 (b)	1.20 $\pm$ 0.10 (b)	1.12 $\pm$ 0.13 (b)
Sex Ratio (% Male)	47.9 $\pm$ 15.1	48.5 $\pm$ 13.7	51.5 $\pm$ 12.7	53.9 $\pm$ 15.6

(a) Significantly correlated with exposure concentration, $p < 0.05$.

(b) Significantly different than control, $p < 0.05$.

TABLE 17. Isoprene Teratology Study: Malformations Observed in Live Mouse Fetuses.

		Fetuses (a)				Litters (a)			
Isoprene (ppm)		0	280	1400	7000	0	280	1400	7000
Total Examined (b)		323	349	333	295	28	29	28	27
Heads Examined (c)		160	176	164	148	28	29	28	27
Skulls Examined (d)		163	173	169	147	28	29	28	27
Viscera Examined (e)		163	173	169	147	28	29	28	27
Malformations:									
Cleft Palate	NO. (%)	0	0	1 (0.3)	1 (0.3)	0	0	1 (3.6)	1 (3.7)
Total Malformations	NO.	0	0	1	1	—	—	—	—
Total Fetuses (Litters) with Malformations	NO. (%)	0	0	1 (0.3)	1 (0.3)	0	0	1 (3.6)	1 (3.7)

- (a) A single fetus or litter may be represented more than once in this table.
 (b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.
 (c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.
 (d) Heads that remained on the fetuses had a skeletal examination; see (b).
 (e) Viscerals performed on approximately 50% of live fetuses and all fetuses with external defects.

TABLE 18. Isoprene Teratology Study: Mean Percent of Live Mouse Fetuses Affected per Litter (Mean $\pm$ SD).

	Isoprene Concentration (ppm)			
	0	280	1400	7000
Number Litters	28	29	28	27
Live Fetuses/Litter	11.5 $\pm$ 3.0	12.0 $\pm$ 1.9	11.9 $\pm$ 2.2	10.9 $\pm$ 1.8
Malformations:				
Cleft Palate	0	0	0.4 $\pm$ 1.9	0.3 $\pm$ 1.6
Total Malformations	0	0	0.4 $\pm$ 1.9	0.3 $\pm$ 1.6
Variations:				
Misaligned Sternebrae	0.8 $\pm$ 2.5	0	0.2 $\pm$ 1.2	0
Supernumerary Rib (b)	21.5 $\pm$ 24.9	23.9 $\pm$ 27.4	34.0 $\pm$ 25.4	40.8 $\pm$ 21.2 (c)
Renal Pelvic Cavitation	0	0	0.7 $\pm$ 3.8	0
Dilated Ureter	1.7 $\pm$ 5.0	0	2.1 $\pm$ 8.3	0
Reduced Ossifications:				
Rib	0.3 $\pm$ 1.6	0.3 $\pm$ 1.5	0	0
Skull	1.0 $\pm$ 3.7	2.1 $\pm$ 5.2	1.2 $\pm$ 6.3	0.9 $\pm$ 4.8
Total Variations and Reduced Ossifications (b)	24.0 $\pm$ 25.6	25.3 $\pm$ 27.0	36.4 $\pm$ 26.4	41.3 $\pm$ 21.8 (c)

- (a) Includes malformations, variations, and reduced ossifications.
 (b) Significantly correlated with exposure concentration, $p < 0.05$.
 (c) Significantly different than controls after arcsine transformation, $p < 0.05$.

TABLE 19. Isoprene Teratology Study: Variations Observed in Live Mouse Fetuses.

		Fetuses (a)				Litters (a)			
Isoprene (ppm)		0	280	1400	7000	0	280	1400	7000
Total Examined (b)		323	349	333	295	28	29	28	27
Heads Examined (c)		160	176	164	148	28	29	28	27
Skulls Examined (d)		163	173	169	147	28	29	28	27
Viscera Examined (e)		163	173	169	147	28	29	28	27
Variations:									
Misaligned Sternebra	NO. (%)	3 (0.9)	0	1 (0.3)	0	3 (10.7)	0	1 (3.6)	0
Supernumerary Ribs	NO. (%)	65 (20.1)	83 (23.8)	112 (33.6)	119 (40.3)	18 (64.3)	19 (65.5)	25 (89.3)	26 (96.3)
Renal Pelvic Cavitation	NO. (%)	0	0	1 (0.6)	0	0	0	1 (3.6)	0
Dilated Ureter	NO. (%)	3 (1.8)	0	3 (1.8)	0	3 (10.7)	0	2 (7.1)	0
Reduced Ossifications:									
Rib	NO. (%)	1 (0.3)	1 (0.3)	0	0	1 (3.6)	1 (3.4)	0	0
Skull	NO. (%)	2 (1.2)	4 (2.3)	2 (1.2)	1 (0.7)	2 (7.1)	4 (13.8)	1 (3.6)	1 (3.7)
Total Variations and Reduced Ossifications (f)	NO.	74	88	119	120	—	—	—	—
Total Fetuses (Litters) with Variations or Reduced Ossifications	NO. (%)	72 (22.3)	88 (25.2)	116 (34.8)	119 (40.3)	20 (71.0)	22 (75.9)	25 (89.3)	26 (96.3)

(a) A single fetus or litter may be represented more than once in this table.

(b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.

(c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.

(d) Heads that remained on the fetuses had a skeletal examination; see (b).

(e) Viscerals performed on approximately 50% of live fetuses and all fetuses with external defects.

(f) There may be >1 variation or reduced ossification per fetus.

APPENDIX A

ANALYTICAL CHEMISTRY NARRATIVE AND DATA FOR
ISOPRENE

Section I

Test Chemical Analysis, Storage and Disposition

Test Material Receipt, Storage and Usage

Receipt

Isoprene was received from the Goodyear Tire and Rubber Company. Isoprene cylinder BNW Lot No. 12102-115-12 (Supplier Lot No. - Not assigned) which was received 3/2/87 was used to conduct prestart testing. Test material for the IRT study was received 10/6/87. A total of 4 cylinders from the 10/6/87 shipment containing approximately 45.0 kg per cylinder of test material were transferred to IRT from the National Toxicology Program (NTP, Contract No. N01-ES-55105-23111-75103). Test material used for animal exposure was identified as BNW Lot No. 12102-127 cylinders 1-4 (Supplier Lot No. - Not assigned).

Storage Conditions

The bulk chemical was stored in its original shipping containers at room temperature in the chemical storage building adjacent to the LSL-II laboratory.

Usage

An average of 4.5 kg isoprene was consumed per exposure day. A total of ~115 kg were required for the IRT study.

Transfer Procedures

Isoprene was delivered directly to the rotary evaporator from the cylinder. Liquid isoprene was forced from the tank by applying low pressure (4-6 psi) nitrogen to the vapor inlet of the tank. Chemical flow rates were adjusted with a metering valve.

Waste Disposal

Excess used test material was volatilized in a chemical hood by sparging with a nitrogen stream.

Surplus Disposal

Used cylinders were transferred back to the National Toxicology Program (NTP, Contract No. N01-ES-55105-23111-75103) for shipment to Radian Corporation, Austin, Texas for disposal.

Chemical Analysis

Analysis at Midwest Research Institute

Chemical characterization of isoprene test material was presented in the September 3, 1986 MRI report. Bulk chemical (MRI assigned Lot No. G080886) was identified as isoprene. Cumulative analytical data indicated a purity greater than 99% as received.

The infrared and nuclear magnetic resonance spectra were consistent with the structure of isoprene and available literature references.

Approximation of the amount of t-butylcatechol (inhibitor) indicated 40 to 48 ppm by color produced with 1.0N sodium hydroxide when compared to freshly prepared t-butylcatechol standards. Determination of peroxides by titration with 0.01N sodium thiosulfate to a colorimetric endpoint indicated 0.290 ± 0.003 (s) meq of peroxide per 1000 g of sample.

Gas chromatographic impurity profiling indicated no impurities greater than 0.1% relative to the major peak. Five dimer peaks at concentrations less than 0.1% relative to the major peak were observed by GC/MS analysis. The largest dimer had a mass spectrum and retention time consistent with limonene. Quantitation of total dimers in the isoprene sample against limonene standards indicated 543 ± 21 ppm. The dimer which was enhanced by the addition of a limonene standard was determined to be 489 ± 19 ppm when quantified against limonene standards.

Stability Studies at Midwest Research Institute

No chemical handling was required for isoprene. The chemical used for test material and analyses was stored in the original metal cylinder at $\sim 25^{\circ}\text{C}$.

Reanalysis at Battelle Pacific Northwest Laboratories

The recommended procedure in the September 3, 1986 MRI report was implemented for reanalysis of the test material. Identity of bulk chemical was confirmed during initial bulk analysis by infrared spectroscopy. Bulk purity analysis was performed by gas chromatography using a 6 ft x 4 mm glass column packed with Porapak QS 80/100. No reference material was retained for relative purity determinations. Dimer analysis was performed by gas chromatography using a 6 ft x 2 mm glass column packed with 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport. Quantitation of limonene (dimer) was made against a limonene standard. Cylinder BNW Lot No. 12102-127-1 was 100.0% pure by area percent and contained approximately 2032 ppm limonene (dimer) when tested on 04/12/88. The contents of each cylinder were analyzed for limonene content within two weeks preceding and following use as exposure material. A cylinder with a limonene concentration of greater than 1% was considered unusable as exposure material. The results of dimer analyses performed on pre- and post-generation cylinder samples are summarized in Table 1. Initial titration of BNW Lot No. 12102-127 on 1/25/88 showed no detectable peroxides. Each lot of test material was assayed for peroxide content within 30 days preceding use as test material. A purity analysis was performed within 30 days of the start of animal exposures. Test material purity was acceptable for the start of the IRT study.

Table 1: Dimer Analyses For Isoprene Exposure Material

<u>Date</u>	<u>TestMaterial</u>	<u>Dimer (ppm)</u>	<u>Sample Status</u>
04/08/88	BNW 12102-127-1*	2032	pre-exposure
04/21/88	BNW 12102-127-1	2377	post-exposure
04/21/88	BNW 12102-127-2	2241	pre-exposure
04/21/88	BNW 12102-127-3	2185	pre-exposure
04/21/88	BNW 12102-127-4	2181	pre-exposure
05/02/88	BNW 12102-127-2	2460	post-exposure
05/10/88	BNW 12102-127-3	2387	post-exposure
05/10/88	BNW 12102-127-4	2353	post-exposure

Note: Pre-exposure samples were taken from the cylinders within two weeks before use as test material and post-exposure samples were taken from the cylinders within two weeks after use as test material.

* Vendor lot number not given.

Section II

Test Chemical Stability Studies

CHEMICAL STABILITY OF ISOPRENE DURING INHALATION TERATOLOGY STUDIES

Stability Studies at BNW

Studies to determine the stability of isoprene were conducted in the occupied and unoccupied 280 and 7000 ppm chambers and the vaporizer flask. Analysis of the exposure chamber atmosphere was accomplished using grab samples collected on standard gas sampling charcoal tubes (Supelco ORBO-32, charcoal tubes) by gas chromatography. Cumulative concentrations of impurities found in the chamber grab samples were less than 0.2% and 0.05% of the total sample area for the unoccupied and occupied chambers respectively. All impurities greater than 0.005% in the chamber grab samples were observed in the pre-exposure cylinder samples. Thus, no detectable degradation of test material was observed due to vapor generation of isoprene. Vaporizer flask samples were taken before the start and at the end of a typical exposure day and analyzed for bulk purity. As expected limonene (dimer) accumulated in the vaporizer flask during the exposure day.

Limonene Determination in Exposure Chambers

The relative concentration of limonene was determined in the occupied and unoccupied chambers during the last hour of a 6 hour run on 2/9/88 and 4/21/88 respectively. Measured volumes of gas were drawn through ORBO-32 standard charcoal tubes. Each ORBO-32 charcoal tube has two separate portions of sorbent. The front portion was analyzed to determine limonene content, while the rear portion was analyzed to evaluate breakthrough during the collection step.

Samples from each of the locations were collected at approximately 1.0 liters per minute (lpm). A summary of the chamber samples taken is given in Table II-1. The charcoal was transferred to GC autosampler vials and desorbed using 1 ml dodecane followed by 5 minutes of ultrasound treatment. Breakthrough for isoprene was approximately 30% to 35%. Conditions of chromatographic analyses are given in Table II-2. A sample chromatogram is shown in Figure II-1.

Standards were prepared by spiking ORBO-32 charcoal tube contents with known volumes of gravimetrically prepared limonene solutions. A series of three standards over the range of 0.05 to 50 mg of limonene placed on charcoal were analyzed. Recovery of approximately 94-99% was observed for limonene when compared to the same series of standards without charcoal. The low level of limonene standard was easily observed by the chromatographic system employed, as shown in Figure II-2. Isoprene standards were also prepared from a pre-exposure cylinder sample and a post-exposure vaporizer flask sample at the level approximating the total quantity of isoprene passed through the sorption tubes during sampling. Recovery of isoprene for the cylinder and flask samples was approximately 95%.

In order to demonstrate the recovery of various classes of compounds, a series of three standards over the range of 0.05 to 50 mg/ml of several compounds containing a variety of functional groups were prepared and analyzed 2/9/88. Approximate retention time and percent recovery for each of the above mentioned standards, calculated from the 50 mg/ml standard, are listed in Table II-5.

The most abundant dimer produced during thermal decomposition of isoprene is limonene and thus is the most sensitive indicator of thermal decomposition products. Limonene was observed at 0.07 and 0.16% of total sample area in the 280 and 7000 ppm unoccupied chamber grab samples respectively. Three impurity peaks were observed in the 280 ppm unoccupied chamber grab sample totalling 0.08% of total sample area. Four impurity peaks with combined area percents of 0.19% in the 7000 ppm unoccupied chamber sample were noted. Both unoccupied chambers exhibited an early eluting peak at approximately 0.01% of the total sample area. Samples taken from the 280 and 7000 ppm chamber with animals showed the early eluting impurity at approximately 0.03%. Limonene was observed at approximately 0.02 and 0.01% of total sample area in the 280 and 7000 ppm occupied chamber grab samples respectively. Three impurity peaks were observed in the 280 ppm occupied chamber grab sample totalling 0.05% of total sample area. Three impurity peaks with combined area percents of 0.04% in the 7000 ppm occupied chamber sample were noted. Results of the GC analysis of ORBO-32 charcoal tube samples are summarized in Table II-3.

The less volatile products (dimers) accumulated in the vaporizer flask during the exposure day. The concentration of the primary dimer increased from 0.6% at the beginning of the exposure day to 16.7% at the end of the exposure day on 2/9/88 and from 0.2% to 7.2% of the total sample area on 4/21/88. The increase in dimer concentration for the post-exposure flask reflects the increase in dimer concentration produced by the selective distillation of isoprene from the generator flask. Note the difference in the concentration factor of the pre- and post-generation dimer contents for the two studies. This reflects day to day variations in the reduction of evaporation flask head at the end of the generation day. If the feed to evaporation flask is stopped sometime before cessation of generation, then the volume in the evaporation flask will be smaller and the concentration of nonvolatile components correspondingly greater.

Trace amounts of t-butylcatechol (~50 ppm) were added to isoprene by the manufacturer as an inhibitor. At the end of a generation day, the evaporation flask would have contained about 0.13% t-butylcatechol. The vapor generation system produced isoprene vapor by refluxing isoprene. This process reduced the concentration of limonene from percent levels in the evaporation flask to trace levels in the generator output. Since t-butylcatechol concentrates to a much lower level than limonene (less than a factor of 10) and has a lower vapor pressure, t-butylcatechol would not have been present in the generator output.

Table II-1: Summary of Chamber Samples

Sample Date: 2/23/88

Exposure Start Time: 0850

<u>Target Concentration (ppm)</u>	<u>Sample Volume (l)</u>	<u>Time Sampled</u>	<u>Total µg Collected</u>
7000	3.1	1408	60,000
7000	3.1	1412	60,000
70	61.5	1417	12,000

Sample Date: 3/21/88

Exposure Start Time: 0856

<u>Target Concentration (ppm)</u>	<u>Sample Volume (l)</u>	<u>Time Sampled</u>	<u>Total µg Collected</u>
7000	3.0	1359	60,000
70	3.0	1404	600
7000	3.0	1416	60,000
70	3.0	1422	600

**Table II-2: Gas Chromatography Parameters for ORBO-32 Standard Charcoal Tube Analysis
used for Determination of Chamber Atmosphere Impurities**

Instrument:	Hewlett Packard 5840 Gas Chromatograph
Column Packing:	100/120 mesh Supelcoport with 20% SP 2100/0.1% Carbowax 1500
Initial Temperature:	50°C
Initial Isotherm Time:	5 minutes
Temperature Program Rate:	10°C/minute
Final Temperature:	200°C
Final Time:	5 minutes
Detector:	FID
Detector Temperature:	250°C
Injector Temperature:	200°C
~RT Isoprene:	1.1 minutes
~RT Limonene	13.6 minutes

Table II-3: GC Analysis of ORBO-32 Tube Samples

280 ppm chamber samples

Unoccupied (~49 mg collected)			Occupied (~46-51 mg collected)			
~RT	Average	% Total	~RT	Average	% Total	
<u>(min)</u>	<u>Area</u>	<u>Area</u>	<u>(min)</u>	<u>Area</u>	<u>Area</u>	<u>Identity</u>
0.9	1325	0.01	0.6	1304	0.03	unknown
1.0	10085711	99.91	0.7	5220713	99.95	isoprene
11.2	452	0.00	1.4*	16	0.00	unknown
14.2	7388	0.07	12.4	1187	0.02	limonene

7000 ppm chamber samples

Unoccupied (~62 mg collected)			Occupied (~58-66 mg collected)			
~RT	Average	% Total	~RT	Average	% Total	
<u>(min)</u>	<u>Area</u>	<u>Area</u>	<u>(min)</u>	<u>Area</u>	<u>Area</u>	<u>Identity</u>
0.9	708	0.01	0.6	2932	0.03	unknown
1.0	5100711	99.80	0.7	10847463	99.96	isoprene
2.2	581	0.01	1.4*	414	0.00	unknown
11.2	646	0.01				
14.2	8283	0.16	12.4	1515	0.01	limonene

* Average peak area at approximately 1.4 minutes for blank runs was subtracted from sample areas at approximately 1.4 minutes.

ND - Not detected

Table II-4: Stability of Isoprene in Vaporizer Flask Results

Bulk Purity Analysis BNW SOP#QB-AC-3A13

<u>Sample ID</u>	<u>% Purity</u>
Pre-exposure cylinder 2/23/88	99.7*
Pre-exposure flask 2/23/88	99.3*
Post-exposure flask 2/23/88	99.6*

Dimer Analysis BNW SOP#QB-AC-3A13

<u>Sample ID</u>	<u>(ppm) d-Limonene</u>
Pre-exposure cylinder 2/23/88	1800
Pre-exposure flask 2/23/88	2009
Post-exposure flask 2/23/88	47732

Peroxide Analysis BNW SOP#QB-AC-3A1P

<u>Sample ID</u>	<u>Peroxide content (meq/kg)</u>
Pre-exposure cylinder 2/23/88	<0.1
Pre-exposure flask 2/23/88	<0.1
Post-exposure flask 2/23/88	<0.1

Degradation Analysis of Exposed Charcoal Tubes, Pre-exposure Cylinder and Post-exposure Flask Samples (without charcoal)- See Table II-1 for Gas Chromatography Parameters

<u>Sample ID</u>	<u>% Purity by Area</u>	<u>% d-Limonene by Area</u>
Pre-exposure cylinder 2/23/88	99.74**	0.17
Pre-exposure flask 2/23/88	99.73**	0.18
Post-exposure flask 2/23/88	94.89**	4.27

<u>Sample ID</u>	<u>% Purity by Area</u>	<u>% d-Limonene by Area</u>
Pre-exposure cylinder 3/21/88	99.88**	0.09
Pre-exposure flask 3/21/88	99.89**	0.09
Post-exposure flask 3/21/88	90.88**	8.23

* It should be noted that the MRI derived bulk purity method does not elaborate dimer peaks. This results in higher area % purity values.

** Area percent purity observed with BNW degradation method elaborates dimer peaks.

Table II-5: Retention Times and % Recovery for Compounds with Various Functional Groups

Major Peak Area Counts for 1 ml Standard Solution on Charcoal:

Standard Identification	~RT for Major Peak	~% Recovery Off of Charcoal	~50 mg/ml Standard	~0.50 mg/ml Standard	~0.05 mg/ml Standard
cyclopentene oxide	5.7	92	17240000	137900	10650
cyclopropyl methyl ketone	5.1	86	16800000	68680	1902
3,4-dihydro-2H-pyran	4.1	96	16550000	143900	11730
trans-2-methyl-2-butenal	5.9	97	14480000	10390	ND
3-methyl-2-butanone	3.1	94	17770000	90200	5437
2-methyl-3-buten-2-ol	2.2	94	20120000	71740	4895
2-methyltetrahydrofuran	3.5	97	17080000	132100	10920
limonene	14.5	89	27040000	224500	20010

ND- No peak detected

Section III
Test Chemical Monitoring

Monitoring System Description (SOW II.D.7.c)

An HP5840 gas chromatograph equipped with a flame ionization detector was used to monitor the exposure chambers, the control chamber, the exposure room and a certified on-line standard of isoprene.

Sampling from multiple positions was accomplished by means of an automated 8 port stream select valve. An HP85B computer remotely controlled the selection of the correct sample stream and the operation of the monitor. Each analysis required about 3 minutes. The equation for the calibration curve was contained in the HP85B and applied to the data transmitted by the on-line GC monitor. The HP85B also accumulated and printed the sample values until all 8 ports of the stream select valve had been measured. These values were then sent to the executive computer for printing and storage. Each value accumulated by the HP85B was compared with limit values for that particular location. If the value was beyond the control limits, the HP85B immediately sent the information to the executive computer which took the appropriate action.

As described in the section that follows, the monitor was calibrated against gravimetrically prepared standards. These standards were related to the on-line monitor through quantitative analysis of grab samples taken from the chambers during generation.

Additionally, the operation of the chamber monitor was checked daily against an on-line standard. This check provides a measure of day-to-day instrument drift. Additional calibration checks by grab sampling was performed to check the monitor calibration when drift of the on-line standard response factor was detected.

The uniformity of the distribution of test chemical in the chamber was checked before the start of the study and once during study exposure.

Calibration of the On-Line Monitor (SOW II.D.7.c)

Calibration of the on-line GC chamber monitor was based on quantitative analysis of bubbler grab samples taken directly from the exposure chambers during a routine exposure period. The normal dynamic operation of the monitor was not disrupted by the collection of these grab samples. The response of the on-line monitor at the time that a grab sample was taken was tied to an independent analysis of the grab sample.

Grab samples were obtained by collecting isoprene in dimethylformamide (DMF) filled bubblers. Gravimetrically prepared standard solutions of isoprene in DMF were used to construct a calibration curve on an independent GC system. The relationship between the peak area observed with the on-line GC and the concentration of isoprene in the chamber was defined using chamber concentrations determined by the gravimetrically calibrated GC. A set of five standards was run for each analysis session. The concentration range of the standards bracketed the concentration range of the chamber grab samples. Two independently weighed stock solutions were used each time the standard series was prepared. The calibration was linear through the range of interest.

On-Line Standard

A certified on-line standard of 2000 ppm isoprene in nitrogen was used to check instrument drift throughout the exposure day. The standard was also checked before the start of each exposure day and then monitored every 8th sample. If the on-line standard was between 5% and 10 % of the target concentration, exposure control personnel were immediately notified and recalibration of the on-line gas chromatograph was accomplished at the discretion of the chemist. Drift in the on-line standard concentration which exceeded 10% required recalibration of the on-line monitor as quickly as practical.

Sensitivity and Specificity (SOW II.D.7.c)

The sensitivity of the GC was estimated from the decay profile for the highest concentration chamber. The minimum detectable limit (MDL) was estimated at 0.04 ppm.

A measure of chromatographic specificity is typically defined by determination of the analyte's partition coefficient. The retention time of methane, assumed to be nonretained, was found to be about 0.09 minutes. The retention time of isoprene was 0.65 minutes. The partition coefficient was approximately 6.2.

Precision, Linearity, and Absolute Recovery (SOW II.D.7.c)

Precision for the on-line monitor was estimated from 8 repeated measurements made using the on-line standard sampled from each of the 8 sample ports on 1/22/88. A standard deviation of 2.53 ppm was observed for a 0.13 % coefficient of variance.

Linearity of the on-line monitor was assured by indirectly calibrating the on-line monitor against a gravimetrically calibrated GC (see "Calibration of the On-Line Monitor " section). The calibration was linear through the range of interest.

Recovery of the bubbler grab sample method was measured by determining breakthrough. Breakthrough was measured every time samples were collected by collection of back-up bubblers from the high concentration chamber. With the 1 liter sample size selected for the study, breakthrough of about 17-18% was encountered. Back-up bubblers were acquired for the high exposure chamber and used to correct the measured chamber concentration at all exposure levels for breakthrough encountered during grab sampling.

Monitoring for Isoprene in Building Exhaust (SOW II.F.9.)

Effluent from the exposure chambers and the exposure generation system was diluted with the exhaust air of the entire LSL-II Building prior to exhausting from the building stack. The isoprene concentration in the exhaust of the building was determined using charcoal gas sampling tubes. The building exhaust was sampled from three areas of the plenum where the exhaust exits the stack. The building exhaust was sampled by collecting a sample, approximately 1 liter of exhaust, through a charcoal gas sampling tube. The expected amount of isoprene in the building exhaust was 1.7 ppm from the IRT study. Based upon the isoprene consumption from the IRT study and the NTP isoprene studies being conducted at the same time, the expected amount of isoprene in the building exhaust was ~ 4.5 ppm. The average concentration of isoprene found in the building exhaust 04/14/88 was 4.1 ppm.

BULK CHEMICAL ANALYSIS

COMPOUND: ISOPRENE
 CAS# 78-79-5
 LOT# BNW# 12102-127-1
 APPEARANCE: Colorless liquid
 RECEIPT DATE: 10/6/87
 ANALYSIS PERIOD: 6 months after receipt
 STORAGE TEMPERATURE: Room temperature
 SAMPLE ANALYSIS DATE: 4/8 to 14/88
 ANALYSIS PROCEDURE: ØB-AC-3A13-ØØ
 NOTEBOOK REFERENCE: BNW 52715-24,25,26 & 30

ASSAY: Gas chromatography using 6ft x4mm glass column packed with Porapak QS 80/100 was employed for the purity by area %.
 Instrument: HP 5840
 A 6ft x2mm glass column packed with 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport was used for the dimer analysis.
 Instrument: HP 5830

RESULTS:

Bulk % Purity

	Ave
100.0	
100.0	100.0% SD=±0.0
100.0	

Isoprene eluted at approximately 13.94 minutes.

Sample injections were allowed to run ~20 minutes past isoprene peak to determine if any impurities were present. No impurities were observed.

Dimer (ppm)

	Ave
2035	
2036	2032 SD= ± 6.7
2022	
2035	

The dimer eluted between 14.42 and 14.49 minutes.

IDENTITY: Infrared spectroscopy using a 10 cm cell with sodium chloride windows scanned from 4000 cm⁻¹ to 600 cm⁻¹ was used for verification of test material identity.

Instrument: Beckman AccuLab 8

RESULTS: The spectrum was similar to that found in the MRI method.

Conclusion: Infrared spectroscopy confirms the identity of lot BNW#12102-127-1. Gas chromatography shows this lot to be 100.0% pure by area percent and acceptable by the suggested MRI purity limit of ≥99%. BNW12102-127-1 contains 2032 ppm dimer which is within the acceptable limit stated in the SOP of 1% (10,000 ppm) dimer.

Signature of Technician: S. A. Barnalough Date: 4-18-88

Signature of Chemist: RB Whitely Date: 5-3-88

SPECTRUM NO. 1DATE 4-12-88SAMPLE BLANK

SOURCE

STRUCTURE

PATH 4000 to 600 cm⁻¹SOLVENT NACONCENTRATION NAPHASE GasCOMMENTS 10 cm gascell with NaCl windowon Beckman Acculab 8ANALYST S.A.B.**Beckman®**INFRARED
SPECTROPHOTOMETER SPECTRUM NO. 2DATE 4-12-88SAMPLE BOWSALIC-22-1(formerly BMW1102-12-1)

SOURCE

STRUCTURE

PATH 4000 to 600 cm⁻¹SOLVENT NA

CONCENTRATION

PHASE VaporCOMMENTS 10 cm gascell with NaCl windowon Beckman Acculab 8ANALYST S.A.B.**Beckman®**INFRARED
SPECTROPHOTOMETER

Copy Attached BW52715-30 4-18-88 SAB

4-13-88 JAB

TIME 22:24:23

RT	AREA	AREA %
10.13	1450000000	90.266
10.50	54500000	0.342
10.52	63110000	0.399
11.70	30000000	0.190
12.94	50000000	0.310
14.00	30000000	0.190
14.21	45440000	0.290

DIL FACTOR: 1.0000 m + 0

Isoprene Bulk Purity by G.C. (IRT)
 Method: 03-AC-3A13-00
 G.C. Run Date: 4-12-88
 G.C.: HP5840 WA10706
 Column: 6ft. x 4mm glass, 2 Porapak
 Q5 80/100
 Methylene Chloride: Jurdick & Jackson,
 Lot # AS122
 Isoprene: 3NW 52715-23-1 (formerly,
 known as 3NW 12102-127-1
 3NW 52713-26
 4-13-88 SAB

HP RUN # 3 APR 11/88 TIME 23:54:21
 ID: 18786 BOTTLE 3
 AREA %

RT	AREA	AREA %
12.11	100000000	95.574
13.93	57100000	5.231
17.48	1950000	0.189
19.58	4900000	0.270
21.73	5540000	0.515
22.78	2150000	0.203
24.11	5950000	0.225
26.26	3134000	0.277
29.34	50000	0.000
38.58	170000	0.100
	1247000	0.070

DIL FACTOR: 1.0000 E+ 0

Dimer Analysis of Isoprene by G.C. (IRT)

Method: 0B-AC-3A13-00

G.C. Run Date: 4-8-88

G.C.: HP5830 N807630

Column: 6ft. x 2mm glass, 20% SP-2100/0.1%
Carbowax 1500 on 100/120 Supelcoport

Limonene: Aldrich, Lot #17143M

Methylene Chloride: Jurdick & Jackson, Lot #A5122

Toluene: MCB, Lot #A12F16

Isoprene Samples: 3NW12299-60-1 = 3NW12299-63-7 & 8

3NW12299-60-2 = 3NW12299-63-9 & 10

3NW1202-127-1 = 3NW12299-63-11 & 12

3NW12299-63 NTP / 3NW52713-24 IRT

4-11-88 SAB

TEMP1 50 50
TIME1 5.0
RHIE 10.00
TEMP2 200
TIME2 5.0
INJ TEMP 200 200
FID TEMP 200 200
OVEN RHX 400

CHI SPD 0.50
HIIN ZT 10
FID SGNL +8
SLP SENS 0.10
HKEH KEJ 1
FLOW H 0
FLOW B 32
UPIN 21
24.0 STOP

SI
0.83

1.34

2.73

3.59

4.97

12.37

SI
BUTLE 24 MeCl₂ BLANK

TIME	HKEH	HKZ
0.32	36	0.00
0.83	199	0.00
1.34	2206000000	99.97
2.73	11910	0.01
3.59	2202	0.00
4.97	55600	0.03

Dimer Analysis of Isoprene by G.C. (IRT)

Method: 83-AC-3A13-88

G.C. Run Date: 4-8-88

G.C.: HP 5830 N807630

Column: 6ft. x 2mm glass, 20% SP-2100/0.1%

Carbowax 1500 on 100/120 Supelcoport

Limonene: Aldrich, Lot #17143M

Methylene Chloride: Burdick & Jackson, Lot #A5122

Toluene: MCB, Lot #A12F16

Isoprene Samples: 3NW12299-60-1 = 3NW12299-63-7 & 8

3NW12299-60-2 = 3NW12299-63-9 & 10

3NW12402-127-1 = 3NW12299-63-11 & 12

3NW12299-63 NTP / 3NW 52715-24 IRT

4-11-88 SAB

APPENDIX B

**EXPOSURE NARRATIVE AND DATA FOR
ISOPRENE**

EXPOSURE DATA AND NARRATIVE FOR ISOPRENE

Animal Exposure Chamber

The Battelle-designed inhalation exposure chamber (commercially available from Harford Systems/Lab Products, Inc., Aberdeen, MD) was used for the inhalation exposures. The 2.3 m³ (1.7 m³ active-mixing volume) stainless steel chamber contained three levels of caging, each level split into two offset tiers (Figure B.1). The drawer-like stainless steel cage units comprised individual animal cages, feed troughs and automatic watering. Stainless steel catch pans for the collection of urine and feces were suspended below each cage unit.

The catch pans, which remained in the chamber during exposure, were designed to aid in maintaining uniform concentrations of aerosol, dust or vapors throughout the chamber. Incoming air was HEPA and charcoal filtered before addition of the test article. Following the addition of the test article the uniform mixture was diverted along the inner surfaces of the chamber. A portion of the flow was "peeled off" by each catch pan thus creating mixing eddies. Exhaust from each tier was cleared through the space between the tiers.

Exposure Suite System Description

The isoprene exposures were conducted using an automated data acquisition and control system in an exposure suite (Figures B.2 and B.3). This system monitored and controlled the basic inhalation test system functions including chamber air flow, vacuum, temperature, relative humidity and test chemical concentration. The system computers, printers, magnetic data storage devices, interface equipment, and monitoring instruments were located in a central control room and interfaced with monitoring and control elements in three exposure rooms. All data acquisition and control originated from an executive computer which controlled a multiplexing interface system. All experimental protocols related to data acquisition and control resided in this computer and were entered into software tables accessed by menus.

Data from each exposure was stored in the exposure control center on separate micro-floppy diskettes. Data and comments from each exposure room were printed on separate printers. Data was printed and stored immediately upon completion of the measurement. At the end of the 24 hour period, the daily data was analyzed and summary and data outlier reports were printed.

A dual point alarm system with user-defined set points was available for each parameter measured. Action taken upon alarm depended on the cause and severity of the alarm and ranged from audio/visual alert to automatic shutoff of the exposure generator. Alarm conditions which might be a threat to the health of the animals alerted a building power operator who was on duty 24 hours per day.

FRONT VIEW

SIDE VIEW

FIGURE B.1. Inhalation Exposure Chamber

FIGURE B.2. Isoprene Exposure Suite

COMPUTER SYSTEM

FIGURE B.3. Data Acquisition System for Isoprene Exposures

Chamber and room temperatures were measured by Resistance Temperature Detectors (RTDs) located at the measurement site. The RTDs were multiplexed to a digital thermometer which was interfaced to the computer. Chamber temperature was controlled primarily by controlling the temperature of the room housing the chambers. Prior to the start of the study RTDs were calibrated to within $\pm 0.5^{\circ}\text{F}$ of a certified mercury thermometer in a temperature controlled water bath.

Relative humidity (RH) was determined by pulling a sample from the measurement location through a Teflon[®] tube into a dewpoint hygrometer located in the control center. Measurements were made from different locations by a valving system which multiplexed the tubes to the hygrometer. Percent RH was calculated by the executive computer from temperature and dewpoint measurements with an accuracy of $\pm 6\%$. Chamber %RH was maintained by a "wet/dry" air source supplied to each chamber. The ratio of "wet" to "dry" air, determined by a computer-controlled mixing valve, determined the chamber %RH.

Chamber air flow was calculated with an accuracy of ± 15 l/min by measurement of the pressure drop across calibrated orifices located at the inlet and exhaust of each chamber. The desired flow orifice was attached by means of a multiplexed valve system to a calibrated pressure transducer located in the control center. Leaks in the chambers could be detected by comparison of the measurement of inlet flow with that of the exhaust. Flow was maintained by a gate valve in the exhaust line of each chamber.

Chamber vacuum, relative to the control center, was measured with an accuracy of ± 0.2 cm H₂O using the same pressure transducer system which measured chamber air flows. Chamber vacuum was maintained at approximately (-) 1" H₂O primarily by inlet resistance provided by the HEPA and charcoal filters.

Isoprene Generation System

A schematic diagram of the isoprene generation and delivery system is shown in Figure B.4. The isoprene generator was housed in a vented cabinet located in the Suite Control Center. The generator employed a rotary evaporation system (Büchi Rotavapor, Model EL-131S) to produce a high purity isoprene vapor. The cylinders in which the bulk isoprene was shipped had both vapor and liquid sample valves. Low pressure nitrogen (4 - 6 psi) was introduced into the vapor inlet of a cylinder, forcing liquid isoprene out at a steady rate. Chemical flow rate was adjusted with a metering valve and monitored with a flowmeter. The liquid was delivered to a rotating evaporator flask immersed in a hot water bath. The resulting vapor was forced out of the mouth of the flask into a chilled water condenser where much of the vapor was recondensed, returning to the evaporator flask. Nitrogen was metered into the bottom of the condenser and flowed out the top. As nitrogen moved through the condenser, it became saturated with isoprene vapor. The temperature of the saturated nitrogen was monitored using a sensor at the top of the condenser. The saturation vapor pressure was calculated and used to determine the output (ppm of isoprene and flow

rate of saturated nitrogen) of the generator. The vapor entered a short distribution manifold where individual delivery lines carried a metered amount of vapor to the exposure chambers. Metering was accomplished by placing vacuum transducer pumps at the chamber end of each line. The pumps generated the negative pressure used to move the isoprene vapor. Within the chemical storage cabinet, each line was connected to the distribution manifold through a fine metering valve and flowmeter. Adjustment of chamber concentration was done with the metering valves and/or adjustment of compressed air pressure to the pumps. Injection of the nitrogen/vapor mix into the conditioned airstream entering the chamber occurred at a point sufficiently removed from the chamber to allow for proper mixing. This assured uniformity of chemical-laden atmosphere within the chamber.

Normal operation called for approximately 20% excess vapor to be exhausted from the manifold through a flowmeter. This caused a slight positive pressure in the manifold and allowed independent adjustment of the chamber flow rates. However, since the vacuum transducer pumps were withdrawing vapor from the manifold, there was the possibility of creating a negative pressure in the manifold and generator which could have drawn air into the nitrogen/isoprene atmosphere. This would have occurred if nitrogen delivery was interrupted or the pump delivery rates were grossly misadjusted. To monitor for this situation, a pressure transducer (Photohelic) measured the pressure drop across the excess vapor flowmeter. A drop in pressure to below 2 cm of water would have resulted in a shutdown of the generation system.

Generation proceeded in stages: warmup, generation and shutdown. During warmup, filling of the evaporating flask and heating of the water bath proceeded together. During this time, some evaporation occurred but all vapor was exhausted from the distribution manifold through the excess flowmeter and at each chamber through pneumatic 3-way valves. These valves allowed for a faster buildup of vapor concentration at startup as well as for more rapid diversion of chemical flow from chambers in the event rapid shutdown was necessitated. After stabilization of the vapor temperature and possible fine adjustments of the vapor delivery and nitrogen flow rates, the generator was in its normal operating stage. At this time, computer-controlled startup of the exposure was initiated by rotation of the pneumatic 3-way valves to the chamber position. During this stage, the generator operated under computer and exposure operator supervision. The exposure operator monitored the fluid level in the flask as well as other operating parameters. The operator adjusted the overall generator output by changing the flow rate of cooling water to the condenser. This affected the temperature of the vapor leaving the condenser and hence, the concentration of chemical in the vapor. Overall generator output could also be controlled by adjusting the flow rate of dilution nitrogen. Individual chamber concentration adjustments were generally done by changing the air pressure to the pressure transducer pumps which were withdrawing vapor from the distribution manifold.

The computer could initiate a shutdown of the generator output under certain conditions by stopping flask rotation and turning off the bath heater. Further reduction in the generator output could then be

FIGURE B.4. Isoprene Generation and Delivery System
B.7

initiated by the operator by stopping the nitrogen flow and opening a valve which introduced chilled water into the water bath.

Shutdown at the end of the generation stage was similar to a computer-initiated shutdown. Following closure of the valves at the chambers and discontinuation of flask rotation, the operator dumped additional cooling water into the bath. The remaining isoprene in the evaporator flask was removed to a waste bottle. Nitrogen continuously purged the generation system until preparation for the next day's generation.

A Gardner Inc. Type CN small particle detector was used to check the chambers and the room for particles during generation before animals were placed in the chambers and once with animals in the chambers. No particles were found in the control chamber or any of the exposure chambers. A count of approximately 200 particles/cm³ was found in the room during generation.

The time (T_{90}), following the start of generation, for the concentration to build up to 90% of the final stable concentration in the chamber and the time (T_{10}), following the stop of generation for the vapor concentration to decay to 10% of the stable concentration were determined before animals were placed in the chambers prior to the start of the study. The resulting curves for all chambers are shown in Figure B.5. The value of T_{90} was found to range from approximately 9 to 11 minutes. At a chamber air flow rate of 15 air changes per hour, the theoretical value for T_{90} is approximately 12.5 minutes. A T_{90} of 12 minutes was chosen for this study. The value of T_{10} ranged from 8 to 10 minutes.

The buildup and decay of concentration with rats and mice present in all the chambers were also checked during the exposure (Figure B.5). The values of T_{90} ranged from 10 to 13 minutes. The decay time, T_{10} , ranged between 11 and 13 minutes.

In order to determine the persistence of the chemical in the chamber following exposure, the concentration of isoprene in the 7000 ppm chamber was monitored overnight following shutoff of the chemical flow to the chamber. Monitoring was performed once during the study when animals were present. Concentration of isoprene in the chamber without animals was below 1% of the initial concentration in less than 28 minutes following shutdown of the vapor generation system compared with approximately 21 minutes with animals in the chambers.

ISOPRENE IRT: 280 ppm Chamber

ISOPRENE IRT: 1400 ppm Chamber

ISOPRENE IRT: 7000 ppm Chamber

Figure B.5. Buildup and Decay of Vapor Concentrations With and Without Animals Present.

Vapor Concentration Uniformity in Chambers

Uniformity of vapor concentration in the exposure chambers was measured prior to the start of and once during the study. The vapor concentration was measured using the on-line GC with the automatic 8-port sample valve disabled to allow continuous monitoring from a single input line. Prior to animal loading, 12 chamber positions (two positions, one in front and one in back, for each of the six possible animal cage unit positions per chamber) were measured. The second set of gas concentration measurements was taken from the front and back positions of the chamber only where cage units contained animals.

The sample point was just above and about 10 cm in from the front or back center of each cage unit. The uniformity data for each chamber during prestart testing and after animals were in place in the chambers are summarized in Table B.1. Complete data are found later in this appendix. Uniformity in all chambers was found acceptable. The possible variation of test chemical concentration measured from one sample port to another during the measurement procedure is termed the Total Port Variability (TPV) and consists of both spatial and temporal variations. Two factors contribute to the TPV. The first, the Between Port Variability (BPV), is the factor of interest as it represents the spatial variation of test chemical distribution within the chamber. The second factor, the Within Port Variability (WPV), represents the temporal fluctuation of the average chemical concentration within the chamber during the time the measurements were taken. This temporal factor includes variations in vapor generation as well as variation of the measurement instrument itself.

The WPV was determined from a minimum of three measurements taken at the on-line monitor port (1B or 2B) before, during and after all other ports were measured.

The TPV was determined from measurements from, at the minimum, the front and back ports at each level on which animals are housed.

The BPV was determined by applying the following equation:

$$BPV = \sqrt{(TPV)^2 - (WPV)^2}$$

Since the WPV is often determined from fewer measurements than the TPV, statistically it is possible for the WPV to be greater than the TPV. In these cases, the BPV is very small, but it cannot be distinguished from the WPV. The BPV can't be determined using the above equation as it yields the square root of a negative number. In this case, it is reported as indistinguishable from the WPV.

TABLE B.1. Teratology Study of Isoprene in Mice and Rats - Summary of Chamber Uniformity Data Obtained Before Exposure (Pre: 2/1/88) and During Exposure with Rats and Mice Present (Post: 4/23/88).

Chamber	TPV (%RSD)		WPV (%RSD)		BPV (%RSD)	
	Pre	Post	Pre	Post	Pre	Post
280 ppm	1.0	0.3	1.6	0.5	*	*
1400 ppm	0.4	0.1	0.7	0.1	*	*
7000 ppm	0.5	0.2	1.0	0.2	*	*

*Indistinguishable from WPV

Chamber Uniformity Limits

WPV $\leq$ 5% RSD

BPV $\leq$ 5% RSD

TPV $\leq$ 7% RSD

Environmental Data During Exposure

Summations of chamber air flow, temperature and relative humidity data for the studies in mice and rats are shown in Tables B.2 and B.3. These tables include the mean, standard deviation, mean expressed as a percentage of the target, the percent relative standard deviation (SD/Mean), maximum, minimum readings, number of readings and the percent of readings for which the value was within the specified operating range.

For the mouse study (Table B.2), the mean values of temperature in all chambers for the entire study were between 74.5 and 75.1°F, all within the specified limits of 72 to 78°F. Temperature extremes ranged from 71.6 to 77.8°F. The percent of temperature readings within the operating range for all chambers were $\geq$ 97%.

The mean values of relative humidity in all chambers for the mouse study were between 53.3 and 55.0%, all within the specified limits of 40 to 70%. Relative humidity extremes (considering all chambers) ranged from 38 to 66%. All but two readings were within the normal operating range.

The mean values of chamber air flow in all chambers for the mouse study were between 14.7 and 15.1 CFM (1 CFM = 1 air change per hour), all within the specified limits of 12 to 18 CFM. Flow extremes (considering all chambers) ranged from 14.4 to 15.4 CFM; all readings were within normal operating limits.

For the rat study (Table B.3), the mean values of temperature in all chambers for the entire study were between 74.4 and 75.5°F, all within the specified limits of 72 to 78°F. Temperature extremes ranged from 70.9 to 77.8°F. The percent of temperature readings within the operating range for all chambers were $\geq$ 98%.

The mean values of relative humidity in all chambers for the rat study were between 52.5 and 55.1%, all within the specified limits of 40 to 70%. Relative humidity extremes (considering all chambers) ranged from 38 to 66%. At least 99% of the readings from each chamber were within operating range.

The mean values of chamber air flow in all chambers for the rat study were between 14.7 and 15.1 CFM (1 CFM = 1 air change per hour), all within the specified limits of 12 to 18 CFM. Flow extremes (considering all chambers) ranged from 14.6 to 15.4 CFM; all readings were within normal operating limits.

A complete summary of the daily chamber environmental data and notations on any readings which exceeded critical limits follows.

TABLE B.2. Inhalation Teratology Study of Isoprene in Mice--Summation of Environmental Data for the Period when Animals were Housed in the Exposure Chambers. Acceptable ranges are also shown.

Temperature (°F)
Acceptable Range = 72 to 78 °F

Target Chamber Conc. (ppm)	Mean ± SD	Percent of Target ±%RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	74.5 ± 1.1	99 ± 2%	77.5	72.2	117	100
Holding	75.1 ± 1.1	100 ± 2%	77.8	72.9	44	100
280	74.6 ± 1.2	100 ± 2%	76.4	71.6	116	97
1400	74.9 ± 1.3	100 ± 2%	77.0	71.8	117	98
7000	74.9 ± 1.2	100 ± 2%	76.7	71.9	117	99

Relative Humidity (% RH)
Acceptable Range = 40 to 70 %RH

Target Chamber Conc. (ppm)	Mean ± SD	Percent of Target ±%RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	53.3 ± 4.0	97 ± 8%	66	40	116	100
Holding	54.3 ± 4.6	99 ± 8%	61	47	46	100
280	53.3 ± 4.7	97 ± 9%	63	38	115	99
1400	55.0 ± 4.0	100 ± 7%	64	43	116	100
7000	54.5 ± 4.0	99 ± 8%	64	38	116	99

Air Flow (CFM)
Acceptable Range = 12 to 18 CFM

Target Chamber Conc. (ppm)	Mean ± SD	Percent of Target ±%RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	15.1 ± 0.1	101 ± 1%	15.2	14.8	114	100
Holding	14.7 ± 0.1	98 ± 1%	14.9	14.4	45	100
280	14.9 ± 0.2	100 ± 1%	15.2	14.7	115	100
1400	15.1 ± 0.1	101 ± 1%	15.4	14.9	115	100
7000	15.0 ± 0.1	100 ± 1%	15.3	14.8	115	100

TABLE B.3. Inhalation Teratology Study of Isoprene in Rats—Summation of Environmental Data for the Period when Animals were Housed in the Exposure Chambers. Acceptable ranges are also shown.

Temperature (°F)
Acceptable Range = 72 to 78 °F

Target Chamber Conc. (ppm)	Mean $\pm$ SD	Percent of Target $\pm$ RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	74.4 $\pm$ 1.2	99 $\pm$ 2%	77.5	71.9	141	99
Holding	75.3 $\pm$ 1.7	100 $\pm$ 2%	77.8	70.9	55	98
280	75.1 $\pm$ 0.7	100 $\pm$ 1%	76.4	73.0	133	100
1400	75.5 $\pm$ 0.8	101 $\pm$ 1%	77.0	72.9	133	100
7000	75.4 $\pm$ 0.7	101 $\pm$ 1%	76.7	72.9	133	100

Relative Humidity (% RH)
Acceptable Range = 40 to 70 %RH

Target Chamber Conc. (ppm)	Mean $\pm$ SD	Percent of Target $\pm$ RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	54.1 $\pm$ 4.8	98 $\pm$ 9%	66	40	140	100
Holding	52.5 $\pm$ 4.6	95 $\pm$ 9%	59	41	55	100
280	54.4 $\pm$ 5.1	99 $\pm$ 9%	65	38	132	99
1400	55.1 $\pm$ 4.2	100 $\pm$ 8%	67	43	133	100
7000	54.6 $\pm$ 4.7	99 $\pm$ 9%	66	38	132	99

Air Flow (CFM)
Acceptable Range = 12 to 18 CFM

Target Chamber Conc. (ppm)	Mean $\pm$ SD	Percent of Target $\pm$ RSD	Maximum	Minimum	Number of Samples	% Samples in Range
0	15.1 $\pm$ 0.1	100 $\pm$ 1%	15.2	14.7	140	100
Holding	14.7 $\pm$ 0.1	98 $\pm$ 0%	14.8	14.6	31	100
280	15.0 $\pm$ 0.1	100 $\pm$ 1%	15.2	14.7	132	100
1400	15.1 $\pm$ 0.1	101 $\pm$ 1%	15.3	14.8	132	100
7000	15.1 $\pm$ 0.2	101 $\pm$ 1%	15.4	14.8	132	100

Exposure Data

Summaries of the concentration data for both the mouse and rat studies for all chambers and the exposure room are included in Tables B.4 and B.5. Summaries of concentration by exposure day follow in this appendix along with graphic illustrations of the daily mean and standard deviation for each chamber.

For the mouse study (Table B.4), the grand means of the concentrations in each chamber for the entire study were between 99 and 100% of the target, with relative standard deviations in the range of 2 to 7%. The daily mean concentrations ranged from 94 to 103% of target (the daily protocol required the daily means to be within $\pm 10\%$ of the target concentrations) and % RSDs were less than 10%. On 4/18/88, a power interruption shut down the primary building exhaust fan which reduced chamber flow by about 25%. Exposures were automatically stopped and not restarted for 19 minutes. This additional time was added to the total length of the exposure day. More than 99% of all individual concentration measurements were within $\pm 10\%$ of the target levels, the specified operating limits. The maximum concentration observed in the control chamber was 0.2 ppm and 0 ppm in the holding chamber. The maximum concentration observed in the room was 0.6 ppm.

For the rat study (Table B.5), the grand means of concentrations in all chambers for the entire study were 100% of the target, with relative standard deviations in the range of 2 to 6%. The daily mean concentrations for all chambers were between 94 and 102% of the target concentrations (the daily protocol required the daily means to be within $\pm 10\%$ of the target concentrations) and % RSDs were less than 10% except for the first day of exposure when a drop in chamber flow due to a building exhaust problem interrupted exposure operations. At least 99% of all individual concentration measurements were within $\pm 10\%$ of the target levels, the specified operating limits. There was no measureable concentration in the control and holding chambers. The maximum concentration observed in the room was 0.8 ppm.

A complete discussion of all concentration excursions is included in this appendix.

TABLE B.4. Inhalation Teratology Study of Isoprene in Mice—Summation of Concentration Data for the Period when Animals were Housed in the Exposure Chambers.

Concentration (PPM)
Acceptable Range = Target $\pm$ 10%

Target Conc. (ppm)	Mean $\pm$ SD	Percent Target $\pm$ RSD	Max	Min	Number Samples	Number in Range	% Samples in Range
Room	0.02 $\pm$ 0.05	-----	0.6	0	270	*270	*100
0	0.00 $\pm$ 0.01	-----	0.2	0	269	*269	*100
Hold	0.00 $\pm$ 0.00	-----	0	0	77	*77	*100
280	278 $\pm$ 6.5	99 $\pm$ 2%	295	223	232	231	>99
1400	1400 $\pm$ 56	100 $\pm$ 4%	1530	695	232	231	>99
7000	6980 $\pm$ 473	100 $\pm$ 7%	7460	31	233	232	>99
St. Gas	2060 $\pm$ 78	95 $\pm$ 4%	2160	1980	242	242	100

* Samples with concentration less than 1 ppm

TABLE B.5. Inhalation Teratology Study of Isoprene in Rats—Summation of Concentration Data for the Period when Animals were Housed in the Exposure Chambers.

Concentration (PPM)
Acceptable Range = Target $\pm$ 10%

Target Conc. (ppm)	Mean $\pm$ SD	Percent Target $\pm$ RSD	Max	Min	Number Samples	Number in Range	% Samples in Range
Room	0.01 $\pm$ 0.05	-----	0.8	0	362	*362	*100
0	0.00 $\pm$ 0.00	-----	0	0	324	*324	*100
Hold	0.00 $\pm$ 0.00	-----	0	0	134	*134	*100
280	279 $\pm$ 6.8	100 $\pm$ 2%	305	223	262	261	>99
1400	1400 $\pm$ 52	100 $\pm$ 4%	1510	695	261	260	>99
7000	6980 $\pm$ 446	100 $\pm$ 6%	7650	31	263	262	>99
St. Gas	2100 $\pm$ 82	98 $\pm$ 4%	2450	1990	333	330	99

* Samples with concentration less than 1 ppm

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: Standard Gas

/Concentration

Range=1.94E+3 to 2.37E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	1.98E+03	92.1%	3.783E+00	.2%	1.99E+03	1.98E+03	17	17	100.0%
14 Apr 1988	1.98E+03	92.1%	4.171E+00	.2%	2.00E+03	1.98E+03	16	16	100.0%
15 Apr 1988	1.99E+03	92.4%	4.220E+00	.2%	2.00E+03	1.99E+03	17	17	100.0%
16 Apr 1988	2.00E+03	92.7%	2.004E+00	.1%	2.00E+03	2.00E+03	17	17	100.0%
17 Apr 1988	2.00E+03	92.7%	2.045E+00	.1%	2.00E+03	2.00E+03	17	17	100.0%
18 Apr 1988	2.00E+03	92.8%	3.226E+00	.2%	2.01E+03	1.99E+03	15	15	100.0%
19 Apr 1988	2.00E+03	92.9%	2.609E+00	.1%	2.01E+03	2.00E+03	17	17	100.0%
20 Apr 1988	2.00E+03	92.9%	1.978E+00	.1%	2.01E+03	2.00E+03	18	18	100.0%
21 Apr 1988	2.00E+03	92.9%	2.669E+00	.1%	2.01E+03	2.00E+03	18	18	100.0%
22 Apr 1988	2.15E+03	99.9%	2.264E+00	.1%	2.16E+03	2.15E+03	15	15	100.0%
23 Apr 1988	2.16E+03	100.0%	2.507E+00	.1%	2.16E+03	2.15E+03	8	8	100.0%
24 Apr 1988	2.15E+03	99.9%	2.808E+00	.1%	2.16E+03	2.15E+03	15	15	100.0%
25 Apr 1988	2.16E+03	100.1%	2.249E+00	.1%	2.16E+03	2.15E+03	18	18	100.0%
26 Apr 1988	2.16E+03	100.1%	2.342E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
27 Apr 1988	2.16E+03	100.1%	1.969E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
Summary	2.06E+03	95.4%	7.771E+01	3.8%	2.16E+03	1.98E+03	242	242	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: Room

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
13 Apr 1988	5.01E-03	2.243E-02	1.00E-01	0.00E+00	20	20	100.0%
14 Apr 1988	1.11E-01	1.308E-01	5.63E-01	0.00E+00	19	19	100.0%
15 Apr 1988	1.76E-02	4.389E-02	1.36E-01	0.00E+00	19	19	100.0%
16 Apr 1988	1.42E-02	3.802E-02	1.49E-01	0.00E+00	19	19	100.0%
17 Apr 1988	5.35E-03	2.395E-02	1.07E-01	0.00E+00	20	20	100.0%
18 Apr 1988	2.07E-02	4.131E-02	1.30E-01	0.00E+00	18	18	100.0%
19 Apr 1988	1.28E-02	3.246E-02	1.15E-01	0.00E+00	19	19	100.0%
20 Apr 1988	5.92E-03	2.648E-02	1.18E-01	0.00E+00	20	20	100.0%
21 Apr 1988	1.39E-03	6.057E-03	2.64E-02	0.00E+00	19	19	100.0%
22 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
23 Apr 1988	1.34E-02	2.509E-02	6.08E-02	0.00E+00	8	8	100.0%
24 Apr 1988	5.73E-03	2.220E-02	8.60E-02	0.00E+00	15	15	100.0%
25 Apr 1988	1.91E-03	8.526E-03	3.81E-02	0.00E+00	20	20	100.0%
26 Apr 1988	1.95E-02	3.538E-02	1.04E-01	0.00E+00	19	19	100.0%
27 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
Summary	1.59E-02	5.046E-02	5.63E-01	0.00E+00	270	270	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 16 Apr 1988

Summary Data for: Holding Chamber

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
13 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
14 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
15 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
16 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
Summary	0.00E+00	0.000E+00	0.00E+00	0.00E+00	77	77	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 0 ppm Chamber

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
13 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
14 Apr 1988	1.19E-02	5.032E-02	2.13E-01	0.00E+00	18	18	100.0%
15 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
16 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
17 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
18 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	18	18	100.0%
19 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
20 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
21 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
22 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
23 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	8	8	100.0%
24 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
25 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
26 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
27 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
Summary	7.94E-04	1.302E-02	2.13E-01	0.00E+00	269	269	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 280 ppm Chamber

/Concentration

Range=2.52E+2 to 3.08E+2

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	2.77E+02	98.8%	6.033E+00	2.2%	2.89E+02	2.67E+02	17	17	100.0%
14 Apr 1988	2.77E+02	98.9%	6.033E+00	2.2%	2.89E+02	2.65E+02	16	16	100.0%
15 Apr 1988	2.79E+02	99.7%	3.874E+00	1.4%	2.88E+02	2.73E+02	16	16	100.0%
16 Apr 1988	2.81E+02	100.4%	2.722E+00	1.0%	2.87E+02	2.78E+02	17	17	100.0%
17 Apr 1988	2.83E+02	101.0%	4.214E+00	1.5%	2.93E+02	2.78E+02	17	17	100.0%
18 Apr 1988	2.76E+02	98.6%	1.661E+01	6.0%	2.95E+02	2.23E+02	15	14	93.3%
19 Apr 1988	2.79E+02	99.7%	5.662E+00	2.0%	2.89E+02	2.72E+02	16	16	100.0%
20 Apr 1988	2.76E+02	98.5%	5.273E+00	1.9%	2.85E+02	2.67E+02	16	16	100.0%
21 Apr 1988	2.79E+02	99.7%	5.031E+00	1.8%	2.89E+02	2.72E+02	16	16	100.0%
22 Apr 1988	2.75E+02	98.3%	6.359E+00	2.3%	2.88E+02	2.61E+02	15	15	100.0%
23 Apr 1988	2.81E+02	100.3%	7.702E+00	2.7%	2.92E+02	2.67E+02	8	8	100.0%
24 Apr 1988	2.77E+02	99.1%	2.931E+00	1.1%	2.84E+02	2.72E+02	15	15	100.0%
25 Apr 1988	2.78E+02	99.1%	4.118E+00	1.5%	2.89E+02	2.71E+02	16	16	100.0%
26 Apr 1988	2.79E+02	99.6%	2.994E+00	1.1%	2.86E+02	2.75E+02	16	16	100.0%
27 Apr 1988	2.80E+02	99.8%	5.429E+00	1.9%	2.95E+02	2.71E+02	16	16	100.0%
Summary	2.78E+02	99.4%	6.518E+00	2.3%	2.95E+02	2.23E+02	232	231	99.6%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 1400 ppm Chamber

/Concentration

Range=1.26E+3 to 1.54E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	1.40E+03	100.0%	4.161E+01	3.0%	1.53E+03	1.34E+03	17	17	100.0%
14 Apr 1988	1.39E+03	99.2%	3.795E+01	2.7%	1.42E+03	1.31E+03	15	15	100.0%
15 Apr 1988	1.40E+03	100.2%	1.742E+01	1.2%	1.44E+03	1.37E+03	16	16	100.0%
16 Apr 1988	1.44E+03	102.7%	1.472E+01	1.0%	1.48E+03	1.42E+03	18	18	100.0%
17 Apr 1988	1.44E+03	102.7%	2.320E+01	1.6%	1.49E+03	1.41E+03	17	17	100.0%
18 Apr 1988	1.36E+03	96.9%	1.870E+02	13.8%	1.47E+03	6.95E+02	15	14	93.3%
19 Apr 1988	1.41E+03	100.5%	3.028E+01	2.2%	1.47E+03	1.37E+03	16	16	100.0%
20 Apr 1988	1.39E+03	99.6%	1.905E+01	1.4%	1.43E+03	1.37E+03	17	17	100.0%
21 Apr 1988	1.40E+03	100.2%	2.415E+01	1.7%	1.44E+03	1.36E+03	16	16	100.0%
22 Apr 1988	1.39E+03	99.2%	5.099E+01	3.7%	1.51E+03	1.27E+03	14	14	100.0%
23 Apr 1988	1.39E+03	99.5%	3.222E+01	2.3%	1.44E+03	1.33E+03	8	8	100.0%
24 Apr 1988	1.41E+03	100.4%	1.538E+01	1.1%	1.44E+03	1.38E+03	15	15	100.0%
25 Apr 1988	1.39E+03	99.3%	2.894E+01	2.1%	1.45E+03	1.32E+03	16	16	100.0%
26 Apr 1988	1.40E+03	100.3%	1.356E+01	1.0%	1.44E+03	1.39E+03	16	16	100.0%
27 Apr 1988	1.40E+03	99.8%	2.161E+01	1.5%	1.45E+03	1.37E+03	16	16	100.0%
Summary	1.40E+03	100.1%	5.641E+01	4.0%	1.53E+03	6.95E+02	232	231	99.6%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 7000 ppm Chamber

/Concentration

Range=6.30E+3 to 7.70E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	7.03E+03	100.5%	1.395E+02	2.0%	7.30E+03	6.80E+03	17	17	100.0%
14 Apr 1988	6.97E+03	99.6%	1.161E+02	1.7%	7.29E+03	6.74E+03	16	16	100.0%
15 Apr 1988	7.01E+03	100.1%	6.795E+01	1.0%	7.14E+03	6.89E+03	17	17	100.0%
16 Apr 1988	7.11E+03	101.6%	5.118E+01	.7%	7.21E+03	7.04E+03	17	17	100.0%
17 Apr 1988	7.13E+03	101.9%	1.051E+02	1.5%	7.38E+03	7.02E+03	17	17	100.0%
18 Apr 1988	6.56E+03	93.7%	1.812E+03	27.6%	7.29E+03	3.13E+01	15	14	93.3%
19 Apr 1988	6.97E+03	99.6%	1.446E+02	2.1%	7.29E+03	6.75E+03	16	16	100.0%
20 Apr 1988	6.93E+03	98.9%	9.956E+01	1.4%	7.10E+03	6.79E+03	17	17	100.0%
21 Apr 1988	6.98E+03	99.7%	7.921E+01	1.1%	7.17E+03	6.84E+03	16	16	100.0%
22 Apr 1988	7.00E+03	100.1%	1.580E+02	2.3%	7.46E+03	6.78E+03	13	13	100.0%
23 Apr 1988	6.99E+03	99.8%	1.192E+02	1.7%	7.12E+03	6.76E+03	7	7	100.0%
24 Apr 1988	7.08E+03	101.1%	9.097E+01	1.3%	7.24E+03	6.85E+03	15	15	100.0%
25 Apr 1988	6.98E+03	99.7%	1.114E+02	1.6%	7.35E+03	6.87E+03	17	17	100.0%
26 Apr 1988	7.00E+03	99.9%	5.573E+01	.8%	7.14E+03	6.93E+03	16	16	100.0%
27 Apr 1988	7.00E+03	99.9%	1.093E+02	1.6%	7.25E+03	6.78E+03	17	17	100.0%
Summary	6.98E+03	99.8%	4.730E+02	6.8%	7.46E+03	3.13E+01	233	232	99.6%

Daily Summation For Isoprene - IRT (Mice)

From 11 Apr 1988 through 16 Apr 1988

Summary Data for: Holding Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
11 Apr 1988	14.6	97.2%	.02	.1%	14.6	14.6	5	5	100.0%
12 Apr 1988	14.7	98.1%	.13	.9%	14.8	14.4	9	9	100.0%
13 Apr 1988	14.8	98.3%	.02	.1%	14.8	14.7	8	8	100.0%
14 Apr 1988	14.8	98.4%	.05	.3%	14.8	14.7	8	8	100.0%
15 Apr 1988	14.8	98.5%	.07	.5%	14.9	14.7	8	8	100.0%
16 Apr 1988	14.7	97.9%	.01	.1%	14.7	14.7	7	7	100.0%
Summary	14.7	98.1%	.09	.6%	14.9	14.4	45	45	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 0 ppm Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	15.0	100.3%	.18	1.2%	15.2	14.8	6	6	100.0%
14 Apr 1988	15.2	101.2%	.04	.3%	15.2	15.1	7	7	100.0%
15 Apr 1988	15.2	101.3%	.03	.2%	15.2	15.1	8	8	100.0%
16 Apr 1988	15.2	101.1%	.02	.1%	15.2	15.1	7	7	100.0%
17 Apr 1988	15.2	101.3%	.03	.2%	15.2	15.2	8	8	100.0%
18 Apr 1988	15.2	101.2%	.05	.3%	15.2	15.1	8	8	100.0%
19 Apr 1988	15.1	100.9%	.03	.2%	15.2	15.1	7	7	100.0%
20 Apr 1988	15.0	99.7%	.07	.5%	15.1	14.9	8	8	100.0%
21 Apr 1988	14.9	99.5%	.02	.1%	14.9	14.9	8	8	100.0%
22 Apr 1988	15.0	99.9%	.03	.2%	15.0	15.0	8	8	100.0%
23 Apr 1988	15.1	100.4%	.02	.1%	15.1	15.0	8	8	100.0%
24 Apr 1988	15.1	100.6%	.01	.1%	15.1	15.1	8	8	100.0%
25 Apr 1988	15.1	100.4%	.03	.2%	15.1	15.0	8	8	100.0%
26 Apr 1988	15.0	100.2%	.04	.2%	15.1	15.0	7	7	100.0%
27 Apr 1988	14.9	99.4%	.07	.5%	15.0	14.8	8	8	100.0%
Summary	15.1	100.5%	.11	.7%	15.2	14.8	114	114	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 280 ppm Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	15.1	100.7%	.13	.9%	15.2	14.9	6	6	100.0%
14 Apr 1988	14.9	99.2%	.20	1.4%	15.2	14.7	8	8	100.0%
15 Apr 1988	14.8	98.5%	.03	.2%	14.8	14.7	8	8	100.0%
16 Apr 1988	14.7	98.3%	.01	.1%	14.7	14.7	7	7	100.0%
17 Apr 1988	14.8	98.4%	.02	.1%	14.8	14.7	8	8	100.0%
18 Apr 1988	14.8	98.4%	.03	.2%	14.8	14.7	8	8	100.0%
19 Apr 1988	14.8	98.8%	.04	.3%	14.9	14.7	7	7	100.0%
20 Apr 1988	14.9	99.5%	.09	.6%	15.0	14.7	8	8	100.0%
21 Apr 1988	15.0	99.8%	.02	.2%	15.0	15.0	8	8	100.0%
22 Apr 1988	15.0	100.3%	.04	.3%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.4%	.02	.2%	15.1	15.0	8	8	100.0%
24 Apr 1988	15.1	100.9%	.02	.2%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.6%	.06	.4%	15.2	15.0	8	8	100.0%
26 Apr 1988	15.1	100.3%	.05	.3%	15.1	15.0	7	7	100.0%
27 Apr 1988	14.9	99.6%	.05	.3%	15.0	14.9	8	8	100.0%
Summary	14.9	99.6%	.15	1.0%	15.2	14.7	115	115	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 1400 ppm Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	15.3	102.0%	.17	1.1%	15.4	15.1	6	6	100.0%
14 Apr 1988	15.3	101.8%	.10	.6%	15.4	15.2	8	8	100.0%
15 Apr 1988	15.2	101.5%	.05	.3%	15.3	15.1	8	8	100.0%
16 Apr 1988	15.2	101.1%	.02	.2%	15.2	15.1	7	7	100.0%
17 Apr 1988	15.2	101.4%	.03	.2%	15.2	15.2	8	8	100.0%
18 Apr 1988	15.2	101.5%	.03	.2%	15.3	15.2	8	8	100.0%
19 Apr 1988	15.2	101.1%	.04	.2%	15.2	15.1	7	7	100.0%
20 Apr 1988	15.2	101.4%	.03	.2%	15.2	15.1	8	8	100.0%
21 Apr 1988	15.0	100.1%	.08	.6%	15.2	15.0	8	8	100.0%
22 Apr 1988	15.1	100.3%	.04	.2%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.6%	.03	.2%	15.1	15.1	8	8	100.0%
24 Apr 1988	15.1	101.0%	.02	.2%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.7%	.05	.3%	15.2	15.0	8	8	100.0%
26 Apr 1988	15.1	100.4%	.05	.3%	15.2	15.0	7	7	100.0%
27 Apr 1988	15.0	99.8%	.07	.5%	15.1	14.9	8	8	100.0%
Summary	15.1	101.0%	.11	.7%	15.4	14.9	115	115	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 7000 ppm Chamber		/Exhaust Air Flow		Range= 12.0 to 18.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	15.2	101.2%	.14	.9%	15.3	15.0	6	6	100.0%
14 Apr 1988	15.0	100.0%	.19	1.3%	15.3	14.8	8	8	100.0%
15 Apr 1988	14.9	99.4%	.06	.4%	15.0	14.8	8	8	100.0%
16 Apr 1988	14.9	99.2%	.05	.3%	15.0	14.8	7	7	100.0%
17 Apr 1988	14.9	99.4%	.04	.3%	15.0	14.9	8	8	100.0%
18 Apr 1988	14.9	99.5%	.06	.4%	15.1	14.9	8	8	100.0%
19 Apr 1988	14.9	99.0%	.07	.4%	15.0	14.8	7	7	100.0%
20 Apr 1988	14.8	98.9%	.04	.3%	14.9	14.8	8	8	100.0%
21 Apr 1988	14.9	99.6%	.08	.5%	15.0	14.8	8	8	100.0%
22 Apr 1988	15.0	100.3%	.05	.3%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.6%	.03	.2%	15.1	15.1	8	8	100.0%
24 Apr 1988	15.1	100.9%	.04	.3%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.7%	.05	.3%	15.2	15.1	8	8	100.0%
26 Apr 1988	15.0	100.3%	.06	.4%	15.2	15.0	7	7	100.0%
27 Apr 1988	15.0	100.3%	.08	.5%	15.1	15.0	8	8	100.0%
Summary	15.0	99.9%	.13	.8%	15.3	14.8	115	115	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 11 Apr 1988 through 16 Apr 1988

Summary Data for: Holding Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
11 Apr 1988	49.4	89.8%	1.34	2.7%	51.0	48.0	5	5	100.0%
12 Apr 1988	55.9	101.6%	4.96	8.9%	61.0	49.0	9	9	100.0%
13 Apr 1988	56.8	103.2%	4.03	7.1%	61.0	51.0	8	8	100.0%
14 Apr 1988	50.6	91.9%	3.13	6.2%	58.0	47.0	9	9	100.0%
15 Apr 1988	54.6	99.3%	4.69	8.6%	59.0	47.0	8	8	100.0%
16 Apr 1988	57.1	103.9%	1.57	2.8%	59.0	55.0	7	7	100.0%
Summary	54.3	98.7%	4.57	8.4%	61.0	47.0	46	46	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 0 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	53.2	96.7%	1.83	3.5%	55.0	50.0	6	6	100.0%
14 Apr 1988	53.8	97.8%	1.20	2.2%	56.0	52.0	9	9	100.0%
15 Apr 1988	51.2	93.2%	1.49	2.9%	53.0	49.0	8	8	100.0%
16 Apr 1988	53.3	96.9%	1.11	2.1%	55.0	52.0	7	7	100.0%
17 Apr 1988	53.2	96.8%	1.91	3.6%	55.0	51.0	8	8	100.0%
18 Apr 1988	51.5	93.6%	2.56	5.0%	54.0	47.0	8	8	100.0%
19 Apr 1988	53.2	96.8%	3.65	6.9%	57.0	48.0	8	8	100.0%
20 Apr 1988	58.3	105.9%	4.62	7.9%	64.0	51.0	8	8	100.0%
21 Apr 1988	58.3	105.9%	2.19	3.8%	62.0	56.0	8	8	100.0%
22 Apr 1988	54.2	98.6%	2.92	5.4%	57.0	50.0	8	8	100.0%
23 Apr 1988	52.0	94.5%	2.39	4.6%	56.0	49.0	8	8	100.0%
24 Apr 1988	48.1	87.5%	4.55	9.5%	53.0	40.0	8	8	100.0%
25 Apr 1988	48.9	88.9%	3.18	6.5%	53.0	45.0	8	8	100.0%
26 Apr 1988	52.6	95.6%	2.51	4.8%	55.0	48.0	7	7	100.0%
27 Apr 1988	58.0	105.5%	4.08	7.0%	66.0	54.0	7	7	100.0%
Summary	53.3	96.9%	4.02	7.5%	66.0	40.0	116	116	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 280 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	54.2	98.5%	1.47	2.7%	56.0	52.0	6	6	100.0%
14 Apr 1988	54.6	99.3%	.92	1.7%	56.0	54.0	8	8	100.0%
15 Apr 1988	56.4	102.5%	2.62	4.6%	59.0	53.0	8	8	100.0%
16 Apr 1988	55.1	100.3%	1.21	2.2%	57.0	54.0	7	7	100.0%
17 Apr 1988	54.7	99.5%	1.98	3.6%	57.0	52.0	8	8	100.0%
18 Apr 1988	52.9	96.1%	2.10	4.0%	55.0	49.0	8	8	100.0%
19 Apr 1988	55.0	100.0%	4.07	7.4%	59.0	49.0	8	8	100.0%
20 Apr 1988	57.0	103.6%	3.21	5.6%	60.0	51.0	8	8	100.0%
21 Apr 1988	55.0	100.0%	2.93	5.3%	59.0	51.0	8	8	100.0%
22 Apr 1988	52.5	95.5%	4.07	7.8%	57.0	46.0	8	8	100.0%
23 Apr 1988	49.7	90.5%	2.49	5.0%	54.0	46.0	8	8	100.0%
24 Apr 1988	45.9	83.4%	4.76	10.4%	52.0	38.0	8	7	87.5%
25 Apr 1988	46.3	84.1%	3.88	8.4%	50.0	40.0	8	8	100.0%
26 Apr 1988	52.1	94.8%	4.81	9.2%	57.0	44.0	7	7	100.0%
27 Apr 1988	59.6	108.3%	1.99	3.3%	63.0	57.0	7	7	100.0%
Summary	53.3	97.0%	4.67	8.8%	63.0	38.0	115	114	99.1%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 1400 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	51.0	92.7%	2.10	4.1%	53.0	48.0	6	6	100.0%
14 Apr 1988	56.3	102.4%	2.35	4.2%	60.0	51.0	9	9	100.0%
15 Apr 1988	57.3	104.1%	2.71	4.7%	61.0	54.0	8	8	100.0%
16 Apr 1988	56.4	102.6%	1.81	3.2%	58.0	53.0	7	7	100.0%
17 Apr 1988	55.7	101.4%	2.55	4.6%	58.0	52.0	8	8	100.0%
18 Apr 1988	52.5	95.5%	2.33	4.4%	55.0	48.0	8	8	100.0%
19 Apr 1988	54.1	98.4%	3.14	5.8%	57.0	49.0	8	8	100.0%
20 Apr 1988	59.8	108.6%	2.25	3.8%	63.0	56.0	8	8	100.0%
21 Apr 1988	58.4	106.1%	1.92	3.3%	60.0	55.0	8	8	100.0%
22 Apr 1988	54.5	99.1%	2.45	4.5%	58.0	51.0	8	8	100.0%
23 Apr 1988	53.7	97.7%	1.83	3.4%	55.0	51.0	8	8	100.0%
24 Apr 1988	49.1	89.3%	4.64	9.5%	54.0	43.0	8	8	100.0%
25 Apr 1988	50.6	92.0%	3.11	6.2%	54.0	46.0	8	8	100.0%
26 Apr 1988	55.1	100.3%	3.98	7.2%	60.0	49.0	7	7	100.0%
27 Apr 1988	59.3	107.8%	2.50	4.2%	64.0	57.0	7	7	100.0%
Summary	55.0	99.9%	4.00	7.3%	64.0	43.0	116	116	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 7000 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	56.7	103.0%	2.94	5.2%	59.0	52.0	6	6	100.0%
14 Apr 1988	57.2	104.0%	1.56	2.7%	60.0	55.0	9	9	100.0%
15 Apr 1988	55.7	101.4%	1.28	2.3%	57.0	54.0	8	8	100.0%
16 Apr 1988	56.6	102.9%	1.51	2.7%	58.0	54.0	7	7	100.0%
17 Apr 1988	55.0	100.0%	2.20	4.0%	58.0	52.0	8	8	100.0%
18 Apr 1988	54.2	98.6%	2.12	3.9%	57.0	51.0	8	8	100.0%
19 Apr 1988	56.3	102.3%	3.20	5.7%	59.0	51.0	8	8	100.0%
20 Apr 1988	58.1	105.7%	3.48	6.0%	62.0	52.0	8	8	100.0%
21 Apr 1988	56.4	102.5%	2.56	4.5%	61.0	52.0	8	8	100.0%
22 Apr 1988	52.7	95.9%	4.27	8.1%	57.0	46.0	8	8	100.0%
23 Apr 1988	51.0	92.7%	2.88	5.6%	55.0	46.0	8	8	100.0%
24 Apr 1988	47.3	85.9%	5.47	11.6%	53.0	38.0	8	7	87.5%
25 Apr 1988	48.4	88.0%	3.70	7.7%	52.0	42.0	8	8	100.0%
26 Apr 1988	53.9	97.9%	4.60	8.5%	59.0	46.0	7	7	100.0%
27 Apr 1988	58.3	106.0%	3.50	6.0%	64.0	54.0	7	7	100.0%
Summary	54.5	99.0%	4.46	8.2%	64.0	38.0	116	115	99.1%

Daily Summation For Isoprene - IRT (Mice)

From 11 Apr 1988 through 27 Apr 1988

Summary Data for: Room

/Temperature

Range= 69.0 to 75.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
11 Apr 1988	71.6	99.5%	.35	.5%	72.2	71.3	5	5	100.0%
12 Apr 1988	72.2	100.3%	.44	.6%	72.8	71.3	9	9	100.0%
13 Apr 1988	72.5	100.6%	.40	.6%	73.0	72.0	8	8	100.0%
14 Apr 1988	72.6	100.9%	.82	1.1%	73.4	71.1	8	8	100.0%
15 Apr 1988	73.3	101.8%	.15	.2%	73.5	73.1	8	8	100.0%
16 Apr 1988	72.9	101.3%	.95	1.3%	73.5	70.6	8	8	100.0%
17 Apr 1988	73.1	101.5%	.23	.3%	73.4	72.7	8	8	100.0%
18 Apr 1988	73.7	102.3%	1.38	1.9%	77.0	72.8	8	7	87.5%
19 Apr 1988	73.4	101.9%	.28	.4%	73.9	73.1	8	8	100.0%
20 Apr 1988	72.8	101.1%	1.13	1.6%	73.8	70.1	8	8	100.0%
21 Apr 1988	72.2	100.3%	1.94	2.7%	73.2	67.4	8	7	87.5%
22 Apr 1988	73.0	101.4%	.31	.4%	73.2	72.3	8	8	100.0%
23 Apr 1988	72.3	100.4%	1.99	2.7%	73.4	67.4	8	7	87.5%
24 Apr 1988	73.2	101.6%	.29	.4%	73.6	72.7	8	8	100.0%
25 Apr 1988	73.1	101.5%	.27	.4%	73.7	72.8	8	8	100.0%
26 Apr 1988	73.1	101.6%	.18	.2%	73.4	72.9	7	7	100.0%
27 Apr 1988	73.2	101.7%	.27	.4%	73.5	72.7	8	8	100.0%
Summary	72.9	101.2%	.97	1.3%	77.0	67.4	133	130	97.7%

Daily Summation For Isoprene - IRT (Mice)

From 11 Apr 1988 through 16 Apr 1988

Summary Data for: Holding Chamber /Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
11 Apr 1988	75.9	101.2%	.32	.4%	76.2	75.5	5	5	100.0%
12 Apr 1988	75.3	100.4%	.37	.5%	75.7	74.5	9	9	100.0%
13 Apr 1988	74.6	99.5%	.25	.3%	75.0	74.3	8	8	100.0%
14 Apr 1988	73.4	97.9%	.43	.6%	74.0	72.9	7	7	100.0%
15 Apr 1988	76.5	102.0%	1.19	1.6%	77.8	73.8	8	8	100.0%
16 Apr 1988	75.0	100.0%	.56	.7%	75.6	74.3	7	7	100.0%
Summary	75.1	100.2%	1.14	1.5%	77.8	72.9	44	44	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 0 ppm Chamber

/Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	72.7	97.0%	.37	.5%	73.3	72.3	6	6	100.0%
14 Apr 1988	73.4	97.9%	.61	.8%	74.1	72.2	7	7	100.0%
15 Apr 1988	74.6	99.5%	.53	.7%	75.3	73.5	8	8	100.0%
16 Apr 1988	75.1	100.1%	.42	.6%	75.5	74.6	7	7	100.0%
17 Apr 1988	76.9	102.5%	1.02	1.3%	77.5	74.5	8	8	100.0%
18 Apr 1988	75.4	100.5%	.87	1.1%	77.3	74.6	8	8	100.0%
19 Apr 1988	75.7	100.9%	.62	.8%	76.5	74.6	8	8	100.0%
20 Apr 1988	75.1	100.1%	1.17	1.6%	77.2	74.0	9	9	100.0%
21 Apr 1988	74.0	98.7%	.23	.3%	74.2	73.5	8	8	100.0%
22 Apr 1988	74.2	99.0%	.19	.3%	74.4	73.9	8	8	100.0%
23 Apr 1988	74.2	98.9%	.19	.3%	74.5	73.9	8	8	100.0%
24 Apr 1988	74.2	98.9%	.45	.6%	74.7	73.5	8	8	100.0%
25 Apr 1988	74.0	98.6%	.38	.5%	74.9	73.7	8	8	100.0%
26 Apr 1988	73.7	98.3%	.19	.3%	74.0	73.4	8	8	100.0%
27 Apr 1988	73.6	98.1%	.23	.3%	73.9	73.1	8	8	100.0%
Summary	74.5	99.3%	1.14	1.5%	77.5	72.2	117	117	100.0%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 280 ppm Chamber

/Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	72.0	96.0%	.30	.4%	72.5	71.7	6	3	50.0%
14 Apr 1988	72.6	96.8%	.62	.9%	73.2	71.6	7	6	85.7%
15 Apr 1988	73.3	97.7%	.19	.3%	73.4	72.8	8	8	100.0%
16 Apr 1988	73.5	98.0%	.16	.2%	73.8	73.3	7	7	100.0%
17 Apr 1988	73.4	97.9%	.09	.1%	73.5	73.2	8	8	100.0%
18 Apr 1988	74.0	98.7%	.57	.8%	74.4	73.0	8	8	100.0%
19 Apr 1988	74.9	99.9%	.36	.5%	75.3	74.2	8	8	100.0%
20 Apr 1988	75.3	100.4%	.25	.3%	75.6	75.0	8	8	100.0%
21 Apr 1988	75.4	100.6%	.29	.4%	75.7	74.8	8	8	100.0%
22 Apr 1988	75.5	100.7%	.24	.3%	75.8	75.1	8	8	100.0%
23 Apr 1988	75.5	100.7%	.35	.5%	76.0	75.0	8	8	100.0%
24 Apr 1988	75.7	101.0%	.45	.6%	76.4	75.1	8	8	100.0%
25 Apr 1988	75.5	100.6%	.40	.5%	76.2	74.9	8	8	100.0%
26 Apr 1988	75.6	100.8%	.33	.4%	76.0	74.8	8	8	100.0%
27 Apr 1988	75.5	100.6%	.44	.6%	76.1	74.6	8	8	100.0%
Summary	74.6	99.5%	1.22	1.6%	76.4	71.6	116	112	96.6%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 1400 ppm Chamber /Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	72.1	96.2%	.20	.3%	72.5	72.0	6	6	100.0%
14 Apr 1988	72.7	97.0%	.68	.9%	73.4	71.8	8	6	75.0%
15 Apr 1988	73.6	98.2%	.30	.4%	74.0	73.0	8	8	100.0%
16 Apr 1988	74.0	98.7%	.15	.2%	74.2	73.8	7	7	100.0%
17 Apr 1988	73.8	98.4%	.21	.3%	74.1	73.6	8	8	100.0%
18 Apr 1988	74.7	99.6%	.60	.8%	75.2	73.4	8	8	100.0%
19 Apr 1988	75.7	100.9%	.40	.5%	76.2	74.9	8	8	100.0%
20 Apr 1988	75.5	100.6%	.35	.5%	75.9	75.1	8	8	100.0%
21 Apr 1988	75.6	100.8%	.51	.7%	76.1	74.7	8	8	100.0%
22 Apr 1988	75.9	101.2%	.52	.7%	76.5	75.0	8	8	100.0%
23 Apr 1988	75.8	101.1%	.46	.6%	76.4	75.0	8	8	100.0%
24 Apr 1988	76.1	101.4%	.68	.9%	77.0	75.0	8	8	100.0%
25 Apr 1988	75.6	100.7%	.67	.9%	76.8	74.8	8	8	100.0%
26 Apr 1988	75.5	100.7%	.43	.6%	76.0	74.6	8	8	100.0%
27 Apr 1988	76.2	101.5%	.40	.5%	76.6	75.4	8	8	100.0%
Summary	74.9	99.9%	1.28	1.7%	77.0	71.8	117	115	98.3%

Daily Summation For Isoprene - IRT (Mice)

From 13 Apr 1988 through 27 Apr 1988

Summary Data for: 7000 ppm Chamber

/Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 Apr 1988	72.2	96.3%	.28	.4%	72.7	72.0	6	6	100.0%
14 Apr 1988	72.9	97.1%	.64	.9%	73.6	71.9	8	7	87.5%
15 Apr 1988	73.9	98.5%	.31	.4%	74.4	73.3	8	8	100.0%
16 Apr 1988	74.1	98.8%	.27	.4%	74.5	73.6	7	7	100.0%
17 Apr 1988	74.1	98.8%	.23	.3%	74.5	73.8	8	8	100.0%
18 Apr 1988	74.3	99.1%	.29	.4%	74.6	73.9	8	8	100.0%
19 Apr 1988	75.0	100.0%	.41	.6%	75.6	74.2	8	8	100.0%
20 Apr 1988	75.7	100.9%	.31	.4%	75.9	75.0	8	8	100.0%
21 Apr 1988	75.9	101.2%	.30	.4%	76.1	75.2	8	8	100.0%
22 Apr 1988	75.9	101.2%	.17	.2%	76.0	75.5	8	8	100.0%
23 Apr 1988	75.8	101.1%	.29	.4%	76.2	75.2	8	8	100.0%
24 Apr 1988	76.1	101.4%	.43	.6%	76.5	75.5	8	8	100.0%
25 Apr 1988	75.9	101.2%	.40	.5%	76.7	75.5	8	8	100.0%
26 Apr 1988	75.8	101.1%	.29	.4%	76.1	75.2	8	8	100.0%
27 Apr 1988	75.8	101.1%	.40	.5%	76.4	75.0	8	8	100.0%
Summary	74.9	99.9%	1.21	1.6%	76.7	71.9	117	116	99.1%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 4 May 1988

Summary Data for: Standard Gas

/Concentration

Range=1.94E+3 to 2.37E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
15 Apr 1988	1.99E+03	92.4%	4.220E+00	.2%	2.00E+03	1.99E+03	17	17	100.0%
16 Apr 1988	2.00E+03	92.7%	2.004E+00	.1%	2.00E+03	2.00E+03	17	17	100.0%
17 Apr 1988	2.00E+03	92.7%	2.045E+00	.1%	2.00E+03	2.00E+03	17	17	100.0%
18 Apr 1988	2.00E+03	92.8%	3.226E+00	.2%	2.01E+03	1.99E+03	15	15	100.0%
19 Apr 1988	2.00E+03	92.9%	2.609E+00	.1%	2.01E+03	2.00E+03	17	17	100.0%
20 Apr 1988	2.00E+03	92.9%	1.978E+00	.1%	2.01E+03	2.00E+03	18	18	100.0%
21 Apr 1988	2.00E+03	92.9%	2.669E+00	.1%	2.01E+03	2.00E+03	18	18	100.0%
22 Apr 1988	2.15E+03	99.9%	2.264E+00	.1%	2.16E+03	2.15E+03	15	15	100.0%
23 Apr 1988	2.16E+03	100.0%	2.507E+00	.1%	2.16E+03	2.15E+03	8	8	100.0%
24 Apr 1988	2.15E+03	99.9%	2.808E+00	.1%	2.16E+03	2.15E+03	15	15	100.0%
25 Apr 1988	2.16E+03	100.1%	2.249E+00	.1%	2.16E+03	2.15E+03	18	18	100.0%
26 Apr 1988	2.16E+03	100.1%	2.342E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
27 Apr 1988	2.16E+03	100.1%	1.969E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
28 Apr 1988	2.15E+03	100.0%	2.873E+00	.1%	2.16E+03	2.15E+03	18	18	100.0%
29 Apr 1988	2.20E+03	102.1%	1.133E+02	5.1%	2.45E+03	2.15E+03	18	15	83.3%
30 Apr 1988	2.16E+03	100.2%	2.152E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
1 May 1988	2.16E+03	100.1%	1.934E+00	.1%	2.16E+03	2.15E+03	18	18	100.0%
2 May 1988	2.15E+03	99.9%	5.426E+00	.3%	2.16E+03	2.15E+03	18	18	100.0%
3 May 1988	2.15E+03	99.9%	1.896E+00	.1%	2.16E+03	2.15E+03	17	17	100.0%
4 May 1988	2.15E+03	99.9%	2.301E+00	.1%	2.16E+03	2.15E+03	18	18	100.0%
Summary	2.10E+03	97.5%	8.160E+01	3.9%	2.45E+03	1.99E+03	333	330	99.1%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 4 May 1988

Summary Data for: Room

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
15 Apr 1988	1.76E-02	4.389E-02	1.36E-01	0.00E+00	19	19	100.0%
16 Apr 1988	1.42E-02	3.802E-02	1.49E-01	0.00E+00	19	19	100.0%
17 Apr 1988	5.35E-03	2.395E-02	1.07E-01	0.00E+00	20	20	100.0%
18 Apr 1988	2.07E-02	4.131E-02	1.30E-01	0.00E+00	18	18	100.0%
19 Apr 1988	1.28E-02	3.246E-02	1.15E-01	0.00E+00	19	19	100.0%
20 Apr 1988	5.92E-03	2.648E-02	1.18E-01	0.00E+00	20	20	100.0%
21 Apr 1988	1.39E-03	6.057E-03	2.64E-02	0.00E+00	19	19	100.0%
22 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
23 Apr 1988	1.34E-02	2.509E-02	6.08E-02	0.00E+00	8	8	100.0%
24 Apr 1988	5.73E-03	2.220E-02	8.60E-02	0.00E+00	15	15	100.0%
25 Apr 1988	1.91E-03	8.526E-03	3.81E-02	0.00E+00	20	20	100.0%
26 Apr 1988	1.95E-02	3.538E-02	1.04E-01	0.00E+00	19	19	100.0%
27 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
28 Apr 1988	2.35E-02	4.279E-02	1.47E-01	0.00E+00	19	19	100.0%
29 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
30 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	17	17	100.0%
1 May 1988	4.91E-03	2.140E-02	9.33E-02	0.00E+00	19	19	100.0%
2 May 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
3 May 1988	1.34E-02	3.295E-02	1.35E-01	0.00E+00	20	20	100.0%
4 May 1988	7.31E-02	1.746E-01	7.58E-01	0.00E+00	18	18	100.0%
Summary	1.16E-02	4.830E-02	7.58E-01	0.00E+00	362	362	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 21 Apr 1988

Summary Data for: Holding Chamber

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
15 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
16 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
17 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
18 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	18	18	100.0%
19 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
20 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
21 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
Summary	0.00E+00	0.000E+00	0.00E+00	0.00E+00	134	134	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 17 Apr 1988 through 4 May 1988

Summary Data for: 0 ppm Chamber

/Concentration

Range=0.00E+0 to 1.00E+0

Date	Mean	Std Dev	Maximum	Minimum	N	N in	% N in
17 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
18 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	18	18	100.0%
19 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
20 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
21 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
22 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
23 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	8	8	100.0%
24 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	15	15	100.0%
25 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
26 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
27 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
28 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
29 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
30 Apr 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	17	17	100.0%
1 May 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
2 May 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	19	19	100.0%
3 May 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	20	20	100.0%
4 May 1988	0.00E+00	0.000E+00	0.00E+00	0.00E+00	18	18	100.0%
Summary	0.00E+00	0.000E+00	0.00E+00	0.00E+00	324	324	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 280 ppm Chamber

/Concentration

Range=2.52E+2 to 3.08E+2

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	2.76E+02	98.6%	1.661E+01	6.0%	2.95E+02	2.23E+02	15	14	93.3%
19 Apr 1988	2.79E+02	99.7%	5.662E+00	2.0%	2.89E+02	2.72E+02	16	16	100.0%
20 Apr 1988	2.76E+02	98.5%	5.273E+00	1.9%	2.85E+02	2.67E+02	16	16	100.0%
21 Apr 1988	2.79E+02	99.7%	5.031E+00	1.8%	2.89E+02	2.72E+02	16	16	100.0%
22 Apr 1988	2.75E+02	98.3%	6.359E+00	2.3%	2.88E+02	2.61E+02	15	15	100.0%
23 Apr 1988	2.81E+02	100.3%	7.702E+00	2.7%	2.92E+02	2.67E+02	8	8	100.0%
24 Apr 1988	2.77E+02	99.1%	2.931E+00	1.1%	2.84E+02	2.72E+02	15	15	100.0%
25 Apr 1988	2.78E+02	99.1%	4.118E+00	1.5%	2.89E+02	2.71E+02	16	16	100.0%
26 Apr 1988	2.79E+02	99.6%	2.994E+00	1.1%	2.86E+02	2.75E+02	16	16	100.0%
27 Apr 1988	2.80E+02	99.8%	5.429E+00	1.9%	2.95E+02	2.71E+02	16	16	100.0%
28 Apr 1988	2.84E+02	101.4%	5.828E+00	2.1%	2.95E+02	2.78E+02	17	17	100.0%
29 Apr 1988	2.81E+02	100.5%	7.233E+00	2.6%	3.05E+02	2.68E+02	16	16	100.0%
30 Apr 1988	2.84E+02	101.3%	5.506E+00	1.9%	2.97E+02	2.79E+02	16	16	100.0%
1 May 1988	2.86E+02	102.0%	3.580E+00	1.3%	2.90E+02	2.79E+02	16	16	100.0%
2 May 1988	2.79E+02	99.6%	1.397E+00	.5%	2.82E+02	2.77E+02	16	16	100.0%
3 May 1988	2.75E+02	98.0%	5.835E+00	2.1%	2.84E+02	2.65E+02	16	16	100.0%
4 May 1988	2.80E+02	100.1%	2.760E+00	1.0%	2.86E+02	2.76E+02	16	16	100.0%
Summary	2.79E+02	99.8%	6.820E+00	2.4%	3.05E+02	2.23E+02	262	261	99.6%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 1400 ppm Chamber

/Concentration

Range=1.26E+3 to 1.54E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	1.36E+03	96.9%	1.870E+02	13.8%	1.47E+03	6.95E+02	15	14	93.3%
19 Apr 1988	1.41E+03	100.5%	3.028E+01	2.2%	1.47E+03	1.37E+03	16	16	100.0%
20 Apr 1988	1.39E+03	99.6%	1.905E+01	1.4%	1.43E+03	1.37E+03	17	17	100.0%
21 Apr 1988	1.40E+03	100.2%	2.415E+01	1.7%	1.44E+03	1.36E+03	16	16	100.0%
22 Apr 1988	1.39E+03	99.2%	5.099E+01	3.7%	1.51E+03	1.27E+03	14	14	100.0%
23 Apr 1988	1.39E+03	99.5%	3.222E+01	2.3%	1.44E+03	1.33E+03	8	8	100.0%
24 Apr 1988	1.41E+03	100.4%	1.538E+01	1.1%	1.44E+03	1.38E+03	15	15	100.0%
25 Apr 1988	1.39E+03	99.3%	2.894E+01	2.1%	1.45E+03	1.32E+03	16	16	100.0%
26 Apr 1988	1.40E+03	100.3%	1.356E+01	1.0%	1.44E+03	1.39E+03	16	16	100.0%
27 Apr 1988	1.40E+03	99.8%	2.161E+01	1.5%	1.45E+03	1.37E+03	16	16	100.0%
28 Apr 1988	1.41E+03	100.7%	4.283E+01	3.0%	1.49E+03	1.35E+03	16	16	100.0%
29 Apr 1988	1.40E+03	100.3%	3.415E+01	2.4%	1.48E+03	1.33E+03	16	16	100.0%
30 Apr 1988	1.40E+03	100.0%	1.815E+01	1.3%	1.45E+03	1.38E+03	16	16	100.0%
1 May 1988	1.40E+03	100.0%	1.592E+01	1.1%	1.42E+03	1.37E+03	16	16	100.0%
2 May 1988	1.39E+03	99.5%	2.919E+01	2.1%	1.43E+03	1.35E+03	16	16	100.0%
3 May 1988	1.41E+03	100.4%	2.339E+01	1.7%	1.44E+03	1.37E+03	16	16	100.0%
4 May 1988	1.41E+03	100.6%	1.541E+01	1.1%	1.44E+03	1.39E+03	16	16	100.0%
Summary	1.40E+03	99.8%	5.191E+01	3.7%	1.51E+03	6.95E+02	261	260	99.6%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 7000 ppm Chamber /Concentration

Range=6.30E+3 to 7.70E+3

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	6.56E+03	93.7%	1.812E+03	27.6%	7.29E+03	3.13E+01	15	14	93.3%
19 Apr 1988	6.97E+03	99.6%	1.446E+02	2.1%	7.29E+03	6.75E+03	16	16	100.0%
20 Apr 1988	6.93E+03	98.9%	9.956E+01	1.4%	7.10E+03	6.79E+03	17	17	100.0%
21 Apr 1988	6.98E+03	99.7%	7.921E+01	1.1%	7.17E+03	6.84E+03	16	16	100.0%
22 Apr 1988	7.00E+03	100.1%	1.580E+02	2.3%	7.46E+03	6.78E+03	13	13	100.0%
23 Apr 1988	6.99E+03	99.8%	1.192E+02	1.7%	7.12E+03	6.76E+03	7	7	100.0%
24 Apr 1988	7.08E+03	101.1%	9.097E+01	1.3%	7.24E+03	6.85E+03	15	15	100.0%
25 Apr 1988	6.98E+03	99.7%	1.114E+02	1.6%	7.35E+03	6.87E+03	17	17	100.0%
26 Apr 1988	7.00E+03	99.9%	5.573E+01	.8%	7.14E+03	6.93E+03	16	16	100.0%
27 Apr 1988	7.00E+03	99.9%	1.093E+02	1.6%	7.25E+03	6.78E+03	17	17	100.0%
28 Apr 1988	7.07E+03	101.0%	1.483E+02	2.1%	7.32E+03	6.85E+03	16	16	100.0%
29 Apr 1988	7.05E+03	100.7%	1.693E+02	2.4%	7.65E+03	6.83E+03	16	16	100.0%
30 Apr 1988	7.02E+03	100.2%	8.646E+01	1.2%	7.23E+03	6.91E+03	16	16	100.0%
1 May 1988	7.05E+03	100.8%	7.674E+01	1.1%	7.14E+03	6.85E+03	16	16	100.0%
2 May 1988	6.92E+03	98.9%	8.658E+01	1.3%	7.07E+03	6.82E+03	17	17	100.0%
3 May 1988	6.98E+03	99.7%	1.144E+02	1.6%	7.14E+03	6.79E+03	17	17	100.0%
4 May 1988	7.04E+03	100.6%	4.705E+01	.7%	7.15E+03	6.98E+03	16	16	100.0%
Summary	6.98E+03	99.7%	4.460E+02	6.4%	7.65E+03	3.13E+01	263	262	99.6%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 21 Apr 1988

Summary Data for: Holding Chamber /Exhaust Air Flow				Range= 12.0 to 18.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	14.7	98.0%	.06	.4%	14.8	14.7	8	8	100.0%
19 Apr 1988	14.7	97.7%	.01	.1%	14.7	14.6	7	7	100.0%
20 Apr 1988	14.7	98.2%	.05	.4%	14.8	14.6	8	8	100.0%
21 Apr 1988	14.8	98.4%	.02	.1%	14.8	14.7	8	8	100.0%
Summary	14.7	98.1%	.06	.4%	14.8	14.6	31	31	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 17 Apr 1988 through 4 May 1988

Summary Data for: 0 ppm Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
17 Apr 1988	15.2	101.3%	.03	.2%	15.2	15.2	8	8	100.0%
18 Apr 1988	15.2	101.2%	.05	.3%	15.2	15.1	8	8	100.0%
19 Apr 1988	15.1	100.9%	.03	.2%	15.2	15.1	7	7	100.0%
20 Apr 1988	15.0	99.7%	.07	.5%	15.1	14.9	8	8	100.0%
21 Apr 1988	14.9	99.5%	.02	.1%	14.9	14.9	8	8	100.0%
22 Apr 1988	15.0	99.9%	.03	.2%	15.0	15.0	8	8	100.0%
23 Apr 1988	15.1	100.4%	.02	.1%	15.1	15.0	8	8	100.0%
24 Apr 1988	15.1	100.6%	.01	.1%	15.1	15.1	8	8	100.0%
25 Apr 1988	15.1	100.4%	.03	.2%	15.1	15.0	8	8	100.0%
26 Apr 1988	15.0	100.2%	.04	.2%	15.1	15.0	7	7	100.0%
27 Apr 1988	14.9	99.4%	.07	.5%	15.0	14.8	8	8	100.0%
28 Apr 1988	14.9	99.5%	.04	.3%	15.0	14.9	8	8	100.0%
29 Apr 1988	15.0	100.3%	.03	.2%	15.1	15.0	8	8	100.0%
30 Apr 1988	15.1	100.5%	.04	.3%	15.1	15.0	8	8	100.0%
1 May 1988	15.1	100.9%	.03	.2%	15.2	15.1	8	8	100.0%
2 May 1988	15.1	100.9%	.05	.3%	15.2	15.1	8	8	100.0%
3 May 1988	15.1	100.8%	.03	.2%	15.2	15.1	8	8	100.0%
4 May 1988	15.0	99.7%	.22	1.5%	15.2	14.7	6	6	100.0%
Summary	15.1	100.3%	.10	.7%	15.2	14.7	140	140	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 280 ppm Chamber /Exhaust Air Flow				Range= 12.0 to 18.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	14.8	98.4%	.03	.2%	14.8	14.7	8	8	100.0%
19 Apr 1988	14.8	98.8%	.04	.3%	14.9	14.7	7	7	100.0%
20 Apr 1988	14.9	99.5%	.09	.6%	15.0	14.7	8	8	100.0%
21 Apr 1988	15.0	99.8%	.02	.2%	15.0	15.0	8	8	100.0%
22 Apr 1988	15.0	100.3%	.04	.3%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.4%	.02	.2%	15.1	15.0	8	8	100.0%
24 Apr 1988	15.1	100.9%	.02	.2%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.6%	.06	.4%	15.2	15.0	8	8	100.0%
26 Apr 1988	15.1	100.3%	.05	.3%	15.1	15.0	7	7	100.0%
27 Apr 1988	14.9	99.6%	.05	.3%	15.0	14.9	8	8	100.0%
28 Apr 1988	14.9	99.6%	.05	.3%	15.0	14.9	8	8	100.0%
29 Apr 1988	15.0	100.3%	.04	.3%	15.1	15.0	8	8	100.0%
30 Apr 1988	15.1	100.4%	.02	.1%	15.1	15.0	8	8	100.0%
1 May 1988	15.1	100.8%	.03	.2%	15.1	15.1	8	8	100.0%
2 May 1988	15.1	100.7%	.03	.2%	15.2	15.1	8	8	100.0%
3 May 1988	15.1	100.7%	.03	.2%	15.1	15.1	8	8	100.0%
4 May 1988	15.0	99.8%	.19	1.3%	15.2	14.8	6	6	100.0%
Summary	15.0	100.1%	.12	.8%	15.2	14.7	132	132	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 1400 ppm Chamber

/Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	15.2	101.5%	.03	.2%	15.3	15.2	8	8	100.0%
19 Apr 1988	15.2	101.1%	.04	.2%	15.2	15.1	7	7	100.0%
20 Apr 1988	15.2	101.4%	.03	.2%	15.2	15.1	8	8	100.0%
21 Apr 1988	15.0	100.1%	.08	.6%	15.2	15.0	8	8	100.0%
22 Apr 1988	15.1	100.3%	.04	.2%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.6%	.03	.2%	15.1	15.1	8	8	100.0%
24 Apr 1988	15.1	101.0%	.02	.2%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.7%	.05	.3%	15.2	15.0	8	8	100.0%
26 Apr 1988	15.1	100.4%	.05	.3%	15.2	15.0	7	7	100.0%
27 Apr 1988	15.0	99.8%	.07	.5%	15.1	14.9	8	8	100.0%
28 Apr 1988	15.0	100.1%	.05	.3%	15.1	14.9	8	8	100.0%
29 Apr 1988	15.1	100.7%	.03	.2%	15.2	15.1	8	8	100.0%
30 Apr 1988	15.1	100.9%	.02	.1%	15.2	15.1	8	8	100.0%
1 May 1988	15.2	101.2%	.04	.3%	15.2	15.1	8	8	100.0%
2 May 1988	15.2	101.1%	.05	.3%	15.2	15.1	8	8	100.0%
3 May 1988	15.1	101.0%	.04	.2%	15.2	15.1	8	8	100.0%
4 May 1988	15.0	100.1%	.21	1.4%	15.2	14.8	6	6	100.0%
Summary	15.1	100.7%	.09	.6%	15.3	14.8	132	132	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 7000 ppm Chamber /Exhaust Air Flow

Range= 12.0 to 18.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	14.9	99.5%	.06	.4%	15.1	14.9	8	8	100.0%
19 Apr 1988	14.9	99.0%	.07	.4%	15.0	14.8	7	7	100.0%
20 Apr 1988	14.8	98.9%	.04	.3%	14.9	14.8	8	8	100.0%
21 Apr 1988	14.9	99.6%	.08	.5%	15.0	14.8	8	8	100.0%
22 Apr 1988	15.0	100.3%	.05	.3%	15.1	15.0	8	8	100.0%
23 Apr 1988	15.1	100.6%	.03	.2%	15.1	15.1	8	8	100.0%
24 Apr 1988	15.1	100.9%	.04	.3%	15.2	15.1	8	8	100.0%
25 Apr 1988	15.1	100.7%	.05	.3%	15.2	15.1	8	8	100.0%
26 Apr 1988	15.0	100.3%	.06	.4%	15.2	15.0	7	7	100.0%
27 Apr 1988	15.0	100.3%	.08	.5%	15.1	15.0	8	8	100.0%
28 Apr 1988	15.1	100.4%	.05	.3%	15.1	15.0	8	8	100.0%
29 Apr 1988	15.2	101.1%	.06	.4%	15.2	15.1	8	8	100.0%
30 Apr 1988	15.2	101.4%	.04	.2%	15.3	15.2	8	8	100.0%
1 May 1988	15.3	101.7%	.05	.3%	15.3	15.2	8	8	100.0%
2 May 1988	15.3	101.7%	.07	.4%	15.4	15.2	8	8	100.0%
3 May 1988	15.2	101.6%	.06	.4%	15.4	15.2	8	8	100.0%
4 May 1988	15.1	100.7%	.22	1.4%	15.4	14.8	6	6	100.0%
Summary	15.1	100.5%	.15	1.0%	15.4	14.8	132	132	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 21 Apr 1988

Summary Data for: Holding Chamber /Relative Humidity				Range= 40.0 to 70.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
15 Apr 1988	54.6	99.3%	4.69	8.6%	59.0	47.0	8	8	100.0%
16 Apr 1988	57.1	103.9%	1.57	2.8%	59.0	55.0	7	7	100.0%
17 Apr 1988	54.9	99.8%	1.81	3.3%	59.0	53.0	8	8	100.0%
18 Apr 1988	53.4	97.0%	1.60	3.0%	55.0	51.0	8	8	100.0%
19 Apr 1988	52.2	95.0%	1.75	3.4%	55.0	50.0	8	8	100.0%
20 Apr 1988	51.7	94.1%	2.12	4.1%	56.0	50.0	8	8	100.0%
21 Apr 1988	43.9	79.8%	2.80	6.4%	50.0	41.0	8	8	100.0%
Summary	52.5	95.4%	4.63	8.8%	59.0	41.0	55	55	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 17 Apr 1988 through 4 May 1988

Summary Data for: 0 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
17 Apr 1988	53.2	96.8%	1.91	3.6%	55.0	51.0	8	8	100.0%
18 Apr 1988	51.5	93.6%	2.56	5.0%	54.0	47.0	8	8	100.0%
19 Apr 1988	53.2	96.8%	3.65	6.9%	57.0	48.0	8	8	100.0%
20 Apr 1988	58.3	105.9%	4.62	7.9%	64.0	51.0	8	8	100.0%
21 Apr 1988	58.3	105.9%	2.19	3.8%	62.0	56.0	8	8	100.0%
22 Apr 1988	54.2	98.6%	2.92	5.4%	57.0	50.0	8	8	100.0%
23 Apr 1988	52.0	94.5%	2.39	4.6%	56.0	49.0	8	8	100.0%
24 Apr 1988	48.1	87.5%	4.55	9.5%	53.0	40.0	8	8	100.0%
25 Apr 1988	48.9	88.9%	3.18	6.5%	53.0	45.0	8	8	100.0%
26 Apr 1988	52.6	95.6%	2.51	4.8%	55.0	48.0	7	7	100.0%
27 Apr 1988	58.0	105.5%	4.08	7.0%	66.0	54.0	7	7	100.0%
28 Apr 1988	61.8	112.3%	4.20	6.8%	66.0	54.0	8	8	100.0%
29 Apr 1988	58.9	107.0%	2.90	4.9%	64.0	55.0	8	8	100.0%
30 Apr 1988	52.0	94.5%	4.69	9.0%	59.0	47.0	8	8	100.0%
1 May 1988	51.4	93.4%	2.26	4.4%	55.0	48.0	8	8	100.0%
2 May 1988	53.0	96.4%	3.12	5.9%	56.0	47.0	8	8	100.0%
3 May 1988	53.9	98.0%	2.70	5.0%	58.0	51.0	8	8	100.0%
4 May 1988	55.3	100.6%	4.08	7.4%	60.0	48.0	6	6	100.0%
Summary	54.1	98.4%	4.76	8.8%	66.0	40.0	140	140	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 280 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	52.9	96.1%	2.10	4.0%	55.0	49.0	8	8	100.0%
19 Apr 1988	55.0	100.0%	4.07	7.4%	59.0	49.0	8	8	100.0%
20 Apr 1988	57.0	103.6%	3.21	5.6%	60.0	51.0	8	8	100.0%
21 Apr 1988	55.0	100.0%	2.93	5.3%	59.0	51.0	8	8	100.0%
22 Apr 1988	52.5	95.5%	4.07	7.8%	57.0	46.0	8	8	100.0%
23 Apr 1988	49.7	90.5%	2.49	5.0%	54.0	46.0	8	8	100.0%
24 Apr 1988	45.9	83.4%	4.76	10.4%	52.0	38.0	8	7	87.5%
25 Apr 1988	46.3	84.1%	3.88	8.4%	50.0	40.0	8	8	100.0%
26 Apr 1988	52.1	94.8%	4.81	9.2%	57.0	44.0	7	7	100.0%
27 Apr 1988	59.6	108.3%	1.99	3.3%	63.0	57.0	7	7	100.0%
28 Apr 1988	60.1	109.3%	3.18	5.3%	65.0	56.0	8	8	100.0%
29 Apr 1988	56.0	101.8%	1.60	2.9%	59.0	55.0	8	8	100.0%
30 Apr 1988	55.2	100.5%	2.25	4.1%	59.0	52.0	8	8	100.0%
1 May 1988	55.0	100.0%	3.70	6.7%	60.0	49.0	8	8	100.0%
2 May 1988	56.4	102.5%	3.11	5.5%	61.0	53.0	8	8	100.0%
3 May 1988	58.7	106.8%	1.50	2.5%	61.0	57.0	7	7	100.0%
4 May 1988	58.4	106.2%	2.99	5.1%	62.0	54.0	7	7	100.0%
Summary	54.4	98.9%	5.10	9.4%	65.0	38.0	132	131	99.2%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 1400 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	52.5	95.5%	2.33	4.4%	55.0	48.0	8	8	100.0%
19 Apr 1988	54.1	98.4%	3.14	5.8%	57.0	49.0	8	8	100.0%
20 Apr 1988	59.8	108.6%	2.25	3.8%	63.0	56.0	8	8	100.0%
21 Apr 1988	58.4	106.1%	1.92	3.3%	60.0	55.0	8	8	100.0%
22 Apr 1988	54.5	99.1%	2.45	4.5%	58.0	51.0	8	8	100.0%
23 Apr 1988	53.7	97.7%	1.83	3.4%	55.0	51.0	8	8	100.0%
24 Apr 1988	49.1	89.3%	4.64	9.5%	54.0	43.0	8	8	100.0%
25 Apr 1988	50.6	92.0%	3.11	6.2%	54.0	46.0	8	8	100.0%
26 Apr 1988	55.1	100.3%	3.98	7.2%	60.0	49.0	7	7	100.0%
27 Apr 1988	59.3	107.8%	2.50	4.2%	64.0	57.0	7	7	100.0%
28 Apr 1988	59.9	108.9%	4.52	7.5%	67.0	53.0	8	8	100.0%
29 Apr 1988	53.5	97.3%	2.20	4.1%	58.0	51.0	8	8	100.0%
30 Apr 1988	53.2	96.8%	3.28	6.2%	57.0	48.0	8	8	100.0%
1 May 1988	53.5	97.3%	3.70	6.9%	58.0	48.0	8	8	100.0%
2 May 1988	54.9	99.8%	2.03	3.7%	59.0	53.0	8	8	100.0%
3 May 1988	56.5	102.7%	3.07	5.4%	59.0	50.0	8	8	100.0%
4 May 1988	58.3	106.0%	2.69	4.6%	62.0	55.0	7	7	100.0%
Summary	55.1	100.1%	4.19	7.6%	67.0	43.0	133	133	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 7000 ppm Chamber

/Relative Humidity

Range= 40.0 to 70.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	54.2	98.6%	2.12	3.9%	57.0	51.0	8	8	100.0%
19 Apr 1988	56.3	102.3%	3.20	5.7%	59.0	51.0	8	8	100.0%
20 Apr 1988	58.1	105.7%	3.48	6.0%	62.0	52.0	8	8	100.0%
21 Apr 1988	56.4	102.5%	2.56	4.5%	61.0	52.0	8	8	100.0%
22 Apr 1988	52.7	95.9%	4.27	8.1%	57.0	46.0	8	8	100.0%
23 Apr 1988	51.0	92.7%	2.88	5.6%	55.0	46.0	8	8	100.0%
24 Apr 1988	47.3	85.9%	5.47	11.6%	53.0	38.0	8	7	87.5%
25 Apr 1988	48.4	88.0%	3.70	7.7%	52.0	42.0	8	8	100.0%
26 Apr 1988	53.9	97.9%	4.60	8.5%	59.0	46.0	7	7	100.0%
27 Apr 1988	58.3	106.0%	3.50	6.0%	64.0	54.0	7	7	100.0%
28 Apr 1988	60.1	109.3%	3.87	6.4%	66.0	53.0	8	8	100.0%
29 Apr 1988	54.9	99.8%	2.64	4.8%	58.0	50.0	8	8	100.0%
30 Apr 1988	53.5	97.3%	3.07	5.7%	57.0	49.0	8	8	100.0%
1 May 1988	54.2	98.6%	3.20	5.9%	58.0	50.0	8	8	100.0%
2 May 1988	54.7	99.5%	2.43	4.4%	59.0	52.0	8	8	100.0%
3 May 1988	56.9	103.4%	3.40	6.0%	61.0	52.0	8	8	100.0%
4 May 1988	58.7	106.7%	3.20	5.5%	64.0	56.0	6	6	100.0%
Summary	54.6	99.3%	4.71	8.6%	66.0	38.0	132	131	99.2%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 4 May 1988

Summary Data for: Room				/Temperature		Range= 69.0 to 75.0			
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
15 Apr 1988	73.3	101.8%	.15	.2%	73.5	73.1	8	8	100.0%
16 Apr 1988	72.9	101.3%	.95	1.3%	73.5	70.6	8	8	100.0%
17 Apr 1988	73.1	101.5%	.23	.3%	73.4	72.7	8	8	100.0%
18 Apr 1988	73.7	102.3%	1.38	1.9%	77.0	72.8	8	7	87.5%
19 Apr 1988	73.4	101.9%	.28	.4%	73.9	73.1	8	8	100.0%
20 Apr 1988	72.8	101.1%	1.13	1.6%	73.8	70.1	8	8	100.0%
21 Apr 1988	72.2	100.3%	1.94	2.7%	73.2	67.4	8	7	87.5%
22 Apr 1988	73.0	101.4%	.31	.4%	73.2	72.3	8	8	100.0%
23 Apr 1988	72.3	100.4%	1.99	2.7%	73.4	67.4	8	7	87.5%
24 Apr 1988	73.2	101.6%	.29	.4%	73.6	72.7	8	8	100.0%
25 Apr 1988	73.1	101.5%	.27	.4%	73.7	72.8	8	8	100.0%
26 Apr 1988	73.1	101.6%	.18	.2%	73.4	72.9	7	7	100.0%
27 Apr 1988	73.2	101.7%	.27	.4%	73.5	72.7	8	8	100.0%
28 Apr 1988	72.6	100.8%	1.30	1.8%	73.3	69.4	8	8	100.0%
29 Apr 1988	72.8	101.2%	.27	.4%	73.2	72.5	8	8	100.0%
30 Apr 1988	72.9	101.3%	.38	.5%	73.4	72.4	8	8	100.0%
1 May 1988	73.4	101.9%	.40	.5%	73.8	72.6	8	8	100.0%
2 May 1988	73.4	101.9%	.28	.4%	73.8	73.0	8	8	100.0%
3 May 1988	73.4	102.0%	.23	.3%	73.8	73.2	8	8	100.0%
4 May 1988	73.5	102.1%	.63	.9%	74.6	72.8	6	6	100.0%
Summary	73.1	101.5%	.90	1.2%	77.0	67.4	157	154	98.1%

Daily Summation For Isoprene - IRT (Rats)

From 15 Apr 1988 through 21 Apr 1988

Summary Data for: Holding Chamber /Temperature				Range=		72.0 to 78.0			
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
15 Apr 1988	76.5	102.0%	1.19	1.6%	77.8	73.8	8	8	100.0%
16 Apr 1988	75.0	100.0%	.56	.7%	75.6	74.3	7	7	100.0%
17 Apr 1988	76.5	102.0%	.45	.6%	77.0	75.7	8	8	100.0%
18 Apr 1988	76.9	102.5%	.64	.8%	77.5	75.9	8	8	100.0%
19 Apr 1988	75.7	101.0%	.91	1.2%	77.6	74.4	8	8	100.0%
20 Apr 1988	73.6	98.1%	1.36	1.9%	76.0	70.9	8	7	87.5%
21 Apr 1988	72.8	97.1%	.51	.7%	74.0	72.5	8	8	100.0%
Summary	75.3	100.4%	1.69	2.2%	77.8	70.9	55	54	98.2%

Daily Summation For Isoprene - IRT (Rats)

From 17 Apr 1988 through 4 May 1988

Summary Data for: 0 ppm Chamber /Temperature				Range= 72.0 to 78.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
17 Apr 1988	76.9	102.5%	1.02	1.3%	77.5	74.5	8	8	100.0%
18 Apr 1988	75.4	100.5%	.87	1.1%	77.3	74.6	8	8	100.0%
19 Apr 1988	75.7	100.9%	.62	.8%	76.5	74.6	8	8	100.0%
20 Apr 1988	75.1	100.1%	1.17	1.6%	77.2	74.0	9	9	100.0%
21 Apr 1988	74.0	98.7%	.23	.3%	74.2	73.5	8	8	100.0%
22 Apr 1988	74.2	99.0%	.19	.3%	74.4	73.9	8	8	100.0%
23 Apr 1988	74.2	98.9%	.19	.3%	74.5	73.9	8	8	100.0%
24 Apr 1988	74.2	98.9%	.45	.6%	74.7	73.5	8	8	100.0%
25 Apr 1988	74.0	98.6%	.38	.5%	74.9	73.7	8	8	100.0%
26 Apr 1988	73.7	98.3%	.19	.3%	74.0	73.4	8	8	100.0%
27 Apr 1988	73.6	98.1%	.23	.3%	73.9	73.1	8	8	100.0%
28 Apr 1988	72.8	97.0%	.43	.6%	73.7	72.3	8	8	100.0%
29 Apr 1988	72.4	96.6%	.33	.4%	73.0	71.9	8	7	87.5%
30 Apr 1988	74.1	98.8%	1.46	2.0%	75.6	72.1	8	8	100.0%
1 May 1988	75.6	100.8%	.24	.3%	76.0	75.2	8	8	100.0%
2 May 1988	74.9	99.8%	.54	.7%	76.1	74.5	8	8	100.0%
3 May 1988	74.6	99.4%	.33	.4%	75.1	74.2	7	7	100.0%
4 May 1988	73.5	98.0%	.60	.8%	74.3	72.8	5	5	100.0%
Summary	74.4	99.2%	1.22	1.6%	77.5	71.9	141	140	99.3%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 280 ppm Chamber /Temperature				Range= 72.0 to 78.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	74.0	98.7%	.57	.8%	74.4	73.0	8	8	100.0%
19 Apr 1988	74.9	99.9%	.36	.5%	75.3	74.2	8	8	100.0%
20 Apr 1988	75.3	100.4%	.25	.3%	75.6	75.0	8	8	100.0%
21 Apr 1988	75.4	100.6%	.29	.4%	75.7	74.8	8	8	100.0%
22 Apr 1988	75.5	100.7%	.24	.3%	75.8	75.1	8	8	100.0%
23 Apr 1988	75.5	100.7%	.35	.5%	76.0	75.0	8	8	100.0%
24 Apr 1988	75.7	101.0%	.45	.6%	76.4	75.1	8	8	100.0%
25 Apr 1988	75.5	100.6%	.40	.5%	76.2	74.9	8	8	100.0%
26 Apr 1988	75.6	100.8%	.33	.4%	76.0	74.8	8	8	100.0%
27 Apr 1988	75.5	100.6%	.44	.6%	76.1	74.6	8	8	100.0%
28 Apr 1988	75.0	99.9%	.35	.5%	75.6	74.6	8	8	100.0%
29 Apr 1988	75.0	100.0%	.43	.6%	75.8	74.4	8	8	100.0%
30 Apr 1988	75.2	100.2%	.40	.5%	75.8	74.5	8	8	100.0%
1 May 1988	75.2	100.3%	.40	.5%	75.8	74.6	8	8	100.0%
2 May 1988	74.7	99.6%	.55	.7%	75.9	74.2	8	8	100.0%
3 May 1988	74.2	98.9%	.47	.6%	75.2	73.8	7	7	100.0%
4 May 1988	73.7	98.3%	.73	1.0%	74.8	73.0	6	6	100.0%
Summary	75.1	100.1%	.68	.9%	76.4	73.0	133	133	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 1400 ppm Chamber

/Temperature

Range= 72.0 to 78.0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	74.7	99.6%	.60	.8%	75.2	73.4	8	8	100.0%
19 Apr 1988	75.7	100.9%	.40	.5%	76.2	74.9	8	8	100.0%
20 Apr 1988	75.5	100.6%	.35	.5%	75.9	75.1	8	8	100.0%
21 Apr 1988	75.6	100.8%	.51	.7%	76.1	74.7	8	8	100.0%
22 Apr 1988	75.9	101.2%	.52	.7%	76.5	75.0	8	8	100.0%
23 Apr 1988	75.8	101.1%	.46	.6%	76.4	75.0	8	8	100.0%
24 Apr 1988	76.1	101.4%	.68	.9%	77.0	75.0	8	8	100.0%
25 Apr 1988	75.6	100.7%	.67	.9%	76.8	74.8	8	8	100.0%
26 Apr 1988	75.5	100.7%	.43	.6%	76.0	74.6	8	8	100.0%
27 Apr 1988	76.2	101.6%	.40	.5%	76.6	75.4	8	8	100.0%
28 Apr 1988	75.6	100.8%	.74	1.0%	76.6	74.6	8	8	100.0%
29 Apr 1988	75.8	101.1%	.33	.4%	76.4	75.3	8	8	100.0%
30 Apr 1988	75.8	101.1%	.38	.5%	76.5	75.2	8	8	100.0%
1 May 1988	76.0	101.3%	.39	.5%	76.5	75.3	8	8	100.0%
2 May 1988	75.2	100.3%	.64	.9%	76.7	74.7	8	8	100.0%
3 May 1988	74.7	99.6%	.52	.7%	75.8	74.4	7	7	100.0%
4 May 1988	73.7	98.3%	.76	1.0%	74.8	72.9	6	6	100.0%
Summary	75.5	100.7%	.75	1.0%	77.0	72.9	133	133	100.0%

Daily Summation For Isoprene - IRT (Rats)

From 18 Apr 1988 through 4 May 1988

Summary Data for: 7000 ppm Chamber /Temperature				Range= 72.0 to 78.0					
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Apr 1988	74.3	99.1%	.29	.4%	74.6	73.9	8	8	100.0%
19 Apr 1988	75.0	100.0%	.41	.6%	75.6	74.2	8	8	100.0%
20 Apr 1988	75.7	100.9%	.31	.4%	75.9	75.0	8	8	100.0%
21 Apr 1988	75.9	101.2%	.30	.4%	76.1	75.2	8	8	100.0%
22 Apr 1988	75.9	101.2%	.17	.2%	76.0	75.5	8	8	100.0%
23 Apr 1988	75.8	101.1%	.29	.4%	76.2	75.2	8	8	100.0%
24 Apr 1988	76.1	101.4%	.43	.6%	76.5	75.5	8	8	100.0%
25 Apr 1988	75.9	101.2%	.40	.5%	76.7	75.5	8	8	100.0%
26 Apr 1988	75.8	101.1%	.29	.4%	76.1	75.2	8	8	100.0%
27 Apr 1988	75.8	101.1%	.40	.5%	76.4	75.0	8	8	100.0%
28 Apr 1988	75.2	100.3%	.55	.7%	75.8	74.5	8	8	100.0%
29 Apr 1988	75.4	100.5%	.43	.6%	76.1	74.7	8	8	100.0%
30 Apr 1988	75.5	100.7%	.36	.5%	76.1	75.0	8	8	100.0%
1 May 1988	75.8	101.0%	.26	.3%	76.3	75.4	8	8	100.0%
2 May 1988	75.2	100.3%	.55	.7%	76.4	74.6	8	8	100.0%
3 May 1988	74.6	99.4%	.47	.6%	75.6	74.3	7	7	100.0%
4 May 1988	73.7	98.2%	.78	1.1%	74.8	72.9	6	6	100.0%
Summary	75.4	100.6%	.73	1.0%	76.7	72.9	133	133	100.0%

EXPOSURE OPERATION DISCUSSION SHEET

INCLUDES DISCUSSIONS AND/OR EXPLANATIONS OF PROBLEMS AFFECTING ANIMAL ENVIRONMENT AND EXPOSURES. EXPLANATIONS ARE INCLUDED FOR DATA IN WHICH THERE WERE EXCURSIONS OF DAILY MEAN OR STANDARD DEVIATION BEYOND ALLOWABLE OPERATING LIMITS OR EXCURSIONS OF INDIVIDUAL DATUM BEYOND CRITICAL LIMITS.

STUDY: IRT Isoprene Rat and Mouse Study

REPORTING PERIOD: April 11-May 4, 1988

NOTE: 24 Hour Data Collection Period extends from ~5:00 a.m. to ~5:00 a.m.

COMPILED BY: R.J. Weigel *RJW*

DATE: 5/7/88

CHAMBER CONCENTRATION

DATE DISCUSSION OR EXPLANATION

4/18/88 At 13:30, primary building exhaust was lost as the result of a short power failure. Air flow through the chambers decreased by about 25% and the generator was stopped. At 13:38, chamber valves were closed. At 13:57, following a period to reacquire the proper generation temperatures, exposures resumed 19 minutes after generation was interrupted. This time was added to the exposure period for the day. As a result of the interruption in delivery of vapor to the chambers, the following readings exceeded the critical low alarm limits:

<u>Chamber</u>	<u>Time</u>	<u>Reading</u>	<u>Alarm Limit</u>
280 ppm	14:00	223 ppm	224 ppm
1400 ppm	13:57	695 ppm	1120 ppm
7000 ppm	13:54	31 ppm	5600 ppm

Also, % RSDs on the 1400 and 7000 ppm chambers were greater than 10% for the day.

TEMPERATURE & RELATIVE HUMIDITY

DATE DISCUSSION OR EXPLANATION

No problems or excursions to report during this period.

CHAMBER FLOW & VACUUM

DATE DISCUSSION OR EXPLANATION

No problems or excursions to report during this period.

CHAMBER UNIFORMITY DATA SHEET

COMPOUND: Isoprene IRT

EXPOSURE ROOM NUMBER: 436

TPV MEASUREMENTS

CHAMBER:		#6/280 ppm		#7/1400 ppm		#8/7000 ppm			
DATE:		4/23/88		4/23/88		4/23/88			
SAMPLE PORT		MONITOR READING	% of Mean	MONITOR READING	% of Mean	MONITOR READING	% of Mean	MONITOR READING	% of Mean
BACK:	1B	363400.0	100.8%	1723000.0	100.0%				
	2B	360000.0	99.9%	1723000.0	100.0%	8646000.0	99.7%		
	3B	360400.0	100.0%	1722000.0	99.9%	8680000.0	100.1%		
	4B	360800.0	100.1%	1723000.0	100.0%	8676000.0	100.1%		
	5B	360800.0	100.1%	1721000.0	99.9%	8674000.0	100.0%		
	6B	360700.0	100.1%	1725000.0	100.1%	8664000.0	99.9%		
FRONT:	1F								
	2F	360300.0	100.0%	1722000.0	99.9%	8668000.0	100.0%		
	3F	359300.0	99.7%	1724000.0	100.1%	8682000.0	100.1%		
	4F	360000.0	99.9%	1723000.0	100.0%	8712000.0	100.5%		
	5F	359900.0	99.9%	1724000.0	100.1%	8650000.0	99.8%		
	6F	359200.0	99.7%	1723000.0	100.0%	8662000.0	99.9%		
MEAN:		360436.4	100.0%	1723000.0	100.0%	8671400.0	100.0%		
TPV:		1123.63	0.3%	1095.45	0.1%	18620.18	0.2%		
BPV:		////	*	////	*	////	*	////	////

* Indistinguishable from WPV

WPV MEASUREMENTS

IN-LINE	1st	363400.0	100.6%	1723000.0	100.1%	8646000.0	99.8%		
	2nd	360100.0	99.6%	1720000.0	99.9%	8660000.0	100.0%		
	3rd	360700.0	99.8%	1720000.0	99.9%	8686000.0	100.3%		
MEAN:		361400.0	100.0%	1721000.0	100.0%	8664000.0	100.0%		
WPV:		1757.84	0.5%	1732.05	0.1%	20297.78	0.2%		

MONITOR TYPE: GC

SERIAL # : N809422

MONITOR DATA LOCATION: Data is part of the daily data file.

COMMENTS: With animals present in chambers

ENTERED BY: LL Trent

DATE: 4/25/88

REVIEWED BY: RJ Weigel

DATE: 9/12/88

CHAMBER UNIFORMITY DATA SHEET

COMPOUND: IRT IsopreneEXPOSURE ROOM NUMBER: 436

TPV MEASUREMENTS

CHAMBER:	#6	#7	#8				
DATE:	2/1/88	2/1/88	2/1/88				
SAMPLE PORT	MONITOR READING	% of Mean	MONITOR READING	% of Mean	MONITOR READING	% of Mean	MONITOR READING % of Mean
BACK: 1B	346200.0	99.5%	1797000.0	100.0%	9014000.0	99.7%	
2B	347800.0	100.0%	1809000.0	100.6%	9038000.0	99.9%	
3B	340200.0	97.8%	1790000.0	99.6%	9114000.0	100.8%	
4B	348900.0	100.3%	1796000.0	99.9%	9028000.0	99.8%	
5B	344300.0	99.0%	1791000.0	99.6%	8996000.0	99.5%	
6B	351900.0	101.1%	1809000.0	100.6%	9022000.0	99.8%	
FRONT: 1F	347500.0	99.9%	1798000.0	100.0%	9160000.0	101.3%	
2F	349500.0	100.4%	1791000.0	99.6%	9074000.0	100.3%	
3F	347500.0	99.9%	1797000.0	100.0%	9032000.0	99.9%	
4F	348700.0	100.2%	1791000.0	99.6%	9024000.0	99.8%	
5F	348900.0	100.3%	1805000.0	100.4%	8990000.0	99.4%	
6F	354000.0	101.7%	1798000.0	100.0%	9030000.0	99.9%	
MEAN:	347950.0	100.0%	1797666.7	100.0%	9043500.0	100.0%	
TPV:	3488.29	1.0%	6786.80	0.4%	49441.43	0.5%	
BPV:	////////////////	*	////////////////	*	////////////////	*	////////////////

* Indistinguishable from WPV.

WPV MEASUREMENTS

IN-LINE 1st	346200.0	101.8%	1797000.0	99.6%	9038000.0	98.8%	
2nd	338400.0	99.5%	1797000.0	99.6%	9202000.0	100.6%	
3rd	335800.0	98.7%	1819000.0	100.8%	9198000.0	100.6%	
MEAN:	340133.3	100.0%	1804333.3	100.0%	9146000.0	100.0%	
WPV:	5412.33	1.6%	12701.71	0.7%	93552.12	1.0%	

MONITOR TYPE: GCSERIAL # : N809422MONITOR DATA LOCATION: Data is kept with prestart recordsCOMMENTS: No animals present. Prestart testing.ENTERED BY: LL TrentDATE: 2/2/88REVIEWED BY: RJ WeigelDATE: 9/12/88

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

(MOUSE DATA)

Isoprene Mouse Teratology Study: Body Weights (g) for Plug-positive Females

C.1	----- 0 ppm Isoprene -----											
	MATNO	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	9 dg Wt (g)	12 dg Wt (g)	15 dg Wt (g)	18 dg Wt (g)	Uter Wt (g)	Pregnant	Liver (g)	Kidney (g)
	1008	33.5	31.7	32.4	31.8	35.5	40.0	45.38	8.733	1	2.726	0.454
	1009	28.8	27.8	28.0	29.8	35.2	43.4	51.62	18.974	1	2.797	0.448
	1012	28.9	27.0	29.9	29.0	29.4	28.5	27.88	0.112	0	1.919	0.424
	1029	25.7	25.8	27.8	30.3	35.2	41.4	48.13	13.483	1	2.945	0.440
	1060	31.0	30.8	32.7	34.7	39.4	46.7	54.01	19.203	1	3.023	0.430
	1062	24.8	24.4	28.9	31.0	35.7	40.8	50.29	17.238	1	2.813	0.409
	1067	28.3	30.0	32.1	33.8	40.4	47.8	54.69	17.580	1	3.504	0.530
	1088	28.4	27.9	30.4	31.2	34.9	38.8	41.38	6.248	1	2.709	0.458
	1101	29.7	28.9	29.9	31.8	38.0	45.5	54.06	19.598	1	3.191	0.487
	1103	30.3	30.1	33.2	34.1	40.0	48.3	50.43	21.366	1	2.914	0.475
	1109	25.4	28.3	28.9	31.0	36.7	45.4	52.95	20.872	1	2.603	0.430
	1112	32.7	31.7	33.0	33.6	38.1	47.7	57.41	21.917	1	2.701	0.426
	1128	31.6	30.0	31.8	33.3	41.4	50.5	62.02	25.092	1	3.348	0.571
	1133	27.7	26.4	28.3	29.1	33.8	40.8	45.78	12.494	1	2.827	0.451
	1138	33.6	35.1	35.0	38.8	42.2	51.0	60.23	23.114	1	3.171	0.457
	1139	31.0	29.2	30.4	32.3	37.8	46.8	54.10	21.009	1	2.859	0.373
	1157	27.7	27.3	31.1	33.1	39.2	48.3	58.91	19.642	1	3.603	0.474
	1189	31.0	30.3	29.2	29.2	29.5	30.9	30.06	0.183	0	2.322	0.530
	1191	24.8	24.7	27.9	29.4	34.4	41.1	49.04	18.921	1	2.770	0.455
	1196	31.3	30.4	34.0	34.2	40.5	48.8	58.23	21.555	1	3.134	0.477
	1201	27.4	27.1	28.2	30.3	35.2	43.6	51.43	19.883	1	2.870	0.452
	1230	27.0	28.4	29.4	31.6	38.8	47.7	57.49	23.455	1	3.158	0.548
	1232	30.3	28.8	30.8	33.9	39.9	49.0	57.87	23.439	1	3.083	0.557
	1284	29.6	28.4	30.4	32.3	39.4	48.5	58.97	24.192	1	3.019	0.483
	1265	31.1	29.6	32.7	35.1	39.9	47.4	53.80	18.965	1	2.877	0.473
	1277	28.1	29.2	29.8	30.8	30.9	31.4	30.83	0.221	0	2.079	0.518
	1287	30.9	27.9	30.5	32.0	37.3	45.7	54.09	22.230	1	2.962	0.472
	1302	27.3	26.5	30.7	32.7	36.9	43.9	51.66	19.348	1	2.510	0.485
	1306	28.3	28.4	30.3	31.6	36.7	42.5	47.65	15.489	1	2.741	0.497
	1307	25.1	24.7	28.7	31.1	38.9	44.7	53.05	19.502	1	3.074	0.484
	1328	31.7	29.5	32.9	35.2	42.2	49.4	59.02	22.359	1	2.973	0.466

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Mouse Teratology Study: Body Weights (g) for Plug-positive Females

----- 280 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	9 dg Wt (g)	12 dg Wt (g)	15 dg Wt (g)	18 dg Wt (g)	Uter Wt (g)	Pregnant	Liver (g)	Kidney (g)
1013	33.3	30.4	33.1	35.0	42.8	50.8	60.71	21.850	1	3.451	0.570
1017	29.1	28.2	30.0	30.1	32.4	40.8	49.31	16.898	1	2.768	0.449
1018	30.4	30.5	31.7	33.7	39.9	48.0	54.21	19.443	1	3.100	0.437
1020	30.6	30.0	30.4	32.4	37.8	44.2	53.38	18.892	1	2.937	0.490
1033	32.8	30.0	34.1	34.6	39.2	49.0	57.90	20.757	1	3.474	0.500
1036	32.4	30.8	32.9	35.5	40.3	49.9	59.57	22.846	1	3.374	0.535
1053	31.1	29.5	31.7	33.2	35.4	43.1	49.23	15.647	1	2.953	0.431
1057	28.4	28.5	30.3	32.0	33.3	42.4	47.93	15.590	1	2.777	0.423
1064	29.4	29.7	30.9	32.1	37.0	44.6	52.47	18.728	1	3.218	0.408
1071	29.1	29.2	32.6	34.4	37.5	47.1	54.63	20.685	1	3.207	0.405
1072	29.1	28.0	30.4	32.8	39.2	45.7	52.39	18.001	1	2.972	0.405
1098	30.2	30.9	33.9	36.8	42.3	53.6	62.14	23.043	1	3.357	0.392
1119	29.3	26.7	29.4	27.0	27.1	29.1	27.34	0.191	0	1.562	0.473
1167	24.5	25.6	27.2	28.8	34.4	40.1	46.24	15.970	1	2.568	0.408
1170	26.4	27.2	29.4	30.0	36.2	44.5	54.00	21.349	1	2.897	0.461
1174	32.4	32.1	32.7	34.7	40.0	47.7	53.09	17.920	1	2.830	0.504
1187	26.0	26.0	29.9	31.5	38.5	45.5	52.91	19.368	1	3.147	0.454
1194	29.7	28.4	30.6	30.3	36.4	43.9	50.58	17.794	1	2.960	0.400
1198	26.6	27.9	29.1	31.6	36.1	43.6	48.90	18.098	1	3.185	0.486
1212	29.8	28.3	31.5	33.3	40.5	48.7	59.53	24.197	1	3.046	0.474
1224	30.8	30.3	34.7	36.3	45.5	54.1	65.92	24.835	1	3.699	0.597
1238	25.1	24.4	29.3	28.9	29.4	28.3	26.42	0.133	0	1.893	0.398
1242	30.1	28.7	30.9	32.8	39.4	46.0	54.20	18.235	1	3.474	0.550
1255	30.2	27.6	30.0	33.8	36.0	45.2	50.22	15.600	1	2.735	0.424
1257	24.9	25.3	26.9	29.7	32.1	40.1	48.89	17.450	1	3.123	0.430
1270	27.7	27.2	28.4	30.0	36.4	42.9	49.39	19.030	1	2.462	0.435
1280	25.0	24.8	27.2	29.1	34.6	41.5	49.61	18.717	1	2.661	0.460
1289	29.4	27.8	28.9	31.5	37.6	46.3	53.32	21.703	1	2.750	0.502
1290	24.9	24.6	25.7	28.3	31.6	40.7	47.18	18.614	1	2.490	0.440
1331	28.8	27.3	29.2	31.4	38.7	46.9	56.22	23.078	1	3.016	0.470
1332	25.8	25.9	26.8	24.7	26.0	26.7	26.53	0.177	0	1.852	0.369
1333	28.2	28.0	30.2	29.9	35.8	42.4	48.18	14.988	1	2.623	0.422

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Mouse Teratology Study: Body Weights (g) for Plug-positive Females

----- 1400 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	8 dg Wt (g)	9 dg Wt (g)	12 dg Wt (g)	15 dg Wt (g)	18 dg Wt (g)	Uter Wt (g)	Pregnant	Liver (g)	Kidney (g)
1002	29.8	29.1	31.3	32.2	37.9	44.7	53.06	16.704	1	3.042	0.520
1003	28.4	27.2	28.8	31.0	35.0	42.4	49.13	15.348	1	3.012	0.498
1034	32.2	29.9	32.9	32.1	38.8	48.9	58.29	19.585	1	3.501	0.552
1041	29.2	27.9	32.3	34.1	39.7	46.1	53.89	18.657	1	3.532	0.485
1042	32.2	29.8	32.9	33.9	38.3	45.1	54.14	18.100	1	3.073	0.487
1043	33.0	31.5	30.5	31.7	38.7	45.8	54.54	18.553	1	3.437	0.517
1048	28.9	27.5	29.8	31.5	35.3	42.4	50.43	16.879	1	2.629	0.430
1052	27.5	27.9	28.9	30.4	35.2	41.8	49.66	15.273	1	3.539	0.496
1073	32.2	29.5	30.3	33.7	39.7	49.3	60.15	21.896	1	3.478	0.478
1074	27.1	26.1	28.1	28.2	28.0	28.7	27.14	0.218	0	2.454	0.580
1075	25.5	25.2	29.8	31.8	38.7	43.8	49.05	16.778	1	2.422	0.442
1078	24.8	25.5	28.2	28.7	31.8	38.8	43.28	10.328	1	2.818	0.387
1079	26.7	28.7	28.3	29.8	34.5	42.8	50.07	18.725	1	2.888	0.447
1080	28.8	25.6	27.9	28.9	25.9	26.5	28.34	0.152	0	1.842	0.434
1093	33.2	31.5	31.4	32.7	32.2	32.3	31.58	0.194	0	2.418	0.620
1095	32.8	31.4	32.3	34.4	38.8	45.0	52.85	19.019	1	3.095	0.428
1116	29.3	26.9	29.5	29.7	27.9	28.8	28.71	0.207	0	1.840	0.402
1118	30.8	30.4	31.3	32.0	28.8	30.1	28.80	0.151	0	2.077	0.497
1121	31.8	29.4	33.0	34.1	37.8	47.8	55.80	20.937	1	3.317	0.552
1124	34.5	31.9	35.1	33.9	40.2	50.0	59.94	20.365	1	3.486	0.552
1145	28.8	28.8	30.1	32.0	43.4	43.4	51.08	18.329	1	3.126	0.434
1171	29.7	28.7	31.8	33.5	38.4	45.5	52.17	18.110	1	3.278	0.495
1184	29.0	28.4	30.7	31.8	38.7	44.1	50.85	15.011	1	3.249	0.454
1226	25.8	26.3	28.6	28.5	35.2	43.2	51.58	18.874	1	3.026	0.444
1238	24.1	24.2	26.1	25.9	32.3	39.8	48.51	15.261	1	3.038	0.495
1239	25.2	24.9	26.8	27.7	34.9	41.8	50.23	19.002	1	2.909	0.408
1240	28.0	27.2	30.6	31.1	37.7	45.5	53.81	20.343	1	3.151	0.437
1244	29.8	27.8	30.4	34.3	42.0	50.3	60.20	24.380	1	3.149	0.509
1250	28.0	28.1	29.7	32.9	38.6	42.8	47.98	13.229	1	3.083	0.578
1268	30.8	30.8	32.8	36.1	42.2	50.1	58.55	22.334	1	2.928	0.557
1275	28.5	28.8	30.1	31.2	34.0	42.8	49.37	17.215	1	2.893	0.447
1300	32.2	30.8	33.0	35.3	40.7	50.0	57.18	22.687	1	3.113	0.478
1313	23.9	25.5	28.6	31.2	35.2	43.2	49.97	16.489	1	2.850	0.383

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Mouse Teratology Study: Body Weights (g) for Plug-positive Females

----- 7000 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	9 dg Wt (g)	12 dg Wt (g)	15 dg Wt (g)	18 dg Wt (g)	Uter Wt (g)	Pregnant	Liver (g)	Kidney (g)
1016	28.7	28.5	31.1	33.3	39.2	45.4	53.38	18.193	1	3.286	0.456
1019	27.8	27.4	29.8	32.4	38.4	44.2	52.27	19.037	1	2.838	0.487
1024	30.8	30.9	32.5	35.4	37.5	43.7	50.38	15.090	1	2.845	0.449
1025	31.0	28.9	28.9	30.8	27.9	30.0	29.68	0.157	0	2.077	0.525
1030	30.9	30.2	32.8	35.0	41.1	45.8	51.38	12.823	1	3.248	0.561
1035	30.6	30.2	31.1	32.1	38.5	43.2	53.91	17.997	1	3.200	0.662
1037	28.4	27.8	30.1	32.0	35.4	44.8	50.83	17.384	1	2.888	0.473
1047	32.0	29.9	33.1	36.4	37.5	43.4	48.85	11.735	1	2.982	0.489
1054	32.5	30.7	31.5	38.2	42.1	47.5	56.99	18.750	1	3.170	0.487
1058	29.3	28.2	28.8	28.7	28.2	28.5	25.87	0.114	0	1.540	0.445
1070	28.1	28.2	29.9	32.0	34.5	41.5	38.02	14.725	1	2.991	0.423
1077	29.7	28.8	29.0	32.5	36.8	42.8	48.54	18.484	1	3.074	0.494
1091	32.8	32.5	34.5	35.8	37.5	45.5	52.47	18.723	1	3.097	0.482
1105	28.5	28.0	28.5	28.0	28.9	27.2	25.58	0.092	0	1.988	0.499
1110	28.5	27.2	30.9	32.7	34.1	43.0	48.98	14.801	1	2.981	0.472
1111	28.7	26.8	28.3	31.2	33.1	41.3	48.08	14.685	1	3.083	0.564
1127	31.2	31.3	33.4	32.8	38.2	44.1	57.41	15.121	1	3.322	0.702
1131	30.9	29.1	31.2	33.0	39.0	45.3	53.47	19.415	1	3.238	0.496
1138	24.7	24.0	27.8	29.3	31.1	40.2	45.48	15.880	1	2.543	0.438
1151	29.8	29.2	30.8	31.8	35.7	43.3	48.79	13.728	1	3.145	0.542
1153	27.1	27.5	28.3	30.3	32.8	39.5	47.22	15.186	1	2.898	0.438
1158	27.8	26.8	29.2	27.8	35.0	40.9	49.78	15.981	1	3.351	0.546
1184	28.7	25.8	27.9	28.9	35.0	41.8	49.38	15.525	1	3.285	0.501
1186	31.1	28.4	30.7	30.8	39.1	48.2	55.98	19.785	1	3.239	0.542
1205	28.3	27.2	28.3	31.1	38.6	41.3	46.00	14.095	1	2.840	0.486
1225	29.8	29.0	30.5	32.7	38.0	45.4	52.33	18.292	1	3.078	0.494
1227	24.2	24.1	27.5	27.2	32.7	37.2	43.08	11.495	1	2.798	0.474
1234	30.7	29.2	32.2	29.2	30.7	30.5	30.11	0.204	0	1.741	0.491
1243	28.3	25.8	28.8	29.3	26.2	28.8	26.93	0.181	0	1.844	0.450
1292	24.8	25.0	27.1	29.7	34.8	40.2	48.85	18.820	1	2.434	0.437
1293	27.7	27.9	30.7	32.4	39.1	45.2	50.40	17.261	1	2.879	0.490
1301	30.2	29.5	31.7	33.8	35.3	43.8	49.05	15.168	1	3.092	0.414

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Mouse Teratology Study: Body Weights (g) for Virgin Females

0 ppm Isoprene

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1089	27.9	29.2	28.8	27.4	27.5
1188	30.8	30.0	30.5	30.0	29.2
1221	31.8	27.5	29.1	29.2	30.8
1262	28.9	28.8	27.1	27.2	28.4
1280	28.3	25.4	28.5	28.8	27.3
1288	28.1	28.5	27.4	28.2	27.2
1291	28.8	28.7	29.2	28.8	29.4
1311	30.3	29.5	29.4	29.7	30.3
1317	29.8	28.2	28.7	28.3	26.5
1330	28.5	27.7	29.1	29.1	22.8

Isoprene Mouse Teratology Study: Body Weights (g) for Virgin Females

----- 280 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1004	28.8	30.0	27.8	29.2	29.1
1068	26.4	24.7	26.2	25.9	25.6
1097	24.3	25.7	26.9	26.7	26.7
1123	31.7	29.6	30.2	31.0	30.6
1149	27.8	28.0	26.7	27.5	27.5
1185	29.6	27.7	29.2	29.1	30.1
1245	27.6	28.2	29.6	29.7	30.3
1262	26.0	27.1	26.6	27.4	27.7
1295	29.6	28.9	27.7	27.7	28.3
1318	29.3	30.8	30.6	30.0	31.4

Isoprene Mouse Teratology Study: Body Weights (g) for Virgin Females

----- 1400 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1020	28.4	27.6	29.0	28.5	29.4
1082	29.6	28.0	27.8	29.2	29.0
1135	29.3	28.7	28.4	29.8	30.1
1141	26.5	25.5	25.3	26.7	25.2
1144	28.7	30.4	28.4	27.8	28.5
1165	28.5	26.6	25.9	28.4	30.5
1209	28.5	29.5	30.5	31.4	32.8
1213	29.7	29.1	29.3	29.9	29.6
1285	26.2	28.1	28.2	28.9	30.1
1329	27.3	27.1	26.8	28.7	29.4

Isoprene Mouse Teratology Study: Body Weights (g) for Virgin Females

----- 7000 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1084	27.2	26.2	25.8	27.1	27.4
1094	32.7	30.9	27.6	29.2	29.2
1129	28.7	28.0	27.5	27.3	27.9
1207	30.3	28.3	27.5	27.8	30.3
1214	24.0	25.3	23.9	24.8	25.0
1220	28.0	27.6	26.4	27.1	27.3
1237	29.9	29.1	28.2	29.2	30.5
1258	29.8	29.5	29.2	28.3	30.5
1274	29.7	27.3	28.2	28.9	28.7
1319	27.7	28.8	27.4	26.9	28.0

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene									
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	
1008	1	1	1.118	2	H				
1008	2	1	1.410	2	V	SURB			
1008	3	1	1.282	1	H				
1008	4	1	1.456	1	V				
1008	5	1	1.401	1	H				
1009	1	1	1.178	1	H				
1009	2	1	1.182	2	V				
1009	3	1	1.333	1	H				
1009	4	1	1.288	1	V				
1009	5	4	.	.					
1009	6	1	1.291	1	H				
1009	7	1	1.238	2	V				
1009	8	1	1.274	2	H				
1009	9	1	1.308	1	V				
1009	10	1	1.335	2	H				
1009	11	1	1.222	2	V				
1009	12	1	1.263	1	H				
1009	13	1	1.308	2	V	DIUR			
1029	1	1	1.308	2	V	SURB			
1029	2	1	1.398	2	H	SURB			
1029	3	1	1.408	2	V				
1029	4	1	1.247	2	H				
1029	5	1	1.387	2	V	SURB			
1029	6	4	.	.					
1029	7	1	1.183	1	H				
1029	8	1	1.378	2	V	SURB			
1029	9	1	1.402	1	H	SURB			
1060	1	1	1.259	2	V				
1060	2	1	1.325	1	H				
1060	3	1	1.295	2	V	SURB			
1060	4	1	1.291	1	H				
1060	5	1	1.181	2	V	SURB			
1060	6	1	1.224	2	H				
1060	7	1	1.269	2	V				
1060	8	1	1.098	2	H				
1060	9	1	1.342	2	V				
1060	10	1	1.353	2	H	RORB			
1060	11	1	1.325	1	V				
1060	12	1	1.295	2	H				
1062	1	1	1.837	2	H				
1062	2	1	1.388	1	V				
1062	3	1	1.502	1	H				
1062	4	2	.	.					
1062	5	2	.	.					
1062	6	1	1.388	2	V				
1062	7	1	1.450	1	H				
1062	8	1	1.298	1	V				

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1002	9	1	1.336	2	H			
1002	10	1	1.404	1	V			
1002	11	1	1.217	2	H			
1002	12	1	1.360	2	V			
1007	1	1	1.500	1	V			
1007	2	4	.	.				
1007	3	1	1.487	2	H			
1007	4	1	1.453	1	V			
1007	5	1	1.510	2	H			
1007	6	1	1.433	1	V			
1007	7	4	.	.				
1007	8	1	1.454	2	H			
1007	9	1	1.392	2	V			
1007	10	2	.	.				
1007	11	1	1.534	1	H			
1007	12	1	1.528	1	V			
1008	1	1	1.084	1	V	SURB		
1008	2	1	1.589	1	H			
1008	3	1	1.582	2	V	SURB		
1101	1	1	1.454	2	H			
1101	2	1	1.310	2	V			
1101	3	1	1.365	1	H			
1101	4	1	1.339	2	V			
1101	5	1	1.330	1	H			
1101	6	1	1.451	1	V			
1101	7	1	1.305	2	H			
1101	8	1	1.275	1	V			
1101	9	1	1.294	1	H			
1101	10	1	1.301	2	V			
1101	11	1	1.321	2	H			
1101	12	1	1.369	1	V			
1103	1	1	1.448	1	V	SURB		
1103	2	1	1.376	1	H	SURB		
1103	3	1	1.360	2	V	SURB		
1103	4	2	.	.				
1103	5	1	1.393	1	H	SURB		
1103	6	1	1.337	2	V			
1103	7	1	1.365	2	H	SURB		
1103	8	1	1.302	1	V			
1103	9	1	1.410	1	H	SURB		
1103	10	1	1.334	1	V			
1103	11	1	1.261	2	H	SURB		
1103	12	1	1.044	2	V	SURB		
1103	13	1	1.332	2	H	SURB		
1103	14	1	1.375	2	V	MAST		
1109	1	1	1.513	1	V			
1109	2	1	1.500	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1109	3	1	1.408	2	V			
1109	4	1	1.477	2	H			
1109	5	1	1.433	2	V			
1109	6	1	1.382	2	H			
1109	7	1	1.321	2	V			
1109	8	1	1.339	2	H			
1109	9	1	1.382	2	V			
1109	10	1	1.270	2	H			
1109	11	1	1.375	2	V			
1109	12	1	1.365	2	H			
1112	1	1	1.110	2	H			
1112	2	1	1.268	1	V			
1112	3	1	1.067	1	H			
1112	4	1	1.045	1	V	SURB		
1112	5	1	1.154	2	H			
1112	6	1	1.094	2	V			
1112	7	1	1.102	2	H			
1112	8	1	1.079	2	V			
1112	9	1	1.129	2	H			
1112	10	1	1.034	2	V			
1112	11	1	1.263	1	H			
1112	12	4	.	.	.			
1112	13	1	1.201	1	V	SURB		
1112	14	1	1.164	2	H			
1112	15	1	1.205	2	V			
1112	16	1	1.093	2	H			
1128	1	1	1.025	1	H	SURB		
1128	2	1	1.336	2	V			
1128	3	1	1.387	1	H			
1128	4	1	1.378	1	V	SURB		
1128	5	1	1.371	2	H			
1128	6	1	1.436	1	V	SURB		
1128	7	1	1.421	2	H			
1128	8	1	1.348	2	V			
1128	9	1	1.451	2	H			
1128	10	1	1.441	1	V			
1128	11	1	1.342	2	H			
1128	12	1	1.276	2	V			
1128	13	1	1.387	2	H			
1128	14	1	1.325	2	V			
1128	15	1	1.423	1	H			
1133	1	1	1.465	1	H			
1133	2	2	.	.	.			
1133	3	1	1.368	1	V			
1133	4	1	1.338	1	H	SURB		
1133	5	1	1.415	2	V			
1133	6	2	.	.	.			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 0 ppm Isoprene -----								
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1133	7	1	1.336	2	H			
1133	8	1	1.380	2	V			
1133	9	1	1.381	2	H			
1136	1	1	1.534	1	V			
1136	2	1	1.436	2	H			
1136	3	1	1.498	1	V			
1136	4	1	1.449	1	H			
1136	5	1	1.329	1	V			
1136	6	1	1.411	2	H			
1136	7	2	.	.				
1136	8	1	1.459	1	V			
1136	9	1	1.468	1	H			
1136	10	1	1.551	1	V			
1136	11	1	1.418	1	H			
1136	12	1	1.463	1	V			
1136	13	1	1.519	1	H			
1136	14	1	1.446	1	V			
1139	1	1	1.828	2	V			
1139	2	1	1.359	1	H			
1139	3	1	1.271	1	V	SURB		
1139	4	2	.	.				
1139	5	1	1.189	2	H			
1139	6	1	1.314	2	V	SURB		
1139	7	1	1.381	2	H			
1139	8	1	1.222	2	V	ROSK		
1139	9	1	1.276	2	H			
1139	10	1	1.383	1	V	SURB		
1139	11	1	1.287	2	H			
1139	12	1	1.372	1	V			
1139	13	1	1.298	2	H			
1139	14	1	1.483	1	V			
1157	1	1	1.320	2	H	SURB		
1157	2	4	.	.				
1157	3	1	1.245	1	V	SURB		
1157	4	1	1.212	2	H			
1157	5	1	1.298	2	V			
1157	6	1	1.291	2	H	SURB		
1157	7	1	1.273	1	V			
1157	8	1	1.276	2	H			
1157	9	1	1.269	1	V	SURB		
1157	10	1	1.287	1	H			
1157	11	1	1.289	1	V	SURB		
1157	12	1	1.184	1	H	SURB		
1157	13	1	1.224	1	V	SURB		
1191	1	1	1.228	1	H	SURB		
1191	2	1	1.094	2	V	DIUR		
1191	3	1	1.219	2	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1191	4	1	1.135	2	V			
1191	5	1	1.184	1	H			
1191	6	1	1.142	2	V			
1191	7	1	1.179	2	H			
1191	8	1	1.268	1	V			
1191	9	1	1.285	2	H			
1191	10	1	1.198	2	V			
1191	11	1	1.199	2	H			
1191	12	1	1.172	2	V	SURB		
1191	13	1	1.181	1	H			
1196	1	1	1.249	2	H			
1196	2	1	1.214	2	V			
1196	3	1	1.274	2	H			
1196	4	1	1.327	1	V			
1196	5	1	1.373	2	H			
1196	6	1	1.288	1	V			
1196	7	1	1.254	1	H			
1196	8	1	1.009	1	V			
1196	9	1	1.104	1	H			
1196	10	1	1.191	1	V			
1196	11	1	1.233	1	H			
1196	12	1	1.241	1	V			
1196	13	2	.	.	.			
1196	14	1	1.238	2	H			
1196	15	1	1.308	1	V			
1201	1	1	1.371	1	H			
1201	2	1	1.275	2	V			
1201	3	1	1.238	2	H			
1201	4	4	.	.	.			
1201	5	1	1.222	1	V			
1201	6	1	1.025	2	H			
1201	7	1	1.261	1	V			
1201	8	1	1.339	2	H			
1201	9	1	1.254	2	V			
1201	10	1	1.232	1	H			
1201	11	1	1.286	2	V			
1201	12	1	1.283	2	H			
1201	13	1	1.212	2	V			
1230	1	1	1.531	2	V			
1230	2	1	1.412	1	H			
1230	3	1	1.568	1	V	SURB	ROSK	
1230	4	1	1.395	2	H			
1230	5	1	1.589	1	V			
1230	6	1	1.518	1	H			
1230	7	1	1.582	1	V	SURB		
1230	8	1	1.405	2	H			
1230	9	1	1.457	1	V	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1230	10	1	1.345	2	H			
1230	11	1	1.462	2	V			
1230	12	1	1.437	1	H	SURB		
1230	13	1	1.539	1	V	SURB		
1232	1	1	1.343	2	H			
1232	2	1	1.392	1	V	DIUR		
1232	3	1	1.376	1	H			
1232	4	1	1.313	2	V			
1232	5	1	1.338	2	H			
1232	6	1	1.407	1	V			
1232	7	1	1.465	2	H			
1232	8	1	1.340	2	V	SURB		
1232	9	1	1.381	2	H			
1232	10	1	1.326	2	V			
1232	11	2	.	.				
1232	12	1	1.415	1	H			
1232	13	1	1.312	2	V			
1232	14	1	1.340	1	H			
1232	15	1	1.430	1	V			
1264	1	1	1.419	1	V	SURB		
1264	2	1	1.531	2	H			
1264	3	1	1.353	1	V			
1264	4	1	1.332	1	H			
1264	5	1	1.381	1	V			
1264	6	1	1.302	1	H			
1264	7	1	1.251	2	V			
1264	8	1	1.409	1	H			
1264	9	1	1.333	2	V			
1264	10	1	1.288	2	H			
1264	11	1	1.172	1	V			
1264	12	1	1.245	2	H			
1264	13	1	1.308	2	V			
1264	14	1	1.318	2	H			
1264	15	1	1.291	1	V	SURB		
1265	1	1	1.458	2	H			
1265	2	1	1.458	1	V			
1265	3	1	1.403	2	H			
1265	4	1	1.349	2	V			
1265	5	1	1.295	2	H			
1265	6	1	1.309	2	V			
1265	7	1	1.517	1	H			
1265	8	1	1.416	1	V			
1265	9	1	1.214	2	H	MAST		
1265	10	1	1.538	1	V			
1265	11	1	1.491	1	H			
1267	1	1	1.182	2	V	MAST	SURB	
1267	2	1	1.124	2	H	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1287	3	1	1.137	2	V	SURB		
1287	4	1	1.171	2	H	SURB		
1287	5	1	0.947	1	V			
1287	6	1	1.071	1	H	SURB		
1287	7	1	1.094	1	V			
1287	8	1	1.174	1	H	SURB		
1287	9	1	1.285	1	V			
1287	10	1	1.277	1	H	SURB		
1287	11	1	1.164	2	V			
1287	12	1	1.274	1	H	SURB		
1287	13	1	1.237	1	V	SURB		
1287	14	1	1.181	1	H	SURB		
1287	15	1	1.110	2	V	SURB		
1302	1	1	1.445	1	V			
1302	2	1	1.484	2	H			
1302	3	1	1.464	2	V			
1302	4	2	.	.				
1302	5	1	1.402	1	H			
1302	6	1	1.472	2	V			
1302	7	1	1.378	2	H			
1302	8	1	1.328	2	V	SURB		
1302	9	1	1.375	1	H			
1302	10	1	1.438	1	V			
1302	11	1	1.411	1	H	SURB		
1302	12	2	.	.				
1302	13	1	1.444	2	V	SURB		
1306	1	1	1.358	2	H			
1306	2	1	1.306	2	V			
1306	3	1	1.398	2	H			
1306	4	1	1.331	2	V	SURB		
1306	5	1	1.610	1	H	SURB		
1306	6	1	1.379	1	V			
1306	7	1	1.447	1	H	SURB		
1306	8	2	.	.				
1306	9	1	1.331	1	V	SURB		
1306	10	1	1.421	1	H	SURB		
1307	1	1	1.399	1	H			
1307	2	1	1.249	2	V			
1307	3	1	1.353	1	H			
1307	4	1	1.235	1	V			
1307	5	1	1.320	1	H			
1307	6	1	1.377	1	V			
1307	7	1	1.290	2	H			
1307	8	1	1.185	2	V			
1307	9	1	1.413	1	H			
1307	10	1	1.331	1	V			
1307	11	1	1.396	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1307	12	1	1.332	2	V			
1328	1	1	1.648	1	V			
1328	2	1	1.485	1	H			
1328	3	1	1.333	2	V			
1328	4	1	1.269	2	H	SURB		
1328	5	1	1.400	1	V			
1328	6	1	1.330	2	H			
1328	7	1	1.355	2	V			
1328	8	1	1.367	1	H			
1328	9	1	1.392	2	V			
1328	10	1	1.441	2	H			
1328	11	1	1.488	2	V			
1328	12	1	1.491	1	H			
1329	13	1	1.355	2	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1013	1	1	1.179	2	H			
1013	2	1	1.171	2	V			
1013	3	1	1.187	1	H			
1013	4	1	1.127	2	V	SURB		
1013	5	1	1.194	1	H			
1013	6	1	1.107	2	V			
1013	7	1	1.061	2	H			
1013	8	1	1.165	2	V			
1013	9	1	1.132	2	H			
1013	10	1	1.078	2	V			
1013	11	1	1.098	2	H			
1013	12	1	1.147	1	V			
1013	13	1	1.185	2	H			
1013	14	1	1.146	1	V			
1013	15	1	1.178	2	H			
1017	1	1	1.137	1	V			
1017	2	1	1.088	2	H			
1017	3	1	1.200	2	V			
1017	4	4	.	.	.			
1017	5	1	1.218	1	V			
1017	6	1	1.109	2	H			
1017	7	1	1.169	2	V	ROSK		
1017	8	1	1.167	1	H			
1017	9	1	1.079	2	V			
1017	10	1	1.177	2	H			
1017	11	2	.	.	.			
1017	12	1	1.124	2	V			
1017	13	1	1.183	2	H			
1018	1	1	1.273	2	V	SURB		
1018	2	1	1.299	1	H	SURB		
1018	3	1	1.199	1	V			
1018	4	1	1.266	1	H			
1018	5	1	1.244	1	V			
1018	6	1	1.268	2	H			
1018	7	1	1.218	1	V			
1018	8	1	1.111	2	H			
1018	9	1	1.121	2	V			
1018	10	1	1.133	2	H			
1018	11	2	.	.	.			
1018	12	1	1.300	2	V	SURB		
1018	13	1	1.344	2	H	SURB		
1018	14	1	1.194	2	V			
1020	1	1	0.976	1	V	SURB		
1020	2	1	1.278	1	H	SURB		
1020	3	1	1.081	1	V	SURB		
1020	4	1	1.307	2	H	SURB		
1020	5	1	1.201	1	V	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1020	6	1	1.094	2	H			
1020	7	1	1.049	2	V	SURB		
1020	8	1	0.865	2	H	SURB		
1020	9	1	1.227	1	V			
1020	10	1	1.217	1	H			
1020	11	1	1.231	2	V	ROSK		
1020	12	1	1.222	1	H	SURB		
1020	13	1	1.090	2	V			
1033	1	1	1.160	2	V			
1033	2	1	1.281	2	H			
1033	3	1	1.193	2	V			
1033	4	1	1.283	1	H			
1033	5	1	1.240	1	V			
1033	6	1	1.218	1	H			
1033	7	1	1.123	1	V			
1033	8	1	1.160	2	H			
1033	9	1	1.198	1	V	ROSK		
1033	10	1	1.107	2	H			
1033	11	1	1.189	1	V			
1033	12	1	1.114	2	H			
1033	13	1	1.181	1	V			
1033	14	1	1.059	2	H			
1036	1	1	1.289	2	H			
1036	2	1	1.311	1	V	ROSK		
1036	3	1	1.194	2	H			
1036	4	1	1.282	2	V			
1036	5	1	1.238	2	H			
1036	6	1	1.155	2	V			
1036	7	1	1.317	1	H			
1036	8	1	1.279	1	V			
1036	9	1	1.322	2	H			
1036	10	1	1.407	1	V			
1036	11	1	1.291	2	H			
1036	12	1	1.504	2	V			
1036	13	1	1.454	1	H			
1036	14	1	1.415	1	V			
1053	1	1	1.241	2	H			
1053	2	1	1.388	1	V			
1053	3	1	1.351	1	H	SURB		
1053	4	1	1.312	2	V			
1053	5	1	1.122	2	H			
1053	6	1	1.232	1	V			
1053	7	1	1.147	2	H			
1053	8	1	1.268	2	V			
1053	9	2	.	.	.			
1053	10	1	1.128	2	H			
1053	11	1	1.258	1	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1057	1	1	1.249	2	V			
1057	2	2	.	.				
1057	3	1	1.060	2	H			
1057	4	1	1.305	2	V			
1057	5	1	1.263	1	H			
1057	6	1	1.151	2	V			
1057	7	1	1.291	1	H			
1057	8	1	1.221	2	V			
1057	9	1	1.216	1	H			
1057	10	2	.	.				
1057	11	1	1.197	2	V			
1057	12	1	1.220	2	H			
1064	1	1	1.095	2	V			
1064	2	1	1.023	2	H			
1064	3	1	1.176	2	V			
1064	4	1	1.217	1	H			
1064	5	1	1.244	2	V			
1064	6	1	1.203	1	H			
1064	7	1	1.185	1	V			
1064	8	1	1.173	2	H			
1064	9	1	1.233	1	V			
1064	10	1	1.132	1	H			
1064	11	1	1.070	2	V			
1064	12	1	1.070	1	H			
1064	13	1	1.109	2	V			
1071	1	1	1.439	1	H			
1071	2	1	1.465	1	V	SURB		
1071	3	1	1.408	2	H	SURB		
1071	4	1	1.458	1	V			
1071	5	2	.	.				
1071	6	1	1.280	1	H	SURB		
1071	7	1	1.258	2	V			
1071	8	1	1.428	1	H			
1071	9	1	1.450	2	V			
1071	10	1	1.498	1	H			
1071	11	1	1.405	1	V			
1071	12	1	1.387	2	H			
1071	13	1	1.379	2	V			
1072	1	1	1.311	1	V			
1072	2	1	1.251	2	H			
1072	3	1	1.182	1	V			
1072	4	1	1.285	2	H			
1072	5	1	1.222	2	V			
1072	6	1	1.234	1	H	SURB		
1072	7	1	0.954	2	V	SURB		
1072	8	1	1.249	2	H	SURB		
1072	9	1	1.220	1	V	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1072	10	1	1.239	1	H			
1072	11	1	0.800	2	V			
1072	12	1	1.201	1	H			
1098	1	1	1.282	2	H			
1098	2	1	1.288	1	V			
1098	3	1	1.293	2	H			
1098	4	1	1.160	2	V			
1098	5	1	1.208	2	H			
1098	6	1	1.246	1	V			
1098	7	1	1.313	1	H			
1098	8	1	1.344	2	V			
1098	9	1	1.254	1	H			
1098	10	1	1.321	1	V			
1098	11	1	1.370	1	H			
1098	12	1	1.300	2	V			
1098	13	1	1.283	1	H			
1098	14	1	1.255	1	V			
1098	15	1	1.334	1	H			
1167	1	1	1.444	1	H			
1167	2	1	1.201	2	V			
1167	3	1	1.349	2	H			
1167	4	1	1.399	1	V			
1167	5	1	0.999	1	H			
1167	6	1	1.382	1	V			
1167	7	6	.	.	.			
1167	8	1	1.373	2	H			
1167	9	1	1.322	1	V			
1167	10	1	1.441	1	H			
1170	1	1	1.345	2	H			
1170	2	1	1.350	2	V			
1170	3	1	1.230	2	H			
1170	4	1	1.294	2	V			
1170	5	1	1.283	1	H			
1170	6	1	1.212	1	V			
1170	7	1	1.200	2	H			
1170	8	1	1.142	2	V			
1170	9	1	1.181	1	H			
1170	10	1	1.248	2	V			
1170	11	4	.	.	.			
1170	12	1	1.210	2	H			
1170	13	1	1.276	2	V			
1170	14	1	1.151	2	H			
1174	1	1	1.345	1	H			
1174	2	4	.	.	.			
1174	3	1	1.240	1	V			
1174	4	1	1.240	1	H			
1174	5	1	1.349	1	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

280 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1174	8	1	1.318	1	H			
1174	7	1	1.283	2	V	SURB		
1174	8	1	1.224	1	H	SURB		
1174	9	1	1.329	1	V			
1174	10	1	1.368	1	H	SURB		
1174	11	1	1.318	2	V	SURB		
1174	12	1	1.401	1	H			
1187	1	1	1.433	1	V			
1187	2	1	1.309	1	H			
1187	3	1	1.269	2	V			
1187	4	1	1.325	2	H			
1187	5	1	1.338	1	V			
1187	6	1	1.278	2	H			
1187	7	1	1.342	1	V	SURB		
1187	8	1	1.239	2	H			
1187	9	1	1.420	1	V			
1187	10	1	1.320	2	H			
1187	11	1	1.232	2	V			
1187	12	1	1.227	2	H			
1194	1	1	1.109	1	H			
1194	2	1	1.126	1	V	SURB		
1194	3	1	1.041	2	H			
1194	4	1	1.181	1	V	SURB		
1194	5	1	1.229	1	H	SURB		
1194	6	1	1.163	1	V	SURB		
1194	7	1	1.226	1	H	SURB		
1194	8	1	1.087	1	V			
1194	9	1	1.093	2	H	SURB		
1194	10	1	1.183	2	V	SURB		
1194	11	1	1.138	2	H	SURB		
1194	12	1	1.183	2	V			
1198	1	1	1.321	2	H	SURB		
1198	2	1	1.413	1	V	SURB		
1198	3	1	1.303	2	H	SURB		
1198	4	1	1.275	1	V	SURB		
1198	5	1	1.382	1	H	SURB		
1198	6	1	1.300	2	V	SURB		
1198	7	1	1.344	2	H	SURB		
1198	8	1	1.287	2	V	SURB		
1198	9	1	1.349	1	H	SURB		
1198	10	1	1.388	1	V			
1198	11	1	1.352	1	H	SURB		
1212	1	1	1.265	1	V			
1212	2	1	1.262	2	H	SURB		
1212	3	1	1.488	1	V	SURB		
1212	4	1	1.388	1	H	SURB		
1212	5	1	1.479	1	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1212	6	1	1.376	2	H	SURB		
1212	7	1	1.412	1	V	SURB		
1212	8	1	1.333	2	H			
1212	9	1	1.462	1	V			
1212	10	1	1.449	1	H	SURB		
1212	11	1	1.455	1	V			
1212	12	1	1.318	2	H	SURB		
1212	13	1	1.444	2	V			
1212	14	1	1.466	1	H	SURB		
1224	1	1	1.398	2	V			
1224	2	1	1.316	1	H	SURB		
1224	3	1	1.428	1	V			
1224	4	1	1.330	1	H			
1224	5	1	1.361	2	V			
1224	6	1	1.217	1	H			
1224	7	1	1.304	1	V			
1224	8	2	.	.	.			
1224	9	1	1.426	1	H			
1224	10	1	1.375	1	V			
1224	11	1	1.408	2	H	SURB		
1224	12	1	1.319	1	V			
1224	13	1	1.285	2	H			
1224	14	1	1.285	2	V			
1224	15	1	1.274	2	H			
1224	16	1	1.386	2	V			
1242	1	2	.	.	.			
1242	2	1	1.224	2	H	SURB		
1242	3	1	1.258	1	V	SURB		
1242	4	1	1.275	1	H	SURB		
1242	5	2	.	.	.			
1242	6	1	1.395	2	V	SURB		
1242	7	1	1.271	2	H	SURB		
1242	8	1	1.424	2	V			
1242	9	1	1.258	1	H	SURB		
1242	10	1	1.136	2	V	SURB		
1242	11	1	1.256	2	H			
1242	12	1	1.308	1	V			
1242	13	1	1.278	2	H	SURB		
1255	1	1	1.594	1	H			
1255	2	1	1.540	2	V			
1255	3	1	1.490	2	H			
1255	4	1	1.543	1	V			
1255	5	1	1.606	1	H			
1255	6	2	.	.	.			
1255	7	2	.	.	.			
1255	8	1	1.624	1	V			
1255	9	1	1.580	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1255	10	1	1.495	2	V			
1257	1	1	1.258	2	V			
1257	2	1	1.389	1	H			
1257	3	1	1.156	2	V			
1257	4	1	1.319	1	H			
1257	5	1	1.182	1	V			
1257	6	1	1.186	2	H			
1257	7	1	1.378	1	V			
1257	8	1	1.273	2	H			
1257	9	1	1.153	1	V			
1257	10	1	1.285	2	H			
1257	11	1	1.253	1	V			
1270	1	1	1.377	2	H			
1270	2	1	1.262	2	V			
1270	3	1	1.432	1	H			
1270	4	1	1.476	2	V			
1270	5	1	1.473	1	H			
1270	6	1	1.419	2	V			
1270	7	1	1.384	1	H			
1270	8	1	1.351	1	V			
1270	9	1	1.343	1	H			
1270	10	1	1.344	2	V			
1270	11	1	1.395	2	H			
1280	1	1	1.258	2	V	SURB		
1280	2	1	1.330	1	H	SURB		
1280	3	1	1.356	2	V	SURB		
1280	4	1	1.285	1	H			
1280	5	1	1.279	1	V	SURB		
1280	6	1	1.110	2	H			
1280	7	1	0.930	1	V			
1280	8	4	.	.	.			
1280	9	1	1.159	2	H	SURB		
1280	10	1	1.283	1	V			
1280	11	1	0.788	2	H			
1280	12	1	1.281	1	V	SURB		
1280	13	1	1.282	1	H	SURB		
1289	1	1	1.318	2	V	SURB		
1289	2	1	1.378	1	H			
1289	3	1	1.294	2	V			
1289	4	1	1.489	1	H	SURB		
1289	5	1	1.401	2	V			
1289	6	2	.	.	.			
1289	7	1	0.981	2	H			
1289	8	1	1.507	1	V			
1289	9	1	1.412	1	H			
1289	10	1	1.264	2	V			
1289	11	1	1.338	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1289	12	1	1.308	2	V			
1289	13	1	1.313	2	H			
1289	14	1	1.458	1	V			
1290	1	1	1.326	1	V			
1290	2	1	1.239	1	H			
1290	3	1	1.224	1	V			
1290	4	1	1.158	1	H			
1290	5	1	1.218	2	V			
1290	6	1	1.197	2	H			
1290	7	4	.	.	.			
1290	8	1	1.228	1	V			
1290	9	1	1.349	1	H	SURB		
1290	10	1	1.342	1	V			
1290	11	1	0.982	2	H	RORB		
1290	12	1	1.301	2	V			
1290	13	1	1.172	2	H			
1331	1	1	1.418	1	V			
1331	2	1	1.387	2	H	SURB		
1331	3	1	1.381	1	V	SURB		
1331	4	1	1.385	2	H			
1331	5	1	1.421	2	V			
1331	6	1	1.355	2	H	SURB		
1331	7	1	1.352	1	V			
1331	8	1	1.273	2	H			
1331	9	1	1.325	2	V			
1331	10	1	1.330	2	H			
1331	11	1	1.334	1	V	SURB		
1331	12	1	1.243	2	H			
1331	13	1	1.237	2	V	SURB		
1331	14	1	1.293	2	H			
1333	1	1	1.436	1	H			
1333	2	1	1.807	2	V			
1333	3	1	1.334	2	H	SURB		
1333	4	2	.	.	.			
1333	5	1	1.402	1	H			
1333	6	1	1.387	2	V			
1333	7	1	1.299	2	H	SURB		
1333	8	5	.	.	.			
1333	9	1	1.513	1	V			
1333	10	2	.	.	.			
1333	11	1	1.422	1	H	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----									
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	
1002	1	1	1.274	2	V				
1002	2	1	1.221	2	H	SURB			
1002	3	2	.	.					
1002	4	1	1.212	2	V				
1002	5	1	1.214	1	H				
1002	6	1	1.244	2	V				
1002	7	1	1.198	1	H				
1002	8	1	1.117	2	V	ROSK			
1002	9	1	1.310	1	H				
1002	10	1	1.195	2	V	ROSK			
1002	11	1	1.171	1	H				
1002	12	1	1.268	1	V				
1003	1	1	1.142	2	H	SURB			
1003	2	1	1.185	2	V	SURB			
1003	3	1	1.126	1	H	SURB			
1003	4	1	1.152	1	V				
1003	5	1	1.129	2	H				
1003	6	1	1.002	2	V				
1003	7	1	1.122	2	H				
1003	8	1	1.130	1	V	SURB			
1003	9	1	1.071	2	H	SURB			
1003	10	1	1.008	2	V	SURB			
1003	11	1	1.008	2	H				
1034	1	1	1.088	2	V	SURB			
1034	2	1	1.162	1	H				
1034	3	1	1.177	1	V	SURB			
1034	4	1	1.079	1	H				
1034	5	1	1.143	1	V	SURB			
1034	6	1	0.952	2	H	SURB			
1034	7	1	1.070	1	V	SURB			
1034	8	1	1.167	2	H				
1034	9	1	1.121	1	V				
1034	10	1	1.089	1	H	SURB			
1034	11	1	1.163	1	V				
1034	12	1	1.120	1	H				
1034	13	1	1.074	1	V				
1034	14	1	1.081	2	H				
1041	1	1	1.104	1	V	SURB			
1041	2	1	1.181	1	H	SURB			
1041	3	1	1.056	2	V	SURB			
1041	4	1	1.109	2	H				
1041	5	1	1.127	1	V				
1041	6	1	1.048	2	H	SURB			
1041	7	1	1.118	1	V				
1041	8	1	1.140	2	H				
1041	9	1	1.245	1	V				
1041	10	1	1.228	1	H				

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1041	11	1	1.155	1	V			
1041	12	1	1.140	2	H			
1041	13	1	1.179	1	V			
1042	1	1	1.232	1	V	SURB		
1042	2	1	1.201	2	H	SURB		
1042	3	1	1.201	1	V	SURB		
1042	4	1	1.128	2	H			
1042	5	1	1.189	2	V			
1042	6	1	1.105	2	H			
1042	7	1	1.112	1	V	SURB		
1042	8	1	1.100	1	H	SURB		
1042	9	1	1.173	1	V	SURB		
1042	10	1	1.135	2	H	SURB		
1042	11	1	1.171	2	V	SURB		
1042	12	1	1.252	2	H			
1042	13	2	.	.				
1042	14	1	1.134	2	V	SURB		
1043	1	1	0.881	1	V			
1043	2	1	1.071	1	H	SURB		
1043	3	1	1.003	2	V	SURB		
1043	4	1	1.116	1	H	SURB		
1043	5	1	1.054	1	V			
1043	6	1	1.188	1	H			
1043	7	1	1.038	2	V	SURB		
1043	8	1	1.027	1	H			
1043	9	1	1.019	2	V			
1043	10	1	1.054	2	H	SURB		
1043	11	1	1.016	2	V			
1043	12	1	0.998	2	H			
1043	13	1	1.013	2	V			
1043	14	1	1.032	2	H			
1048	1	1	1.370	2	V	SURB		
1048	2	1	1.327	1	H			
1048	3	1	1.414	2	V			
1048	4	1	1.305	1	H			
1048	5	1	1.354	1	V			
1048	6	4	.	.				
1048	7	1	1.167	2	V			
1048	8	1	1.211	1	H			
1048	9	1	1.301	1	V			
1048	10	1	1.423	1	H			
1048	11	2	.	.				
1048	12	1	1.328	2	V			
1052	1	1	1.085	2	V	SURB		
1052	2	1	1.113	2	H	SURB		
1052	3	1	1.150	1	V	SURB		
1052	4	1	1.168	1	H	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1052	5	1	1.068	2	V	SURB		
1052	6	1	1.164	1	H	SURB		
1052	7	1	1.150	1	V	SURB		
1052	8	1	1.033	2	H	SURB		
1052	9	1	1.099	2	V			
1052	10	1	1.122	1	H	SURB		
1052	11	4	.	.				
1052	12	1	1.040	1	V	SURB		
1073	1	1	1.320	1	H			
1073	2	1	1.250	2	V			
1073	3	1	1.172	2	H			
1073	4	1	1.259	2	V	SURB		
1073	5	1	1.303	1	H	SURB		
1073	6	1	1.235	2	V	SURB		
1073	7	1	1.212	1	H	SURB		
1073	8	1	1.121	2	V	SURB		
1073	9	1	1.173	1	H	SURB		
1073	10	1	1.192	2	V	SURB		
1073	11	1	1.201	2	H			
1073	12	1	1.324	1	V	SURB		
1073	13	1	1.211	2	H	SURB		
1073	14	1	1.202	1	V			
1075	1	1	1.207	1	H			
1075	2	1	1.167	2	V			
1075	3	1	1.211	1	H			
1075	4	1	1.145	2	V			
1075	5	1	1.228	1	H			
1075	6	1	1.203	1	V			
1075	7	2	.	.				
1075	8	1	1.285	1	H			
1075	9	1	1.163	1	V	SURB		
1075	10	1	1.321	1	H			
1075	11	1	1.122	1	V			
1075	12	1	1.265	2	H			
1078	1	1	0.934	1	V	SURB		
1078	2	1	1.161	1	H	SURB		
1078	3	1	1.220	2	V	SURB		
1078	4	1	1.115	1	H	SURB		
1078	5	1	1.168	1	V	SURB		
1078	6	1	1.032	1	H			
1078	7	1	1.094	2	V	SURB		
1079	1	1	1.338	1	V			
1079	2	1	1.234	1	H			
1079	3	1	1.301	2	V	SURB		
1079	4	1	1.335	1	H			
1079	5	1	1.222	1	V			
1079	6	1	1.208	2	H	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1079	7	1	1.307	1	V			
1079	8	1	1.210	2	H			
1079	9	1	1.278	2	V			
1079	10	1	1.355	1	H			
1079	11	1	1.304	1	V			
1079	12	1	1.267	2	H			
1095	1	1	1.247	1	H	SURB		
1095	2	1	0.989	2	V			
1095	3	1	1.102	1	H	SURB		
1095	4	1	1.242	1	V			
1095	5	1	1.079	2	H	SURB		
1095	6	1	1.204	1	V			
1095	7	1	1.060	2	H	SURB		
1095	8	1	1.146	1	V	SURB		
1095	9	1	0.995	2	H	SURB		
1095	10	1	0.986	1	V	SURB		
1095	11	1	1.044	2	H	SURB		
1095	12	1	1.025	2	V			
1095	13	1	1.077	1	H	SURB		
1095	14	1	1.079	1	V			
1121	1	1	1.149	1	V			
1121	2	1	1.070	2	H			
1121	3	1	1.151	1	V	SURB		
1121	4	1	1.218	2	H	SURB		
1121	5	1	0.872	2	V	SURB		
1121	6	1	1.041	2	H			
1121	7	1	1.183	1	V	SURB		
1121	8	1	1.056	1	H			
1121	9	1	1.075	1	V			
1121	10	1	1.072	2	H			
1121	11	4	.	.				
1121	12	1	1.106	2	V			
1121	13	1	1.078	1	H	SURB		
1121	14	1	1.084	2	V			
1121	15	1	1.023	1	H			
1121	16	1	0.995	2	V			
1124	1	1	1.421	1	H			
1124	2	1	1.339	2	V			
1124	3	1	1.390	1	H	SURB		
1124	4	1	1.394	1	V			
1124	5	1	1.334	2	H	SURB		
1124	6	1	1.340	2	V			
1124	7	1	1.367	1	H			
1124	8	1	1.333	1	V			
1124	9	1	1.398	1	H			
1124	10	1	1.352	2	V			
1124	11	1	1.404	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----									
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	
1124	12	1	1.232	2	V	SURB			
1124	13	2	.	.					
1145	1	1	1.410	1	H				
1145	2	1	1.337	1	V				
1145	3	1	1.358	2	H				
1145	4	1	1.310	2	V				
1145	5	4	.	.					
1145	6	1	1.324	2	H				
1145	7	1	1.171	2	V	SURB			
1145	8	1	1.207	1	H	SURB			
1145	9	1	1.267	2	V				
1145	10	1	1.210	1	H				
1145	11	1	1.150	2	V				
1145	12	2	.	.					
1145	13	1	1.235	2	H	SURB			
1171	1	1	1.162	2	V				
1171	2	1	1.251	2	H	SURB			
1171	3	1	1.214	2	V				
1171	4	1	1.321	1	H				
1171	5	1	1.220	2	V				
1171	6	1	1.308	1	H	SURB	CLPA		
1171	7	1	1.203	2	V				
1171	8	1	1.305	2	H				
1171	9	1	1.198	1	V				
1171	10	1	1.260	2	H				
1184	1	1	1.240	1	V	SURB			
1184	2	1	1.330	2	H				
1184	3	1	1.229	1	V				
1184	4	1	1.117	2	H				
1184	5	1	1.182	2	V	DIUR			
1184	6	1	1.060	2	H	SURB			
1184	7	1	1.152	1	V	DIUR			
1184	8	1	1.060	1	H				
1184	9	1	1.084	2	V	SURB			
1184	10	1	1.179	2	H	SURB			
1226	1	1	1.269	2	H				
1226	2	1	1.273	2	V				
1226	3	1	1.237	1	H				
1226	4	1	1.220	2	V				
1226	5	1	1.193	1	H				
1226	6	1	1.270	1	V				
1226	7	1	1.219	2	H				
1226	8	1	1.239	1	V				
1226	9	1	1.280	1	H				
1226	10	1	1.251	2	V				
1226	11	1	1.300	1	H				
1226	12	1	1.277	2	V				

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1236	1	1	1.390	2	V			
1236	2	1	1.377	2	H	SURB		
1236	3	1	1.360	2	V	SURB		
1236	4	1	1.283	2	H	SURB		
1236	5	1	1.432	1	V	SURB		
1236	6	1	1.409	1	H			
1236	7	1	1.398	1	V	RPCA	DIUR	SURB
1236	8	1	1.354	1	H			
1236	9	1	1.316	2	V			
1239	1	1	1.240	1	H			
1239	2	1	1.253	1	V			
1239	3	1	1.257	1	H			
1239	4	1	1.123	2	V			
1239	5	1	1.209	2	H			
1239	6	1	0.765	2	V			
1239	7	1	1.246	1	H			
1239	8	1	1.242	2	V			
1239	9	1	0.661	1	H			
1239	10	1	1.296	2	V			
1239	11	1	1.191	2	H			
1239	12	1	1.204	2	V			
1239	13	1	1.195	1	H			
1240	1	1	1.285	2	V			
1240	2	1	1.258	2	H			
1240	3	1	1.332	2	V			
1240	4	1	1.323	1	H			
1240	5	1	1.259	1	V			
1240	6	1	1.295	1	H			
1240	7	1	1.202	1	V	SURB		
1240	8	1	1.294	1	H			
1240	9	1	1.275	1	V			
1240	10	1	1.274	1	H			
1240	11	1	1.155	2	V			
1240	12	1	1.230	1	H			
1240	13	1	1.149	2	V	SURB		
1244	1	1	1.428	1	H			
1244	2	1	1.287	2	V	SURB		
1244	3	1	1.303	1	H			
1244	4	1	1.252	2	V			
1244	5	1	1.400	1	H			
1244	6	1	1.409	1	V			
1244	7	1	1.330	2	H			
1244	8	1	1.341	2	V			
1244	9	1	1.328	1	H	SURB		
1244	10	1	1.273	2	V			
1244	11	1	1.164	1	H	SURB		
1244	12	1	1.378	1	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1244	13	1	1.230	2	H			
1244	14	1	1.250	2	V			
1244	15	1	1.241	2	H			
1250	1	1	1.339	1	V			
1250	2	1	1.203	1	H			
1250	3	2	.	.				
1250	4	4	.	.				
1250	5	1	1.183	2	V	SURB		
1250	6	1	1.106	2	H	SURB		
1250	7	2	.	.				
1250	8	1	1.214	1	V	SURB		
1250	9	1	1.372	1	H			
1250	10	1	1.286	1	V			
1250	11	1	1.273	2	H			
1260	1	1	1.476	2	H	SURB		
1260	2	1	1.363	2	V	SURB		
1260	3	1	1.346	2	H	SURB		
1260	4	1	1.509	1	V			
1260	5	1	1.380	2	H			
1260	6	1	1.409	1	V			
1260	7	1	1.375	2	H	SURB		
1260	8	1	1.462	1	V	SURB		
1260	9	1	1.338	2	H	SURB		
1260	10	1	1.441	1	V	SURB		
1260	11	1	1.443	1	H			
1260	12	1	1.414	2	V			
1260	13	1	1.298	2	H			
1275	1	1	1.367	2	V			
1275	2	1	1.340	1	H			
1275	3	1	1.263	2	V			
1275	4	1	1.252	2	H			
1275	5	1	1.299	1	V			
1275	6	1	1.273	1	H			
1275	7	1	1.210	1	V			
1275	8	1	1.268	2	H			
1275	9	1	1.275	1	V			
1275	10	1	1.332	2	H			
1275	11	1	1.224	2	V			
1300	1	1	1.210	2	V	SURB		
1300	2	1	1.287	1	H	MAST	SURB	
1300	3	1	1.210	1	V	SURB		
1300	4	1	1.240	1	H			
1300	5	1	1.250	2	V			
1300	6	1	1.180	2	H			
1300	7	1	1.079	1	V	SURB		
1300	8	2	.	.				
1300	9	1	1.115	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1300	10	1	1.010	1	V			
1300	11	1	1.132	2	H			
1300	12	1	1.044	2	V	SURB		
1300	13	1	1.214	1	H			
1300	14	1	1.074	1	V			
1300	15	1	1.233	1	H			
1300	16	1	1.178	1	V			
1300	17	1	1.167	2	H			
1313	1	1	1.350	2	V			
1313	2	1	1.370	1	H			
1313	3	1	1.290	2	V			
1313	4	1	1.341	1	H			
1313	5	1	1.392	1	V			
1313	6	2	.	.	.			
1313	7	1	1.319	1	H	SURB		
1313	8	1	1.413	1	V			
1313	9	1	1.348	1	H			
1313	10	1	1.310	2	V			
1313	11	1	1.352	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1018	1	1	1.403	1	V			
1018	2	1	1.207	2	H	SURB		
1018	3	1	1.360	1	V			
1018	4	1	1.341	1	H	SURB		
1018	5	1	1.310	1	V			
1018	6	1	1.316	1	H			
1018	7	1	1.240	2	V			
1018	8	1	1.269	2	H	SURB		
1018	9	1	1.359	1	V	SURB		
1018	10	1	1.010	1	H	SURB		
1019	1	1	1.095	2	H	SURB		
1019	2	1	1.245	1	V	SURB		
1019	3	1	1.143	2	H			
1019	4	1	1.144	2	V	SURB		
1019	5	1	1.178	1	H			
1019	6	1	1.111	2	V			
1019	7	1	1.064	2	H			
1019	8	1	1.051	2	V	SURB		
1019	9	1	1.030	1	H			
1019	10	1	1.016	2	V	SURB		
1019	11	1	1.148	1	H			
1019	12	1	1.062	2	V	SURB		
1019	13	1	1.097	2	H	SURB		
1019	14	1	1.020	2	V	SURB		
1024	1	1	0.899	1	H	CLPA		
1024	2	1	0.988	2	V			
1024	3	2	.	.				
1024	4	1	0.950	1	H	SURB		
1024	5	1	0.988	1	V	SURB		
1024	6	1	1.009	1	H	SURB		
1024	7	1	0.953	1	V	SURB		
1024	8	1	0.963	1	H			
1024	9	1	0.957	1	V			
1024	10	1	0.988	2	H			
1024	11	1	0.874	2	V			
1024	12	1	0.939	2	H	SURB		
1024	13	2	.	.				
1024	14	1	0.921	2	V	SURB		
1030	1	1	1.290	1	H			
1030	2	1	1.255	2	V			
1030	3	1	1.245	2	H	SURB		
1030	4	2	.	.				
1030	5	2	.	.				
1030	6	1	1.325	2	V			
1030	7	1	1.213	2	H	SURB		
1030	8	1	1.319	1	V			
1030	9	2	.	.				

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1030	10	1	1.338	1	H			
1030	11	1	1.181	2	V	SURB		
1030	12	2	.	.				
1035	1	1	0.628	2	V			
1035	2	1	1.001	2	H	SURB		
1035	3	1	1.052	2	V	SURB		
1035	4	1	1.063	2	H			
1035	5	1	1.001	1	V			
1035	6	1	0.870	2	H			
1035	7	1	0.988	2	V			
1035	8	1	0.972	2	H	SURB		
1035	9	1	0.983	1	V			
1035	10	1	0.941	2	H	SURB		
1035	11	1	0.926	2	V	SURB		
1035	12	1	1.019	2	H	SURB		
1035	13	1	1.012	1	V			
1035	14	1	1.058	1	H	SURB		
1037	1	1	1.302	2	V			
1037	2	1	1.393	2	H			
1037	3	2	.	.				
1037	4	1	1.237	2	V			
1037	5	1	1.412	1	H	SURB		
1037	6	1	1.385	2	V	SURB		
1037	7	1	1.266	2	H			
1037	8	1	1.248	2	V			
1037	9	1	1.070	2	H	SURB		
1037	10	1	1.319	2	V			
1037	11	1	1.033	1	H	SURB		
1037	12	1	1.278	1	V	SURB		
1047	1	1	1.209	1	H	SURB		
1047	2	1	0.971	1	V	SURB		
1047	3	1	1.148	2	H	SURB		
1047	4	1	1.205	2	V			
1047	5	1	0.891	2	H	SURB		
1047	6	1	1.133	2	V			
1047	7	1	1.122	2	H			
1047	8	1	0.978	1	V			
1054	1	1	1.122	2	H	SURB		
1054	2	1	1.224	2	V			
1054	3	1	1.183	1	H	SURB		
1054	4	1	1.220	1	V			
1054	5	1	1.160	1	H			
1054	6	1	1.208	1	V			
1054	7	1	1.111	2	H			
1054	8	1	1.148	2	V			
1054	9	1	1.166	1	H			
1054	10	1	1.086	2	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1054	11	1	1.142	1	H			
1054	12	1	1.180	1	V			
1054	13	1	1.093	1	H			
1070	1	2	.	.				
1070	2	1	1.158	2	V			
1070	3	1	1.108	2	H			
1070	4	1	1.238	2	V			
1070	5	1	1.261	1	H			
1070	6	1	1.170	1	V			
1070	7	1	1.189	2	H			
1070	8	1	1.211	1	V			
1070	9	1	1.205	2	H			
1070	10	1	1.089	1	V			
1070	11	1	1.243	1	H			
1070	12	2	.	.				
1077	1	1	1.164	2	V			
1077	2	1	1.192	2	H			
1077	3	1	1.128	1	V			
1077	4	1	1.115	2	H			
1077	5	1	1.063	1	V			
1077	6	1	1.086	1	H			
1077	7	1	1.003	2	V			
1077	8	1	1.025	1	H			
1077	9	1	1.218	1	V			
1077	10	1	0.992	2	H	SURB		
1077	11	1	1.049	1	V			
1077	12	1	1.165	1	H			
1091	1	1	1.140	2	H	SURB		
1091	2	2	.	.				
1091	3	1	1.221	2	V	SURB		
1091	4	1	1.147	1	H	SURB		
1091	5	1	1.110	2	V	SURB		
1091	6	1	1.091	2	H	SURB		
1091	7	1	1.177	1	V	SURB		
1091	8	1	1.038	2	H			
1091	9	4	.	.				
1091	10	1	1.063	1	V			
1091	11	1	1.021	2	H	SURB		
1091	12	1	1.063	2	V			
1091	13	1	1.063	2	H	SURB		
1091	14	1	1.050	1	V	SURB		
1110	1	1	0.927	2	V			
1110	2	1	0.840	1	H	SURB		
1110	3	1	0.918	1	V	SURB		
1110	4	1	1.094	1	H	SURB		
1110	5	1	1.085	2	V	SURB		
1110	6	1	0.989	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1110	7	1	0.941	1	V			
1110	8	1	1.004	1	H	SURB		
1110	9	1	1.008	1	V	SURB		
1110	10	1	1.062	2	H	SURB		
1110	11	1	0.993	1	V	SURB		
1111	1	1	1.215	2	H			
1111	2	1	1.223	2	V			
1111	3	1	1.211	1	H			
1111	4	1	1.088	1	V			
1111	5	1	1.129	1	H	SURB		
1111	6	4	.	.				
1111	7	4	.	.				
1111	8	1	1.180	1	V	SURB		
1111	9	1	1.089	2	H			
1111	10	1	1.124	2	V	SURB		
1111	11	1	1.104	2	H	SURB		
1111	12	1	1.135	1	V	SURB		
1127	1	1	1.148	2	H	SURB		
1127	2	1	1.123	1	V			
1127	3	1	1.072	1	H	SURB		
1127	4	1	1.139	1	V	SURB		
1127	5	1	1.071	2	H	SURB		
1127	6	2	.	.				
1127	7	1	0.977	2	H			
1127	8	1	1.089	1	V	SURB		
1127	9	1	1.159	2	H	SURB		
1127	10	1	0.924	1	V	SURB		
1127	11	1	1.057	2	H			
1127	12	1	0.682	2	V	SURB		
1127	13	2	.	.				
1131	1	1	1.385	1	V			
1131	2	1	1.344	1	H			
1131	3	1	1.098	2	V			
1131	4	1	1.333	1	H			
1131	5	1	1.369	1	V			
1131	6	1	1.371	1	H			
1131	7	1	1.383	2	V	SURB		
1131	8	1	1.334	1	H			
1131	9	1	1.385	1	V			
1131	10	1	1.322	2	H			
1131	11	1	1.374	1	V			
1131	12	1	1.263	2	H			
1138	1	1	1.284	1	V			
1138	2	1	1.214	2	H			
1138	3	1	1.118	2	V	SURB		
1138	4	1	1.246	1	H			
1138	5	1	1.233	1	V	SURB		

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

7000 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1138	6	1	1.159	1	H			
1138	7	1	1.094	2	V	SURB		
1138	8	1	1.201	1	H			
1138	9	1	1.110	2	V	SURB		
1138	10	1	1.117	1	H			
1138	11	2	.	.				
1138	12	1	1.061	2	V			
1151	1	1	1.485	1	H	SURB	ROSK	
1151	2	1	1.369	1	V	SURB		
1151	3	1	1.452	1	H	SURB		
1151	4	2	.	.				
1151	5	1	1.298	1	V			
1151	6	1	1.354	2	H	SURB		
1151	7	1	1.350	1	V	SURB		
1151	8	2	.	.				
1151	9	1	1.404	1	H			
1151	10	1	1.538	1	V			
1153	1	4	.	.				
1153	2	1	1.015	2	H	SURB		
1153	3	1	1.013	2	V			
1153	4	1	1.040	1	H	SURB		
1153	5	1	1.068	1	V			
1153	6	1	1.011	1	H			
1153	7	1	1.124	1	V	SURB		
1153	8	1	1.036	2	H	SURB		
1153	9	1	0.939	1	V	SURB		
1153	10	1	1.048	2	H			
1153	11	1	1.004	2	V			
1153	12	1	1.058	1	H			
1158	1	2	.	.				
1158	2	1	1.149	1	H	SURB		
1158	3	1	1.208	1	V			
1158	4	1	1.108	1	H			
1158	5	1	0.973	2	V			
1158	6	1	1.064	2	H	SURB		
1158	7	1	1.154	1	V			
1158	8	1	1.050	2	H			
1158	9	1	1.100	1	V			
1158	10	1	1.150	2	H			
1158	11	1	1.198	2	V			
1158	12	1	1.183	1	H	SURB		
1164	1	1	1.088	1	V			
1164	2	1	1.094	2	H			
1164	3	1	1.037	1	V			
1164	4	1	0.984	2	H	SURB		
1164	5	1	1.092	2	V	SURB		
1164	6	1	1.045	1	H			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1104	7	1	1.068	1	V			
1104	8	1	1.022	2	H			
1104	9	1	0.967	2	V	SURB		
1104	10	1	1.109	1	H	SURB		
1104	11	1	1.134	1	V	SURB		
1108	1	1	1.242	1	V			
1108	2	1	1.148	2	H			
1108	3	1	0.797	1	V			
1108	4	1	1.301	1	H			
1108	5	1	1.011	1	V			
1108	6	1	1.249	2	H			
1108	7	1	1.145	2	V			
1108	8	1	1.262	2	H			
1108	9	1	1.229	2	V			
1108	10	1	1.226	2	H			
1108	11	1	1.173	1	V	SURB		
1108	12	1	1.351	1	H			
1108	13	1	1.173	1	V			
1205	1	1	1.249	1	H	SURB		
1205	2	1	1.378	1	V			
1205	3	1	5.508	2	H			
1205	4	1	1.252	2	V			
1205	5	1	1.191	2	H			
1205	6	1	1.245	1	V	SURB		
1205	7	1	1.339	1	H			
1205	8	1	1.227	2	V	SURB		
1205	9	1	1.234	1	H			
1205	10	2	.	.	.			
1225	1	1	1.194	1	H			
1225	2	1	1.054	1	V	SURB		
1225	3	1	0.953	1	H			
1225	4	1	0.944	2	V			
1225	5	1	1.113	1	H			
1225	6	2	.	.	.			
1225	7	1	0.885	1	V			
1225	8	1	0.989	1	H	SURB		
1225	9	1	0.938	2	V	SURB		
1225	10	1	1.185	1	H	SURB		
1225	11	1	1.207	1	V			
1225	12	1	1.279	1	H			
1225	13	1	1.305	1	V			
1225	14	1	1.250	1	H			
1227	1	1	1.052	1	V	SURB		
1227	2	1	1.170	2	H	SURB		
1227	3	1	0.978	1	V			
1227	4	1	1.248	1	H	SURB		
1227	5	1	1.195	2	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3
1227	6	1	0.795	2	H			
1227	7	1	0.529	2	V	SURB		
1227	8	2	.	.				
1227	9	4	.	.				
1227	10	4	.	.				
1227	11	1	1.295	1	H	SURB		
1292	1	1	1.455	2	H			
1292	2	1	1.472	1	V			
1292	3	1	1.416	2	H			
1292	4	1	1.318	2	V			
1292	5	1	1.336	1	H			
1292	6	1	1.276	1	V	SURB		
1292	7	1	1.386	1	H			
1292	8	1	1.351	1	V	SURB		
1292	9	1	1.304	1	H			
1292	10	1	1.253	1	V	SURB		
1293	1	1	1.222	1	V			
1293	2	4	.	.				
1293	3	1	1.191	2	H	SURB		
1293	4	1	1.134	1	V			
1293	5	1	1.238	2	H			
1293	6	1	0.794	2	V	SURB		
1293	7	1	1.154	2	H			
1293	8	1	1.271	1	V			
1293	9	1	1.281	1	H	SURB		
1293	10	1	0.970	1	V	SURB		
1293	11	1	1.184	1	H	SURB		
1293	12	1	1.125	2	V	SURB		
1293	13	1	1.326	1	H	SURB		
1301	1	1	1.082	2	H			
1301	2	1	1.150	1	V			
1301	3	1	1.114	2	H	SURB		
1301	4	1	1.105	1	V	SURB		
1301	5	4	.	.				
1301	6	1	1.078	2	H			
1301	7	2	.	.				
1301	8	1	1.040	2	V			
1301	9	1	1.118	1	H			
1301	10	1	1.140	2	V			
1301	11	1	1.177	1	H			
1301	12	1	1.071	1	V			

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 32 in this Appendix) for Identification of abnormalities [ABNn]

Isoprene Mouse Teratology Study: Raw Fetal Data

Code Sheet Identification for Fetal Abnormalities

SURB	Supernumerary Rib
DIUR	Dilated Ureter
RORB	Reduced Ossification Rib
MAST	Misaligned Sternebrae
ROSK	Reduced Ossification Skull
CLPA	Cleft Palate
RPCA	Renal Pelvic Cavitation

ISOPRENE MOUSE TERATOLOGY: CALENDAR OF EVENTS

Exposure levels; treatments 1-4	0, 280, 1400, 7000 ppm
Ordered mice	2/16/88
Received mice (ARS# 880044)	3/16/88
Health screen	4/4/88
Eartagged and weighed females	4/4/88
Virgins placed into individual caging	4/6/88
Virgins weighed and randomized	4/11/88
Released from quarantine	4/11/88
Mated 0dg (# positive)	(A) 4/7/88 (43)
weighed, randomized and individually caged	(B) 4/8/88 (24)
	(C) 4/9/88 (80; 40 on study)
	(D) 4/10/88 (47; 25 on study)
Moved to exposure room	4/11/88
Exposure (6 hours/day; 6-17dg)	(A) 4/13 to 4/24/88
	(B) 4/14 to 4/25/88
	(C) 4/15 to 4/26/88
	(D) 4/16 to 4/27/88
Weighed (6dg) start exposure	(A-D) 4/13 to 4/16/88
Weighed (9dg)	(A-D) 4/16 to 4/19/88
Weighed (12dg)	(A-D) 4/19 to 4/22/88
Weighed (15dg)	(A-D) 4/22 to 4/25/88
Sacrificed (18dg)	(A) 4/25/88
	(B) 4/26/88
	(C) 4/27/88 terminal serology
	(D) 4/28/88
Virgins - exposed 12 days	4/14 to 4/25/88
Weighed, exposure day 1	4/14/88
Weighed, exposure day 5	4/18/88
Weighed, exposure day 10	4/23/88
Sacrificed, one day post-exposure	4/26/88
Fetal specimen exams completed	6/3/88

ISOPRENE MOUSE TERATOLOGY STUDY DISPOSITION

Exposure Group	Treatment	Virgins	Plug-Positive Teratology Mice			
			On Study	Removed From Study	Sacrifice	Litters Examined
Control (0 ppm)	1	10	33	2(a,b)	32	28
280 ppm	2	10	33	1(a)	32	29
1400 ppm	3	10	33	0	33	28
7000 ppm	4	10	33	1(a)	32	27

(a) One dam removed from study, premature delivery.

(b) One dam removed from study, ≤ 2 implants.

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

(RAT DATA)

Isoprene Rat Teratology Study: Body Weights (g) for Sperm-positive Females

----- 0 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	8 dg Wt (g)	10 dg Wt (g)	14 dg Wt (g)	17 dg Wt (g)	20 dg Wt (g)	Uter Wt (g)	LIVER	KIDNEY	Pregnant
1403	213.4	219.2	234.1	240.8	259.8	277.1	303.48	51.26	12.24	1.89	1
1411	257.9	280.5	307.5	321.7	346.6	372.4	414.05	74.58	13.72	2.18	1
1420	229.1	236.9	251.2	266.7	292.9	308.3	337.16	61.36	13.79	1.58	1
1423	255.2	262.4	274.0	281.5	297.1	305.8	335.18	57.26	12.46	1.72	1
1429	246.1	261.5	292.9	312.8	326.1	348.9	397.33	81.99	16.05	1.97	1
1430	238.0	243.2	258.5	269.9	288.0	308.7	341.12	58.88	13.92	2.00	1
1433	242.8	258.8	289.7	302.1	327.8	349.2	394.36	79.08	17.01	2.01	1
1444	209.6	222.5	236.1	252.0	269.4	301.9	342.90	81.81	14.96	1.86	1
1448	220.0	241.7	263.9	284.9	297.3	330.8	368.99	74.26	15.08	1.80	1
1448	236.4	248.7	260.9	270.5	238.0	225.2	212.22	0.32	7.51	1.73	0
1457	229.1	244.6	262.4	269.2	281.9	248.8	239.93	0.40	8.83	2.02	0
1459	261.7	279.7	308.4	324.8	350.7	365.0	381.45	40.37	15.87	2.24	1
1464	246.8	261.9	270.7	292.5	302.6	330.3	357.37	80.42	15.21	1.86	1
1473	231.1	242.8	267.6	272.8	293.0	305.3	333.82	65.84	14.10	1.93	1
1479	224.0	232.1	255.3	267.3	283.5	301.4	330.58	66.70	13.74	1.88	1
1483	197.7	212.1	235.8	196.3	233.9	269.8	322.17	79.40	14.49	1.95	1
1490	235.8	261.0	273.7	294.7	305.7	337.3	355.90	59.40	14.97	2.10	1
1505	231.1	245.8	269.3	271.0	293.0	309.6	340.63	63.84	14.24	1.78	1
1508	237.6	249.2	269.7	272.8	296.4	314.7	347.98	68.04	14.19	1.84	1
1512	211.1	226.0	253.2	265.7	287.8	307.4	334.30	59.23	13.17	1.71	1
1514	246.9	251.3	267.4	288.8	309.6	334.6	381.96	86.38	15.06	2.01	1
1517	215.4	223.9	247.5	253.8	277.3	300.3	323.87	62.14	13.23	1.64	1
1532	283.8	299.4	324.0	342.5	364.2	392.2	429.84	81.98	16.49	2.12	1
1542	256.1	273.1	290.5	311.0	339.2	366.8	411.42	88.50	16.78	2.16	1
1543	226.0	241.6	274.7	294.9	312.0	344.7	369.73	81.15	13.52	1.91	1
1554	236.0	246.6	271.6	286.7	304.2	333.8	367.00	70.52	15.83	1.91	1
1571	253.3	271.1	298.4	312.2	330.6	366.9	394.27	77.38	15.70	1.98	1
1636	230.0	236.2	258.9	270.3	265.9	284.8	251.85	0.38	9.98	1.97	0
1647	189.9	204.8	238.0	253.1	268.1	294.2	324.99	68.47	13.15	1.78	1

C.43

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Rat Teratology Study: Body Weights (g) for Sperm-positive Females

----- 280 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	8 dg Wt (g)	10 dg Wt (g)	14 dg Wt (g)	17 dg Wt (g)	20 dg Wt (g)	Uter Wt (g)	LIVER	KIDNEY	Pregnant
1401	221.9	225.6	258.3	288.4	294.2	309.4	338.19	83.90	13.84	1.80	1
1414	265.8	282.1	295.1	307.4	332.7	358.8	382.77	79.62	13.82	2.01	1
1427	248.9	258.8	275.3	289.5	310.6	333.7	377.00	74.91	15.35	2.03	1
1440	230.7	247.6	248.0	258.1	258.7	259.2	261.71	0.58	10.61	2.08	0
1445	230.2	254.8	271.1	285.4	308.4	328.0	359.52	81.03	14.80	1.58	1
1452	221.3	224.3	253.8	288.3	283.7	307.1	342.72	69.29	13.58	1.94	1
1463	240.9	249.4	278.9	300.2	317.0	344.2	388.18	79.04	18.06	1.91	1
1489	230.8	241.8	285.1	277.0	294.1	318.4	383.39	72.33	14.88	2.02	1
1475	252.0	282.8	278.7	293.5	319.4	337.0	368.35	71.53	14.31	2.08	1
1477	230.8	241.8	283.8	282.4	288.1	287.9	279.35	0.44	13.77	2.09	0
1485	215.8	229.2	243.2	253.3	283.8	254.1	248.30	0.82	9.59	1.77	0
1488	240.2	247.4	277.7	291.1	310.2	337.8	384.15	88.27	13.92	1.90	1
1489	248.5	281.8	277.0	293.4	318.7	338.8	383.79	59.18	15.54	2.03	1
1495	231.9	244.9	257.7	278.7	300.9	324.8	359.45	81.75	13.84	1.88	1
1503	218.1	232.6	237.2	254.5	284.8	280.0	304.91	83.31	13.40	1.70	1
1504	194.0	202.0	221.5	232.8	252.3	287.2	289.43	83.71	9.08	1.54	1
1524	238.9	252.7	280.7	298.7	328.1	351.7	377.82	81.06	15.00	1.93	1
1528	222.9	228.1	247.7	281.3	285.8	300.1	323.74	61.10	12.92	1.80	1
1540	219.1	235.1	252.2	275.7	291.5	313.1	333.22	88.35	13.94	1.84	1
1546	230.9	244.4	258.1	275.5	292.4	321.3	359.48	81.59	14.70	2.00	1
1560	227.0	243.7	272.7	293.9	319.5	347.3	387.21	90.54	18.29	2.23	1
1570	221.9	234.8	253.8	284.5	283.8	302.4	327.18	73.82	12.15	1.84	1
1575	250.8	279.2	293.3	319.8	342.1	387.9	410.92	72.85	19.35	2.49	1
1588	227.8	221.7	249.1	254.0	285.2	288.1	426.73	80.95	17.83	1.98	1
1604	213.7	218.7	227.8	239.7	258.3	279.8	314.54	81.57	14.14	1.70	1
1629	289.6	292.9	318.1	330.4	348.2	383.1	317.75	81.90	12.31	1.73	1
1630	232.4	248.0	281.1	283.3	297.5	315.9	341.27	81.29	18.70	2.27	1
1631	257.1	273.3	303.8	317.6	329.4	354.8	385.97	83.00	16.08	2.08	1

C.44

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Rat Teratology Study: Body Weights (g) for Sperm-positive Females

----- 1400 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	6 dg Wt (g)	10 dg Wt (g)	14 dg Wt (g)	17 dg Wt (g)	20 dg Wt (g)	Uter Wt (g)	LIVER	KIDNEY	Pregnant
1405	270.1	276.1	304.3	320.1	336.1	364.5	399.37	72.67	15.58	2.18	1
1409	237.0	254.0	275.7	292.1	311.7	338.1	376.61	56.16	16.29	2.12	1
1410	235.2	252.4	277.3	298.2	314.9	347.8	380.93	83.01	14.19	1.96	1
1412	239.3	258.4	293.9	310.9	333.4	366.3	400.24	68.60	17.03	2.20	1
1428	232.9	238.5	255.8	263.7	267.8	265.1	258.47	0.31	10.75	2.13	0
1436	227.2	235.3	251.4	265.9	259.5	270.6	271.20	0.44	10.31	2.02	0
1438	249.9	260.3	291.3	295.2	320.8	338.0	366.02	76.28	12.34	1.81	1
1441	208.6	212.6	230.6	242.0	249.6	265.9	286.09	47.51	11.40	1.69	1
1443	249.8	260.8	282.6	294.8	316.8	344.9	373.32	62.83	14.36	1.82	1
1453	286.0	315.2	332.9	358.5	373.2	408.4	462.09	105.86	17.54	2.30	1
1461	239.2	246.9	267.5	274.4	298.1	320.5	348.62	68.77	13.64	2.17	1
1484	230.8	244.2	269.5	281.0	300.8	319.0	344.71	60.40	14.75	2.23	1
1487	217.2	228.7	249.4	262.8	280.1	309.7	338.69	78.21	12.64	1.86	1
1491	220.6	229.4	254.5	268.4	292.7	324.1	356.72	75.07	15.24	1.92	1
1494	225.6	238.0	271.4	284.3	310.7	345.7	381.23	75.55	16.75	2.01	1
1496	250.5	270.3	298.8	314.9	334.6	368.4	403.73	75.41	14.91	1.89	1
1525	236.0	247.3	271.1	294.0	314.9	338.2	364.92	63.74	16.24	1.95	1
1526	218.8	223.0	247.5	260.4	280.8	302.1	331.03	60.89	14.56	1.96	1
1530	225.4	233.2	255.8	265.0	282.1	283.7	252.56	0.43	9.12	1.81	0
1531	230.8	241.1	253.1	281.0	281.4	307.7	340.11	71.59	12.90	2.03	1
1541	251.2	267.0	289.4	296.2	323.0	340.8	378.27	77.61	14.64	1.92	1
1549	258.7	278.3	311.4	337.2	362.1	389.7	429.53	86.23	18.74	2.40	1
1552	212.4	219.9	248.4	258.9	278.2	303.2	338.40	78.65	15.80	1.76	1
1558	212.3	229.3	242.8	258.9	277.5	301.9	333.32	66.56	12.94	1.56	1
1563	241.3	258.7	301.5	309.1	329.5	358.5	404.23	80.61	17.37	2.33	1
1564	211.4	224.0	241.6	252.8	268.1	294.1	323.29	62.29	12.34	1.90	1
1573	231.6	244.4	266.3	292.6	316.6	356.6	392.70	79.27	14.55	2.11	1
1579	245.8	249.5	265.3	272.3	266.8	259.8	258.50	0.67	9.99	1.97	0
1650	214.9	227.4	246.2	264.6	284.7	302.9	334.35	66.72	14.56	1.84	1

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Rat Teratology Study: Body Weights (g) for Sperm-positive Females

----- 7000 ppm Isoprene -----											
MATNO	Pre-study Wt (g)	0 dg Wt (g)	8 dg Wt (g)	10 dg Wt (g)	14 dg Wt (g)	17 dg Wt (g)	20 dg Wt (g)	Uter Wt (g)	LIVER	KIDNEY	Pregnant
1400	241.6	245.1	288.0	285.9	280.2	280.7	277.73	0.38	11.71	2.27	0
1415	199.2	208.5	245.1	254.0	279.5	300.8	320.82	63.88	11.51	2.00	1
1417	228.8	240.8	270.8	278.1	297.5	309.9	319.25	20.34	15.28	2.13	1
1418	240.0	252.6	260.6	269.0	293.0	321.9	357.87	69.63	16.33	2.14	1
1421	246.3	260.9	280.0	290.9	308.9	339.8	375.18	66.17	18.48	2.31	1
1425	240.1	259.8	289.1	290.9	310.6	330.0	372.41	70.24	15.91	2.03	1
1434	245.3	282.3	289.8	298.4	316.6	340.2	378.08	80.20	15.69	2.26	1
1454	209.8	219.4	245.8	252.9	270.0	302.0	337.94	68.34	13.53	1.78	1
1456	256.6	271.8	292.0	293.4	315.9	343.7	380.00	71.00	14.51	1.84	1
1465	242.7	247.1	270.0	276.3	298.9	323.4	355.63	54.30	17.19	2.29	1
1472	242.5	257.0	264.9	260.9	285.3	303.2	334.74	60.54	13.61	1.80	1
1497	226.0	237.1	254.9	258.7	278.2	302.1	332.42	65.12	13.25	1.68	1
1499	226.4	242.5	271.8	281.0	295.8	321.3	343.82	63.41	16.06	2.18	1
1500	249.7	266.1	283.4	283.7	298.0	327.1	367.49	84.87	14.94	1.97	1
1510	248.3	262.2	280.0	287.5	302.7	327.2	359.61	70.66	15.18	1.90	1
1511	208.7	222.6	233.6	241.6	259.9	279.5	310.77	54.33	14.07	1.71	1
1513	266.9	282.0	297.7	283.0	309.9	339.4	365.76	65.36	15.78	1.94	1
1529	232.4	240.0	280.3	272.6	293.4	322.5	353.29	63.30	14.13	1.84	1
1536	236.8	245.5	266.0	272.9	282.8	278.2	283.25	0.31	9.37	2.08	0
1548	271.6	283.8	308.8	314.2	337.4	359.3	391.96	72.95	15.59	2.22	1
1555	231.3	248.2	260.0	290.8	311.9	340.2	370.91	73.19	16.07	1.95	1
1557	221.3	230.5	239.7	247.4	269.8	291.7	305.98	58.70	12.04	1.70	1
1558	230.3	245.8	282.7	290.0	316.0	341.0	367.45	70.86	14.50	2.13	1
1561	218.4	228.2	247.6	253.7	241.5	247.5	233.53	0.47	8.97	1.89	0
1566	216.1	228.1	243.4	251.2	268.7	298.3	315.80	58.86	12.69	1.77	1
1597	239.4	250.4	266.7	281.0	300.1	330.7	352.14	73.56	14.91	1.82	1
1599	219.2	218.8	235.3	245.0	246.1	241.8	240.02	0.35	10.59	1.88	0
1602	269.1	275.0	280.1	287.6	312.6	342.0	380.87	71.58	17.98	2.30	1

C.46

Pregnant: 1=Pregnant 0=Non-Pregnant

Isoprene Rat Teratology Study: Body Weights (g) for Virgin Females

0 ppm Isoprene

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1623	229.8	237.7	242.8	250.1	259.18
1582	263.4	278.7	277.8	282.0	278.49
1591	210.0	220.0	221.4	224.1	238.08
1615	237.9	246.4	240.8	248.0	247.98
1583	240.5	253.0	250.0	263.0	281.09
1610	286.9	304.8	299.2	309.0	311.38
1608	224.0	234.2	235.8	244.4	245.50
1648	217.4	230.3	239.3	244.1	240.80
1585	247.8	258.8	253.0	265.1	272.29
1619	281.3	259.4	269.2	275.4	290.42

Isoprene Rat Teratology Study: Body Weights (g) for Virgin Females

----- 280 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1612	212.7	221.1	216.4	229.2	236.05
1620	259.2	277.0	272.2	284.6	282.43
1607	229.8	238.4	237.0	251.7	252.67
1595	230.1	247.8	242.6	249.8	258.77
1625	233.1	250.2	256.1	271.6	285.40
1617	227.3	235.3	226.0	237.4	249.38
1621	260.1	281.6	277.0	281.2	300.05
1613	214.6	233.0	226.3	240.6	251.28
1594	250.6	256.9	259.4	281.6	286.68
1600	280.7	290.0	297.6	311.9	312.30

Isoprene Rat Teratology Study: Body Weights (g) for Virgin Females

----- 1400 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1686	222.2	229.3	220.8	231.3	249.74
1652	221.5	225.3	228.8	244.5	247.36
1608	246.0	267.2	248.1	260.6	277.23
1603	235.2	234.6	249.4	253.8	255.22
1654	277.2	284.2	283.3	294.3	297.04
1637	225.2	248.3	248.2	260.8	263.93
1639	251.3	254.7	253.5	256.3	269.93
1598	237.3	241.6	243.2	251.4	247.88
1590	227.3	244.1	242.0	253.1	259.35
1632	266.9	283.4	290.4	308.2	322.91

Isoprene Rat Teratology Study: Body Weights (g) for Virgin Females

----- 7000 ppm Isoprene -----

MATNO	Pre-study Wt	Exposure Day1	Exposure Day5	Exposure Day10	Sacrifice Wt
1640	233.1	246.4	242.1	252.4	258.51
1577	216.1	226.4	230.0	232.4	227.24
1642	211.7	226.0	224.4	228.9	234.94
1596	231.6	237.1	233.9	237.5	250.54
1611	245.2	253.3	250.2	262.3	257.34
1655	258.5	279.4	280.8	282.1	289.02
1591	277.1	298.5	304.8	310.4	313.00
1628	241.6	260.9	260.4	261.5	273.79
1605	232.8	251.7	254.6	258.7	258.96
1626	228.1	242.1	226.3	233.1	232.36

Isoprene Rat Teratology Study: Raw Fetal Data

----- 0 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1403	1	1	2.983	1	H							
1403	2	1	3.208	1	V							
1403	3	1	2.871	2	H							
1403	4	1	2.853	1	V							
1403	5	1	2.981	1	H							
1403	6	2	.	.	.							
1403	7	1	3.033	2	V							
1403	8	1	2.935	2	H							
1403	9	1	3.020	2	V							
1403	10	1	2.914	1	H							
1403	11	1	3.012	1	V							
1403	12	1	2.754	2	H							
1411	1	1	3.144	1	H							
1411	2	1	3.192	1	V							
1411	3	1	2.944	2	H				ROPH			
1411	4	1	3.310	1	V							
1411	5	1	3.002	2	H				ROST			
1411	6	1	3.047	2	V				ROST			
1411	7	1	2.891	1	H							
1411	8	1	3.146	1	V							
1411	9	1	3.187	1	H							
1411	10	1	2.988	2	V				ROST			
1411	11	1	3.306	1	H							
1411	12	1	3.208	2	V							
1411	13	1	3.398	1	H							
1411	14	1	3.497	1	V							
1411	15	1	3.425	1	H							
1420	1	1	3.043	2	V							
1420	2	1	3.654	1	H							
1420	3	1	3.296	2	V							
1420	4	1	3.636	2	H							
1420	5	1	3.442	1	V				ROVE			
1420	6	1	3.437	2	H							
1420	7	1	3.399	1	V							
1420	8	1	3.583	1	H							
1420	9	1	3.677	1	V							
1420	10	1	3.676	1	H							
1420	11	1	3.227	1	V							
1420	12	1	3.389	1	H							
1423	1	1	2.829	2	H							
1423	2	1	3.283	2	V							
1423	3	1	3.287	2	H							
1423	4	1	3.393	2	V							
1423	5	1	2.990	1	H							
1423	6	1	3.278	1	V							
1423	7	1	3.042	1	H							
1423	8	1	3.273	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1423	9	1	3.183	1	H							
1423	10	1	3.143	1	V							
1423	11	4	.	.	.							
1423	12	1	3.114	2	H							
1423	13	1	3.459	2	V							
1429	1	1	3.043	2	V	ROST	ROVE					
1429	2	1	3.145	1	H	ROST	ROVE					
1429	3	1	3.468	1	V	ROST						
1429	4	1	3.418	1	H							
1429	5	1	3.308	1	V							
1429	6	1	3.685	1	H							
1429	7	1	3.409	1	V							
1429	8	1	3.315	1	H	ROST						
1429	9	1	3.950	1	V							
1429	10	1	3.107	1	H	ROST						
1429	11	1	3.918	1	V							
1429	12	1	3.008	2	H	ROST						
1429	13	2	.	.	.							
1429	14	1	3.355	1	V							
1429	15	1	3.753	1	H							
1429	16	1	3.529	2	V	ROVE						
1429	17	1	3.902	1	H							
1430	1	4	.	.	.							
1430	2	1	2.977	1	H	ROST						
1430	3	1	3.038	1	V							
1430	4	1	2.991	1	H							
1430	5	1	2.903	1	V							
1430	6	1	2.894	2	H							
1430	7	1	2.603	1	V	ROST	ROPB	ROPH				
1430	8	1	2.959	2	H							
1430	9	1	3.243	1	V							
1430	10	1	3.067	1	H							
1430	11	1	2.780	2	V							
1430	12	1	2.901	2	H							
1430	13	1	2.528	1	V	ROST	ROPH					
1430	14	1	3.033	1	H							
1433	1	1	3.203	1	V							
1433	2	1	3.438	1	H							
1433	3	1	3.029	2	V							
1433	4	1	3.066	2	H							
1433	5	1	3.127	2	V							
1433	6	1	3.209	2	H							
1433	7	1	3.176	2	V							
1433	8	1	3.233	1	H							
1433	9	1	2.901	2	V							
1433	10	1	3.288	2	H							
1433	11	1	3.242	2	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1433	12	1	3.149	1	H							
1433	13	1	3.234	2	V							
1433	14	1	2.908	2	H							
1433	15	1	3.240	1	V							
1433	16	1	3.179	2	H							
1444	1	1	3.501	2	V							
1444	2	1	3.415	2	H							
1444	3	1	3.276	2	V							
1444	4	1	4.045	1	H							
1444	5	1	3.548	1	V							
1444	6	1	3.538	2	H							
1444	7	1	3.471	1	V							
1444	8	1	3.778	1	H							
1444	9	1	3.199	2	V							
1444	10	1	3.494	2	H							
1444	11	1	3.550	2	V							
1444	12	1	3.373	2	H							
1444	13	1	3.305	2	V							
1444	14	1	3.597	2	H							
1444	15	1	3.879	2	V							
1444	16	1	3.539	1	H							
1446	1	1	3.294	2	V							
1446	2	1	3.405	1	H							
1446	3	1	3.725	1	V							
1446	4	1	3.440	2	H							
1446	5	1	3.558	2	V							
1446	6	1	3.308	1	H							
1446	7	1	3.753	1	V							
1446	8	1	3.841	2	H							
1446	9	1	3.702	1	V							
1446	10	1	3.874	2	H							
1446	11	1	3.287	2	V							
1446	12	1	3.772	2	H							
1446	13	1	3.402	1	V							
1446	14	1	3.460	1	H							
1459	1	1	3.335	1	H							
1459	2	1	3.478	1	V							
1459	3	1	3.594	2	H							
1459	4	1	3.926	1	V							
1459	5	1	3.777	2	H							
1459	6	1	3.838	1	V							
1459	7	1	3.778	2	H							
1464	1	1	3.277	1	V							
1464	2	1	3.502	2	H							
1464	3	1	3.241	1	V							
1464	4	1	3.498	2	H							
1464	5	1	3.639	1	V							

ROST

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 0 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1484	8	1	3.470	2	H							
1484	7	1	3.211	1	V							
1484	8	1	3.749	1	H							
1484	9	1	3.569	2	V							
1484	10	1	3.258	2	H							
1484	11	1	3.429	2	V							
1484	12	1	3.805	1	H							
1484	13	1	3.622	2	V							
1484	14	1	3.533	2	H							
1484	15	1	3.250	2	V							
1484	16	1	3.309	2	H							
1473	1	1	3.336	2	V							
1473	2	1	3.350	2	H							
1473	3	1	3.301	1	V							
1473	4	1	3.191	1	H							
1473	5	1	3.388	1	V							
1473	6	1	3.374	1	H							
1473	7	1	3.523	1	V							
1473	8	1	3.092	2	H							
1473	9	1	3.194	2	V							
1473	10	1	3.208	2	H							
1473	11	1	3.158	2	V							
1473	12	1	3.473	1	H							
1473	13	1	3.265	1	V							
1479	1	1	2.875	2	H	ROPH						
1479	2	1	2.893	2	V							
1479	3	1	3.057	2	H							
1479	4	1	3.346	2	V							
1479	5	1	2.987	1	H	ROST						
1479	6	1	2.893	2	V	ROSK						
1479	7	1	2.833	1	H	ROST	ROPB					
1479	8	1	3.090	2	V	ROSK						
1479	9	1	2.788	2	H							
1479	10	1	2.957	2	V	ROSK	ROST					
1479	11	1	2.998	2	H	ROST	ROPB					
1479	12	2	.	.	.							
1479	13	1	3.089	1	V	ROSK	ROST					
1479	14	1	3.085	1	H	ROST						
1479	15	1	3.193	2	V	ROSK	ROST					
1483	1	1	2.864	2	H	ROST						
1483	2	1	3.083	1	V	ROST						
1483	3	1	3.004	1	HV	UHER	ROST					
1483	4	1	3.015	2	V							
1483	5	1	3.051	2	H							
1483	6	1	3.319	1	V							
1483	7	1	3.018	1	H							
1483	8	1	3.058	2	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 0 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1483	9	1	3.432	1	H							
1483	10	1	3.230	1	V	ROPB						
1483	11	1	3.142	1	H							
1483	12	1	2.990	2	V							
1483	13	1	3.561	1	H							
1483	14	1	3.286	2	V							
1483	15	1	3.830	1	H							
1483	16	1	3.171	2	V							
1490	1	1	8.837	2	V	DIUR						
1490	2	2	.	.	.							
1490	3	1	3.419	2	H							
1490	4	1	2.929	1	V							
1490	5	1	3.288	2	H							
1490	6	1	3.568	1	V	DIUR						
1490	7	1	2.700	2	H							
1490	8	1	3.184	2	V							
1490	9	1	3.624	1	H							
1490	10	1	3.342	1	V							
1490	11	1	3.361	1	H							
1490	12	1	3.683	1	V	ROST						
1505	1	1	2.223	1	HV	EXCE	RACH	ROST	MAST	ROVE	ROPB	ADPT
1505	2	1	3.223	1	V							
1505	3	1	8.020	2	H							
1505	4	1	3.059	2	V							
1505	5	1	3.022	2	H	ROVE						
1505	6	1	3.142	2	V							
1505	7	1	2.700	1	H							
1505	8	1	3.172	2	V							
1505	9	1	2.869	2	H	ROST	ROPB					
1505	10	1	3.238	1	V							
1505	11	1	3.098	1	H							
1505	12	1	3.479	1	V							
1505	13	1	3.023	1	H							
1508	1	1	3.454	2	V							
1508	2	1	3.392	1	H							
1508	3	1	3.554	2	V							
1508	4	1	3.295	2	H							
1508	5	1	3.929	1	V							
1508	6	1	3.708	1	H							
1508	7	1	3.757	2	V							
1508	8	1	3.432	2	H							
1508	9	1	3.588	2	V	DIUR						
1508	10	1	3.607	2	H							
1508	11	1	3.489	1	V							
1508	12	1	3.589	1	H							
1508	13	1	3.334	2	V							
1512	1	4	.	.	.							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1512	2	1	3.180	2	H							
1512	3	1	3.571	2	V							
1512	4	1	3.495	2	H							
1512	5	1	3.781	1	V							
1512	6	1	3.696	1	H							
1512	7	2	.	.	.							
1512	8	1	3.640	1	V							
1512	9	1	3.889	1	H							
1512	10	1	3.369	1	V							
1512	11	1	3.689	1	H							
1512	12	1	3.953	1	V							
1512	13	1	3.765	1	H							
1514	1	1	3.657	1	V							
1514	2	1	3.496	1	H							
1514	3	1	3.469	1	V							
1514	4	1	3.372	1	H							
1514	5	1	3.709	1	V							
1514	6	1	3.878	1	H							
1514	7	1	3.356	2	V							
1514	8	1	2.924	2	H							
1514	9	1	3.522	2	V							
1514	10	1	3.328	1	H							
1514	11	1	3.768	1	V							
1514	12	1	3.445	1	H							
1514	13	1	3.618	1	V							
1514	14	1	3.544	2	H							
1514	15	1	3.661	1	V							
1514	16	1	3.492	2	H							
1517	1	1	3.600	1	H							
1517	2	1	3.412	1	V							
1517	3	1	3.230	1	H							
1517	4	1	4.129	1	V							
1517	5	1	3.817	1	H							
1517	6	1	3.879	2	V							
1517	7	1	3.681	1	H							
1517	8	4	.	.	.							
1517	9	1	3.649	1	V							
1517	10	1	3.788	1	H							
1517	11	1	3.657	2	V							
1517	12	1	3.811	1	H							
1532	1	1	3.348	2	H							
1532	2	1	3.308	1	V							
1532	3	1	3.240	2	H							
1532	4	1	3.102	1	V							
1532	5	1	3.123	2	H							
1532	6	1	3.310	2	V							
1532	7	1	3.694	1	H							

ROST

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 0 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1532	8	1	3.434	2	V							
1532	9	1	3.403	1	H							
1532	10	1	3.518	1	V							
1532	11	1	3.282	1	H							
1532	12	1	3.483	1	V							
1532	13	1	3.253	2	H							
1532	14	1	2.956	1	V							
1532	15	1	3.514	1	H							
1532	16	1	3.478	2	V							
1542	1	1	2.943	1	V							
1542	2	1	2.895	2	H	ROST						
1542	3	1	2.913	2	V	ROST						
1542	4	1	2.900	2	H							
1542	5	1	3.098	1	V							
1542	6	1	2.787	1	H							
1542	7	1	3.143	2	V							
1542	8	1	3.252	1	H							
1542	9	1	3.220	1	V							
1542	10	1	3.422	1	H							
1542	11	1	3.084	2	V							
1542	12	1	3.468	1	H							
1542	13	1	3.011	1	V							
1542	14	1	2.974	2	H							
1542	15	1	3.527	1	V							
1542	16	1	3.340	1	H							
1542	17	1	3.433	1	V	DIUR						
1542	18	1	3.598	1	H							
1543	1	1	3.320	1	H							
1543	2	1	3.564	1	V							
1543	3	1	3.546	2	H							
1543	4	1	3.532	1	V							
1543	5	1	3.623	2	H							
1543	6	1	3.745	1	V	ROST						
1543	7	1	3.815	1	H							
1543	8	1	3.247	1	V							
1543	9	1	3.405	2	H							
1543	10	1	3.303	2	V							
1543	11	1	3.867	1	H							
1543	12	1	3.622	2	V							
1543	13	1	.	1	H							
1543	14	1	3.457	1	V							
1543	15	1	3.647	2	H							
1554	1	1	2.931	2	H	ROST						
1554	2	1	2.841	2	V							
1554	3	1	3.150	2	H	ROST	MAST					
1554	4	1	3.295	2	V							
1554	5	1	2.977	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

0 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1554	6	1	3.163	2	V							
1554	7	1	3.211	2	H							
1554	8	1	3.314	2	V							
1554	9	1	3.288	1	H							
1554	10	1	3.112	2	V							
1554	11	1	3.276	2	H							
1554	12	1	3.401	1	V							
1554	13	1	3.424	1	H							
1554	14	1	3.217	1	V							
1554	15	1	3.249	1	H							
1554	16	2	.	.	.							
1571	1	1	3.351	1	H							
1571	2	1	3.514	2	V							
1571	3	1	3.533	2	H							
1571	4	1	3.775	1	V							
1571	5	1	3.643	2	H							
1571	6	1	3.700	1	V	ROST						
1571	7	1	3.591	2	H	ROST						
1571	8	1	3.678	2	V							
1571	9	1	3.945	2	H							
1571	10	1	3.454	2	V							
1571	11	1	3.729	1	H							
1571	12	1	3.751	1	V							
1571	13	1	2.876	1	H							
1571	14	1	4.113	1	V							
1571	15	1	3.729	2	H							
1847	1	1	2.468	2	V							
1847	2	1	3.049	2	H							
1847	3	1	3.420	1	V							
1847	4	1	3.398	1	H							
1847	5	1	3.511	1	V							
1847	6	1	3.512	1	H							
1847	7	1	3.073	2	V	MIIN						
1847	8	1	3.148	2	H							
1847	9	1	3.217	1	V	ROST						
1847	10	1	3.108	2	H							
1847	11	1	3.208	2	V							
1847	12	1	3.098	2	H							
1847	13	1	3.195	1	V							
1847	14	1	3.186	1	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1401	1	1	2.037	2	H							
1401	2	1	3.092	1	V							
1401	3	1	3.133	2	H							
1401	4	1	3.228	1	V							
1401	5	1	3.073	2	H							
1401	6	1	3.248	2	V							
1401	7	1	3.174	2	H							
1401	8	1	3.225	2	V							
1401	9	1	3.427	1	H							
1401	10	1	3.351	2	V							
1401	11	1	3.423	2	H							
1401	12	1	3.282	1	V							
1401	13	1	3.457	2	H							
1414	1	1	3.104	1	V							
1414	2	1	3.015	2	H							
1414	3	1	3.319	1	V							
1414	4	1	3.043	2	H							
1414	5	1	3.325	1	V							
1414	6	1	3.481	1	H							
1414	7	1	2.757	1	V							
1414	8	1	3.101	1	H							
1414	9	1	3.031	1	V							
1414	10	1	3.231	2	H							
1414	11	1	3.550	1	V							
1414	12	1	3.214	2	H							
1414	13	1	3.304	1	V							
1414	14	1	3.109	1	H							
1414	15	1	3.071	2	V							
1414	16	1	2.717	2	H							
1414	17	1	3.384	1	V							
1427	1	1	3.219	2	V							
1427	2	1	3.248	2	H							
1427	3	1	3.488	1	V							
1427	4	1	3.423	1	H							
1427	5	1	3.182	2	V							
1427	6	1	3.389	2	H							
1427	7	1	2.473	2	V							
1427	8	1	3.197	2	H							
1427	9	1	2.709	2	V							
1427	10	1	3.504	1	H							
1427	11	1	3.203	2	V							
1427	12	1	2.969	1	H							
1427	13	2	.	.	.							
1427	14	1	3.093	2	V							
1427	15	1	3.444	2	H							
1427	16	1	3.568	2	V							
1445	1	1	3.339	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1445	2	1	3.502	2	V							
1445	3	1	3.338	1	H							
1445	4	1	3.243	2	V							
1445	5	1	3.287	1	H							
1445	6	1	3.439	1	V							
1445	7	1	3.412	2	H							
1445	8	1	3.459	2	V	DIUR						
1445	9	1	3.310	1	H							
1445	10	1	3.287	2	V							
1445	11	1	3.314	2	H							
1445	12	1	3.257	2	V							
1452	1	1	3.590	1	V							
1452	2	1	3.584	1	H							
1452	3	1	3.928	1	V							
1452	4	1	3.571	2	H							
1452	5	1	3.448	1	V							
1452	6	1	3.471	2	H							
1452	7	1	3.498	2	H							
1452	8	1	3.115	2	V	ROVE						
1452	9	1	3.384	1	H							
1452	10	1	3.383	2	V							
1452	11	1	3.532	2	H							
1452	12	1	3.728	1	V							
1452	13	1	3.763	1	H	DIUR						
1483	1	1	2.813	2	H							
1483	2	1	2.823	2	V							
1483	3	1	3.288	2	H							
1483	4	1	2.885	2	V							
1483	5	1	3.121	1	H	ROVE						
1483	6	1	3.488	2	V							
1483	7	1	2.555	2	H							
1483	8	1	2.147	2	V	ROSK	ROST	ROPB	ROPH			
1483	9	1	2.579	2	H							
1483	10	1	3.008	2	V							
1483	11	1	3.211	2	H							
1483	12	1	3.311	2	V							
1483	13	1	3.218	2	H							
1483	14	1	3.305	1	V							
1483	15	1	3.188	2	H							
1483	16	1	2.707	2	V							
1483	17	1	3.048	2	H							
1489	1	1	3.487	1	H							
1489	2	1	3.313	2	V							
1489	3	1	3.545	1	H							
1489	4	1	3.089	2	V							
1489	5	1	3.043	2	H							
1489	6	1	3.528	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1489	7	1	3.313	1	H							
1489	8	1	3.240	1	V							
1489	9	1	3.370	1	H							
1489	10	1	3.448	1	V							
1489	11	1	3.505	1	H							
1489	12	1	3.828	1	V							
1489	13	1	3.090	2	H							
1489	14	1	3.551	1	V							
1476	1	1	3.582	1	V	DIUR						
1476	2	1	3.470	2	H							
1476	3	1	3.384	2	V							
1476	4	1	3.892	1	H							
1476	5	1	3.413	1	V							
1476	6	1	3.452	2	H							
1476	7	2	.	.	.							
1476	8	1	3.350	2	V							
1476	9	1	3.339	1	H							
1476	10	1	3.347	1	V							
1476	11	1	3.179	2	H							
1476	12	1	3.449	1	V	DIUR						
1476	13	1	3.384	2	H							
1476	14	1	3.477	1	V							
1476	15	1	2.881	2	H							
1488	1	1	3.104	1	V							
1488	2	1	3.329	1	H							
1488	3	1	3.680	1	V							
1488	4	1	3.581	1	H							
1488	5	1	3.436	1	V	ROSK	ROST					
1488	6	1	3.184	2	H	ROPB	ROST	ROPH				
1488	7	1	3.258	1	V							
1488	8	1	3.264	2	H	ROST						
1488	9	1	3.402	2	V							
1488	10	1	3.477	1	H							
1488	11	2	.	.	.							
1488	12	1	3.785	1	V							
1488	13	1	3.348	2	H							
1488	14	2	.	.	.							
1488	15	1	3.224	2	V	ROPB						
1489	1	1	3.489	1	V							
1489	2	1	3.410	1	H							
1489	3	2	.	.	.							
1489	4	1	3.418	2	V							
1489	5	1	2.967	2	H							
1489	6	1	2.864	1	V							
1489	7	1	3.148	2	H							
1489	8	2	.	.	.							
1489	9	1	3.058	2	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1489	10	1	3.175	1	H							
1489	11	1	3.388	2	V							
1489	12	1	2.913	2	H							
1489	13	1	2.928	2	V							
1489	14	1	3.368	1	H							
1495	1	1	3.438	2	V							
1495	2	1	3.445	2	H							
1495	3	1	3.594	2	V							
1495	4	1	3.647	1	H							
1495	5	1	3.875	2	V							
1495	6	1	3.693	1	H							
1495	7	1	3.429	2	V							
1495	8	1	3.776	2	H							
1495	9	1	3.179	2	V							
1495	10	1	3.828	1	H							
1495	11	1	3.751	1	V							
1495	12	1	3.533	1	H							
1495	13	1	3.788	1	V							
1495	14	1	3.670	2	H							
1495	15	1	3.682	1	V							
1495	16	1	3.439	2	H							
1503	1	1	3.042	1	V							
1503	2	1	3.170	1	H							
1503	3	1	3.126	2	V							
1503	4	1	3.269	1	H							
1503	5	1	2.921	1	V							
1503	6	1	3.210	1	H							
1503	7	1	3.260	1	V							
1503	8	1	3.101	1	H							
1503	9	1	3.278	1	V							
1503	10	1	3.129	1	H							
1503	11	1	3.182	2	V							
1503	12	1	3.173	2	H							
1503	13	1	3.181	2	V							
1503	14	1	3.198	2	H							
1504	1	1	3.143	2	V							
1504	2	1	3.189	1	H							
1504	3	1	3.085	1	V							
1504	4	1	3.452	1	H							
1504	5	1	3.082	1	V							
1504	6	1	3.485	2	H							
1504	7	1	3.028	2	V							
1504	8	1	3.297	2	H							
1504	9	1	3.457	1	V							
1504	10	1	3.442	1	H							
1504	11	1	3.498	1	V							
1504	12	1	3.221	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1504	13	1	3.248	2	V							
1524	1	1	3.648	1	H	ROST						
1524	2	1	3.738	1	V							
1524	3	1	3.651	2	H							
1524	4	1	3.789	1	V							
1524	5	1	3.333	2	H							
1524	6	1	3.844	2	V	DIUR						
1524	7	1	3.482	2	H							
1524	8	1	3.499	2	V							
1524	9	1	3.938	1	H							
1524	10	1	3.625	1	V							
1524	11	1	4.240	1	H							
1528	1	1	2.842	2	V							
1528	2	2	.	.	.							
1528	3	1	3.359	1	H							
1528	4	1	3.304	2	V							
1528	5	1	3.134	1	H	UHER						
1528	6	1	3.679	1	V							
1528	7	1	3.322	2	H							
1528	8	1	3.274	2	V							
1528	9	1	3.222	2	H							
1528	10	2	.	.	.							
1528	11	1	3.478	2	V							
1528	12	1	3.479	2	H							
1528	13	1	3.417	1	V							
1528	14	1	3.447	1	H	ROVE						
1540	1	1	3.500	1	V							
1540	2	1	3.342	2	H							
1540	3	1	3.970	1	V							
1540	4	2	.	.	.							
1540	5	1	3.770	1	H							
1540	6	1	3.775	1	V							
1540	7	1	3.462	2	H							
1540	8	1	3.488	1	V							
1540	9	1	3.580	2	H							
1540	10	1	3.963	1	V							
1540	11	2	.	.	.							
1540	12	2	.	.	.							
1540	13	1	3.135	1	H							
1540	14	1	3.970	1	V							
1540	15	1	3.987	1	H							
1546	1	1	3.757	1	H							
1546	2	1	3.781	1	V							
1546	3	1	3.857	2	H							
1546	4	1	3.571	2	V							
1546	5	1	3.891	2	H							
1546	6	1	3.594	2	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1548	7	1	3.758	1	H							
1548	8	1	3.558	2	V							
1548	9	1	3.686	1	H							
1548	10	1	3.317	2	V							
1548	11	1	3.700	2	H							
1548	12	1	3.708	2	V	MAST	ROVE					
1548	13	1	3.671	2	H	ROVE						
1548	14	1	3.348	2	V							
1548	15	1	3.374	2	H							
1580	1	1	3.819	2	H							
1580	2	1	3.980	2	V							
1580	3	1	3.890	2	H							
1580	4	1	3.833	1	V							
1580	5	1	4.114	1	H							
1580	6	1	4.051	2	V							
1580	7	1	4.242	1	H							
1580	8	1	4.035	2	V							
1580	9	1	3.989	1	H							
1580	10	1	4.077	1	V							
1580	11	1	4.059	1	H							
1580	12	1	3.935	2	V							
1580	13	1	4.019	2	H							
1580	14	1	4.084	1	V							
1580	15	1	3.952	2	H							
1570	1	1	3.131	2	H							
1570	2	1	3.108	2	V	DIUR						
1570	3	1	3.492	1	H							
1570	4	1	3.432	2	V							
1570	5	1	3.588	1	H							
1570	6	1	3.411	2	V							
1570	7	1	3.549	1	H							
1570	8	1	3.275	1	V							
1570	9	1	3.131	2	H							
1570	10	1	3.293	1	V							
1570	11	1	3.449	2	H							
1570	12	1	3.591	2	V							
1570	13	1	3.255	2	H	ROST	ROPH					
1570	14	1	3.305	2	V							
1570	15	1	3.301	2	H							
1575	1	1	2.788	2	H							
1575	2	1	2.818	1	V	ROVE						
1575	3	1	2.941	1	H							
1575	4	1	3.048	1	V							
1575	5	1	3.101	1	H							
1575	6	1	3.857	1	V							
1575	7	1	3.392	1	H							
1575	8	1	2.832	2	V	ROST						

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1575	9	1	2.950	2	H							
1575	10	1	3.180	2	V							
1575	11	1	3.000	2	H							
1575	12	1	3.251	2	V							
1575	13	1	3.155	1	H							
1575	14	2	.	.	.							
1575	15	1	3.490	2	V							
1580	1	1	3.150	1	H							
1580	2	1	3.310	1	V							
1580	3	1	3.175	1	H							
1580	4	1	3.163	1	V							
1580	5	1	3.050	2	H							
1580	6	1	3.150	2	V							
1580	7	1	3.305	2	H							
1580	8	2	.	.	.							
1580	9	1	3.570	1	V							
1580	10	1	3.332	2	H							
1580	11	1	3.130	1	V							
1580	12	1	3.245	1	H	ROST						
1580	13	1	3.100	1	V							
1580	14	1	3.300	1	H							
1580	15	1	3.105	1	V							
1580	16	1	3.251	2	H							
1580	17	1	3.350	1	V							
1604	1	1	3.207	1	V							
1604	2	1	3.434	1	H							
1604	3	4	.	.	.							
1604	4	4	.	.	.							
1604	5	1	3.520	1	V							
1604	6	1	3.084	2	H							
1604	7	1	3.810	1	V							
1604	8	1	2.690	1	H							
1604	9	1	3.580	1	V							
1604	10	1	3.370	1	H	RURB						
1604	11	1	3.635	1	V							
1604	12	1	3.650	2	H							
1604	13	1	3.800	2	V							
1629	1	1	2.075	2	H	ROST	ROPB	ROPH	ROVE			
1629	2	1	2.721	1	V	ROST	ROPB					
1629	3	1	2.870	1	H	ROST	ROPB					
1629	4	1	2.641	2	V	ROVE						
1629	5	1	2.740	1	H	ROST	ROVE	ROPH				
1629	6	1	2.283	2	V	ROST	ROVE	ROPB				
1629	7	1	2.740	2	H	ROST	ROPB					
1629	8	1	2.594	1	V	ROST	ROVE	ROPB	ROPH			
1629	9	1	2.093	2	H	ROST	ROVE	ROPB	ROPH			
1629	10	1	2.700	2	V	ROST						

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 280 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1629	11	1	3.170	2	H	ROPB						
1629	12	1	2.913	1	V	ROPB	ROST	ROVE				
1629	13	1	2.977	1	H	ROST	ROPB					
1629	14	1	2.506	2	V	ROST	ROPB	ROVE				
1630	1	1	3.778	1	V							
1630	2	2	.	.	.							
1630	3	1	4.038	1	H	ROVE						
1630	4	1	3.695	1	V							
1630	5	1	3.731	2	H							
1630	6	1	3.798	1	V							
1630	7	1	3.465	2	H							
1630	8	1	3.569	2	V							
1630	9	1	3.589	2	H							
1630	10	1	3.301	2	V							
1630	11	1	3.480	2	H							
1630	12	1	3.435	1	V							
1630	13	1	3.924	1	H							
1630	14	1	3.621	2	V							
1630	15	1	3.976	1	H							
1630	16	1	3.977	2	V							
1631	1	1	3.653	2	H							
1631	2	1	3.732	2	V							
1631	3	1	3.609	2	H							
1631	4	1	3.882	1	V							
1631	5	1	3.447	2	H							
1631	6	1	3.445	2	V							
1631	7	1	3.623	1	H							
1631	8	1	3.760	1	V							
1631	9	1	3.828	1	H							
1631	10	1	4.031	2	V							
1631	11	1	3.447	2	H							
1631	12	1	3.904	1	V							
1631	13	1	3.913	2	H							
1631	14	1	3.652	2	V							
1631	15	1	4.045	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1405	1	1	3.287	1	V							
1405	2	1	3.226	1	H							
1405	3	1	3.253	2	V							
1405	4	1	3.379	2	H							
1405	5	2	.	.	.							
1405	6	1	3.652	2	V							
1405	7	1	3.138	2	H							
1405	8	1	3.103	1	V							
1405	9	1	3.053	2	H							
1405	10	1	3.210	1	V							
1405	11	1	3.458	2	H							
1405	12	1	3.199	2	V							
1405	13	1	3.247	2	H							
1405	14	1	3.835	2	V							
1405	15	1	3.420	2	H							
1409	1	1	3.009	1	H							
1409	2	1	3.052	1	V							
1409	3	1	3.021	2	H							
1409	4	1	3.540	1	V							
1409	5	1	3.217	1	H							
1409	6	2	.	.	.							
1409	7	1	3.142	2	V	ROST						
1409	8	1	3.190	1	H							
1409	9	1	3.322	2	V							
1409	10	1	3.090	2	H							
1409	11	2	.	.	.							
1409	12	1	3.413	2	V							
1409	13	1	3.142	2	H							
1410	1	1	3.490	1	V	ROST						
1410	2	1	3.500	1	H	ROST						
1410	3	1	3.500	1	V	ROST						
1410	4	1	4.020	1	H							
1410	5	1	3.405	2	V							
1410	6	1	3.361	2	H	ROST						
1410	7	1	3.695	1	V							
1410	8	1	3.101	1	H	ROST						
1410	9	1	3.139	2	V							
1410	10	1	3.007	1	H							
1410	11	1	3.510	1	V	ROST						
1410	12	1	3.545	1	H							
1410	13	1	3.804	2	V							
1410	14	1	3.510	2	H	ROST						
1410	15	1	3.334	2	V							
1410	16	1	3.634	2	H							
1412	1	1	2.896	2	H	ROVE						
1412	2	1	3.101	1	V	ROVE						
1412	3	1	3.169	1	H	ROVE						

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1412	4	1	3.039	1	V							
1412	5	1	3.269	2	H							
1412	6	1	3.132	1	V	DIUR						
1412	7	1	2.950	2	H							
1412	8	1	3.287	1	V	ROVE						
1412	9	1	3.128	1	H	ROVE						
1412	10	1	2.730	2	V							
1412	11	1	2.984	2	H	ROST						
1412	12	1	2.865	2	V							
1412	13	1	3.049	2	H							
1412	14	1	3.825	2	V							
1412	15	1	3.044	2	H							
1430	1	1	3.617	2	V							
1430	2	1	3.367	2	H							
1430	3	1	3.608	2	V	DIUR	RPCA					
1430	4	1	3.579	2	H							
1430	5	1	3.377	2	V							
1430	6	1	3.692	1	H							
1430	7	1	2.840	2	V	DIUR	RPCA	ROST				
1430	8	1	3.647	1	H							
1430	9	1	3.724	1	V							
1430	10	1	3.921	1	H							
1430	11	1	3.670	1	V							
1430	12	1	3.450	2	H							
1430	13	1	3.504	1	V							
1430	14	1	3.696	2	H							
1441	1	1	3.070	2	V							
1441	2	1	3.437	1	H							
1441	3	1	3.112	1	V							
1441	4	1	3.284	2	H							
1441	5	1	3.214	2	V							
1441	6	1	3.442	1	H							
1441	7	2	.	.	.							
1441	8	2	.	.	.							
1441	9	1	3.238	1	V							
1441	10	1	3.047	2	H							
1441	11	1	3.063	2	V							
1441	12	1	2.157	1	H	ROST	ROPB					
1443	1	1	3.617	1	H							
1443	2	1	3.616	1	V							
1443	3	1	3.424	2	H							
1443	4	1	3.254	2	V							
1443	5	1	3.611	2	H							
1443	6	1	3.676	2	V							
1443	7	1	3.182	1	H							
1443	8	4	.	.	.							
1443	9	1	3.788	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1443	10	1	3.415	1	H							
1443	11	1	3.183	1	V	ROVE						
1443	12	1	3.508	2	H							
1443	13	1	3.854	1	V							
1453	1	1	2.720	2	H	ROST						
1453	2	1	3.144	2	V	RURB	RORB					
1453	3	1	3.234	2	H							
1453	4	1	3.319	2	V							
1453	5	1	3.477	1	H							
1453	6	1	3.753	1	V							
1453	7	1	3.392	2	H	RURB						
1453	8	1	3.975	1	V							
1453	9	1	3.792	1	H							
1453	10	1	3.437	2	V							
1453	11	1	3.225	2	H							
1453	12	1	3.394	2	V							
1453	13	1	3.405	1	H							
1453	14	1	3.225	2	V							
1453	15	2	.	.	.							
1453	16	1	3.410	1	H	RURB	RORB					
1453	17	1	3.490	2	V							
1453	18	1	3.850	1	H							
1453	19	1	3.833	1	V							
1453	20	1	3.578	2	H							
1453	21	1	3.767	1	V							
1461	1	1	3.211	1	H							
1461	2	1	3.452	1	V							
1461	3	1	3.185	2	H							
1461	4	1	2.722	2	V							
1461	5	1	3.392	1	H							
1461	6	1	3.322	2	V							
1461	7	1	3.502	2	H							
1461	8	1	3.196	1	V							
1461	9	1	3.738	1	H							
1461	10	1	3.532	2	V							
1461	11	1	3.730	1	H							
1461	12	1	3.492	1	V							
1461	13	1	3.320	1	H							
1461	14	1	3.347	1	V							
1484	1	1	3.085	1	H							
1484	2	1	3.265	1	V							
1484	3	1	3.013	2	H							
1484	4	1	3.307	1	V							
1484	5	1	3.399	1	H							
1484	6	2	.	.	.							
1484	7	1	3.180	2	H							
1484	8	1	2.958	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1484	9	1	3.221	2	H							
1484	10	1	3.238	2	V							
1484	11	1	3.332	2	H							
1484	12	1	3.318	1	V							
1484	13	1	3.239	1	H							
1487	1	1	2.939	2	H							
1487	2	1	3.439	1	V							
1487	3	1	3.120	2	H							
1487	4	1	3.183	1	V							
1487	5	1	3.388	1	H							
1487	6	1	3.188	2	V							
1487	7	1	3.331	2	H							
1487	8	1	3.812	2	V							
1487	9	1	3.291	2	H							
1487	10	1	3.308	2	V							
1487	11	1	3.532	1	H							
1487	12	1	3.838	1	V							
1487	13	1	3.501	1	H							
1487	14	1	3.435	1	V							
1487	15	1	3.189	2	H							
1487	16	1	3.137	2	V							
1491	1	1	3.185	1	H							
1491	2	1	3.017	2	V							
1491	3	1	2.908	2	H							
1491	4	1	3.195	2	V							
1491	5	1	3.428	1	H							
1491	6	1	2.981	2	V							
1491	7	1	3.344	2	H							
1491	8	1	3.234	1	V							
1491	9	1	3.044	2	H							
1491	10	1	2.958	2	V							
1491	11	1	3.208	1	H							
1491	12	1	3.118	2	V							
1491	13	1	3.242	1	H							
1491	14	1	3.305	2	V							
1491	15	1	3.473	1	H							
1494	1	1	2.793	2	H							
1494	2	1	3.128	1	V							
1494	3	1	3.097	1	H							
1494	4	1	3.029	2	V							
1494	5	1	3.541	1	H							
1494	6	1	1.900	2	HV							
1494	7	1	3.208	2	H							
1494	8	1	3.302	2	V							
1494	9	1	3.331	2	H							
1494	10	1	3.531	1	V							
1494	11	1	3.299	2	H							

RURB
ROVE

ROST ROPB ROPH AOPT

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
 Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1494	12	1	3.423	1	V							
1494	13	1	3.276	2	H							
1494	14	1	3.446	1	V							
1494	15	1	3.252	1	H							
1496	1	1	2.881	2	V	ROPB						
1496	2	1	3.199	1	H							
1496	3	1	3.341	1	V	ROVE						
1496	4	1	2.941	1	H							
1496	5	1	3.002	2	V	ROST						
1496	6	1	3.131	1	H							
1496	7	1	3.283	2	V							
1496	8	1	2.878	2	H							
1496	9	1	2.750	2	V							
1496	10	1	3.185	1	H							
1496	11	1	2.835	2	V	MIIN						
1496	12	1	3.294	1	H							
1496	13	1	3.018	2	V							
1496	14	1	3.258	1	H							
1496	15	1	3.236	2	V							
1496	16	1	3.182	2	H	ROVE						
1525	1	1	3.323	2	H							
1525	2	1	3.290	2	V							
1525	3	2	.	.	.							
1525	4	1	3.791	1	H							
1525	5	1	3.726	2	V							
1525	6	1	3.899	1	H							
1525	7	1	3.561	2	V							
1525	8	1	3.413	2	H							
1525	9	1	3.381	1	V							
1525	10	1	3.356	2	H							
1525	11	1	3.483	2	V							
1525	12	1	3.524	2	H							
1525	13	1	3.488	2	V							
1525	14	2	.	.	.							
1526	1	4	.	.	.							
1526	2	1	2.892	2	H	ROST	ROPB	ROPH				
1526	3	1	2.589	2	V	ROPB						
1526	4	2	.	.	.							
1526	5	1	2.583	2	HV	UHER	ROST	ROPH				
1526	6	1	3.391	1	V							
1526	7	1	3.486	1	H							
1526	8	1	2.789	2	V							
1526	9	1	3.348	1	H							
1526	10	1	2.921	2	V							
1526	11	1	3.113	2	H							
1526	12	1	3.292	1	V							
1526	13	1	3.087	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 83 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1520	14	1	3.384	1	V							
1526	15	1	3.048	2	H							
1531	1	1	3.062	2	H							
1531	2	1	2.995	2	V							
1531	3	1	3.313	2	H							
1531	4	1	3.572	1	V							
1531	5	1	3.784	1	H							
1531	6	1	3.390	2	V							
1531	7	1	3.828	1	H							
1531	8	1	3.397	1	V							
1531	9	1	3.084	2	H							
1531	10	1	3.835	1	V	DIUR	RPCA					
1531	11	1	3.492	2	H							
1531	12	1	3.584	1	V							
1531	13	1	3.378	2	H							
1531	14	1	3.215	2	V							
1541	1	1	3.259	1	H							
1541	2	1	3.455	1	V							
1541	3	1	3.730	2	H							
1541	4	1	3.759	2	V							
1541	5	1	3.743	1	H							
1541	6	1	3.612	2	V							
1541	7	1	3.606	2	H							
1541	8	1	3.708	1	V	ROVE						
1541	9	1	3.578	2	H							
1541	10	1	3.832	1	V							
1541	11	1	3.498	1	H							
1541	12	2	.	.	.							
1541	13	1	3.584	2	V							
1541	14	1	3.598	1	H							
1541	15	1	3.400	2	V							
1549	1	1	2.703	2	H							
1549	2	1	3.414	1	V							
1549	3	1	3.276	2	H							
1549	4	1	3.390	1	V							
1549	5	1	3.289	2	H							
1549	6	1	3.482	1	V							
1549	7	1	3.510	1	H							
1549	8	2	.	.	.							
1549	9	1	3.032	1	V							
1549	10	1	3.062	1	H							
1549	11	1	3.118	1	V							
1549	12	1	2.750	2	H							
1549	13	1	3.272	2	V							
1549	14	1	3.424	2	H							
1549	15	1	3.410	1	V							
1549	16	1	3.504	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1549	17	1	3.299	2	V							
1549	18	1	3.608	1	H							
1552	1	1	3.800	2	H							
1552	2	1	3.852	2	V							
1552	3	1	3.999	1	H							
1552	4	1	4.055	1	V							
1552	5	1	3.844	1	H							
1552	6	1	3.849	2	V							
1552	7	1	3.898	1	H							
1552	8	1	3.718	2	V							
1552	9	1	4.274	1	H							
1552	10	1	3.521	2	V							
1552	11	1	4.116	1	H							
1552	12	1	3.993	1	V							
1552	13	1	3.788	2	H							
1552	14	1	3.911	2	V							
1558	1	1	2.877	1	H							
1558	2	1	3.972	1	V							
1558	3	1	3.668	1	H							
1558	4	1	3.357	1	V							
1558	5	1	3.194	2	H							
1558	6	1	3.359	1	V							
1558	7	1	3.579	1	H							
1558	8	1	3.434	2	V							
1558	9	1	3.538	1	H							
1558	10	1	3.317	1	V							
1558	11	1	3.302	1	H							
1558	12	1	3.122	1	V							
1558	13	1	3.333	2	H							
1583	1	1	3.192	2	V	ROVE						
1583	2	1	3.281	1	H							
1583	3	1	3.325	2	V							
1583	4	1	3.345	2	H							
1583	5	1	3.607	1	V	DIUR						
1583	6	1	3.474	1	H							
1583	7	1	3.828	2	V	ROST						
1583	8	1	2.815	2	H	ROST						
1583	9	1	3.314	2	V							
1583	10	1	3.380	2	H							
1583	11	1	3.481	1	V							
1583	12	4	.	.	.							
1583	13	1	3.588	2	H							
1583	14	1	3.698	2	V							
1583	15	1	3.740	2	H							
1583	16	1	3.603	2	V							
1583	17	1	3.385	1	H							
1584	1	2	.	.	.							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 83 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 1400 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1584	2	1	3.822	1	H	ROVE						
1584	3	1	3.588	2	V							
1584	4	1	3.711	1	H							
1584	5	1	3.955	2	V							
1584	6	1	3.357	2	H							
1584	7	1	4.072	1	V							
1584	8	1	3.812	2	H							
1584	9	1	4.511	1	V							
1584	10	1	2.929	2	H							
1584	11	1	2.900	1	V							
1584	12	1	2.748	2	H							
1584	13	1	2.819	2	V							
1584	14	2	.	.	.							
1573	1	1	3.864	1	H							
1573	2	1	3.845	2	V							
1573	3	1	4.155	1	H							
1573	4	1	3.342	2	V							
1573	5	1	3.487	2	H							
1573	6	1	3.867	2	V							
1573	7	1	3.938	1	H							
1573	8	1	3.892	2	V							
1573	9	1	3.550	2	H							
1573	10	1	3.571	2	V							
1573	11	1	3.859	2	H							
1573	12	1	4.023	2	V							
1573	13	1	4.013	2	H							
1573	14	4	.	.	.							
1573	15	1	3.939	2	V							
1850	1	1	3.077	2	V							
1850	2	2	.	.	.							
1850	3	1	3.158	1	H	ROST	ROPB					
1850	4	1	3.245	2	V							
1850	5	2	.	.	.							
1850	6	1	3.362	2	H							
1850	7	1	3.435	2	V							
1850	8	1	3.298	1	H	ROST	MAST					
1850	9	1	3.292	2	V							
1850	10	1	3.841	1	H							
1850	11	1	3.528	1	V	DIUR						
1850	12	1	3.786	1	H							
1850	13	1	3.349	2	V	MAST						
1850	14	1	3.361	2	H	ROST						
1850	15	1	3.489	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

7000 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1415	1	1	3.169	1	H	ROST						
1415	2	1	3.076	1	V							
1415	3	1	3.398	1	H							
1415	4	1	3.030	1	V							
1415	5	1	3.117	1	H							
1415	6	1	3.109	2	V							
1415	7	1	3.450	1	H							
1415	8	1	3.051	2	V							
1415	9	1	3.070	2	H							
1415	10	1	3.372	2	V							
1415	11	1	3.067	2	H							
1415	12	1	3.163	2	V							
1415	13	2	.	.	.							
1415	14	1	3.448	1	H							
1417	1	2	.	.	.							
1417	2	1	3.153	2	H							
1417	3	1	3.527	1	V							
1417	4	1	2.949	2	H							
1417	5	1	3.148	1	V							
1418	1	1	2.842	2	H	ROST						
1418	2	1	3.422	1	V							
1418	3	1	2.778	2	H	ROST						
1418	4	1	3.523	1	V							
1418	5	1	3.476	1	H							
1418	6	1	3.589	1	V							
1418	7	1	2.930	2	H	ROST						
1418	8	1	3.271	1	V							
1418	9	1	3.441	1	H							
1418	10	1	3.337	1	V							
1418	11	1	3.431	2	H							
1418	12	1	3.275	2	V							
1418	13	1	3.170	2	H							
1418	14	1	3.447	1	V							
1421	1	1	3.103	2	H							
1421	2	1	3.013	2	V							
1421	3	1	2.948	2	H							
1421	4	1	2.615	2	V							
1421	5	1	3.053	1	H							
1421	6	1	2.788	1	V							
1421	7	1	3.197	1	H							
1421	8	1	2.879	2	V	ROVE						
1421	9	1	3.176	2	H							
1421	10	2	.	.	.							
1421	11	1	3.033	2	V							
1421	12	1	3.028	2	H							
1421	13	1	3.237	1	V							
1421	14	1	3.103	2	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----												
Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1421	16	1	3.050	2	V							
1425	1	2	.	.	.							
1425	2	1	3.228	2	H							
1425	3	1	3.301	1	V							
1425	4	1	3.854	1	H							
1425	5	1	3.482	2	V							
1425	6	1	3.636	1	H							
1425	7	1	3.279	2	V							
1425	8	1	3.238	1	H							
1425	9	1	3.201	1	V							
1425	10	1	3.273	1	H							
1425	11	1	2.923	2	V							
1425	12	1	3.317	1	H							
1425	13	1	3.077	2	V	ROPB						
1425	14	1	3.477	1	H	ROVE	ROPB					
1425	15	1	3.470	2	V							
1434	1	1	2.553	2	V	ROST	ROVE					
1434	2	1	3.076	1	H							
1434	3	1	3.165	2	V							
1434	4	1	3.139	2	H							
1434	5	1	3.292	2	V							
1434	6	1	3.130	1	H	ROVE						
1434	7	1	2.800	2	V							
1434	8	1	3.339	1	H							
1434	9	1	3.253	2	V							
1434	10	1	3.358	1	H							
1434	11	1	3.308	2	V							
1434	12	1	3.449	1	H							
1434	13	1	3.335	2	V	DIUR						
1434	14	1	3.269	1	H							
1434	15	1	2.803	1	V	ROSK						
1434	16	1	3.283	1	H	ROST						
1454	1	1	2.646	1	V							
1454	2	1	3.139	2	H							
1454	3	1	3.549	1	V							
1454	4	1	3.351	1	H							
1454	5	1	3.322	1	V							
1454	6	1	3.305	2	H							
1454	7	1	3.243	2	V							
1454	8	1	3.365	1	H	ROST						
1454	9	1	3.331	2	V							
1454	10	1	3.540	1	H							
1454	11	1	3.350	1	V							
1454	12	1	3.528	1	H							
1454	13	1	3.504	2	V							
1454	14	1	3.615	1	H							
1458	1	1	2.240	2	H	ROST						

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

7000 ppm Isoprene

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1458	2	1	2.983	1	V	ROVE	ROST					
1458	3	1	2.989	1	H	ROVE						
1458	4	1	3.208	1	V	ROVE						
1458	5	1	3.136	1	H							
1458	6	1	2.602	2	V	ROVE	ROST					
1458	7	1	2.784	2	H	ROST	ROPB					
1458	8	1	3.179	1	V	ROST						
1458	9	1	2.539	2	H	ROST						
1458	10	1	3.166	2	V	ROVE						
1458	11	1	2.874	2	H							
1458	12	1	2.897	1	V	ROVE	ROST	ROPB				
1458	13	1	2.785	2	H	ROVE						
1458	14	1	2.914	1	V	ROVE						
1458	15	1	3.142	1	H							
1458	16	1	3.088	2	V							
1465	1	1	3.000	1	V							
1465	2	1	3.164	2	H							
1465	3	1	3.530	1	V							
1465	4	1	3.292	2	H							
1465	5	1	3.604	1	V	ROVE						
1465	6	1	3.485	1	H							
1465	7	1	3.371	2	V							
1465	8	1	3.528	1	H							
1465	9	1	2.486	2	V	ROST	ROVE					
1465	10	1	3.213	1	H							
1465	11	1	3.416	1	V	ROVE						
1472	1	1	2.930	2	H							
1472	2	1	3.516	1	V	DIUR						
1472	3	1	3.004	2	H	RURB	RORB					
1472	4	1	3.338	2	V	RURB						
1472	5	1	3.348	2	H							
1472	6	1	3.441	2	V							
1472	7	1	3.150	2	H	RURB						
1472	8	1	3.208	1	V							
1472	9	1	3.444	1	H							
1472	10	1	3.320	1	V	ROVE						
1472	11	1	3.149	1	H	RURB						
1472	12	1	3.167	2	V							
1497	1	1	3.383	2	H							
1497	2	1	3.558	1	V	ROSK						
1497	3	1	3.384	1	H							
1497	4	1	3.702	2	V							
1497	5	1	3.660	1	H							
1497	6	1	3.659	2	V							
1497	7	1	3.398	2	H							
1497	8	1	3.598	1	V							
1497	9	1	3.789	1	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1497	10	1	3.417	2	V							
1497	11	1	3.823	1	H							
1497	12	1	3.423	1	V							
1499	1	1	3.183	1	V							
1499	2	1	3.242	2	H							
1499	3	1	2.873	2	V	ROST						
1499	4	1	3.144	1	H							
1499	5	1	3.088	1	V							
1499	6	1	2.895	1	H							
1499	7	1	3.382	1	V	ROST						
1499	8	1	3.151	2	H							
1499	9	1	3.106	2	V							
1499	10	1	2.645	2	H	ROST						
1499	11	2	.	.	.							
1499	12	1	3.339	2	V							
1509	1	1	3.070	1	H							
1509	2	1	3.044	1	V							
1509	3	1	3.301	1	H							
1509	4	1	2.855	2	V							
1509	5	1	3.243	1	H							
1509	6	1	3.095	1	V							
1509	7	1	3.259	2	H							
1509	8	1	3.205	1	V							
1509	9	1	3.538	1	H							
1509	10	1	3.293	1	V							
1509	11	1	3.128	2	H							
1509	12	1	3.221	2	V							
1509	13	1	3.380	1	V	ROPB						
1509	14	1	3.535	1	H	ROST						
1509	15	1	3.249	1	V							
1509	16	1	3.242	1	H							
1509	17	1	3.123	1	V	ROSK	ROST					
1509	18	1	3.470	2	H							
1510	1	1	3.531	1	V							
1510	2	1	3.559	2	H							
1510	3	1	3.632	1	V							
1510	4	1	3.824	1	H							
1510	5	1	3.891	1	V							
1510	6	1	3.417	1	H							
1510	7	1	3.291	2	V							
1510	8	1	3.240	2	H							
1510	9	1	3.118	2	V							
1510	10	1	3.115	2	H							
1510	11	1	3.824	1	V							
1510	12	1	3.395	2	H							
1510	13	1	3.540	2	V							
1510	14	1	3.801	1	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1511	1	1	2.893	2	V	ROST						
1511	2	2	.	.	.							
1511	3	1	2.991	2	H	ROST						
1511	4	1	3.255	1	V							
1511	5	1	3.182	1	H							
1511	6	1	3.099	2	V	ROST						
1511	7	1	3.047	2	H							
1511	8	1	2.980	1	V							
1511	9	1	2.816	2	H							
1511	10	1	3.020	1	V	ROST						
1511	11	1	3.214	2	H							
1511	12	2	.	.	.							
1511	13	1	3.398	1	V							
1511	14	1	3.007	2	H							
1513	1	1	2.957	1	V							
1513	2	1	3.216	2	H							
1513	3	1	3.308	2	V							
1513	4	1	3.088	1	H	ROVE						
1513	5	1	3.289	1	V							
1513	6	1	3.094	2	H							
1513	7	1	3.076	1	V							
1513	8	1	3.232	2	H	ROVE						
1513	9	1	3.238	1	V							
1513	10	2	.	.	.							
1513	11	1	3.021	2	H							
1513	12	1	3.319	1	V							
1513	13	1	3.272	2	H							
1513	14	1	3.291	2	V							
1513	15	1	3.263	2	H							
1529	1	1	3.661	1	V							
1529	2	1	3.725	2	H							
1529	3	1	3.282	2	V							
1529	4	1	3.453	2	H							
1529	5	1	3.038	1	V							
1529	6	1	3.661	1	H	ROVE						
1529	7	1	3.935	1	V							
1529	8	1	3.335	2	H							
1529	9	1	3.429	2	V							
1529	10	2	.	.	.							
1529	11	1	3.749	1	H	ROVE						
1529	12	1	3.032	1	V							
1529	13	1	3.914	1	H							
1548	1	1	3.050	1	V							
1548	2	1	3.164	2	H							
1548	3	1	4.125	1	V							
1548	4	1	3.991	1	H							
1548	5	1	3.784	1	V							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1548	8	1	3.702	2	H							
1548	7	1	3.947	2	V							
1548	8	1	3.827	2	H							
1548	9	1	3.547	1	V							
1548	10	1	3.833	2	H							
1548	11	1	3.859	1	V							
1548	12	1	3.997	2	H							
1548	13	1	3.898	2	V							
1555	1	1	2.884	1	H							
1555	2	1	3.401	1	V							
1555	3	1	3.138	2	H							
1555	4	1	3.148	2	V							
1555	5	1	2.943	2	H							
1555	6	1	3.371	1	V							
1555	7	1	3.036	2	H							
1555	8	1	2.989	2	V							
1555	9	1	3.271	2	H							
1555	10	2	.	.	.							
1555	11	1	2.815	2	V							
1555	12	1	3.070	2	H							
1555	13	1	3.288	1	V							
1555	14	1	3.178	2	H							
1555	15	1	3.153	2	V							
1555	16	1	3.246	2	H							
1555	17	1	3.464	2	V							
1557	1	1	3.249	2	V							
1557	2	1	3.737	2	H							
1557	3	1	4.061	1	V							
1557	4	1	3.703	1	H							
1557	5	1	3.924	1	V							
1557	6	2	.	.	.							
1557	7	1	3.677	1	H							
1557	8	1	3.845	1	V							
1557	9	1	3.789	1	H							
1557	10	1	4.141	1	V							
1557	11	2	.	.	.							
1557	12	1	3.053	2	H							
1557	13	1	4.060	1	V							
1558	1	1	3.309	1	H							
1558	2	1	3.676	1	V							
1558	3	1	3.873	1	H							
1558	4	1	3.314	2	V							
1558	5	1	3.502	2	H							
1558	6	1	3.450	1	V							
1558	7	1	3.642	2	H							
1558	8	1	3.654	1	V							
1558	9	1	3.665	1	H							

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1558	10	1	3.845	1	V							
1558	11	1	3.780	2	H							
1558	12	1	3.055	2	V							
1558	13	1	4.113	1	H							
1566	1	1	3.009	2	V							
1566	2	1	3.567	1	H							
1566	3	1	3.205	2	V							
1566	4	1	3.499	1	H							
1566	5	2	.	.	.							
1566	6	1	3.470	2	V							
1566	7	1	3.300	1	H							
1566	8	1	3.040	1	V							
1566	9	2	.	.	.							
1566	10	1	2.788	2	H							
1566	11	1	3.145	2	V							
1566	12	1	3.343	1	H							
1566	13	1	3.390	2	V							
1566	14	1	3.238	2	H							
1597	1	2	.	.	.							
1597	2	1	3.041	2	H	ROVE						
1597	3	1	3.173	2	V							
1597	4	1	3.103	2	H							
1597	5	2	.	.	.							
1597	6	1	3.614	1	V							
1597	7	1	3.184	1	H							
1597	8	1	3.705	1	V	ROVE						
1597	9	1	3.125	2	H							
1597	10	1	3.481	2	V							
1597	11	1	3.301	1	H							
1597	12	1	3.041	1	V							
1597	13	1	3.490	2	H							
1597	14	1	3.458	1	V							
1597	15	1	3.347	2	H							
1597	16	1	3.400	2	V							
1597	17	1	3.500	1	H							
1602	1	1	3.158	1	H							
1602	2	2	.	.	.							
1602	3	1	3.534	1	V							
1602	4	1	3.685	1	H							
1602	5	1	3.125	2	V							
1602	6	1	2.717	2	H							
1602	7	1	3.338	1	V							
1602	8	1	3.666	1	H							
1602	9	1	3.375	1	V	ROVE						
1602	10	1	3.332	1	H	ROST						
1602	11	1	3.268	2	V	ROVE						
1602	12	1	3.442	1	H	ROST						

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

Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

----- 7000 ppm Isoprene -----

Matno	Site	Status	Fetal Wt(g)	Sex	Head or Visceral	ABN1	ABN2	ABN3	ABN4	ABN5	ABN6	ABN7
1002	13	1	3.764	1	V							
1002	14	1	3.648	1	H							
1002	15	1	3.274	1	V							

C.82

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2; See Code Sheet (pg 33 in Appendix) for Identification of abnormalities [ABNn]

Isoprene Rat Teratology Study: Raw Fetal Data

Code Sheet Identification for Fetal Abnormalities

ROPH	Reduced Ossification Phalanges
ROST	Reduced Ossification Sternebrae
ROVE	Reduced Ossification Vertebrae
ROPB	Reduced Ossification Pelvic
ROSK	Reduced Ossification Skull
RORB	Reduced Ossification Rib
UHER	Umbilical Hernia
DIUR	Dilated Ureter
EXCE	Exencephaly
RACH	Rachishisis
MAST	Misaligned Sternebrae
AOPT	Anophthalmia
MIIN	Missing Innominate Artery
RURB	Rudimentary Rib
RPCA	Renal Pelvic Cavitation

ISOPRENE RAT TERATOLOGY: CALENDAR OF EVENTS

Exposure levels; treatments 1-4	0, 280, 1400, 7000 ppm
Ordered rats	2/16/88
Received rats (ARS# 880043)	3/16/88
Health screen	4/4/88
Eartagged & weighed females	4/5/88
Released from quarantine	4/11/88
Virgins individually caged	4/12/88
Virgins weighed and randomized	4/14/88
Mated 0dg (# positive)	(A) 4/12/88 (48)
weighed, randomized, individually caged	(B) 4/13/88 (36)
	(C) 4/14/88 (15)
	(D) 4/15/88 (17)
Moved to exposure room; (A-C)	4/15/88
(D & Virgins)	4/17/88
Exposure (6 hours/day; 6-19dg)	(A) 4/18 to 5/1/88
	(B) 4/19 to 5/2/88
	(C) 4/20 to 5/3/88
	(D) 4/21 to 5/4/88
Weighed (6dg) start exposure	(A-D) 4/18 to 4/21/88
Weighed (10dg)	(A-D) 4/19 to 4/25/88
Weighed (14dg)	(A-D) 4/26 to 4/29/88
Weighed (17dg)	(A-D) 4/29 to 5/2/88
Sacrificed (20dg)	(A) 5/2/88
	(B) 5/3/88 terminal serology
	(C) 5/4/88
	(D) 5/5/88
Virgins - exposed 14 days	4/20 to 5/3/88
Weighed exposure day 1	4/20/88
Weighed exposure day 5	4/24/88
Weighed exposure day 10	4/29/88
Sacrifice one day post-exposure	5/4/88
Fetal specimen exams completed	6/28/88

ISOPRENE RAT TERATOLOGY STUDY DISPOSITION

Exposure Group	Treatment	Virgins	Sperm-Positive Teratology Rats			
			On Study	Removed From Study	Sacrifice	Litters Examined
Control (0 ppm)	1	10	29	0	29	26
280 ppm	2	10	28	0	28	25
1400 ppm	3	10	29	0	29	25
7000 ppm	4	10	28	0	28	24

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

(CONTEMPORARY CONTROL)

Contemporary Control Data for Swiss (CD-1) Mice
(N=111 Litters; Mean $\pm$ SD).

	Number	Percent
Maternal Weight; 18 dg	54.3 $\pm$ 4.9	—
Gravid Uterine Weight	19.9 $\pm$ 3.9	—
Extra-gestational Weight Gain	6.6 $\pm$ 2.0	—
Implants	12.5 $\pm$ 2.4	—
Live Fetuses	11.7 $\pm$ 2.4	93.7 $\pm$ 7.2
Early Resorptions	0.6 $\pm$ 0.8	4.4 $\pm$ 6.2
Late Resorptions	0.2 $\pm$ 0.5	1.9 $\pm$ 3.8
Dead Fetuses	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Total Intrauterine Death	0.8 $\pm$ 0.9	6.3 $\pm$ 7.2
Litters with Resorptions	72	64.9
Fetal Weight	1.35 $\pm$ 0.13	—
Male	1.38 $\pm$ 0.12	—
Female	1.33 $\pm$ 0.12	—

Contemporary Control Data on Swiss (CD-1) Mouse Teratology Studies:
Malformations and Variations.

		Fetuses (a) Number (Percent)	Litters Number (Percent)	Mean Percent per Litter ($\pm$ SD)
Total examined (b)		1144	111	—
Heads examined (c)		—	—	—
Skulls examined (d)		—	—	—
Malformations				
Exencephaly	No. (%)	1 (0.1)	1 (0.9)	0.1 ± 1.1
Folded Retina	No. (%)	2 (0.2)	2 (1.8)	0.2 ± 1.3
Limb Flexure	No. (%)	12 (1.0)	8 (7.2)	0.8 ± 3.3
Total Fetuses (Litters) with Malformations	No. (%)	14 (1.4)	10 (12.0)	1.0 ± 3.5
Variations				
Misaligned Sternebrae	No. (%)	26 (2.3)	17 (15.3)	2.0 ± 5.8
Supernumerary Rib	No. (%)	207 (18.1)	65 (58.6)	18.0 ± 24.4
Reduced Ossifications				
Sternebrae	No. (%)	35 (3.1)	24 (21.6)	2.7 ± 5.8
Skull	No. (%)	9 (0.8)	5 (4.5)	0.8 ± 4.0
Total Fetuses (Litters) with Variations or Reduced Ossifications	No. (%)	269 (23.6)	83 (74.8)	23.2 ± 24.5

- (a) A single fetus may be represented more than once in this table.
 (b) All fetuses examined for external, visceral and skeletal defects. All fetuses stained with alcian blue and alizarin red S, one-half had heads removed prior to staining.
 (c) Heads removed from fetuses and fixed in Bouin's solution then examined for soft-tissue cranio-facial malformations.
 (d) Heads remained on the fetuses that were stained for skeletal examination; see a) above.

Contemporary Control Data for Sprague-Dawley Rats
(N=106 Litters; Mean $\pm$ SD).

	Number	Percent
Maternal Weight; 20 dg	393.6 $\pm$ 35.7	—
Gravid Uterine Weight	77.2 $\pm$ 17.7	—
Extra-gestational Weight Gain	46.5 $\pm$ 14.6	—
Implants	15.4 $\pm$ 2.8	—
Live Fetuses	14.5 $\pm$ 3.1	93.6 $\pm$ 8.3
Early Resorptions	0.7 $\pm$ 1.0	5.3 $\pm$ 7.9
Late Resorptions	0.2 $\pm$ 0.5	1.1 $\pm$ 3.2
Dead Fetuses	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Total Intrauterine Death	0.9 $\pm$ 1.1	6.4 $\pm$ 8.3
Litters with Resorptions	57	53.8
Fetal Weight	3.50 $\pm$ 0.32	—
Male	3.58 $\pm$ 0.37	—
Female	3.41 $\pm$ 0.31	—

Contemporary Control Data for Sprague-Dawley Rats: Malformations.

		Fetuses (a) Number (Percent)	Litters Number (Percent)	Mean Percent per Litter ($\pm$ SD)
Total examined (b)		1531	106	—
Heads examined (c)		—	—	—
Skulls examined (d)		—	—	—
Malformations				
Exencephaly	No. (%)	2 (0.1)	1 (0.9)	0.1 ± 1.1
Microphthalmia	No. (%)	1 (0.1)	1 (0.9)	0.1 ± 0.6
Rudimentary Rib	No. (%)	1 (0.1)	1 (0.9)	0.1 ± 0.6
Anophthalmia	No. (%)	1 (0.1)	1 (0.9)	0.1 ± 0.7
Rachischisis	No. (%)	2 (0.1)	1 (0.9)	0.1 ± 1.1
Ectopic Ovaries	No. (%)	1 (0.1)	1 (0.9)	0.1 ± 0.5
Total Fetuses (Litters) with Malformations	No. (%)	5 (0.3)	5 (4.7)	0.3 ± 1.5

- (a) A single fetus or litter may be represented more than once in this table.
 (b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.
 (c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.
 (d) Heads that remained on the fetuses had a skeletal examination; see (b).

Contemporary Control Data for Sprague-Dawley Rats:
Variations and Reduced Ossifications.

		Fetuses (a) Number (Percent)	Litters Number (Percent)	Mean Percent per Litter ($\pm$ SD)
Total examined (b)		1531	106	—
Heads examined (c)		—	—	—
Skulls examined (d)		—	—	—
Variations				
Misaligned Sternebrae	No. (%)	6 (0.4)	6 (5.7)	0.4 ± 1.6
Supernumerary Rib	No. (%)	38 (2.5)	17 (16.0)	2.4 ± 7.4
Renal Pelvic Cavitation	No. (%)	8 (0.5)	4 (3.8)	0.5 ± 2.9
Dilated Ureter	No. (%)	36 (2.4)	18 (17.0)	2.5 ± 7.8
Missing Innominate Artery	No. (%)	3 (0.2)	3 (2.8)	0.2 ± 1.2
Reduced Ossifications				
Sternebrae	No. (%)	130 (8.5)	52 (49.1)	8.8 ± 14.4
Vertebrae, centra	No. (%)	59 (3.9)	32 (30.2)	3.9 ± 9.2
Phalanges	No. (%)	13 (0.8)	9 (8.5)	1.0 ± 3.8
Pelvic	No. (%)	27 (1.8)	14 (13.2)	2.2 ± 8.7
Skull	No. (%)	20 (1.3)	8 (7.5)	1.4 ± 6.3
Total Fetuses (Litters) with Variations or Red. Ossif.	No. (%)	253 (16.5)	85 (80.2)	16.8 ± 18.0

(a) A single fetus or litter may be represented more than once in this table.

(b) All fetuses examined for external and skeletal defects. One-half had heads removed prior to skeletal staining.

(c) Heads fixed in Bouin's solution for soft-tissue craniofacial evaluations.

(d) Heads that remained on the fetuses had a skeletal examination; see (b).

APPENDIX D

ANIMAL HEALTH SCREEN

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 4/4/88

Lab no: R-68
Animal/Shipment no: 880044
Date rc'd: 3/16/88
Source: CR P08
Species/Strain: Mice/CD-1
Sex: M/F Age: BD 1/16/88

Status: Ten mice (#1-5 male, #6-10 female) submitted for pre-exposure health screen

Gross Necropsy

1/10* Mass A 2mm diameter roughly spherical mass, yellow, soft; located in connective tissue with attachment to seminal vesicles and mesentary. This is probably a focus of necrotic fat. (#2)

*Number affected/number examined

Nasopharyngeal culture

0/10 * Beta hemolytic streptococci
0/10 Bordetella bronchiseptica
0/10 Citrobacter freundii
1/10 Coagulase positive staphylococci
0/10 Klebsiella oxytoca
0/10 Klebsiella pneumoniae
0/10 Pasturella multocida
0/10 Pseudomonas aeruginosa
0/10 Streptococcus pneumoniae

*Number of positive cultures/number cultured

Serology: Mouse

0/10 * Mycoplasma pulmonis
0/10 Sendai virus
0/10 Pneumonia virus of mice
0/10 Mouse hepatitis virus
0/10 GD VII virus

*Number of positive tests/number tested

Histopathology

3/10 * Liver Rare tiny focus of inflammation in hepatic parenchyma (#1,2,8)
1/10 Lung Alveolar bronchiolar adenoma (#3)

*Number affected/number examined

Correlation/Summary

All findings are satisfactory. Coagulase positive staphylococci are not primary pathogens for the mouse. The liver lesions reported from 3 of the mice are commonly seen in newly received mice and are not considered an indication of significant infection or disease. The lung tumor is highly usual particularly in a mouse at this age but there is no reason to suspect any increased incidence or susceptibility in the remainder of the group.

Released for Study on 4/11/88.

Released from Quarantine on 4/11/88.

RE Farrell 4/12/88
Technologist

John Elmer 4/12/88
Veterinarian

Mast
✓Evanoff
Brown

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 4/27/88

Lab no: R-80
Animal/Shipment no: 880044
Date rc'd: 3/16/88
Source: CR P08
Species/Strain: Mice/CD-1
Sex: M/F Age: BD 1/18/88

Status: Ten mouse blood specimens submitted for terminal sacrifice serology

Serology: Mouse

0/10 *	<u>Mycoplasma pulmonis</u>
0/10	Sendai virus
0/10	Pneumonia virus of mice
0/10	Mouse hepatitis virus
0/10	GD VII virus

*Number of positive tests/number tested

Correlation/Summary

The 10 sera submitted were negative for antibodies to those common rodent pathogens listed above. This is good evidence that no study animals were infected by any of these pathogens.

AE Farrell 5/6/88
Technologist

Agnes J. Lane 5/6/88
Veterinarian

Mast
✓ Evans
Brown

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 4/4/88

Lab no: R-69 (addendum)
Animal/Shipment no: 880043
Date rec'd: 3/16/88
Source: CR P03
Species/Strain: Rat/CD
Sex: M/F Age: BD 1/18/88

Status: Ten rats (#1-5 male, #6-10 female) submitted for pre-exposure health screen

Serology: Rat
0/10 * Mycoplasma pulmonis

* Number positive/number tested

Correlation/Summary

None of the sera tested had antibodies to M. pulmonis.

5/24/88 A E Jancell
Technologist

Stef E Rone 5/24/88
Veterinarian

Mast
Evanoff
Brown

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 4/4/88

Lab no: R-69
Animal/Shipment no: 850043
Date rec'd: 3/16/88
Source: CR P03
Species/Strain: Rat/CD
Sex: M/F Age: ED 1/18/88

Status: Ten rats (#1-5 male, #6-10 female) submitted for pre-exposure health screen

Gross Necropsy

No significant lesions

Nasopharyngeal culture

0/10 * Beta hemolytic streptococci
0/10 Bordetella bronchiseptica
0/10 Citrobacter freundii
7/10 Coagulase positive staphylococci
0/10 Klebsiella oxytoca
0/10 Klebsiella pneumoniae
0/10 Pasturella multocida
0/10 Pseudomonas aeruginosa
0/10 Streptococcus pneumoniae

*Number of positive cultures/number cultured

Serology: Rat

0/10 Sendai virus
0/9 Pneumonia virus of mice (#1 Non-specific activity of sera)
1/10 RCV/SDAV (#6)
0/10 KRV/H1

*Number of positive tests/number tested

Histopathology

3/10 * Liver Rare pericholangial focus of inflammatory cells, mostly lymphocytes (#1,4,5)
3/10 Liver Rare tiny focus of inflammation in hepatic parenchyma (#3,9,10)
4/10 Liver Occasional tiny focus of inflammation in hepatic parenchyma (#4,5,7,8)
1/10 Subman. lymph node Hyperplasia (#7)

*Number affected/number examined

Correlation/Summary

No microscopic lesions were found in rat #6 or any other rats in the group which would indicate infection by rat coronavirus (RCV) or sialodacryoadenitis virus (SDAV). Therefore the ELISA reaction for RCV/SDAV in rat #6 is presumed to be a false positive. Such reactions occur occasionally with ELISA. Additional ELISA testing will be done at the end of the study.

All other findings were satisfactory. Coagulase positive staphylococci are not primary pathogens in rats and the microscopic lesions reported are considered incidental and not to be an indication of significant infection or disease.

The Mycoplasma pulmonis test was not run because the reagents are on backorder from the manufacturer. These will be run when the reagents are received.

Released for Study on 4-11-88.

Released from Quarantine 4-11-88.

DeJurell 4/15/88
Technologist

Stacy Kone 4/15/88
Veterinarian

Hast
Evanoff
Brown

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 5/3/88

Lab no: R-83
Animal/Shipment no: 880043
Date rc'd: 3/16/88
Source: CR P03
Species/Strain: Rat/CD
Sex: M/F Age: BD 1/18/88

Status: Ten rat blood specimens submitted for terminal sacrifice serology

Serology: Rat

0/10	Sendai virus
0/10	Pneumonia virus of mice
0/10	RCV/SDAV
0/10	KRV/H1

*Number of positive tests/number tested

Correlation/Summary

The 10 sera submitted were negative for antibodies to those common rodent pathogens listed above. This is good evidence that no study animals were infected by any of these pathogens. This data supports the previous presumption that the one reaction to RCV/SDAV in the 10 pre-exposure health screen sera was a false positive. Neither the pre-exposure sera nor these sera were tested for antibodies to Mycoplasma pulmonis since the reagents have been on back order from the manufacturer for some time. These will be run when the reagents are obtained.

AE Garrell 5/6/88
Technologist

John C. Rowe 5/6/88
Veterinarian

Mast
Evansoff
Brown

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: IRT Isoprene
Building: LSL II
Room: 433
Date initiated: 5/3/88

Lab no: R-83 (addendum)
Animal/Shipment no: 880043
Date rec'd: 3/16/88
Source: CR P03
Species/Strain: Rat/CD
Sex: M/F Age: BD 1/18/88

Status: Ten rat blood specimens submitted for terminal sacrifice serology

Serology: Rat

0/10 * Mycoplasma pulmonis

*Number of positive tests/number tested

Correlation/Summary

None of the sera tested had antibodies for M.pulmonis.

CEG/AMU 5/24/88
Technologist

Stacy E. Rowe 5/24/88
Veterinarian

Mast
Evanoff
Brown

APPENDIX E

QUALITY ASSURANCE STATEMENT

TERATOLOGY STUDY OF ISOPRENE IN MICE AND RATS
(Final Report)

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, 3/01/88 - 5/15/88, or specifically for this study and the dates the reviews were performed and findings reported to management. (All findings were reported to the study director or his designee at the time of the review.)

Phase/Procedure Reviewed	Review Date	Date Findings Submitted in Writing to Study Director/Management
Animal Receipt	1/19-20/88*	1/20/88
Animal Receipt	2/25/88*	2/26/88
Dosing	3/14/88	3/30/88
Health Screen	4/04/88*	4/08/88
Identification	4/04/88*	4/08/88
Body Weights	4/04/88*	4/08/88
Necropsy	4/27/88 & 5/05/88*	7/25/88
Data	5/03/88*	5/03/88
Data	5/25-27/88*	6/20/88
Data	6/14 & 7/04/88*	7/04/88
Data	7/22,25-27/88*	8/10/88
Final Report	2/6-8 & 17/89*	2/17/89

*Reviewed specifically for this study

[Quality Assurance Unit]

2/17/89

APPENDIX F

PROTOCOL AND CAGE MAPS

STUDY PROTOCOL

**Inhalation Teratology Study of Isoprene
in Mice and Rats**

Submitted to:

**Dr. Bernard Schwetz
Dr. Richard Morrissey
National Toxicology Program
National Institute Environmental Health Sciences
Research Triangle Park, NC**

Submitted by:

**Dr. Terryl J. Mast
Battelle - Pacific Northwest Laboratory
Richland, WA 99352**

February 6, 1988

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INHALATION REPRODUCTIVE TOXICOLOGY STUDY PROTOCOL
ISOPRENE

I. TITLE: TERATOLOGY STUDY OF ISOPRENE IN MICE AND RATS

II. INTRODUCTION

Isoprene, originally isolated as a pyrolysis product of natural rubber, is now used in large quantities for the manufacture of polyisoprene, and in smaller proportions as a copolymer with isobutylene for the synthesis of butyl rubber (Saltman, 1981). Worldwide production of isoprene was reported to be 650,000 metric tons in 1976. Isoprene is also a basic building block in many natural products, e.g. terpenes, camphors, and vitamins A and K, and is a normal constituent of human breath. Isoprene occurs naturally in the atmosphere as a result of volatilization from plant surfaces and from combustion.

PHYSICAL AND CHEMICAL PROPERTIES

Table 1. Summary of Physical and Chemical Properties

Isoprene ^a	
Synonym: 2-methyl-1,3-butadiene	MW: 68.1
Molecular Formula: C ₅ H ₈	CAS No.: 78-79-5
Colorless, flammable, volatile liquid	RTECS No.: NT4Ø37ØØØ
Forms peroxides upon standing	
Melting Point: -145.95°C	Boiling Point: 34.1°C (93°F)
Flash Point: -54°C (-65°F)	Specific Gravity: 0.6759 g/cm ³
(25°C)	
Vapor Density: 2.4 (air = 1)	
Flammability Limits (by volume):	
Lower: 15,000 ppm	Upper: 89,000 ppm
Solubility:	
Miscible in most common hydrocarbons	
Practically insoluble in water, DMSO, ethanol, acetone	
TLV: None established	

^a Condensed from Little (1987) and references therein.

Isoprene is a highly reactive, branched diene and undergoes reactions similar to those of butadiene (e.g. peroxide and dimer formation). Acting as both a diene and a dienophile it readily forms dimers via a Diels-Alder addition mechanism; the predominant product is limonene. The chemical is no longer considered suitable for use in inhalation exposures when the limonene dimer concentration reaches a level of >1%. An inhibitor, 40-48 ppm t-butylcatechol (MRI, 1986), is added to isoprene to prevent formation of dangerous peroxides. [Significant levels of either peroxides or the limonene dimer are prevented from reaching animal exposure chambers by isoprene vapor generation methodology (BNW, 1986).]

METABOLISM AND PHARMACOKINETICS

Isoprene may be metabolized *in vitro* to either of two epoxides (compounds II and III, Figure 1) which can then be further oxidized to diols, or in the case of compound III, to the mutagenic diepoxide, compound IV. Formation of these oxidation products has been shown to occur in liver microsomes prepared from rats, mice, rabbits, or hamsters, and the reactions are presumably catalyzed by the P_{450} -monooxygenase complex (Longo, Citti, and Gervasi, 1985). Pre-treatment with phenobarbital resulted in an increased V_{max} for the microsomal oxidation of compound III in all species tested.

Inhalation studies in male Wistar rats and B6C3F1 mice (Peter et al. 1987) have shown that the rate of isoprene metabolism ($\mu\text{mol/h}\cdot\text{kg}$) is directly proportional to chamber concentrations up to about 300 ppm. At greater exposure concentrations saturation kinetics apply and the maximal rate appears to be about 130 and 400 $\mu\text{mol/h}\cdot\text{kg}$ for rats and mice, respectively. Thus, the half-life of the parent compound, isoprene, for exposure concentrations above 300 ppm is approximately 44 min for rats and 18 min for mice. The half-life for isoprene at exposure concentrations <300 ppm is 6.8 min in rats and 4.4 min in mice. Unfortunately, neither the duration of the exposures nor the number of exposure days test animals were exposed were reported for this study.

A recent study on the fate of inhaled isoprene in rats (Dahl et al. 1987) provided considerable insight into the toxicokinetics of isoprene during, and following, a single exposure. Male F344 rats were exposed to 8, 266, 1480, or 8200 ppm ^{14}C -isoprene for a duration of up to 6 hr. They found that: 1) 5% of the metabolites associated with isoprene exposure were excreted in the urine within a 66-hr post-exposure period, 2) 3 to 20% of the metabolites were excreted in the feces or exhaled as CO_2 , and 3) 8-18% remained in the body after 66 hr. The concentration of circulating metabolites generally increased with increasing exposure concentration, as well as with the duration of exposure. The percent of original material present as the isoprene diepoxide and/or as the diols remained relatively constant as a function of time for the two lower concentrations, but increased as the exposure concentration increased. The percent of inhaled ^{14}C -isoprene retained by the animal immediately after exposure decreased with increasing dose (e.g., from 19% at 8 ppm to 4.5% at 8200 ppm). The half-life for urinary excretion of ^{14}C in the rat was 10.2 ± 1 hr (mean $\pm$ SE), considerably longer than the half-life of less than one hour reported by Peter et al. (1987) for the parent compound only. Since it is the metabolites of isoprene that are suspected of causing genotoxicity (see below), the half-life for urinary excretion is probably of more toxicological significance than is the half-life for the parent compound.

Dahl et al. (1987) also reported that the diepoxide/diol metabolites achieved maximal blood levels following a 6-hr exposure to 1480 ppm isoprene. Exposure to a higher concentration, 8200 ppm, for 6 hr did not increase the blood levels of these metabolites. Furthermore, blood levels of the parent compound, isoprene, appeared to be maximal immediately following a 2-hr exposure to 8200 ppm, and did not increase with a longer exposure period. Tissue distribution studies showed that fat, followed by blood, had the highest diepoxide/diol metabolite concentrations following a 6-hr exposure to 1480 ppm isoprene. Both isoprene and metabolite levels had decreased substantially after an 18-hr recovery period.

Figure 1. Proposed metabolism of isoprene by liver microsomes (modified from Gervasi et al. 1985). Compound IV is highly mutagenic.

In summary, Dahl et al. (1987) demonstrated that isoprene is metabolized to a considerable extent in male F344 rats; however, the metabolic capacity is apparently saturated by exposure concentrations at or above 1480 ppm. Since these data were collected following single exposures, the potential for the induction of the metabolizing capabilities during repeated exposures cannot be assessed. Furthermore, there are apparent conflicts between these results and those of Peter et al. (1987) who reported saturation of the metabolic rate at a lower exposure concentration, ≈300 ppm. Resolution of these discrepancies is difficult since the methodology used to generate data in the report of Peter et al. (1987) is not well defined.

Isoprene, which has a high octanol to water partition coefficient, should be readily absorbed via the lung. This was shown to be the case by Egle and Gochberg (1975) who found that: 1) the retention of inhaled isoprene in the dog was 74-76%, and 2) that the amount retained was not affected by the ventilatory rate. The amount of isoprene retained remained in this range up to an atmospheric concentration of approximately 0.72 µg/ml (≈264 ppm) and then declined. At a concentration of 0.96 µg/ml (≈367 ppm) the amount of isoprene retained dropped to ≈40 percent. The decrease in the percent of isoprene retained as the exposure concentration increases

may in part account for the discrepancy between the retention values reported by Egle and Gochberg (1975) for the dog (74-76%), and the considerably lower values reported by Dahl et al. (1987) for the rat. In the latter study where the rats were exposed to concentrations as high as 8000 ppm the retention values were only 5-19%.

TOXICOLOGY

In vitro

Salmonella mutagenicity assays in strains TA1530, TA1535, TA100, TA98, or TA1538, in the presence or absence of liver microsomes from Aroclor-induced rats, were negative (deMeester et al., 1981). Isoprene was also negative in Ames/*Salmonella* assays conducted by the NTP (unpublished results).

Although isoprene itself was not found to be mutagenic in the above mentioned studies, work by Gervasi, et al. (1985) showed that a diepoxy metabolite of isoprene, 2-methyl-1,2,3,4-diepoxybutane (Del Monte, Citti, and Gervasi, 1985), was highly mutagenic to *Salmonella* strains TA98 and TA100. Furthermore this compound was shown to have a half-life and mutagenic and alkylating activities similar to the well known mutagenic, clastogenic, and carcinogenic compound, 1,2,3,4-diepoxybutane.

Recent studies in B6C3F1 male mice conducted by the NTP assessed the cytogenetic toxicity of isoprene (Tice et al. 1987). Using bone marrow and peripheral red blood cells the following endpoints were measured: 1) the average generation time (AGT), 2) mitotic index (MI), 3) chromosomal aberrations (CA), 4) sister-chromatid exchange (SCE), 5) percent polychromatic erythrocytes (%PCE), 6) micronucleated PCE (MN-PCE), and 7) micronucleated normochromatic erythrocytes (MN-NCE). Multiple exposures of 4-5 week old male mice (exposed 12 out of 16 days) to 0, 438, 1750, or 7000 ppm isoprene for 6 h/day caused an exposure-correlated increase relative to controls in the AGT, MN-PCE and MN-NCE. The mean frequencies for SCE and CA were also elevated above controls, but values plateaued above 438 ppm isoprene. Increases in frequencies for CA, SCE, and/or MN-PCE or MN-NCE were indicative of the induction of genotoxic damage, while alterations in AFT, MI, and %PCE reflected cytotoxicity resulting from either genotoxic damage or from independent mechanisms. Results from these studies indicate that isoprene exposure induces somatic genotoxicity in these mice. The increase in micronucleated erythrocytes is consistent with the induction of DNA damage observed in the presence of an S-phase dependent clastogen. The plateau effect observed in the elevation of micronucleated erythrocytes and SCE frequencies suggests a saturation of the capacity of the mice to metabolize isoprene. The apparent saturation of the capacity of experimental animals to metabolize isoprene at higher exposure concentrations is consistent with the results reported by Dahl et al. (1987) and Peter et al. (1987), mentioned above.

Animal Studies

Acute:

Isoprene has been considered to be more toxic than butadiene. The LC₅₀ value for 2-hour exposure to isoprene is about 50,000 ppm for mice, while the LC₅₀ value for rats exposed to isoprene for 4 hours was 64,500 ppm (Shugaev, 1969; Sandmeyer, 1981). Gage (1970) observed no signs of

toxicity or histopathologic changes in rats after 15 6-hour exposures to 1670 ppm or after six 6-hour exposures to 6000 ppm (two rats/sex/group).

A Russian study (Mamedov, 1979) reported a decreased cellularity and mitotic index in the thymus as well as a reduced thymus weight one day after a single inhalation exposure to 8.4 mg/L (=3,200 ppm) isoprene [species not reported]. The first two indices normalized after two days. At a higher dose level, 21.4 mg/L (=8,180 ppm), the number of circulating lymphocytes also increased. Subacute experiments revealed similar affects after 2-4 days of exposure, but by the end of the 30-day exposure period most parameters had normalized. Chronic [sic] exposure of 4 months duration (0.0108 (=4 ppm) and 0.116 (=44 ppm) mg/L; 4 h/day) were reported to cause "unfavorable" changes in the lymphoid tissue. [This information was obtained from an abstract, not the original article.]

Repeated Dose:

A repeated dose study designed to characterize the toxicity, to identify target organs, to determine the "no-effect" level, to establish the differences in sensitivity between species and sexes, and to determine the slope of the dose-response curve associated with two weeks of inhalation exposure to isoprene has been conducted in mice and rats (BNW, 1987). Male and female F344/N rats and B6C3F1 mice were exposed to 0, 438, 875, 1750, 3500 and 7000 ppm isoprene, 6 hr/day, 5 day/wk, for two weeks. Animals were exposed for a total of 12 days.

Results from the rat study indicated that isoprene, at the above-listed exposure levels, caused no deaths and no clinical signs of toxicity. When treated animals were compared to controls there were no significant differences in body weight gain or in the organ to body weight ratios. Hematology parameters, clinical chemistry measures, and urinalysis values were not altered with respect to controls after 4 days of exposure. Neither gross lesions nor histopathological changes attributable to isoprene exposure were observed at terminal necropsy.

In the mouse study isoprene exposure did not result in deaths or cause clinical signs of toxicity. However, body weight gain with respect to controls, as well as the mean testis to body weight ratios, were decreased in male mice in an exposure-related fashion. Body weights of female mice were not affected. In both sexes liver to body weight ratios were increased, and thymus and spleen ratios were decreased, for all exposure levels. Changes in these ratios were directly proportional to exposure concentrations in all cases. The increase in the liver to body weight ratio as compared to controls was statistically significant for all exposure levels for both sexes.

Clinical pathology results in animals after 4 exposures indicated a slight non-regenerative anemia in all exposure levels, but there were no observable effects on hepatic or renal function. Focal, raised or thickened areas at the pole of the forestomach were observed in all exposure concentrations for both sexes at trimming. Subsequent histopathological evaluations demonstrated the presence of forestomach epithelial hyperplasia. Histopathological evaluations also showed olfactory epithelial degeneration at 7000, 3500, and 1750 ppm in male mice, and testicular atrophy at 7000 ppm. Male mice also had vacuolized hepatocellular cytoplasm at all exposure concentrations.

Subchronic:

No effect on weight gain in mice, rabbits, or rats with respect to controls was observed following 4 to 5 months of 4 hr/day exposures to 790 - 1750 ppm isoprene (Sandmeyer, 1981). However, prolonged exposure to isoprene has been suggested to affect the function of the central and autonomic nervous system of mice, rabbits, and rats (CRCS, 1984).

Chronic:

No information was found addressing the chronic toxicity of isoprene.

Reproductive and Developmental:

Isoprene administered orally to pregnant female Wistar rats at 0, 22, 379, or 1895 mg/kg from 9-12 days of gestation (dg) had no effect on maternal weight gain, but caused increased fetal death and retarded ossification of the sternebrae with respect to controls (Komatsu, 1971 cited in CRCS, 1984). These effects were not dose-related.

Human

No studies addressing chronic effects of human exposure to isoprene were found in the literature.

SUMMARY

Repeated exposure of F344 rats or B6C3F1 mice to isoprene concentrations as high as 7000 ppm did not result in clinical signs of toxicity. However, there was considerable evidence that isoprene, or one or more of its metabolites, caused either cyto- or genotoxicity. The capacity of rodents to metabolize isoprene apparently becomes saturated at exposure concentrations greater than ~400 ppm. However, since both *in vitro* and *in vivo* results indicate that exposure to isoprene induces the P₄₅₀-monooxygenase system, the metabolic capacity of the animals may increase with repeated exposures. Studies on the retention of inhaled isoprene indicate that retention appears to decline with increasing exposure concentrations.

RECOMMENDATIONS

Based on the results of the cytotoxicity studies, isoprene may have a significant potential to cause fetotoxicity in offspring exposed *in utero*. Therefore, a two species teratology study in Sprague-Dawley rats and CD-1 mice is recommended. Exposure concentrations of 0, 280, 1400, and 7000 ppm are suggested on days 6-17 of gestation in mice, and 6-19 in rats, for a duration of 6 hours per day. Since there is some indication that isoprene exposure may result in induction of the P₄₅₀-monooxygenase complex maternal liver, kidney, and adrenal weights should be obtained in addition to whole body and uterine weights.

III. SPONSOR AND SPONSOR'S REPRESENTATIVE

A. Sponsor:

National Institute of Environmental Health Sciences
National Toxicology Program (NTP)
P.O. Box 12233;
Research Triangle Park, N.C. 27709

B. Sponsor's Representatives:

Dr. Bernard Schwetz
Dr. Richard Morrissey

IV. TESTING LABORATORY

A. Facility

Battelle - Pacific Northwest Laboratory (PNL)
P.O.Box 999; Richland, Washington 99352

B. Study Director:

Dr. Terryl J. Mast

V. PROPOSED SCHEDULE OF EVENTS (THIS PROPOSED SCHEDULE MAY BE
ALTERED. ALL CHANGES WILL BE APPENDED TO THE PROTOCOL.)

	<u>Mice</u>	<u>Rats</u>
A. Animals arrive week of:	1/18/88	1/18/88
B. Identification of females:	2/11/88	2/16/88
C. Health screen:	2/8/88	2/8/88
D. Prestart audit for GLP compliance:		2/11/88
E. Initiate breeding procedures:	2/17/88	2/22/88
F. Initiate exposure :	2/24/88	2/29/88
G. Initiate necropsy:	3/7/88	3/14/88
H. Complete exposure:	3/10/88	3/17/88
I. Evaluate fetal specimens:	3/21/88	4/4/88
		<u>Combined</u>
I. Submit draft report:		5/15 88
J. Submit final report:		7/15 88

VI. TEST SYSTEM

A. Species: mice and rats

B. Strain: Mice: CrI:CD-1(ICR)BR; rats: Sprague-Dawley
[CrI:CD(SD)BR]

C. Number of Animals and Supplier:

Mice from Charles River Breeding Laboratories, Raleigh, NC.
Mice: 90 males
330 females

Rats from Charles River Breeding Laboratories, Portage, MI
Rats: 55 males
250 females

D. Age of Animals Upon Arrival: Mice: 7-8 weeks
Rats: 7-8 weeks

E. Experimental Animals (Females): 40 virgin female mice or rats will be randomly selected and assigned to four dose groups (10/group) from the total female pool (ØB-DT-3BØB). The remaining females will be mated by placing at least two females with one male overnight in a breeding cage (ØB-DT-3BØD). Nine AM of the day that copulation is established will be designated as 0 dg (ØB-DT-3BØD).

F. Number of Animals in Study: A [~~minimum~~ approximately]^{6A} of 33 plug-positive female mice or 30 sperm-positive rats (to obtain 20 pregnant females) will comprise each of the four treatment groups; the minimum number of mated females to be exposed will be 132 mice or 120 rats. There will also be 10 virgins (females) of each species per exposure level.

VII. EXPERIMENTAL DESIGN AND DOSE LEVELS

A. Experimental Design: Four groups of mated female mice will be exposed to the test chemical on 12 consecutive days (6 dg - 17 dg). The animals will be necropsied on 18 dg for maternal and fetal evaluations.

Four groups of mated female rats will be exposed to the test chemical on 14 consecutive days (6-19 dg). The rats will be necropsied on 20 dg for maternal and fetal evaluations.

In addition, 10 virgin females of each species will be added to each exposure group for the purpose of obtaining ovaries to be used for quantitative ovarian follicle counts. These

^{6A} Changed 9/6/88 Amendment A.

animals will be exposed, 12 consecutive days for mice and 14 consecutive days for rats, concurrently with the mated females and sacrificed one day after their last exposure period.

- B. Exposure Regimen: Chamber atmospheric concentrations of isoprene will be 0 (filtered air), 280, 1400, and 7,000 ppm. Plug-positive and virgin mice will be exposed for 6 hrs/day for 12 consecutive days (6 dg - 17 dg); sperm-positive and virgin rats for 14 consecutive days (6 dg - 19 dg), 6 hr/day. The exposure chamber doors will be closed throughout the exposure and non-exposure periods, except during animal care procedures. Exposure chamber temperatures will be maintained at $75 \pm 3^{\circ}\text{F}$ and relative humidities at $55 \pm 15\%$. Air flow will be maintained at 15 ± 3 cfm and the chamber pressure at approximately 1" water negative with respect to room pressure.
- C. Selection of Atmospheric Concentrations: Exposure chamber concentrations are based partly on information obtained from previously published reports on inhalation toxicology studies of isoprene and partly on safety considerations. Safety considerations limit the maximum exposure concentration to 50% of the lower explosion limit ($\approx 15,000$ ppm) which is 7,000 ppm.

VIII. TEST SYSTEM HOUSING, HANDLING AND ENVIRONMENTAL CONDITIONS

A. Quarantine and Acclimatization (ØB-AR-3FØ3)

1. Animal shipping crates will be examined upon arrival for evidence of conditions likely to permit exposure to pathogens (soiled, wet or otherwise damaged).
2. The uncrating will be conducted at the door of the quarantine room. While being removed from the crates the animals will be examined for evidence of shipping stress.
3. The animals will be quarantined and acclimatized in the LSL-II Building for 3-4 weeks prior to the start of the study.
4. During part of the quarantine/acclimatization period the animals will be housed by sex, approximately 10 mice or 5 rats per cage in wire cages on flush racks. The cage space will meet the requirements stated in the NIH "Guide for Care and Use of Laboratory Animals".
5. During the breeding period the animals will be housed in the quarantine room.
6. Plug-positive mice or sperm-positive rats will be acclimated from 0 dg in individual compartments of wire-mesh cages within exposure chambers (with chamber doors open). Virgin females will be acclimated for approximately 1 week prior to exposure under the same conditions.
7. Room temperature during the acclimatization and exposure periods will be maintained at $75 \pm 3^{\circ}\text{F}$ and relative humidity at $50 \pm 15\%$. These measurements will be recorded at least twice daily.

8. Twelve hours light and twelve hours dark will be maintained with light starting at 0600.
9. At least ten animals from each shipment will be randomly selected for pre-exposure health screening (ØB-AR-3FØ2). They will be examined by gross necropsy, histopathology and nasopharyngeal culture for evidence of disease and the presence of potentially pathogenic organisms.
10. The clinical veterinarian will make a visual inspection of the animals to be used in the study just prior to their release for the study (documented on the quarantine/ acclimatization record).
11. As an added screen for viral infection, 5 animals from the control group and 5 animals from the highest dose group will be tested promptly after sacrifice at BNW for viral pathogens (ØB-AR-3B1R).
12. Females not selected for the study or health screen will be discarded during the first exposure week. The disposition of these females will be recorded on the Animal Disposition Record and retained in the study files (ØB-AR-3FØ3). Males, (they are not individually identified) will also be discarded.

B. Feed (ØB-AR-3FØ5)

1. NTP pre-approved NIH-07 Open Formula Diet (pellets) from Ziegler Bros., Inc., Gardner, PA will be used during the quarantine/acclimatization periods and throughout the duration of the experiment.
2. Feed will be provided ad libitum in slot feeders during the experiment, except during exposure hours.

C. Water

1. Fresh softened water (ion exchange softener, Illinois Water Treatment Company, Model 2R-2240, Rockford, IL) will be supplied ad libitum at all times. The hardness of the water will be checked approximately once every week. Records will be retained in the LSL-II Building Engineer's office.
2. The automatic watering system (Edstrom Industries, Waterford, WI) will be used for the quarantine/acclimatization period and throughout the duration of the study.
3. A representative sample of animal drinking water from one of the NTP study rooms will be analyzed for contaminants at least once each calendar year.

- D. Randomization:** Virgin females will be randomly chosen from the pool of female animals based on the first body weight (taken at the time of ear tagging). During the week prior to the start of exposure virgins will be weighed and randomly assigned to a treatment group by means of a computer-assisted randomization program which is based on a single blocking factor,

[randomization program which is based on a single blocking
factor, body weight (ØB-DT-3BØB).]^{+A}

^{+A} Added 9/6/88.

On the day of plug or sperm detection (0 dg), the mated animals will be weighed and assigned to dose groups as described above.

E. Identification:

1. All female animals will be individually identified by metal ear tags during the first weighing session (ØB-AR-3FØC)
2. Cage maps (ØB-DT-3BØ3) showing placement of individual animals in each cage unit of the exposure chamber will be prepared and updated as needed. Each exposure chamber will be identified by chamber number and exposure level. The proposed arrangement of the exposure chambers is included in Figure 2.

IX. TEST ARTICLE

A. Chemical name: Isoprene

B. Formula: C_5H_8

C. CAS No.: 78-79-5

D. Manufacturer: Goodyear Tire and Rubber Co.
Beaumont Chemical Plant
Beaumont, TX 77704

E. BNW LOT No.: 12102-115

F. The vehicle control will be filtered air.

G. Storage conditions: The reservoir is maintained in a flammable storage cabinet at room temperature in the LSL-II Building. The remaining inventory is stored at or below 75°F in a chemical storage facility adjacent to the LSL-II building.

H. Analytical Chemistry

1. Upon receipt, identity and gross purity analyses of the bulk chemical will be performed by infrared spectroscopy. Bulk purity is periodically determined using gas chromatography.
2. Isoprene concentrations within the exposure chambers will be monitored using an HP-5840 gas chromatographic system.

Detector: Flame Ionization
Column: 1 ft x 1/8" OD nickel
Packing: 1½ SP-1000 on Carbopack B
Column Temperature: 120°C

Figure 2. Layout of Exposure Room for Isoprene

Carrier: Nitrogen
Carrier Flow: 20-30 ml/min
Sample Valve: Hastalloy C mounted in GC oven (Valco)
Sample Loop: One ml nickel
Stream Select Valve: 12-port, Hastalloy C mounted in GC oven (Valco)

On-Line Standard: 2000 ppm isoprene in N₂
(MG Industries)

Calibration Frequency: Daily check against on-line standard, additional checks against grab samples as indicated by the on-line standard and as indicated by I.8.

Control Range: Target concentration $\pm 10\%$

Critical Limits: Target concentration $+20\%$, alarmed
(shut off gas flow to the chamber)

Target concentration -20% , alarmed
(operator makes necessary adjustments and documents the excursion).

3. The calibration of the on-line chamber monitor is based on analysis of bubbler grab samples. The calibration of the on-line monitor is directly tied to gravimetrically prepared standard solutions in dimethylformamide (DMF) through a GC which is off-line. The gravimetrically calibrated off-line GC is used to measure the quantity of isoprene collected from exposure chambers in DMF filled bubblers. The relationship between the peak area observed with the on-line GC and the concentration of isoprene in the chamber is then defined using chamber concentrations determined by the gravimetrically calibrated GC. The analysis of bubbler grab samples is performed using a HP5840 GC with a 1.8m by 2mm i.d. glass column packed with 20% SP2100/0.1% Carbowax 1500 on 100/120 mesh Supelcoport with an oven temperature of 55°C (with follow-up temperature programming to elute the DMF solvent peak).
4. The major product of dimerization of isoprene is limonene. Test material with a limonene concentration greater than 10,000 ppm (1%) limonene is unacceptable for use as test material. The concentration of the limonene dimer is determined using a gas chromatographic internal standard method with a column packed with 20% SP2100/0.1% Carbowax 100/120 Supelcoport.
5. Peroxide in the bulk test material is determined using an iodometric titration with a potentiometric endpoint.
6. Building exhaust effluent is analyzed for residual test material by sample collection on charcoal followed by DMF spiked with hexane internal standard desorption and analysis by gas chromatography.
7. Chamber samples are analyzed for degradation products by sample collection on charcoal followed by dodecane desorption and analysis by gas chromatography.

Gas Chromatographic Conditions for Analysis of Charcoal
Absorption Tubes

Instrument:	Hewlett Packard 5830
Column:	Six foot by 4 mm ID glass, 100/120 mesh Supelcoport with 20% SP 2100/0.1% Carbowax 1500
Initial Temperature:	50°C
Initial Isothermal Time:	5 min
Temperature Program rate:	10°C/min
Final Temperature:	200°C
Final Time:	9 min
Detector:	FID
Detector Temperature:	250°C
Injector Temperature:	200°C
RT Unk Bulk Impurity:	~1.3 min
RT Isoprene:	~1.65 min
RT limonene:	~15.1 min
RT Dodecane (desorbent):	~18.7 min

I. Analysis Schedule

1. Purity analysis will be performed on the bulk chemical upon receipt, at four month intervals thereafter, and will be performed within 30 days of the start of animal exposures.
2. The highest concentration exposure chamber will be monitored for residual isoprene before the start and during the study.
3. The building exhaust will be monitored for residual chemical once during the study.
4. The composition of residual test material taken from the generator at the end of an exposure day will be characterized prior to the start of the study. This will include a determination of peroxide and limonene content.
5. The stability of the test material in the highest and lowest concentration exposure chambers will be characterized prior to the start of the study. This characterization will be repeated with occupied chambers following the initiation of animal exposures.
6. Each lot of test material will be assayed for peroxide content within 30 days preceding use as test material.
7. Dimer content of the bulk test material will be determined within two weeks preceding and following use as test material.
8. During exposures the on-line monitor calibration will be confirmed by quantitative analysis of grab samples during the first week of exposure and every other week thereafter.
9. Drift of the on-line monitor calibration will be checked daily against an on-line compressed gas standard.

X. DESCRIPTION OF INHALATION EXPOSURE SYSTEM

The inhalation chambers will be located in Room 436 of the LSL-II building. A detailed description of the inhalation exposure system to be used in this study is included in Attachment 2 of this protocol. The location of the exposure room and chamber layout are shown in Figure 2.

A. Environmental Monitoring

1. Air filtration: HEPA and charcoal filters will be used for intake air, and a HEPA filter will be used for exhaust air.
2. Temperatures will be monitored by RTDs multiplexed to a digital thermometer with computer data acquisition at approximately 4-hour cycles for 24 hours per day. The control range is $75 \pm 3^{\circ}$ F with critical limits, <70 or $>80^{\circ}$ F. Any chamber temperature excursion beyond the critical limits will be recorded and alarmed automatically.
3. Relative humidity will be monitored by a single dew point hygrometer in conjunction with a multiplexed sampling system with computer data acquisition at approximately 4-hour cycles, 24 hours per day. The control range is $55 \pm 1\%$ with critical limits of $<35\%$ or $>75\%$. Any relative humidity excursion beyond the critical limits will be recorded and alarmed automatically.
4. Chamber air flow will be monitored at an exhaust orifice using a multiplexed Validyne pressure transducer system with computer data acquisition at approximately 4-hour cycles, 24 hours per day. The control range is 15 ± 3 air changes/hour (15 ± 3 CFM) with critical limits of <10 CFM or >20 CFM. Any chamber flow excursion beyond critical limits will be recorded and alarmed automatically. A critically low flow will result in automatic termination of the exposure. Isoprene concentrations in the chambers will be controlled primarily by the adjustment of chamber air flow.
5. Chamber vacuum will be monitored using a multiplexed Validyne pressure transducer system with computer data acquisition at approximately 4-hour cycles, 24 hours per day. The control range is -0.2 to -2.0 inches of water pressure with critical limits set at the same values. Any chamber vacuum excursion beyond the critical limits will be recorded and alarmed automatically. If chamber vacuum exceeds the limits of -0.2 inch of water, the exposure will be automatically terminated.
6. Uniformity of the concentration of the test chemical in each of the chambers will be determined during the development of exposure generation without animals. Chamber uniformity will be verified within the first week of the rat teratology study and again within the first week of the mouse study. A between port and within port variability of $\leq 5\%$ RSD will be considered acceptable.
7. The exposure chambers test chemical buildup and decay time will be determined prior to start of the study to determine the T_{90} value. These curves will be verified within the first

week of the rat study and again within the first week of the mouse study.

8. Prior to the start of the study and once in the high level chamber during the rat study, samples will be taken from all chambers using a Gardner condensation nuclei counter to assure that the vapor generation does not produce an aerosol of Isoprene.
9. A study of test material stability in the exposure chambers and in the generator reservoir will be conducted during the developmental work without animals in the chambers and once during the first week of the mouse exposures. The chamber samples will be taken from the high and low dose chambers during the last hour of exposure. A generator reservoir sample will be taken at the end of an exposure day.

B. Effluent Treatment

Chamber exhaust will be diluted to comply with applicable State and Federal Regulations prior to release from the building exhaust stack.

XI. EXPERIMENTAL OBSERVATIONS

- A. Clinical Observations: The animals will be observed daily for mortality, morbidity, and signs of toxicity (JB-DT-3B03). The date and time of death or euthanasia of moribund animals will be recorded and the animals will be necropsied by trained prosectors (JB-DT-3B0F).
- B. Body Weights: All females will be weighed prior to mating. Plug-positive mice will be weighed on 0, 6, 9, 12, 15, and 18 dg (JB-DT-3B0C). Sperm-positive rats will be weighed on 0, 6, 10, 14, 17, and 20 dg. Virgin females will be weighed on the 1st, 5th, 10th day of exposure and at sacrifice.
- C. Scheduled Necropsy: The mice are scheduled to be euthanized with CO₂ on 18 dg and the rats on 20 dg. At necropsy (JB-DT-3B0G) maternal animals will be weighed and examined for gross tissue abnormalities. Maternal liver, ~~adrenals~~^{-A} and kidney weights will be obtained at the time of sacrifice. In order to document the presence of lesions which may be due to chemical exposure, any organs or tissues with lesions will be preserved in neutral buffered formalin (NBF); in this case, comparable organs or tissues from approximately 20% of the control animals will be preserved in NBF; all other tissues will be discarded.

^{-A} Deleted 9/6/88 Amendment A. F.20

The uterus will be removed and weighed, and the number, position and status of implants will be recorded. The placentas will be examined. Any apparently non-gravid uteri will be stained with 10% ammonium sulfide to detect implantation sites. The identity of live fetuses (by study, dam number and uterine position) will be retained throughout all examinations and archiving. Live fetuses will be examined for gross defects and weighed. Following euthanasia, a complete visceral examination will be performed on 50% of all fetuses and on any fetuses with gross abnormalities.

(ØB-DT-3BØG). Sex will be determined on all fetuses by internal examination. All skeletons will be double-stained and examined for cartilage formation and centers of ossification (ØB-DT-3BØG); however, ~50% of these will have had their heads removed. These fetal heads will be examined by razor-blade sectioning fixation in Bouin's fluid (Wilson, 1965; [ØB-DT-3BØI]). Records of morphologic lesions observed in gross and visceral examinations will include photographs (ØB-DT-3BØJ) of significant representative lesions.

Both ovaries from the virgin females and one ovary from each of the pregnant females will be collected at the time of sacrifice. (ØB-DT-3BØG). Collected ovaries will be fixed for 24 hr in Bouin's fluid then transferred to 70% ethanol, ~~and sent to Dr. Donald Mattison at the National Center for Toxicological Research for sectioning and quantitative follicle counts.~~ Rm 2/9/88

D. Indices of Effects: The following parameters, expressed as mean $\pm$ STD, when appropriate, will be computed from data for inseminated animals and their litters and will be presented in the Final Report for each treatment group:

- Number of dead maternal animals, animals removed from the study and reason for removal
- Summary of maternal toxicity, including incidence of changes detected during clinical observations
- Number and percent pregnant
- Maternal body weights:
 - Mice on 0, 6, 9, 12, 15 and 18 dg
 - Rats on 0, 6, 10, 14, 17, and 20 dg
- Weight of gravid uterus
- Maternal liver, adrenal, and kidney weights
- Extragestational weight and weight gain
- Number of implantation sites/litter
- Number of litters with live fetuses
- Number and percent of live fetuses/litter
- Body weight of live fetuses/litter
- Body weight of male and female fetuses/litter
- Sex ratio of fetuses/litter
- Number and percent of early and late resorptions/litter
- Number and percent of non-live/litter (early and late resorptions and dead fetuses)
- Listing of malformations and variations observed in fetuses/litters

(ØB-DT-3BØG) Sex will be determined on all fetuses by internal examination. All skeletons will be double-stained and examined for cartilage formation and centers of ossification (ØB-DT-3BØG); however, ~50% of these will have had their heads removed. These fetal heads will be examined by razor-blade sectioning [after]^{+A} fixation in Bouin's fluid (Wilson, 1965; [ØB-DT-3BØI]). Records of morphologic lesions observed in gross and visceral examinations will include photographs (ØB-DT-3BØJ) of significant representative lesions.

Both ovaries from the virgin females and [~~one ovary from each~~ ^{+A} the pregnant females will be collected at the time of sacrifice. (ØB-DT-3BØG). Collected ovaries will be fixed for 24 hr in Bouin's fluid then transferred to 70% ethanol and sent to [~~Dr. Donald Mattison at the National Center for Toxicological Research for the NTP for future~~]^{+A} sectioning and quantitative follicle counts.

D. Indices of Effects: The following parameters, expressed as mean $\pm$ STD, when appropriate, will be computed from data for inseminated animals and their litters and will be presented in the Final Report for each treatment group:

- Number of dead maternal animals, animals removed from the study and reason for removal
- Summary of maternal toxicity, including incidence of changes detected during clinical observations
- Number and percent pregnant
- Maternal body weights:
 - Mice on 0, 6, 9, 12, 15 and 18 dg
 - Rats on 0, 6, 10, 14, 17, and 20 dg
- Weight of gravid uterus
- Maternal liver, [~~adrenal~~]^{+A} and kidney weights
- Extragestational weight and weight gain
- Number of implantation sites/litter
- Number of litters with live fetuses
- Number and percent of live fetuses/litter
- Body weight of live fetuses/litter
- Body weight of male and female fetuses/litter

^{+A} Added 9/6/88 by Amendment A.

^{-A} Delete 9/6/88 by Amendment A.

^{+A} Changed 9/6/88 by Amendment A.

- Sex ratio of fetuses/litter
- Number and percent of early and late resorptions/litter
- Number and percent of non-live/litter (early and late resorptions and dead fetuses)
- Listing of malformations and variations observed in fetuses/litters

- Number and percent of malformed fetuses /litter *pm*
- Number and percent of litters with malformed fetuses

XII. PROPOSED STATISTICAL METHODS

The methods proposed for the statistical analyses of representative maternal, reproductive and fetal indices of effects are: summary statistics, N, mean, standard deviation, with accompanying ANOVA based on multiple comparisons where appropriate. Arc sin transformations will be performed on proportional incidence data. Further statistical analyses may be performed at discretion of sponsor.

XIII. RECORDS RETENTION

Records that accumulate during the study will be retained at BNW until requested and shipped to NTP archives. Some of these records may be presented as part of the protocol or reports. These will include but not be limited to the following records:

A. Personnel Records

1. List of BNW personnel participating in the study.
2. Name, address, and function of any outside consultant(s).
3. Record of removal of any individual from direct contact of the test system due to illness.

B. Health and Safety Records (original records and five copies of microfiche will be submitted to NTP within approximately two months after the end of each fiscal year). Chemical specific records will be submitted with the study. Facility specific records will be submitted annually.

1. Medical records of all personnel participating in the study. These records will be retained by Hanford Environmental Health Foundation (HEHF), P.O. Box 100, Richland, WA 99352 for a minimum of 40 years. A letter verifying this arrangement will be retained for each test material file.
2. Records and results of any biological monitoring on laboratory personnel (if applicable).
3. NTP Health and Safety package for Isoprene.
4. BNW biohazard protocols and BNW Health and Safety Plan.
5. Chemical specific health and safety training records.
6. Waste disposal records.
7. Respiratory protection program with documentation of user training (specific fit testing if needed) for each type of respirator.
8. Building ventilation system, hoods and exhausting system monitoring records (pertinent to NTP studies).

9. Health and Safety Section of the Monthly Progress Reports.
10. Accident/injury reports for personnel involved in this study.
11. NTP site visit reports, attention items and related correspondence on health and safety.

C. Protocols

1. Approved and dated BNW study protocol.
2. Protocol amendments including NTP technical contract modifications which affect the study.
3. Documentation of any deviation from the protocol.
4. Documenting any unforeseen circumstances that may affect the integrity of the study and corrective actions taken.

D. Test Material Records

1. Test material identity records including manufacturer, quantity, lot number(s), purity grade and date(s), etc.
2. NTP analytical contractor characterization reports.
3. NTP analytical contractor bulk stability reports.
4. NTP analytical contractor shipment records (if available).
5. BNW test chemical receipt records.
6. BNW storage records including storage conditions.
7. BNW bulk analysis and degradation records.
8. BNW method development records.
9. Chemical exposure generation system description and procedures.
10. Chamber concentration monitoring records, including GC tracings.
11. Uniformity (chamber balance) records.
12. Gas chromatograph calibration records.
13. Generation and chamber degradation study records.
14. BNW test material inventory and usage records.
15. Records of shipment to NTP repository of any unused test material.
16. Gas chromatograph maintenance records.
17. Aerosol determination records.

18. Chamber concentration buildup, decay, and overnight monitoring records.
19. Exposure generation operating parameter records.

E. Animal Records - Pretest

1. Animal receiving records including supplier, species, strain, birth week, sex, number of animals for each sex, receiving date and receiving conditions (photocopy of a representative animal shipping crate label).
2. Quarantine and acclimatization records.
3. Pretest health screening records and animal health notebook.
4. Randomization records.
5. Animal identification records.
6. Written release records from clinical veterinarian.
7. Disposal of excess animals.
8. Bedding type.

F. Animal Records - On Test

1. Exposure room location and chamber layout records.
2. Chamber cage map.
3. Cage type, rack type and the rotation scheme during study.
4. Cageboard type.
5. Type of watering system.
6. Body weight records.
7. Daily observation records
8. Clinical signs of toxicity records.
9. Serology data and reports.
10. Pathological specimen inventory records.

G. Feed

1. Feed tags with manufacturer, lot numbers and milling dates.
2. Feed analysis records as provided by NTP analytical contract laboratory.

H. Water

1. Annual water analysis.

2. Weekly water hardness check (records will be maintained in building engineer and/or building manager's office).

I. Quarantine Room, Exposure Room, and Inhalation Exposure Chamber Records

1. Exposure chamber description.
2. Exposure suite control center description.
3. Temperature raw data and daily and monthly summation reports.
4. Relative humidity raw data and daily and monthly summation reports.
5. Air flow raw data and daily and monthly summation reports.
6. Chamber vacuum raw data and daily and monthly summation reports.
7. Exposure system monitors calibration and maintenance records.
8. Description of the lighting system and light/dark regimen.
9. Sanitation procedures and pest control program.

J. All Relevant Correspondence

K. Reports

1. Monthly Progress Report.
2. Special study reports if any:
3. Incident reports (if applicable).
4. Final Teratology Report.

L. Internal Computer Generated Forms and Tables

1. Teratology results and statistical analyses.
2. Analytical chemistry results.
3. Exposure suite control center computer printouts.
4. XYBION printouts (if any).

XIV. OTHER SPECIFICATIONS

- A. This study will be performed in compliance with the FDA Good Laboratory Practice Regulations for Non-Clinical Laboratory Studies (21 CFR 58) except where deviations are required by the NTP January, 1984 General Statement of Work and subsequent modifications.
- B. This Protocol will be the controlling document in case of discrepancies between the Protocol and SOPs. If this occurs the Study Director is to be notified immediately for clarification.

- C. A list of all relevant Standard Operating Procedures (SOPs) for this study are present in Attachment I.

XV. HEALTH AND SAFETY

BNW's Health and Safety Plan (ØB-HS-3S1C) has been approved by NTP. In addition, a respiratory program is instituted. This is supplemented by using supplied-air respirators (ØB-HS-3S19) which will be worn by personnel during periods of animal care while the chambers are open and by having available self-contained breathing apparatus for use when entering a room under emergency conditions following a leak.

XVI. APPROVAL BY PNL

Terrell J. Mast
Study Director

Date: 2/8/88

R. A. Gelman
Quality Assurance Auditor

Date: 2/8/88

XVII. APPROVAL BY NTP

Bernard A. Schuety
Co-Study Officer

Date: 9 Feb 88

Richard E. Monissey
Co-Study Officer

Date: 2/9/88

XVIII. REFERENCES

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XIX. AMENDMENTS TO PROTOCOL

9/6/88 Amendment A

Page 8 VI.F: Changed "minimum" to "approximately".

Reason: To allow for natural experimental variation.

Page 10a VIII.D: Added "randomization program which is based on
a single blocking factor, body weight (ØB-DT-3BØB)."

Reason: Accidentally omitted in original protocol.

Page 16 XI.C: Deleted "adrenal".

Reason: Adrenal weight data are not sufficiently accurate.

Page 17 XI.C: Deleted "one ovary from each of".

Reason: The statement as originally written was incorrect.

Page 17 XI.C: Changed "Dr. Donald Mattison at the National
Center for Toxicological Research for" to "the NTP for future."

Reason: Change requested by Sponsor.

Page 17 XI.D: Deleted "adrenal".

Reason: See above.

ATTACHMENT 1

STANDARD OPERATING PROCEDURES FOR INHALATION REPRODUCTIVE
TOXICOLOGY STUDIES

REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY

ØB-DT-3BØ3	Cage Location Maps and Daily Observations
ØB-DT-3BØB	Randomization of Animals
ØB-DT-3BØD	Rodent Mating Procedures
ØB-DT-3BØF	Necropsies for Health Evaluation and of Dead or Moribund Animals
ØB-DT-3BØG	Developmental Evaluations for Teratology Studies
ØB-DT-3BØI	Examination of Fetal Heads Fixed in Bouin's Solution
ØB-DT-3BØY	Examination of Double-stained Fetal Rat and Mouse Skeletons.
ØB-DT-3B1J	Preparation of the Reproductive System for Histologic Evaluation
ØS-SI-3EØ1	Macintosh Data Collection System using Arbor Balance for Teratology and Dominant Lethal Sacrifice.
ØS-SI-3EØ3	Data Transfer from Macintosh to VAX using MacTerminal
ØB-HI-3GØ9	Operation of Sealer
ØB-HI-3FØ2	Shipping Histology Materials
ØB-BE-3B2M	Inhalation Room Procedures During Exposure Periods
ØB-AR-3GØH	Rodent Weighing using Toledo 8142 Automatic System
ØB-AR-3FØC	Rodent Identification with Ear Tags
ØB-AR-3DØ1	Handling and Care of Calibrated Standard Weights
ØB-AR-3FØT	Guidelines for Euthanasia
ØB-AR-3BØN	Moving Animals From the LSLII Animal Resources Section

ANIMAL FACILITIES

ØB-AR-3BØG	Barrier Procedures for LSL-II Animal Facility
ØB-AR-3GØ1	Pre-Cleaning Equipment and Operation of Cages - Bottle and Rack Washers
ØB-AR-3BØ3	Handling and Changing Out Exposure Chambers and Cage Units

ØB-AR-3BØ8	Handling Escaped Small Animals
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ØB-AR-3FØ2	Pre-Exposure Health Screening of Rodents
ØB-AR-3FØ3	Quarantine of Animals
ØB-AR-3FØ5	Management of Animal Feed
ØB-AR-3FØB	Selection and Notification Procedures, Moribund Sacrifice Animals and Animals Found Dead
ØB-AR-3B1R	Pathogen Monitoring
ØB-AR-3FØA	Daily Care of Bioassay Animals and Cleaning of Exposure Rooms
ØB-AR-3B23	Inhalation Room Procedures for Animal Care Personnel

INHALATION EXPOSURE AND BIOENGINEERING

ØB-BE-3B3H	Buildup and Decay and Overnight Concentration Monitoring
ØB-BE-3B24	Inhalation Exposure Chamber Balance
ØB-BE-3CØL	RTD Thermometer Calibration
ØB-BE-3DØE	Exposure Suite QC, Maintenance, and Calibration
ØB-BE-3EØ9	Study Protocol Entry Into Exposure Suite Computers
ØB-BE-3GØ4	Exposure Suite Routine Computer Operation
ØB-BE-3EØB	Exposure Suite Data Analysis Program Operation
ØB-BE-3CØJ	EG&G Hygrometer: Operation, Maintenance, and Calibration
ØB-BE-3CØV	Calibration and Check of Chamber Airflow Using Digital Anemometer
ØB-BE-3B1X	Relative Humidity Determination via Use of Dewpoint Hygrometer
ØB-BE-3GØ3	Operating Procedures for the Gardner Type CN Small-Particle Detector
ØB-BE-3C13	General FGD Calibration-Exposure Chamber and Generator Cabinets
ØB-BE-3B3K	Isoprene Exposure System Daily Operating Procedure (Teratology)
ØB-BE-3DØU	Isoprene Exposure System QC, Maintenance, and Calibration (Teratology)

ANALYTICAL CHEMISTRY

ØB-AC-3A13	Bulk Analysis of Isoprene
ØB-AC-3A1N	Isoprene: Analysis of Building Exhaust
ØB-AC-3DØ2	Routine Maintenance of the HP 5840

ISOPRENE
MOUSE AND RAT TERATOLOGY
ATTACHMENT 1

ØB-DT-1FØN-ØØ-Ø141
Page: 3 of 3

ØB-AC-3CØU Isoprene: Calibration of the Chamber Monitor

ØB-AC-3A1P Determination of Peroxide Content in Isoprene

SAFETY

ØB-HS-3S19 The 3M Brand W-2860 Hardcap, Continuous-Flow Air Line
Respirator

ØB-HS-3S1C Bioassay Studies: Health and Safety Plan

ØB-HS-3S1A Scott Presur-Pak II Self-contained Breathing Apparatus

ØB-HS-3S1B Bioassay Studies: Respiratory Protection Program

ØB-HS-3S1M Biohazard Protocol - Isoprene

NTP PROJECT OFFICE

ØB-9A-3EØ6 Data Handling and Storage of NTP Study Documents and
Materials

ØB-QA-3EØA Filling Out Data Sheets

ØB-QA-3BØ7 Job Orientation and Training

INHALATION EXPOSURE SYSTEM DESCRIPTION

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INHALATION EXPOSURE SYSTEM DESCRIPTION

I. Animal Exposure Chamber

The animals will be exposed and maintained in inhalation exposure chambers developed at BNW (U.S. Patent No. 4,261,741, August 12, 1980; Moss, 1980; Brown and Moss, 1981; Moss et al., 1982) and now commercially produced by the Harford Division of Lab Products, Inc., Aberdeen, MD. The chamber (Figure 1A) facilitates multiple-tier exposures of various laboratory rodent species to aerosol- and vapor-laden atmospheres. The total volume of the chamber is 2.3 m³ with an active mixing volume of 1.7 m³, the remainder being the inlet and exhaust volumes where animals are not placed. There are three levels of caging, each level split into two tiers which are offset from each other and from the chamber walls (Figure 1B). Drawer-like stainless steel cage units composed of individual animal cages are suspended in the space above each tier. Stainless steel catch pans for the collection of urine and feces are suspended below each cage unit. Catch pans are left in position during each exposure period. Cageboard is added to these catch pans during non-exposure periods to reduce ammonia concentrations.

The chamber was designed so that uniform aerosol or vapor concentrations can be maintained throughout the chamber when the catch pans are left in position. Incoming air containing a uniform mixture of test material is diverted so that it flows vertically along the inner surfaces of the chamber. Eddies are formed (Figure 1B) at each tier as the aerosol or vapor flows past the catch pans. Stagnant zones that would normally exist above each pair of catch pans are cleared by exhaust flow through the space between the tiers. Aerosol or vapor reaching the lowest level is deflected across the bottom tiers by metal strips in the space between the catch pan and the wall. Tests have shown that aerosol or vapor concentration homogeneous to within 8% throughout the chamber can be obtained repeatedly provided the aerosol or vapor is uniformly mixed before passing through the chamber inlet (Griffis, LC et al., 1981).

The dimensions of the individual cages are as follows:

Animal Species	Cages/ Unit	Floor Dimensions (cm)	Floor Area (cm ²)	Height (cm)
Mouse	60	14.0 x 7.6	106	15.0
Mouse	40	14.0 x 11.4	159	15.2
Rat (female)	24	27.9 x 9.7	271	20.3
Rat (male)	16	27.9 x 14.5	405	20.3
Golden Hamster	52	14.0 x 8.9	125	17.8

Figure 1. Inhalation Exposure Chamber Designed at BNW
(A. Oblique Cutaway View of the Chamber; B. Airflow
Patterns).

F.38

II. Exposure Suite System Description

The exposures will be conducted using an automated data acquisition and control system in an exposure Suite (Figure 2) consisting of three exposure rooms and a Suite Control Center room (only one of the exposure rooms will be used for this study). A central computer monitors the basic chamber functions (i.e., test chemical concentration, air flow, vacuum, temperature, and relative humidity) in each of the three exposure rooms. The executive computer is a Hewlett-Packard (HP) Model 9816. All data acquisition and system control originates from this computer. All experimental protocols related to the data acquisition and control system (such as data channel assignments, monitoring frequencies and alarm settings) reside in the executive computer and are entered into tables accessed by menus.

Data input to the executive computer is accomplished through several interface instruments. All on-line chemical monitor data are collected and preconditioned by HP-85B computers, one for each of the exposure rooms. Conditioned data are transferred to the executive computer for analysis, concentration control, data storage, and printing. Data from all monitoring equipment other than chemical monitors are inputted through a Colorado Data Systems (CDS) model 53A-IBX Intelligent Interface System (IIS).

System control is provided from the computer by means of control relays in the CDS IIS. These relays control such devices as valves, drive motors, audible alarms, indicator lamps, etc.

Data and comments from each exposure room are stored on separate magnetic diskettes by HP Model 9121 micro-floppy disk drives. Data and comments from each exposure room are printed on separate thermal dot matrix printers (HP Model 2671G). Data are printed and stored immediately upon completion of the measurement to the "Daily Log". At the end of the day (24-hour period), the daily data are analyzed and a summary is printed. This summary includes the the mean, standard deviation, % relative standard deviation, maximum, minimum, and number of measurements for each set of data for the 24-hour period. A second printout provides a table of outliers (i.e. all data points which are beyond the critical limits defined in the protocol). This outlier table allows rapid determination of problem areas in the data. A third printout provides a list of all comments generated by the computer and operators. This allows rapid inspection of generation start and stop times and any problem areas.

A complete description of the software for this system is contained in BNW documents ØB-BE-5EØ1. Maintenance of this system is detailed in SOP # ØB-BE-3DØE. Routine operation of the system software and hardware are detailed in SOP # ØB-BE-3GØ4.

Figure 2. Detailed layout of the exposure rooms of the Exposure Suite in which the Isoprene Study will be conducted.

III. Test Article Generation and Monitoring

A. Test Article Generation System

A schematic diagram of the isoprene vapor generation and delivery system is shown in Figure 3. The isoprene generator is housed in a vented cabinet located in the Suite Control Center.

The vapor generator will employ a rotary evaporation system (Bucchi Rotavapor, Model EL-131S) to produce a nearly pure isoprene vapor. The cylinders in which the bulk isoprene are shipped have both vapor and liquid sample valves. Low pressure nitrogen (4 - 6 psi) will be introduced into the vapor inlet of a tank, forcing liquid isoprene out at a steady rate. Chemical flow rate will be adjusted with a metering valve and monitored with a flowmeter. The liquid will be delivered to a rotating (40 rpm) flask immersed in a hot water bath at 65°C. The resulting vapor will be forced out of the mouth of the flask into a chilled water condenser where much of the vapor will be recondensed, returning to the evaporator flask. Nitrogen will be metered into the bottom of the condenser and will flow out its top. As nitrogen moves through the condenser, it will become saturated with isoprene vapor. The temperature of the saturated nitrogen will be monitored using a sensor at the top of the condenser. The saturation vapor pressure can be calculated and is used to determine the output (ppm of isoprene and flow rate of saturated nitrogen) of the generator. For example, at an exit temperature of 9°C, the isoprene concentration will be approximately 400,000 ppm at a typical flow rate of 11 lpm. The vapor will enter a short distribution manifold from which individual delivery lines will carry a metered amount of vapor to the exposure chambers. Vacuum transducer pumps at the chamber end of each line will generate the negative pressure needed to move the isoprene vapor. Within the chemical storage cabinet, each line will be connected to the distribution manifold through a fine metering valve and flowmeter. Adjustment of chamber concentration will be done with the metering valves and/or adjustment of compressed air pressure to the pumps. Injection of the nitrogen/vapor mix into the conditioned airstream entering the chamber will occur at a point sufficiently removed from the chamber to allow for proper mixing. This will assure uniformity of chemical-laden atmosphere within the chamber.

Normal operation will call for approximately 20% excess vapor to be exhausted from the manifold through a flowmeter. This will cause a slight positive pressure in the manifold and allows independent adjustment of the chamber flow rates. However, there will be the possibility of creating a negative pressure in the manifold and generator which could draw air into the nitrogen/isoprene atmosphere since the vacuum transducer pumps are will be withdrawing vapor from the manifold. This would occur if nitrogen delivery is interrupted or the pump delivery rates are grossly misadjusted. To monitor for this situation, a pressure transducer (Photohelic) will measure the pressure drop across the excess vapor flowmeter. A drop in pressure to below 2 cm of water will result in a shutdown of the generation system.

Generation will proceed in stages: warmup, generation and shutdown. During warmup, filling of the evaporating flask and heating of the water bath will proceed together. During this time, some evaporation will occur but all vapor will be exhausted from the distribution manifold through the excess flow exhaust. When the bath temperature and fluid level reach the correct values, computer-controlled startup of the delivery pumps will be initiated. Until concentration is equilibrated in the delivery lines,

nitrogen/isoprene vapor will be vented to exhaust at each chamber through pneumatic 3-way valves. These valves will allow for the more rapid diversion of chemical flow from chambers in the event rapid shutdown is necessary. After stabilization of the vapor temperature and possible fine adjustments of the vapor delivery and nitrogen flow rates, the generator will be in its normal operating stage. During this stage, the generator will operate under computer and exposure operator supervision. The exposure operator will monitor the fluid level in the flask as well as other operating parameters. The operator can adjust the overall generator output by changing the flow rate of cooling water to the condenser. This will affect the temperature of the vapor leaving the condenser and hence, the concentration of chemical in the vapor. Overall generator output could also be controlled by adjusting the flow rate of dilution nitrogen. The computer will be able to initiate a shutdown of the generator output under certain conditions by stopping flask rotation and turning off the bath heater. Further reduction in the generator output could then be initiated by the operator by reducing the nitrogen flow and tripping a solenoid-controlled valve which will introduce chilled water into the water bath.

Shutdown at the end of the generation stage will be similar to a computer-initiated shutdown. Following closure of the valves at the chambers and discontinuation of flask rotation, the operator will trip the solenoid, dumping additional cooling water into the bath. The remaining isoprene in the evaporating flask will be removed to a waste bottle. Nitrogen will continuously purge the generation system until preparation for the next day's generation.

Routine operation of the generation system is detailed in SOP# ØB-BE-3B3K. Maintenance and calibration of the system is contained in SOP# ØB-BE-3DØU.

F.43

Figure 3. Schematic Diagram of the Isoprene Generation and Delivery System

B. Test Article Concentration Monitoring

A single gas chromatograph (GC) with a flame ionization detector will be used to monitor the 3 exposure chambers, the control chamber, the holding chamber, the room, a certified standard vapor of isoprene in nitrogen, and a nitrogen blank. Sampling from the multiple positions will be accomplished by means of an automated, multiplexed 8-port stream select valve. Samples from each location are continuously drawn by a vacuum pump through polytetrafluoroethylene-lined stainless steel tubes to a location near the input of the stream select valve. This assures fresh sample at the monitor location. The sample time per port will be less than three minutes assuring that all ports are sampled at least once per hour.

Sample values are accumulated from the GC and printed by a Hewlett-Packard Model 85B computer until samples for all 8 ports of the stream select valve have been measured. These values are then sent to the executive computer for printing and storage. Each value accumulated by the HP 85B is compared with limit values for that particular location. If the value is beyond the control limits, the HP 85B will immediately send the information to the executive computer which will take the appropriate alarm action.

The monitor will be calibrated against quantitatively analyzed bubbler samples in air. Standards will be prepared gravimetrically. Additionally, the operation of the chamber monitor will be checked daily against an on-line standard. This check provides a measure of day-to-day instrument drift. Additional calibration checks by grab sampling will be performed to check the monitor calibration when drift of the on-line standard response factor is detected.

Daily operation procedures for the concentration monitoring system are contained in SOP# ØB-AC-3B1M. Maintenance and calibration of the monitoring system is contained in SOP# ØB-AC-3CØU.

The uniformity of the distribution of the test chemical in the chamber will be checked following SOP# ØB-BE-3B24.

The buildup and decay curves of the concentration in the chambers, the determination of T_{90} , and the determination of the persistence of the test article in the chambers following termination of test article generation (i.e., overnight monitoring) will be done following SOP# ØB-BE-3B3H.

IV. Chamber Environmental Control and Monitoring

A. Temperature

Nearly all of the heat load contributed to the exposure chamber by the animals is dissipated from the chamber by radiation through the chamber wall (Bernstein and Drew, 1980). Temperature of the air supplied to the chamber has little effect on the temperature of the chamber. On the other hand, temperature of the room housing the the chamber has a great deal of effect. Consequently, chamber temperature is maintained in the proper range primarily by controlling the room temperature.

Temperatures of the exposure chambers, exposure room and, if necessary, test chemical generators are measured by Resistance Temperature Devices (RTDs). The RTDs are placed in a representative location in each chamber (a top sample port on the back side). Each RTD is connected to an Omega Model 412B Digital Thermometer by either a manual select switch or by computer controlled scanner relays. This allows the temperature to be read manually or to be recorded automatically by the exposure system executive computer. Temperatures are automatically recorded at regular intervals during each 24 hour day. All temperature measurement equipment except the RTDs is located in the Exposure Suite Control Center. RTDs are calibrated to within 0.5°F of a certified mercury thermometer (SOP# ØB-BE-3CØL) before the start of each study and at least every two months thereafter.

B. Relative Humidity

Relative humidity (RH) in the exposure chambers is controlled by the system depicted in Figure 4. Equipment located in the RH Control Equipment Room (Room 335 of the LSL-II basement) provides separate ducts of dry and moist air to each exposure chamber. Filtered air with a maximum dewpoint of about 53°F is supplied to the RH Control Equipment by the building HVAC system. This air is evenly delivered to two ducts. Air from the first duct passes into a plenum where steam, generated from city tap water with no additional additives, is injected to bring the air to a dewpoint of about 60°F. This provides the moist air source for the chambers. The air from the second duct passed through a refrigeration coil which reduces the moisture content of the air to a dewpoint of about 40°F. This provides the source of "dry" air for the chambers. A manually controlled mixing valve for each chamber mixes the proper proportions of the moist and dry air to maintain the proper RH in each chamber. The mixing valve can also be controlled by the computer providing automatic control of chamber RH.

Relative Humidity is measured using an EG&G Model 910 dewpoint hygrometer located in the Exposure Suite Control Center. Air from the exposure chambers is sampled from a representative location (a top port on the back side). A teflon filter is placed at the chamber end of the sample line if the test article is an aerosol. Samples of the air from each measurement location are continuously pulled through polytetrafluoroethylene (PTFE) tubing to a central location in the Exposure Suite Control Center. This assures a fresh sample at the dewpoint hygrometer. Sample air from a particular location is routed by a multiplexed valve system to either the exposure system exhaust or the dewpoint hygrometer for RH determination. The valves are controlled by either a manual switch or by a computer controlled relay. This allows RH to be measured manually or automatically by the exposure system executive computer. RH is automatically recorded at regular intervals during the 24 hour day.

Figure 4. Schematic Diagram of the Chamber Relative Humidity Control System

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Once the dewpoint has been determined by the hygrometer, the RH is automatically calculated by the exposure system executive computer using the dewpoint value and the temperature (measured simultaneously at the same location by the RTD system). The following equation is used for this calculation:

$$\%RH = \frac{10^{\left[9.91 - \frac{2714.55}{(5/9)(T_1 - 32) + 293.13}\right]}}{10^{\left[9.91 - \frac{2714.55}{(5/9)(T_2 - 32) + 293.13}\right]}} \times 100$$

Where: T_1 = dewpoint temperature ($^{\circ}F$)
 T_2 = drybulb temperature ($^{\circ}F$)

Calibration of the dewpoint hygrometer is established prior to the start of the study and checked at least once every two months following SOP# ØB-BE-3B1X. Initial calibration requires comparison at three RH levels ($\approx$ 30%, 50% and 70%) of the RH calculated by the monitor to measurements made by a calibrated portable hygrometer and RTD located near the chamber.

C. Chamber Airflow

Air flow in the chambers is maintained by the vacuum in the central chamber exhaust duct. This vacuum is created by the chamber exhaust flow fans located in the South Equipment Room of the LSL-II Building. There are two parallel exhaust fans, one operating at a time with the other providing backup. Both fans operate from emergency power.

Chamber air flow rate is controlled by a gate valve in each individual chamber exhaust duct. A drive motor attached to the stem of this valve, allows the control of chamber flow either by computer or manually from the Exposure Control Center.

Fine control of exposure concentration can be accomplished by automatically or manually adjusting the valve position to control chamber dilution air flow within the allowable limits. Gross adjustment of concentration must be done manually by adjusting the generation system.

Chamber air flow is measured by a multiplexed orifice-meter system consisting of a calibrated orifice located in each chamber exhaust, a Validyne Model DP-45 pressure transducer, a Validyne Model CD-18 carrier demodulator, and a Validyne Model PM-12 digital voltmeter. The pressure transducer is multiplexed to each chamber's flow orifice by valves remotely controlled either manually or by means of the executive computer. This allows flow to be measured either manually or automatically. Flow is automatically recorded at regular intervals during the 24 hour day.

Calibrated flow orifice meters are located at both the inlet and exhaust to each chamber. By comparing the measured flow at the inlet and exhaust, leaks in the chamber can be detected. A leak check is automatically performed by the executive computer when each chamber is closed. If a leak is detected, the executive computer will notify the operator and will not allow exposures to proceed until the leak is repaired. This system is

sensitive to very small leaks which may cause an imbalance of test article concentration within the chamber.

Calibration of the flow orifices will be done before the start of each study and will be checked once every two months following SOP # ØB-BE-3CØV.

D. Chamber Vacuum

The chambers are maintained at a slight negative pressure compared to the room in order to reduce the possibility of escape of test article. This negative pressure is created by the pressure drop across the HEPA and charcoal filters at the inlet to each chamber.

The same Validyne pressure transducer system used to measure chamber flows is used to measure chamber vacuum. Vacuum in the chamber is measured relative to atmospheric pressure in the Suite Control Room. Vacuum is automatically recorded at regular intervals during the 24 hour day.

Vacuum is also continuously monitored by a mechanical pressure switch attached to each chamber. In the event of leak in the chamber, the pressure switch will immediately shut off the flow of test article to the chamber and activate an audio alarm.

V. Animal Facility Air Handling System

Supply air enters the building through two identical parallel air handling systems (Figure 5). Each system consists of a pre-heat coil, a filter system, a heating coil, a chilling coil, and a supply fan. The pre-heat coil heats the air to a minimum of 45°F. The filter system, comprising a roll filter, pre-filter, and a bag filter, rids the air of most particles. The heating and chilling coils maintain the temperature of the air exiting the air conditioning system at about 53°F. The chilling coils also dry the air to a dewpoint not greater than 53°F.

Although simultaneous operation of both of the parallel air supply systems is necessary to provide the 20 air changes per hour typically supplied to each animal room, only one of these systems, which can be operated from the emergency power system, is required to maintain the rooms within the temperature and flow specifications required by the protocol. Exposure of the animals to the test article can continue in the event of the failure of one of the air supply systems.

The air from the two parallel building air supply systems is mixed together by an air mixing unit and is divided into two ducts which feed the rooms on the East and West sides of the animal quarters. If necessary, steam is injected into the air in these ducts to maintain the relative humidity of all rooms in the basement at a minimum of 35%. In rooms where further room RH control is necessary, it is provided by individual steam generators located in the room. Prior to entering the animal room, the air is filtered through a HEPA filter.

Figure 5. Air Handling System for Animal Rooms of the Life Science II Building

Air for exposure chambers is supplied to a chamber relative humidity conditioning system from the building air supply systems. A single supply system is sufficient to supply air to the RH conditioning systems for all exposure chambers in the facility.

Exhaust from the animal room is filtered by a room HEPA filter and again through a bank of building exhaust HEPA filters assuring no escape of aerosol particles from the facility. Three parallel exhaust fans provide exhaust from the rooms. Two of these fans are in operation with the third as a backup unit. One fan can be operated from the emergency power system in case of power failure.

A separate exhaust duct system for the chambers allows for the addition of scrubbers to remove particles or vapors before exhausting from the building. Because the chamber exhaust system has a separate fan, failure of one of the building exhaust fans will not prevent the continuation of exposures.

VI. Exposure Suite Alarm System

An extensive system of alarms has been incorporated into the exposure suite automated data acquisition and control system to provide safety for the system operators, protect the health of the animals and ensure the integrity of the study. There are actually two separate alarm systems; one provided by the computer and a separate "physical" alarm system which provides redundancy for some of the computer alarm functions.

Following each function measured by the computer, the value is compared to the alarm limit values (stored in the computer memory) for that function. There are four limit values for each function and location monitored by the computer; high and low non-critical and high and low critical. For example, chamber flows may have the following limits:

Critical low	10	air changes per hour
Non-critical Low.....	12	
Non-critical High.....	18	
Critical High.....	20	

The result of an alarm condition depends on the function measured and the measurement location. Each function and location has an alarm response assignment in the computer. Again using chamber flow as an example, flows exceeding the non-critical limits but remaining within the critical limits will cause the computer to print a "beyond-non-critical-limits" symbol, "(" if low and ")" if high, next to the data on the daily log printed by the computer. A chamber flow which exceed the critical limits will cause the computer to print a "beyond-critical-limits" symbol, ">" if high and "<" if low, on the daily log and to turn on the critical alarm audio alert. A critical low flow alarm will also shut off the flow of test article to the chamber. Although it is possible for the computer to make automatic corrections to air flow in the chamber, this is not done because to do so would affect concentration of the test article in the chamber. A critical low negative pressure in a chamber (which may be the result of a leak in the chamber) will also cause the computer to shut off the flow of test article to the chamber. Similar responses result from alarms arising from temperature and relative humidity measurements in the chambers, however these alarms have no affect on the operation of the test article generator.

All critical alarms arising from measurements of generator function (such as vaporizer temperature) will result in all functions of the generator being turned off. The physical alarm system includes the following continuously monitoring devices:

- Chamber pressure (also detects critically low flow if it is the result of pump failure and not a clogged chamber inlet duct)
- Generator cabinet exhaust flow
- Chamber exhaust system flow
- Building exhaust system flow
- Explosive level detectors monitoring the chambers & generator cabinet (present only if test article is flammable)

In all cases an alarm condition from any one of these monitors is considered critical and results in the test article generator being shut off.

VII. Chamber Exhaust and Waste Treatment

The exhaust from the central chamber exhaust duct is mixed with the exhaust from the entire animal facility ($\approx 75,000$ cfm) prior to being exhausted from the building stack. Dilution of the chamber exhaust with the building exhaust results in an acceptable stack concentration on the order of one-tenth the Threshold Limit Value for the test article.

VIII. Data Recording and Handling

Data from each exposure room are stored in the Exposure Suite Control Center on separate magnetic disks by Hewlett-Packard (HP) Model 9121 micro-floppy disc drives. Data and comments from each exposure room are printed by separate thermal dot matrix printers (HP Model 2171G) or by ink jet printers (HP Model 2225A). Data are printed and stored immediately upon completion of the measurement to a Daily Log (example, Figure 6). Both the Daily Log and the disks will be maintained in the study files. The Daily Log will be considered the raw data. The Daily Log includes the time of measurement, the measurement location (such as chamber), the measurement function (such as temperature), the value of the measurement, the percent of target, an alarm code, and a status code. See Figure 6-continued for an explanation of the alarm and status codes.

At the end of the day (24 hour period), the daily data are analyzed and three summaries are printed. The first (example, Figure 7) includes the mean, % of target, standard deviation, % relative standard deviation, maximum, minimum, and number of measurements for each function (such as temperature) and location (such as chamber) monitored over the 24 hour period. The second (example, Figure 8) provides a list of outliers; that is, all data points which were beyond the defined critical operating limits. This printout allows for quick review of data which is outside of the operating limits. The final summary (example, Figure 9) is a printout of all comments made by the computer, Exposure Specialist, and Exposure Operator during the 24-hour period. This includes comments on startup time, exposure termination, new calibration factors entered and other information. This summary allows a quick review of events that occurred during the day.

Data handling and analysis procedures are described in SOPs ØB-BE-3EØB and ØB-BE-3EØE.

11 Jun 1987 Hexachlorocyclopentadiene Program: 87.01 page 5

Time	Data Origin	Function	Data	
	HCC- 200 pcc-R	-T90 Time Expires-Including Conc Data		
	HCC- 50 pcc-M	-T90 Time Expires-Including Conc Data		
	HCC- 50 pcc-R	-T90 Time Expires-Including Conc Data		
	HCC- 10 pcc-M	-T90 Time Expires-Including Conc Data		
09:54	Hewlett Packard 9616 (Access Level: Programmer)			
	HCC- 10 pcc-R	-T90 Time Expires-Including Conc Data		
09:55	Hewlett Packard 856 (Access Level: Specialist)			
	HCC- 10 pcc-R	GC Data Expires-Data Time<T90 Time & Data<Target		
	Low Limit Exceeded. (Data not stored to disk)			
09:55	HCC- 50 pcc-R	GC#16-30556	OKI 4.44E+1 pcc	99%
	High Limit Exceeded. (Data not stored to disk)			
10:02	HCC- 50 pcc-M	GC#16-30556	OKI 5.54E+1 pcc	113%
	High Limit Exceeded. (Data not stored to disk)			
10:09	HCC- 200 pcc-M	GC#16-30556	OKI 2.22E+2 pcc	111%
09:40	HCC- Room	GC#16-30556	OKI 0.00E+0 pcc	0%
09:43	HCC- 0 pcc-R	GC#16-30556	OKI 0.00E+0 pcc	0%
09:46	HCC- 0 pcc-R	GC#16-30556	OKI 0.00E+0 pcc	0%
09:50	HCC- 0 pcc-M	GC#16-30556	OKI 0.00E+0 pcc	0%
09:53	Hewlett Packard 856 (Access Level: Specialist)			
	HCC- 10 pcc-R	GC Data Expires-Data Time<T90 Time & Data<Target		
09:53	HCC- 10 pcc-R	GC#16-30556	OKI 5.99E+0 pcc	99%
09:53	HCC- 10 pcc-M	GC#16-30556	OKI 5.11E+0 pcc	99%
09:53	HCC- 50 pcc-M	GC#16-30556	OKI 4.44E+1 pcc	99%
10:02	HCC- 50 pcc-M	GC#16-30556	OKI 5.54E+1 pcc	113%
10:05	HCC- 200 pcc-R	GC#16-30556	OKI 2.04E+2 pcc	103%
10:09	HCC- 200 pcc-M	GC#16-30556	OKI 2.22E+2 pcc	111%
10:15	HCC- Standard Gas	GC#16-30556	OKI 5.80E+1 pcc	99%
10:21	HCC- Room	GC#16-30556	OKI 0.00E+0 pcc	0%
10:24	HCC- 0 pcc-R	GC#16-30556	OKI 0.00E+0 pcc	0%
10:28	HCC- 0 pcc-R	GC#16-30556	OKI 0.00E+0 pcc	0%
10:31	HCC- 0 pcc-M	GC#16-30556	OKI 0.00E+0 pcc	0%
10:34	HCC- 10 pcc-M	GC#16-30556	OKI 1.05E+1 pcc	107%
10:37	HCC- 10 pcc-M	GC#16-30556	OKI 5.57E+0 pcc	94%
10:40	HCC- 50 pcc-R	GC#16-30556	OKI 4.89E+1 pcc	99%
10:44	HCC- 50 pcc-M	GC#16-30556	OKI 5.43E+1 pcc	109%
10:47	HCC- 200 pcc-R	GC#16-30556	OKI 1.83E+2 pcc	97%
10:50	HCC- 200 pcc-M	GC#16-30556	OKI 2.05E+2 pcc	103%
10:56	HCC- Standard Gas	GC#16-30556	OKI 5.81E+1 pcc	99%
11:12	HCC- Vaporizer Temperature		OKI 180.1 F	100%
11:14	HCC- Room Temperature		OKI 55.0 F	99%
11:32	HCC- 200 pcc-M	Relative Humidity	OKI 54.0 %	99%
11:35	HCC- 200 pcc-M	Relative Humidity	OKI 50.0 %	91%

Figure 6. Example of 24-Hour "Daily Log" Printout from Data Acquisition and Control Computer. See Following Page for Explanation of Columns.

Figure 6. (continued)

DESCRIPTION OF COMPUTER "DAILY LOG" OUTPUT

The date, exposure name, program version and page number will be printed at the top of each page of the daily log.

Column 1: Time -- time that measurement was taken

Column 2: Location -- location of measurement (for example, chamber)

Column 3: Function -- measurement function (for example, temperature)

Column 4: Data --

Alarm Code -- "(" Indicates data < non-critical low but ≥ critical low alarm value
")" Indicates data > non-critical high but ≤ critical high alarm value
"<" Indicates data < critical low alarm value
">" Indicates data > critical high alarm value

Status Code -- "OK" Indicates monitoring instrument is functioning properly and is calibrated
"BS" Indicates service time of monitoring instrument has expired. (Usually indicates that instrument calibration should be checked. Does not necessarily mean that data are not valid)
"I" Indicates data will be included in summary
"E" Indicates data will be excluded from summary

Data Value -- Data may be expressed in scientific notation (x.xxxEyy)

Units Label -- Units of measurement (e.g., ppm, °F, mg/m³)

Summation for the File: Jun_11_87 Exposure: hexachlorocyclopentadiene

Exhaust Air Flow	Mean	% Target	Std Dev	Z PSD	Maximum	Minimum	Run X's
200	14.7	98%	.14	1%	14.8	14.4	10
200	14.9	100%	.07	0%	15.0	14.6	10
50	14.8	100%	.05	0%	14.9	14.7	10
50	14.8	100%	.12	1%	15.0	14.7	10
10	14.9	100%	.05	0%	15.0	14.8	10
10	15.0	100%	.07	0%	15.1	14.9	10
0	14.8	100%	.19	1%	15.0	14.3	10
0	14.2	95%	.03	5%	15.1	13.5	10
0	15.0	100%	.04	0%	15.0	14.9	10
Vacuum	Mean	% Target	Std Dev	Z PSD	Maximum	Minimum	Run X's
200	.8	75%	.03	2%	.8	.8	10
200	1.0	100%	.01	1%	1.0	.9	10
50	1.0	100%	.02	2%	1.0	.9	10
50	1.0	100%	.01	1%	1.0	.9	10
10	1.2	100%	.01	1%	1.2	1.2	10
10	1.0	100%	.01	1%	1.0	.9	10
0	1.0	104%	.02	2%	1.1	1.0	10
0	1.1	108%	.10	9%	1.2	1.0	10
0	1.1	100%	.01	1%	1.1	1.0	10
Relative Humidity	Mean	% Target	Std Dev	Z PSD	Maximum	Minimum	Run X's
200	58.1	100%	4.56	10%	65.0	45.0	10
200	58.2	100%	11.57	10%	70.0	47.0	10
50	58.0	100%	4.47	10%	65.0	47.0	10
50	58.0	100%	11.60	10%	70.0	45.0	10
10	58.0	100%	4.10	10%	65.0	45.0	10
10	58.0	100%	7.13	10%	65.0	45.0	10
0	58.0	100%	4.24	10%	65.0	45.0	10
0	58.0	100%	11.24	10%	65.0	45.0	10
0	58.0	100%	11.1	10%	65.0	50.0	10
Temperature	Mean	% Target	Std Dev	Z PSD	Maximum	Minimum	Run X's
Vaporizer	180.2	100%	.13	0%	180.4	180.0	10
200	73.9	97%	.10	1%	70.5	78.0	10
200	74.7	100%	.75	1%	75.2	73.2	10
200	74.5	100%	.48	1%	75.1	73.6	10
50	74.5	97%	.48	1%	75.2	73.2	10
50	75.5	100%	.74	1%	76.5	74.2	10
10	74.3	100%	.61	1%	75.1	73.1	10
10	75.2	100%	.41	1%	75.8	74.5	10
0	74.5	100%	.73	1%	75.5	74.1	10
0	74.2	100%	.68	0%	74.6	73.5	10
0	75.2	100%	.49	1%	75.0	74.1	10
Flow	Mean	% Target	Std Dev	Z PSD	Maximum	Minimum	Run X's
200	2.00E+2	100%	1.00E+0	0%	2.00E+2	1.99E+2	10
200	2.00E+2	100%	1.00E+0	0%	2.12E+2	1.96E+2	10

Figure 7. Example of 24-Hour "Data Summation" Printout From Data Acquisition and Control Computer.

Outlier Table for the File: Jun_11_87 Exposure: HexaChloroCycloPentadiene

Origin	Instrument	Time	Data	Lower	Target	Higher
No Outlier (Critical Limits exceeded) data points found.						

Figure 8. Example of 24-Hour "Data Outlier Table" Printout from Data Acquisition and Control Computer. Table Shows Data Which Were Beyond the Defined Critical Limits.

Daily Comments	Hexachlorocyclopentadiene	File: Jun_11_87
Time Operator Comment		
09:14 David J. Bailey	Chamber Leak Check for HCC- 10 ppm-H	
09:14 David J. Bailey	Exhaust Flow=14.9 Inlet Flow=14.5 (2.7% leak)	[Acceptable]
09:15 David J. Bailey	Chamber Leak Check for HCC- 10 ppm-R	
09:15 David J. Bailey	Exhaust Flow=15 Inlet Flow=14.9 (.7% leak)	[Acceptable]
09:16 David J. Bailey	Chamber Leak Check for HCC- 0 ppm-H	
09:16 David J. Bailey	Exhaust Flow=14.5 Inlet Flow=14.5 (0% leak)	[Acceptable]
09:16 David J. Bailey	Chamber Leak Check for HCC- 0 ppm-R	
09:16 David J. Bailey	Exhaust Flow=14.9 Inlet Flow=14.9 (0% leak)	[Acceptable]
09:17 David J. Bailey	Chamber Leak Check for HCC- 0 ppm-H-SC	
09:17 David J. Bailey	Exhaust Flow=15 Inlet Flow=15.3 (-2% leak)	[Acceptable]
09:17 David J. Bailey	All Chambers have been found ACCEPTABLE.	
09:28 Hewlett Packard 9815	HCC- Standard Gas-CC Data Excludes no Exposure at Data Time	
09:32 Hewlett Packard 9815	HPSC found Parameters Okay & ready for Exposure Start.	
09:33 Hewlett Packard 9815	Exposure Timing started.	[Time=1(0)]
09:33 Hewlett Packard 9815	Generator ON	
09:34 Hewlett Packard 9816	HCC- 200 ppm-H -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 200 ppm-R -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 50 ppm-H -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 50 ppm-R -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 10 ppm-H -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 10 ppm-R -ON Exposure-Enable Environ Data Collection	
09:34 Hewlett Packard 9816	HCC- 200 ppm-H -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 200 ppm-R -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 50 ppm-H -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 50 ppm-R -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 10 ppm-H -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 10 ppm-R -T90 Time Excludes-Including Conc Data	
09:34 Hewlett Packard 9816	HCC- 10 ppm-H-CC Data Excludes-Data Time<T90 Time & Data<Target	
09:34 Hewlett Packard 9816	HCC- 10 ppm-R-CC Data Excludes-Data Time<T90 Time & Data<Target	
10:34 Hewlett Packard 9816	Exposure Terminated. Exposure timers stopped.	
10:34 Hewlett Packard 9816	Generator OFF	
15:34 Hewlett Packard 9816	HCC- 200 ppm-H -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 200 ppm-R -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 200 ppm-H -Total Exposure Time=06:00:09	
15:34 Hewlett Packard 9816	HCC- 200 ppm-R -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 200 ppm-R -Total Exposure Time=06:00:11	
15:34 Hewlett Packard 9816	HCC- 50 ppm-H -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 50 ppm-H -Total Exposure Time=06:00:12	
15:34 Hewlett Packard 9816	HCC- 50 ppm-R -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 50 ppm-R -Total Exposure Time=06:00:14	
15:34 Hewlett Packard 9816	HCC- 10 ppm-H -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 10 ppm-H -Total Exposure Time=06:00:16	
15:34 Hewlett Packard 9816	HCC- 10 ppm-R -OFF Exposure-Enable Environ Data Collection	
15:34 Hewlett Packard 9816	HCC- 10 ppm-R -Total Exposure Time=06:00:17	
16:13 Hewlett Packard 9816	Environmental Data from Chambers 'Off-line' not monitored.	
16:13 Hewlett Packard 9816	HCC- 200 ppm-H -OFF Exposure-Disable Environ Data Collection	
16:13 Hewlett Packard 9816	HCC- 200 ppm-R -OFF Exposure-Disable Environ Data Collection	
16:13 Hewlett Packard 9816	HCC- 50 ppm-H -OFF Exposure-Disable Environ Data Collection	
16:13 Hewlett Packard 9816	HCC- 50 ppm-R -OFF Exposure-Disable Environ Data Collection	
16:13 Hewlett Packard 9816	HCC- 10 ppm-H -OFF Exposure-Disable Environ Data Collection	
16:13 Hewlett Packard 9816	HCC- 10 ppm-R -OFF Exposure-Disable Environ Data Collection	

Figure 9. Example of 24-Hour "Comment Summary" Printout from Data Acquisition and Control Computer. Table shows a Summary of all comments recorded on "Daily Log" printout.

IX. Equipment and Power Failure Protection Systems

Power is provided to the Battelle complex from two separate city substations through an automatic switching device. This significantly reduces the possibility of losing city power. Power from the city is routed to equipment in the LSL-II building through two types of motor control centers. One type can switch power from the LSL-II diesel generator. The other has access only to city power. The emergency-power-type motor control center has a low voltage detector on each leg of the three-phase input power. If the city supplied power should fail or "brown out", these detectors automatically start the emergency power diesel generator and route the emergency power to the equipment connected to the emergency-power-type motor control center.

All equipment critical to the well-being of the animals is connected to the emergency-power-type motor control center including:

- Emergency lighting and electrical outlets
- Building air conditioning chillers #1 and #2
- Building heating boilers and feedwater pump systems #1 and #2
- Air compressors #1 and #2
- Air supply fans #1 and #2
- Air exhaust fans #1 and #2

Note that there are two identical units of all equipment that is vital to the well-being of the animals (heating, cooling, supply air, exhaust air, and compressed air). Either of the two units has sufficient capacity to maintain the animal environment within a safe range. In all cases, the emergency power system will operate one of the two identical systems.

All building or chamber systems which are essential to the survival of the animals are alarmed. If a system malfunctions, an alarm is tripped in the Power Operator's office. A Power Operator is on duty 24 hours/day, 7 days/week. If the Power Operator is not authorized to correct the problem that caused the alarm, he immediately calls the appropriate personnel of the programs affected.

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From Isoprene Study Protocol: Pg 7; Section V.

ACTUAL ISOPRENE STUDY CALENDAR

	<u>Mice</u>	<u>Rats</u>
A. Animals arrive week of:	3/16/88	3/16/88
B. Identification of females:	4/4/88	4/5/88
C. Health screen:	4/4/88	4/4/88
D. Prestart audit for GLP compliance:	4/11/88	
E. Initiate breeding procedures:	4/6/88	4/11/88
F. Initiate exposure :	4/13/88	4/18/88
G. Initiate necropsy:	4/29/88	5/2/88
H. Complete exposure:	4/27/88	5/4/88
I. Evaluate fetal specimens:	5/9/88	5/23/88
	<u>Combined</u>	
J. Submit draft report:	9/15/88	
K. Submit final report:	45 days after receipt of NTP-reviewed draft report.	

EXPOSURE CHAMBER LOCATION

PROJECT: NTP-IRT
 STUDY: MOUSE AND RAT TERATOLOGY
 ROOM: 436

CHEMICAL: ISOPRENE
 CHAMBER: 1 Ø PPM
 DATE: 4-21-88 to 4-24-88

BSW

LEVEL 2 MICE

1315			
1306		1337	
1287		1302	
1265		1264	
1139		1196	
1136	1277	1128	1328
1109	1232	1101	1307
1103	1230	1088	1191
1062	1201	1067	1157
1060	1189	1029	1133
1012	1112	1009	1008
GRP A	GRP B	GRP C	GRP D

LEVEL 1

LEVEL 4 RATS

1542	
1517	
1512	
1508	1647
1505	1635
1479	1571
1473	1543
1433	1490
1423	1464
1420	1459
1411	1448
1403	1446
GRP A	GRP B

LEVEL 3 MICE

1330			
1317			
1311			
1291			
1268			
1260			
1252			
1221			
1168			
1089			

VIRGINS

LEVEL 5 RATS

	1646
	1623
	1619
	1615
	1610
	1606
1554	1591
1532	1585
1457	1583
1444	1582

GRP C

VIRGINS

LEVEL 6 RATS

1514	
1483	
1430	
1429	
GRP D	

EXPOSURE CHAMBER LOCATION

PROJECT: NTP-IRT
 STUDY: MOUSE AND RAT TERATOLOGY
 ROOM: 436

CHEMICAL: ISOPRENE
 CHAMBER: 2 280 PPM
 DATE: 4-21-88 to 4-24-88
380

LEVEL 2 MICE

1290			
1257		1331	
1255		1270	
1119		1242	
1098		1212	
1071	1294	1187	1333
1057	1289	1167	1332
1053	1280	1072	1238
1036	1198	1020	1224
1033	1174	1018	1194
1017	1064	1013	1170
GRP A	GRP B	GRP C	GRP D

LEVEL 1

LEVEL 4 RATS

1570	
1560	
1528	1631
1524	1630
1504	1546
1495	1540
1489	1477
1486	1463
1485	1452
1475	1445
1401	1414
GRP A	GRP B

LEVEL 3 MICE

1318			
1295			
1262			
1245			
1185			
1149			
1123			
1097			
1068			
1004			
VIRGINS			

LEVEL 6 RATS

1604	
1575	
1469	
1440	
1427	
GRP D	

LEVEL 5 RATS

	1625
	1621
	1620
	1617
	1613
	1612
	1607
1629	1600
1588	1595
1503	1594
GRP C	VIRGINS

EXPOSURE CHAMBER LOCATION

PROJECT: NTP-IRT
 STUDY: MOUSE AND RAT TERATOLOGY
 ROOM: 436

CHEMICAL: ISOPRENE
 CHAMBER: 3 1400 PPM
 DATE: 4-21-88 to 4-24-88
BSW

LEVEL 2 MICE

1300		1313	
1275		1244	
1121		1171	
1095		1118	1240
1080	1266	1116	1239
1079	1250	1145	1236
1075	1078	1093	1226
1052	1073	1074	1184
1046	1043	1041	1124
1042	1003	1002	1034

GRP A GRP B GRP C GRP D

LEVEL 4 RATS

1552	
1541	
1531	
1494	1579
1491	1573
1487	1556
1484	1526
1461	1525
1443	1496
1441	1453
1438	1428
1405	1410

GRP A GRP B

LEVEL 6 RATS

1650	
1549	
1436	
1409	

GRP D

LEVEL 1

LEVEL 3 MICE

1329			
1285			
1213			
1209			
1165			
1144			
1141			
1135			
1082			
1028			

VIRGINS

LEVEL 5 RATS

	1654
	1652
	1639
	1637
	1632
	1608
1564	1603
1563	1598
1530	1540
1412	1586

GRP C

VIRGINS

EXPOSURE CHAMBER LOCATION

PROJECT: NTP-IRT
STUDY: MOUSE AND RAT TERATOLOGY
ROOM: 436

CHEMICAL: ISOPRENE
CHAMBER: 4 7000 PPM.
DATE: 4-21-88 to 4-24-88
BSW

LEVEL 2 MICE

1301			
1138		1293	
1111		1242	
1110		1205	
1091		1105	
1070	1243	1131	1298
1058	1225	1077	1234
1047	1153	1054	1227
1037	1151	1030	1166
1025	1127	1019	1164
1024	1035	1016	1158
GRP A	GRP B	GRP C	GRP D

LEVEL 4 RATS

1561	
1558	
1557	1597
1548	1566
1529	1555
1497	1536
1472	1513
1456	1510
1434	1454
1418	1421
1415	1417
GRP A	GRP B

LEVEL 6 RATS

1602	
1599	
1465	
1425	
GRP D	

LEVEL 1

[illegible]

LEVEL 3 MICE

1319			
1274			
1258			
1237			
1220			
1214			
1207			
1129			
1094			
1084			
VIRGINS			

LEVEL 5 RATS

	1655
	1642
	1640
	1628
	1626
	1611
1511	1605
1509	1596
1499	1581
1400	1577
GRP C	VIRGIN

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