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Final Report

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May 1988

Prepared for the
National Institute of Environmental Health Sciences, National Toxicology Program
under a Related Services Agreement with
the U.S. Department of Energy
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Pacific Northwest Laboratory
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INHALATION DEVELOPMENTAL TOXICOLOGY STUDIES: TERATOLOGY STUDY OF n-HEXANE IN MICE

Final Report
No. NIH-Y01-ES-70153

T.J. Mast, Study Director

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SUMMARY

Timed-pregnant (≈33 females per group) and virgin (10 females per group) Swiss (CD-1) mice were exposed to 0 (filtered air), 200, 1000, and 5000 ppm n-hexane (99.2% purity) vapor in inhalation chambers, 20 h/day, for a period of 12 consecutive days. Plug-positive females were exposed on 6-17 days of gestation (dg). Maternal body weight at sacrifice (18 dg) and total cumulative weight gain for dams in the 5000-ppm exposure group were significantly reduced with respect to controls; however, this was due to an exposure-correlated reduction in gravid uterine weight, not to a decrease in extragestational gain. An exposure-correlated decrease in the gravid uterine weight to extragestational weight gain ratio (significant for the 5000-ppm group) occurred in the absence of an effect on placental weight.

Gestational exposure to n-hexane resulted in an increase in the number of resorbed fetuses for all exposure groups relative to the control group; however, the increases were not directly correlated to exposure concentration. The differences were statistically significant for the 200-ppm group with respect to total intrauterine death (early plus late resorptions), and with respect to late resorptions for the 5000-ppm group. A small, but statistically significant, reduction in female (but not male) fetal body weight relative to the control group was observed at the 5000-ppm exposure level. There were no exposure-related increases in any individual fetal malformation or variation, nor was there any increase in the incidence of combined malformations or variations.

Gestational exposure of CD-1 mice to n-hexane vapors appeared to cause a degree of concentration-related developmental toxicity in the absence of overt maternal toxicity, but the test material was not found to be teratogenic. This developmental toxicity was manifested as an increase in the number of resorptions per litter for all exposure levels, and as a decrease in the uterine:extra-gestational weight gain ratio at the 5000-ppm exposure level. Because of the significant increase in the number of resorptions at the 200-ppm exposure level, a no observable effect level (NOEL) for developmental toxicity was not established for exposure of mice to 200, 1000, or 5000-ppm n-hexane vapors.

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INTRODUCTION

The straight-chain hydrocarbon, n-hexane, is commonly used as a solvent for the extraction of oil seeds, as a reaction medium in the production of polyolefins, elastomers and pharmaceuticals, and as a component of quick-drying cements, lacquers and adhesives. The production of n-hexane, which was estimated to be four billion pounds per year in 1979, utilizes stocks of straight-run gasoline and higher boiling liquid products stripped from natural gas or paraffinic fractions of refinery streams. It is also found as a minor component of gasoline and its combustion products, hence petroleum products are a major source of environmental hexane contamination. Due to the large-scale production and widespread use of hexane, including teaching laboratories, the opportunity for industrial, incidental, environmental, or volitional (glue-sniffing) exposure to hexane vapors is significant. This study was prompted by the extensive human exposure to n-hexane vapors and the need to further evaluate its potential to cause developmental toxicity in a laboratory animal model.

An excellent review concerning hexacarbon toxicity and metabolism is available in Experimental and Clinical Neurotoxicology (edited by Spencer and Schaumberg, 1980). In summary, polyneuropathies have been reported following exposure of workers to n-hexane contained in adhesives, when used as an industrial solvent, or following repeated exposure by glue-sniffing. A metabolite, 2,5-hexanedione, has been shown to be responsible for most, if not all, of the neurotoxicity. Younger rats appear to be less sensitive to n-hexane neurotoxicity than older animals. It has been suggested that this difference may be due to their having shorter axons with smaller diameters, or to a greater rate of growth and repair of peripheral nerves as compared to that of adults (Howd et al. 1983; Kimura et al. 1971). Likewise, Graham and Gottfried (1984) hypothesized that mice are less sensitive than rats to gamma-diketones, such as 2,5-hexanedione, because myelinated axons in mice are shorter and have smaller diameters than the corresponding axons in larger species.

Pharmacokinetic and distribution studies of inhaled n-hexane have indicated that the saturation concentration of n-hexane in organs is directly proportional to their lipid content, and that blood contains more hexane in relation to its lipid content than do organs (Andersen 1981; Bohlen et al. 1973). Baker and Rickert (1981) found that the metabolism and elimination of n-hexane were dependent upon exposure concentration, but that the tissue concentration of the metabolite, 2,5-hexanedione, was not directly related to n-hexane exposure concentration. Bus et al. (1981), using ^{14}C-labeled n-hexane in 6-hour inhalation exposures, found that the distribution of radioactivity was dependent on the exposure concentration.

In studies designed to address the possibility that exposure to hexane may affect prenatal development in rats, Bus et al. (1979) also determined the distribution and half-lives of n-hexane ($t_{1/2}$=1.2 h) and 2,5-hexanedione ($t_{1/2}$=3.9 h) in maternal organs and fetuses exposed to n-hexane during gestation. Concentrations of n-hexane and its metabolites in fetuses were approximately equal to those in maternal blood. Nevertheless, they observed no statistically significant effects on intrauterine mortality, fetal body weights, or in the incidence of fetal anomalies following daily inhalation exposures to 1000 ppm of n-hexane from 8-12, 12-16, or 8-16 days of gestation (dg) for 6 h/day. Growth of the exposed pups was impaired during the first three postnatal weeks in the group exposed 8-16 dg, but the possibility of maternally mediated effects or postnatal exposure via milk was not examined.

Other developmental studies included those of Marks et al. (1980) who found that oral administration of n-hexane (2.2 g/kg/day) from 6-15 dg in rats produced one maternal death, but no adverse fetal effects. When they administered 2.8, 7.9 or 9.9 g/kg/day of n-hexane subdivided into three oral doses per day, maternal mortality was increased and fetal weight was reduced in a dose-related manner for the two higher exposure levels. No fetal malformations were observed.

Exposure of female rats for 7 h/day to hexane vapor at concentrations up to 10,000 ppm for 15 days prior to conception and through 18 dg produced neither signs of neuropathy nor indications of effects on postnatal maturation

and growth of the pups (Howell and Cooper 1981; Howell 1979). No effects on the visual (VER) or interhemispheric (IHR) evoked responses of anesthetized offspring were found in the first series of experiments. However, in a second set of experiments, there was an increased amplitude of the VER peaks in unanesthetized 45-day old pups in the high-concentration group.

These studies are rather convincing relative to the absence of morphologic effects following gestational exposure to n-hexane vapors (despite the low exposure concentration of 1000 ppm employed in one rat study). While it is tempting to conclude that fetal and neonatal rats and mice are relatively resistant to the effects of n-hexane exposure, these conclusions are based on incomplete evidence. In order to provide more definitive information regarding the developmental toxicity of n-hexane, the following study in mice was conducted with the goal of maximizing maternal exposure during gestation. An analogous study in Sprague-Dawley rats was also conducted; results are reported elsewhere (Mast 1987).

Since it appears that the toxicity for most chemicals is a function of concentration versus duration of exposure over certain concentration ranges, an adequate assessment of the teratologic potential of n-hexane requires evaluations after gestational exposure to a series of concentrations, the highest of which causes some maternal toxicity. To achieve this goal, this study in mice employed multiple exposure levels, 0, 200, 1000 and 5000 ppm for 20 h/day. The maximum exposure concentration was limited by safety considerations to 50% of the lower explosion limit (LEL), ≈11,000 ppm, for n-hexane (NIOSH, 1987). The two lower exposure concentrations, 200- and 1000-ppm, were chosen with the goal of obtaining a no observable effect level (NOEL) or at least observing a graded toxicological response. The exposure concentrations employed in this study were significantly greater than the human TLV (threshold limit value) for occupational exposure to n-hexane, which is 50 ppm (ACGIH 1985), and the 10-h TWA (time-weighted average) set by NIOSH (1987), which is 100 ppm. NIOSH (1987) has also set a 15-min ceiling of 510 ppm for n-hexane.

Exposures of plug-positive females extended throughout the late implantation, organogenic, and fetal developmental stages (i.e., 6-17 dg). Fetal evaluations were performed on 18 dg.

Reported effects on lipid metabolism suggested the possibility that the ovaries and/or ovulation may be affected by exposure to n-hexane vapors. Although the limited data of Howell and Cooper (1981) regarding preconception and preimplantation exposure indicated that the ovary was not a target organ for n-hexane toxicity, the lack of information on the uptake of n-hexane or its metabolites into the ovary was of concern. Since the need for a specific study was not immediately justified, the ovaries from the pregnant animals in this study were preserved at necropsy for later morphological evaluation. An additional group of virgin females was exposed concurrently with the plug-positive females to determine the effect of n-hexane exposure on the ovaries of non-pregnant mice. Furthermore, body weight data obtained on the virgin females also served as a baseline from which the effects of pregnancy on the toxicity of the test material to adult females could be assessed. Results from this segment of the study, other than body weight data, are not reported here since the ovaries were sent to another laboratory (designated by the sponsor) for evaluation and follicle counts.

MATERIALS AND METHODS

Four groups of Swiss (CD-1) mice (Charles River, Raleigh, NC), each consisting of 35 randomly selected, sperm-positive females and 10 randomly selected virgin females, were exposed to 0 (filtered air), 200, 1000, or 5000 ppm n-hexane vapor for 12 consecutive days, 20 h/day. Plug-positive females were exposed on 6-17 days of gestation (dg). The day of plug detection was designated as 0 dg. Exposures commenced at 12 NOON On 6 dg and continued for 20 h/day, or until 8 A.M. on the following morning. The last day of exposure began at 12 NOON on 17 dg and ended at 8 A.M. on the morning of 18 dg. Control animals (0 ppm) were housed in an exposure chamber in the same room, and were handled in the same manner as the mice that were exposed to the test chemical. Animals remained in the exposure chambers and were supplied with fresh air,

food, and water during the daily 4-h period when n-hexane exposures were not in progress. (See ANIMAL HUSBANDRY section for details.) The long daily exposure period for n-hexane was chosen in order to maximize exposures to n-hexane since the maximum vapor concentration in the chambers was not allowed to exceed 50% of the LEL (lower explosion limit), which is -11,000 ppm (NIOSH, 1987).

VAPOR GENERATION AND CHEMICAL ANALYSES

Bulk chemical purity analyses were performed on the single lot of n-hexane used for mouse exposures. Analytical procedures employed infrared spectroscopy and gas chromatography for the initial identity and purity determinations. The purity of the n-hexane used during the exposures was 299.2% (Research Triangle Institute [RTI] lot no. H-222).

On-line measurements of the n-hexane chamber concentrations were performed with an HP5840 gas chromatographic system (GC) equipped with a flame ionization detector. A computer-controlled, rotating 8-port valve allowed measurement of n-hexane concentrations in the control chamber, exposure room, and the on-line standard in addition to levels in the exposure chambers. All ports were sampled at least once every 40 minutes. The GC was equipped with a 1/8" o.d., one-foot nickel column packed with 1% SP-1000 on 60/80 mesh Carbopack B. The oven operating temperature was 120°C. An on-line standard, 1000 ppm n-hexane in nitrogen (MG Industries Scientific Gases, 11705 S. Alameda St., Los Angeles, CA), was used to check instrument drift throughout the exposure day (see Appendix A for more detail). The minimum detectable limit of n-hexane was estimated from the decay profile of the 5000 ppm chamber and found to be 0.15 ppm. The calibration curve for this analysis showed good linearity over an extended range and was monitored at intervals by routine analysis of bubbler-samplers.

Inhalation exposures were conducted in Battelle-designed chambers (Moss, Decker and Cannon, 1982; Brown and Moss, 1981). The 2.3 m^3 (1.7 m^3 active-mixing volume) stainless steel chambers contained three levels of caging, each of which was split into two offset tiers. Air containing a uniform mixture of

the test article flowed through the chamber at approximately 15 air changes per hour. The air was HEPA- and charcoal-filtered before addition of the test article.

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

Generation of the n-hexane vapor was achieved by metered pumping of the liquid chemical from a reservoir, through inert delivery tubes, to a vaporizer located at the fresh air inlet of each animal exposure chamber. The vaporizer was comprised of a stainless steel cylinder covered with a glass fiber wick from which the liquid was vaporized. The operating temperature of the vaporizer was maintained below 50°C (the boiling point of n-hexane is ≈70°C). All generation equipment which came into contact with the n-hexane was stainless steel, Teflon®, or Viton®. All equipment was contained in the vented, explosion-proof generator cabinet. Chamber air flows were maintained by a computer-controlled pump in the exhaust line of each chamber. The exposure suite data acquisition and control computer automatically controlled the concentration of n-hexane in the chambers by adjusting the flow rate of dilution air through individual chambers.

The buildup and decay of n-hexane concentrations without animals in the chambers were checked before the start of the study, and with animals in the chambers during the first week of the study (Figure 1). The time required to reach 90% of the target concentration (T_{90}) ranged from 7-9 min. The decay time (the time required to decline to 10% of the target concentration after cessation of exposure [T_{10}]) with animals present ranged from 7-9 min. Uniformity of vapor concentration in the exposure chambers was measured prior to

the start of (without animals), and once during the study (with animals). Uniformity in all chambers was found acceptable (e.g. ±5%).

ANIMAL HUSBANDRY

Upon receipt mice were maintained on wire racks equipped with automatic watering systems (12 mice per cage). Males and females were housed separately. Prior to the start of the study, five females and five males were killed and examined for internal and external parasites and bacterial pathogens. Serum from each of these animals was tested for antibodies to selected pathogens, and histopathologic examinations of lung, liver, kidney, ileum, colon, and heart were performed (Appendix D). Animals remained under quarantine status throughout the course of the study due to the presence of a *Streptococcus* Group 'C' in some animals. The presence of this organism had no apparent effect on the health of the animals and they were released for study by the veterinarian (See Appendix D for details). Another check for antibodies to selected viral pathogens was performed on serum collected from five females in the control group and five females in the 5000-ppm group at the time of sacrifice. All results were negative. All animals were observed daily for mortality, morbidity, and overt signs of toxicity throughout the study.

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. Due to the long daily duration of the exposures, 20 h, food was left in place during the exposures and replaced daily at approximately 11 A.M. Water was provided ad *libitum* with automatic waterers. Room lighting was maintained on a 12-hour on-off cycle (On 6 A.M. to 6 P.M., and off 6 P.M. to 6 A.M.). During the quarantine period animal room temperature was maintained at 73±3°F and humidity was maintained 50±15%.

During the exposure period all chambers were maintained within the limits of 75±3°F. Actual temperature means were between 72.8 and 76.3°F, all within the specified limits. Mean relative humidity in all exposure chambers was between 47.6 and 52.1%; these values were within the specified limits of

55 ± 15%. The average air flow in all chambers for the study was between 14.6 and 15.5 CFM (1 CFM = 1 air change per hour); all flows were 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

All female mice were weighed and individually identified during the week prior to mating. At this time forty (40) females were randomly chosen, by using body weight as a blocking variable, for assignment to the study as virgins. The remaining females were bred by caging one or two females overnight with one male. Copulation was established on the following morning by examination for a vaginal plug; if a plug was found, this day was designated as 0 dg. At this time, the plug-positive females were weighed and randomly assigned to exposure groups, again using body weight as the blocking variable. Mating was conducted for five successive nights to obtain the desired number of plug-positive females. At least three days prior to the start of the exposure, virgins and plug-positive females were placed into an inhalation chamber for acclimatization.

Plug-positive females were weighed on 0, 6, 9, 12, and 18 dg and virgins were weighed 12 days prior to the start of exposure, on exposure days 1, 4, and 7, and at the time of sacrifice. The pregnant females were removed from the exposure chambers on the morning of 18 dg, weighed and euthanized with CO_2 and their uteri were removed and weighed. Virgins were killed on the day after their last day of exposure. Following sacrifice, females were examined grossly for manifestations of toxicity and any unusual findings were recorded.

Apparently nongravid uteri from positively mated females were stained with ammonium sulfide to detect possible implantation sites. The number, position and status of implants was recorded for each gravid uterus and placentas were examined and weighed. Live fetuses were weighed and examined for gross defects. Live fetuses were then euthanized with an injection of Nembutal® (sodium pentobarbital) and examined by dissection for visceral defects. Their sex was also confirmed at this time. Skeletal examinations

were performed on all fetuses except that approximately one-half of the fetuses in each litter were decapitated prior to staining. Consequently, only one-half of the heads were examined for skeletal abnormalities. Cartilage as well as ossified bone was visualized by double-staining fetal carcasses with alcian blue and alizarin red S. The removed heads were fixed in Bouin's solution and sectioned with a razor blade to examine them for soft-tissue cranio-facial abnormalities rather than skeletal defects.

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, pp 434-506) with an analysis of variance (ANOVA) model for unbalanced data. Response variables, either body weight or the arcsin transformations of proportional incidence data, were analyzed against the class variable, treatment, in a one-way ANOVA model. 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 use of an orthogonal trend test (Winer, 1971). In the case of proportional data this test was performed on transformed variables. The litter was used as the basis for analysis of fetal variables.

RESULTS

Summaries of the concentration data obtained during animal exposures are shown in Table 1. The daily mean concentrations for all chambers were within 10% of the target concentrations. More detailed summaries of the concentration data and summaries of the environmental data are included in Appendix B along with graphic illustrations of the daily means and standard deviations for each chamber. Since actual n-hexane exposure chamber concentrations so closely approximated target exposure concentrations, all groups will be referred to by their target concentration throughout this report.

Decomposition of n-hexane was not anticipated under the storage and generation conditions employed; however, test material stability for a reservoir sample aged five days was confirmed. The five-day aging period was conservative since reservoirs were renewed daily during exposure periods. The bulk purity of the aged reservoir sample was 99.1% relative to reference material and the impurity profile exhibited no significant differences from those in the reference sample. Analyses for potential degradation products were performed on samples collected from the high and low chambers before and during animal exposures. No evidence of impurities or degradation products was found in samples taken from the exposure chambers.

Each exposure group, 0, 200, 1000, or 5000 ppm, consisted of 35 plug-positive female mice and 10 virgin female mice. No clinical signs of toxicity were noted and there were no maternal deaths. All animals were killed following the 12^{th} consecutive day of exposure, 6-17 days of gestation for plug-positive females. The pregnancy rate of all plug-positive females was found to be 80% at the time of sacrifice on 18 dg.

The mean body weights of virgin female mice were not significantly affected by exposure to n-hexane vapors (Table 2). However, pregnant females exposed to 5000 ppm n-hexane showed a significant reduction in mean body weight on 18 dg when compared to that of control animals (Table 3). The mean cumulative weight gain for pregnant mice in the 5000-ppm group from 6-18 dg was also significantly less than that for controls (Figure 2). Since there was no associated reduction in extra-gestational weight gain (EGWG; body weight at the time of sacrifice minus the 0-dg weight minus the gravid uterine weight), the lower mean maternal body weight at the time of sacrifice for the 5000-ppm group was due to a reduction in the gravid uterine weight (Table 3). Indeed, the mean gravid uterine weight was significantly reduced relative to the controls for the 200- and 5000-ppm exposure groups. The lack of a treatment-related effect on EGWG was also substantiated by the fact that the weight gain of the virgin females was not affected by exposure to n-hexane. The mean ratio of uterine weight to EGWG for all treatment groups was less

than that for the control groups and the difference was statistically significant for the 5000-ppm group (Figure 3).

Exposure to n-hexane vapors on 6-17 dg had no statistically significant effect on the number of implantations or on the fetal sex ratio (Tables 4 and 5). However, the mean number of implantations per litter for the 5000-ppm group is less than that for the control group by 1.3 implants per litter (also compare with contemporary control data[1] [Table 61). Although implantation of the embryo should be complete by 6 dg, the first day of exposure, the possibility of a test-material-induced effect cannot be completely disregarded in this case since we found in another study (Mast et al. 1988) that very early resorptions in the mouse could not be detected visually without the aid of a stain (10% ammonium sulfide). All uteri that did not have any apparent implantation sites were stained to determine if they had ever been pregnant; however, uteri that had distinct implants were not stained. Thus, the presence of very early resorptions in gravid uteri would not have been noted.

The number of live implants per litter for all three n-hexane exposure levels was less than the control group, but the difference was statistically significant for only the 5000-ppm group (Table 4). Furthermore, the number of live implants for all three of the exposed groups was less than the value for the contemporary control data (Table 6). The mean percent of live implants was reduced for the 200- and 5000-ppm groups, but not for the 1000-ppm group relative to contemporary controls. The mean percent intrauterine death (early and late resorptions combined) was greater for all exposed groups than for the control group, but the difference was statistically significant only for the 200-ppm group. There was no significant correlation of these parameters with increasing exposure concentration. The percent incidence of late resorptions was significantly greater than controls for the 5000-ppm group and a trend

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[1] Contemporary control data were collected on Swiss (CD-1) mice supplied by Charles River Laboratories from March 1987 through November 1987. Data for the control group of this study are included in contemporary control group means. All of these animals were subjected to the same housing and exposure chamber conditions.

analysis showed the percent incidence of late resorptions to be positively and significantly correlated with exposure concentration.

Fetal weights, presented as means of litter means in Table 5 (male and female combined) were slightly, but not significantly, reduced for all treatment groups when compared to controls; however; the decrease was significantly correlated to increasing n-hexane concentration. When compared to contemporary control data (Table 6) fetal weights for the animals used in this study were greater than the mean fetal weight for contemporary control animals, and mean fetal weights for the n-hexane exposed groups were never less than the mean for contemporary control data. Mean fetal weights examined on the basis of sex showed that male weights for n-hexane exposed groups were not significantly affected as compared to the control group; however, mean female fetal weights were significantly reduced for the 5000-ppm group when compared to the control group in this study. The reduction in mean female fetal weight was also significantly correlated with increasing n-hexane concentration. The percent reduction in mean fetal weights for fetuses in the 5000-ppm group was =3% for males and ≈6% for females.

Malformations were found in only 10 fetuses (seven litters), one fetus (one litter) had exencephaly and nine fetuses (six litters) had abnormal limb flexure (Table 7). None of these appeared to be treatment related. Although the one exencephalic fetus was in the 5000-ppm exposure group, the lack of similar or associated malformations in other fetuses and litters in this group, and the presence of this malformation in the contemporary control group (Table 8), indicated it was not treatment related. The statistically significant increase noted in the incidence of exencephaly in the highest exposure group is a spurious result due to the extremely low background incidence of this abnormality and is not biologically significant.

Variations observed included dilated ureters, rib anomalies, and reduced ossification sites in the sternebrae and the skull (Table 7). There was a nonsignificant increase in the mean percent incidence per litter of supernumerary ribs relative to controls for all n-hexane exposed groups which appeared to be treatment related (Table 9). In fact, the incidence of

supernumerary ribs in the contemporary control data (Table 8) is greater than for the 5000-ppm group in this study.

DISCUSSION

This study indicated that a low degree of developmental toxicity was caused by the exposure of pregnant Swiss (CD-1) mice to 200, 1000, or 5000 ppm n-hexane vapors on days 6-17 of gestation. Although the toxicity was not severe at any of the three exposure concentrations, some effects were observed even at the lowest exposure level. For instance there was a statistically significant decrease in the gravid uterine weight for the 200- and 5000-ppm levels of the exposed animals relative to that of the control group. The decrease in the mean gravid uterine weight, which was significantly correlated to increasing exposure concentration, occurred in the absence of a corresponding reduction in either mean placental weight or maternal extra-gestational weight gain. The uterine weight decrease was probably due to the lower number of live fetuses per litter in the groups exposed to the test material. The constancy of the extra-gestational weight gain across exposure groups resulted in a treatment-correlated decrease in uterine:extra-gestational body weight ratios (Figure 3).

The effects of gestational exposure to increasing concentrations of n-hexane on the mean number of live fetuses per litter, as well as on the incidence of resorptions per litter, also indicated the existence of some fetotoxicity. However, the increase in the incidence of total resorptions was not directly correlated to increasing exposure concentration since the percent of resorptions per litter was greater for the 200 and 5000 ppm groups than it was for the 1000-ppm group. On the other hand, orthogonal trend tests on arcsine-transformed data did indicate a significant relationship between the exposure levels and the resorption incidence for late resorptions. This treatment-correlated increase in the incidence of late resorptions was probably the most biologically significant effect since the percent of late resorptions per litter was greater for all treatment groups than for the control group or for the contemporary control data.

A slight, but statistically significant reduction in fetal body weights was observed for female fetuses at the 5000-ppm exposure concentration, but not for males, indicating that females may have been more susceptible. The lack of any affect of exposure on the placental weights, for either female or male fetuses, was also indicative of the lack of maternal toxicity. Gestational exposure to n-hexane did not alter the fetal sex distribution.

No statistically significant, treatment-related increases in the incidence of fetal malformations were observed although there was an apparent increase in the incidence of supernumerary ribs. This increase may not have been due to the test material since the mean percent incidence per litter in contemporary controls was greater than that observed for the highest n-hexane exposure group (Tables 8 and 9). However, increases in the incidence of supernumerary ribs in rodents in general, and specifically in this strain of mice (CD-1), have been repeatedly correlated to stress, physical or chemical, during pregnancy (Chernoff et al. 1987; Schardein 1987).

An attempt was made to compare the results of this study with those produced following oral exposure of pregnant Swiss (CD-1) mice to n-hexane (Marks et al. 1980); however, since the data are not presented in a similar manner some comparisons, e.g. uterine weight versus extra-gestational weight gain, are not possible. Although maternal toxicity, evident as an increasing incidence of maternal death, was present in the higher dose groups of Marks' study, there was no concurrent increase in the incidence of malformations or variations. There was a treatment-associated reduction in fetal body weight which became statistically significant for the two highest dose groups which received a total of 7.92 and 9.90 g/kg/day (administered three times/day). It is possible to compare the oral doses with the approximate inhalation dose given the following assumptions: 1) 5000 ppm n-hexane equivalent to 18000 mg/m^3 n-hexane; 2) the minute volume of the mouse is 0.024 l/min (Altman and Ditmar, 1974) and the average body weight is 45 g; and 3) approximately 80% of the test material is absorbed. On this basis the dose of n-hexane to an adult mouse in the 5000-ppm group would be approximately 11.5 g/kg/day, a value only slightly higher than the highest oral dose level employed by Marks

et al. (1980). In summary, although there is no obvious conflict between the results reported by Marks et al. (1980) and the results of this study, their study does not indicate significant developmental toxicity in the absence of maternal toxicity.

Another inhalation study, also conducted for the National Toxicology Program under the same conditions as described herein for Swiss (CD-1) mice (Mast, 1987), produced no evidence of developmental toxicity in Sprague-Dawley rats in the absence of maternal toxicity. Extra-gestational weight gain in the rat was reduced for all n-hexane exposure groups and was relatively more pronounced than the corresponding decrease in uterine weight. There was no exposure-related increase in the incidence of malformations, although there was an increase in the incidence of reduced sternebral ossifications. Interestingly, if the same dose calculation is applied to the rat that was used above for the mouse, the dose for the rat is considerably lower. Assuming an average body weight of 350 g and a minute volume of 0.073 l/min (Altman and Ditmar, 1980), the daily dose for the rat at 5,000-ppm level is approximately 4.5 g/kg/day, less than one-half the dose calculated for the mouse.

In summary, exposure of Swiss (CD-1) mice to 200, 1000, or 5000 ppm n-hexane during gestation resulted in some exposure-correlated developmental toxicity in the absence of maternal toxicity. This developmental toxicity was revealed by exposure concentration-related increases in the incidence of late resorptions and decreases in gravid uterine weight, and by decreases in gravid uterine weight to maternal extra-gestational weight gain ratios. There was no increase in the incidence of specific malformations or variations, nor in the incidence of total malformations or variations.

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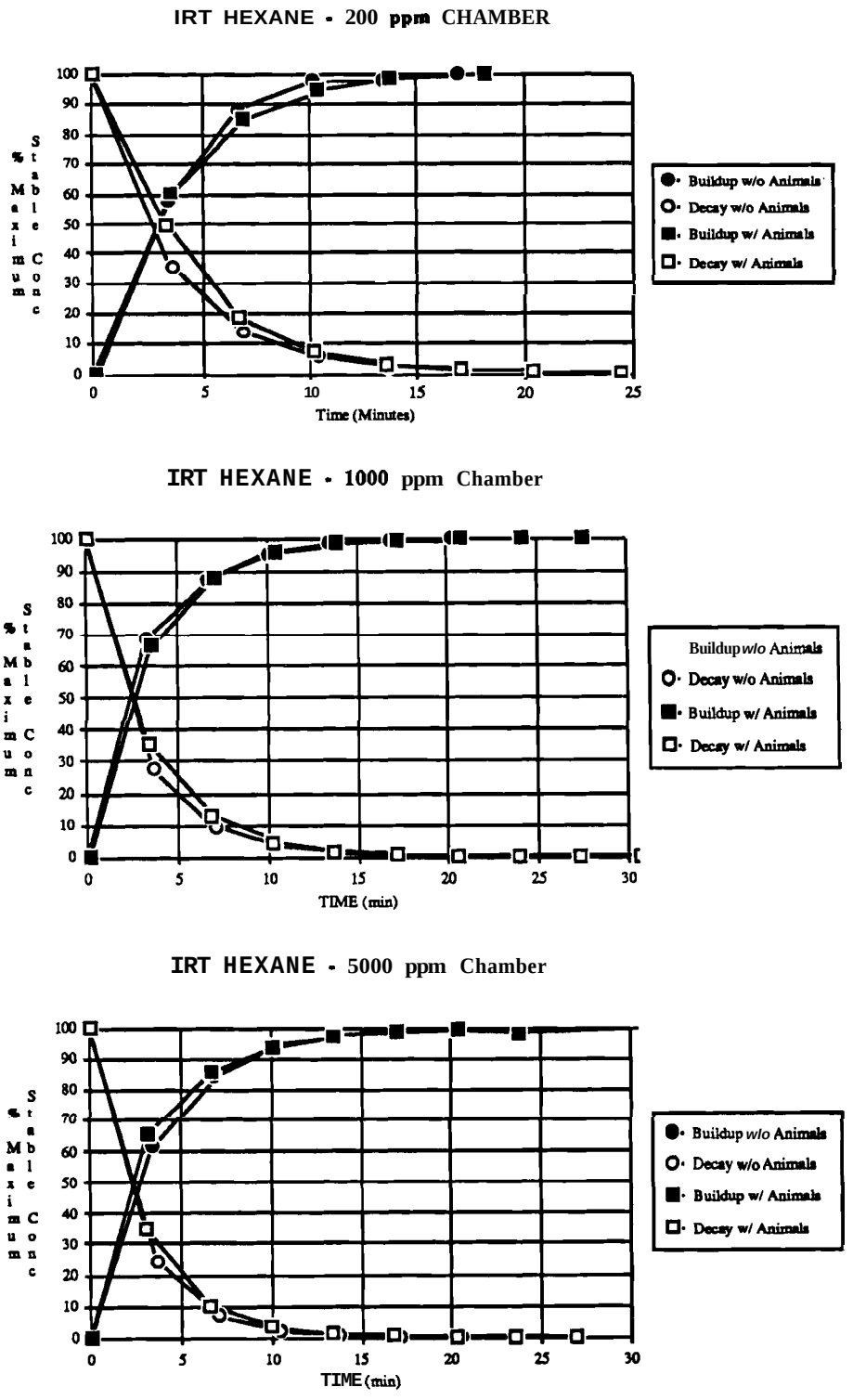


FIGURE 1. Buildup and Decay of n–Hexane Vapor Concentrations in the 200, 1000 and 5000 ppm Chambers (With and Without Animals Present).

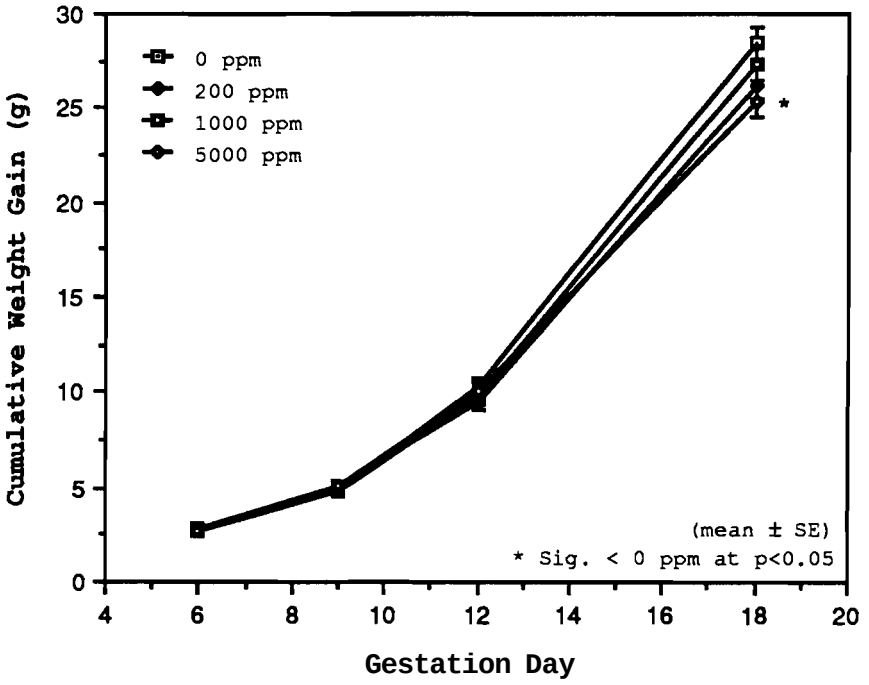
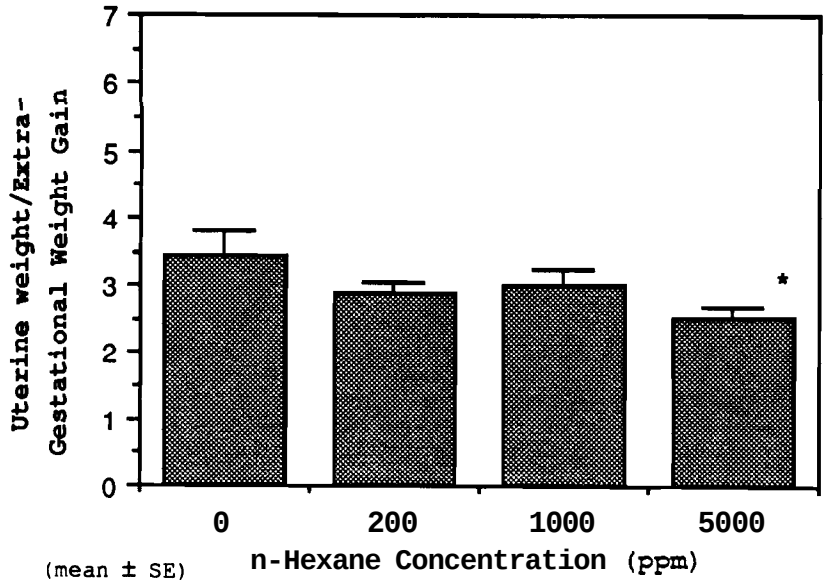


FIGURE 2 Cumulative Weight Gain for Pregnant Dams (6-18 days of gestation) Exposed to n-Hexane Vapors During Gestation.



* Significantly **less** than control, p<0.05.

FIGURE 3. The Ratio of Gravid Uterine Weight to Maternal Extra-gestational Weight Gain at 18 dg. The decreasing ratio is linearly correlated to increasing exposure concentration, p<0.05.

TABLE 1. n–Hexane Mouse Teratology: Average Daily Exposure Chamber Concentrations

0 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	0	0	0%	0	0
2	0	0	0%	0	0
3	0	0	0%	0	0
4	0	0	0%	0	0
5	0	0	0%	0	0
6	0	0	0%	0	0
7	0	0	0%	0	0
8	0	0	0%	0	0
9	0	0	0%	0	0
10	0	0	0%	0	0
11	0	0	0%	0	0
12	0	0	0%	0	0
13	0	0	0%	0	0
14	0	0	0%	0	0
15	0	0	0%	0	0
16	0	0	0%	0	0
Summary	0	0	0%	0	0

200 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	166	56	34%	0	207
2	196	19	10%	169	260
3	214	21	10%	163	291
4	196	11	6%	181	211
5	209	15	7%	116	215
6	204	3	2%	199	215
7	204	3	1%	195	210
8	202	16	8%	100	207
9	204	1	1%	200	207
10	211	3	2%	198	214
11	207	2	1%	204	214
12	204	25	12%	42	212
13	205	1	1%	200	207
14	208	1	0%	206	210
15	209	1	1%	206	213
16	207	3	2%	203	216
Summary	203	21	10%	0	291

1000 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	1050	105	10%	418	1260
2	1050	7	1%	1010	1060
3	1020	77	7%	671	1160
4	1040	5	0%	1030	1050
5	1030	132	13%	201	1060
6	1020	8	1%	1010	1040
7	1020	4	0%	1010	1020
8	1000	5	1%	988	1010
9	1000	7	1%	977	1010
10	1010	17	2%	970	1030
11	1010	6	1%	992	1030
12	991	50	5%	679	1020
13	983	58	6%	637	1020
14	1020	5	1%	1000	1030
15	1030	7	1%	1000	1040
16	1030	17	2%	974	1050
Summary	1020	53	5%	201	1260

5000 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	5110	58	1%	5020	5230
2	5070	74	1%	4740	5250
3	5000	662	13%	1200	5670
4	5100	37	1%	5020	5170
5	4980	798	16%	4630	5180
6	5090	29	1%	5040	5160
7	5140	30	1%	5080	5200
8	5160	33	1%	5080	5210
9	5140	45	1%	4990	5220
10	4980	35	1%	4910	5050
11	4960	46	1%	4780	5070
12	4910	81	2%	4490	5020
13	4940	101	2%	4380	5050
14	5090	26	1%	5040	5140
15	5120	33	1%	5010	5180
16	4990	87	2%	4870	5180
Summary	5050	267	5%	4630	5670

TABLE 2. n-Hexane Mouse Teratology: Mean Body Weights for Virgins (g ± SD).

Exposure Concentration	N	Exposure Day 1 Mean ±SD	Exposure Day 4 Mean ±SD	Exposure Day 7 Mean ±SD	Exposure Day 12 Mean ±SD
0 ppm	10	29.7f2.0	29.3f1.9	29.2k2.2	29.5f2.3
200 ppm	10	28.7 ±1.8	28.4 ±1.8	28.2k2.0	28.0f1.9
1000 ppm	10	29.5f1.5	29.8f1.7	29.8f1.6	29.8 ±1.7
5000 pprn	10	28.7 f2.1	29.4 ±2.2	29.7 f1.9	30.4 f2.0

TABLE 3. n-Hexane Mouse Teratology Study: Mean Body, Uterine, and Extra-gestational Weights for Preqnant Dams (q ± SD).

Exposure Concentration	N	DG 6 Mean f SD	DG 9 Mean ± SD	DG 12 Mean ± SD	DG 18 (a) Mean ± SD	Uterine (a) Mean ±SD	Extra-gestational Gain Mean ±SD
0 ppm	27	31.5 ±1.6	33.5 ±1.8	39.0f2.7	57.0f5.0	21.4 f3.8	7.0 f1.9
200 ppm	27	31.3f1.5	33.6f1.9	38.0f2.2	54.8f4.0	19.2 ±3.4(b)	7.0 f1.7
1000 ppm	28	31.1 ±1.3	33.2f1.8	38.1f2.7	55.7 ±4.9	20.2 f3.5	7.2 f1.9
5000 ppm	25	31.0 ±1.6	33.5 f2.0	38.5 ±2.9	53.7 f4.6 (b)	17.8 f3.9 (c)	7.5 f1.7

a = Decrease in weights linearly correlated with increasing exposure concentration, p<0.05.
b = Significantly different from control groups at p<0.05.
c = Significantly different from control groups at p<0.01.

~~TABLE 4.~~ n-Hexane Mouse Teratology Study: Reproductive Measures (mean ± SD).

	n-Hexane Chamber Concentration (ppm)			
NUMBER OF:	0	200	1000	5000
Plug-positive mice exposed	35	35	35	35
Number pregnant mice	29 (a)	28 (b)	29 (b)	26 (b)
Pregnant mice (%)	83	80	83	74
Litters with live fetuses	27	27	28	25
Implantations/dam	12.6 ± 2.6	12.2 ± 2.1	12.2 ± 2.3	11.3 ± 2.6
Live fetuses/litter (c)	12.0 ± 2.6	10.6 ± 2.2	11.4 ± 2.4	10.2 ± 2.7 (d)
Resorptions/litter	0.6 ± 0.7	1.6 ± 1.7 (d)	0.8 ± 0.9	1.1 ± 1.2
Early	0.5 ± 0.6	1.2 ± 1.4	0.4 ± 0.7	0.6 ± 1.0
Late (c)	0.0 ± 0.2	0.4 ± 0.9	0.4 ± 0.6	0.5 ± 0.8 (d)
Dead fetuses/litter	0	0	0	0
PERCENTAGE OF:				
Live fetuses/litter	95.5 ± 5.6	87.2 ± 12.2 (e)	93.5 ± 7.2	89.7 ± 12.4
Resorptions/litter	4.5 ± 5.6	12.8 ± 12.2 (e)	6.5 ± 7.2	10.3 ± 12.4
Early	4.3 ± 5.3	9.4 ± 10.9	3.5 ± 5.6	5.8 ± 9.5
Late (c)	0.3 ± 1.3	3.4 ± 6.6	2.9 ± 4.6	4.5 ± 6.5 (e)

(a) Two pregnant females removed from study (see Appendix C).
(b) One pregnant female removed from study (see Appendix C).
(c) Values correlated to increasing exposure concentrations, $p<0.05$.
(d) Significantly different from controls, $p<0.05$ (Tukey's t-test).
(e) Significantly different from controls following arcsin transformation of proportional data, $p<0.05$ (Tukey's t-test).

TABLE 5. n–Hexane Mouse Teratology Study: Average Fetal and Placental Weights (Mean of Litter Means; g ± SD).

	n–Hexane Chamber Concentration (ppm)			
	0	200	1000	5000
Litters examined	27	27	28	25
Fetuses examined	325	287	319	255
Heads examined	163	142	160	128
Proportion Male	0.46 ± 0.13	0.48 ± 0.18	0.53 ± 0.15	0.44 ± 0.16
Fetal weight (a)	1.42 ± 0.11	1.40 ± 0.10	1.37 ± 0.10	1.35 ± 0.11
Placental weight	0.09 ± 0.01	0.09 ± 0.01	0.09 ± 0.01	0.09 ± 0.01
Fetal weight:				
Male	1.45 ± 0.12	1.45 ± 0.16	1.40 ± 0.12	1.40 ± 0.12
Female (a)	1.39 ± 0.10	1.37 ± 0.10	1.35 ± 0.10	1.31 ± 0.11(b)
Placental weight				
Male	0.10 ± 0.01	0.10 ± 0.01	0.10 ± 0.01	0.10 ± 0.02
Female	0.09 ± 0.01	0.09 ± 0.01	0.09 ± 0.01	0.09 ± 0.02

(a) Values linearly correlated with increasing exposure concentration, $p<0.05$.
(b) Significantly less than controls at $p<0.05$.

TABLE 6. Contemporary Control Data for Swiss (CD-1) Mice (N=83 Litters; Mean ± SD).

		Percent
Maternal Weight; 18 dg (g)	54.6 ± 4.9	---
Gravid Uterine Weight (g)	20.2 ± 3.6	---
Extra-gestational Weight Gain (g)	6.8 ± 2.0	---
Implants/Litter	12.6 ± 2.1	---
Live Fetuses/Litter	11.7 ± 2.2	93.5 ± 7.3
Early Resorptions/Litter	0.6 ± 0.8	4.6 ± 6.3
Late Resorptions/Litter	0.2 ± 0.5	1.9 ± 3.7
Dead Fetuses/Litter	0.0 ± 0.0	0.0 ± 0.0
Total Intrauterine Death/Litter	0.8 ± 1.0	6.5 ± 7.3
Fetal Weight (g)	1.36 ± 0.11	---
Male (g)	1.39 ± 0.11	---
Female (g)	1.34 ± 0.10	---

TABLE 7. n-Hexane Mouse Teratology Study: Alterations Observed in Live Fetuses.

		Fetuses (a)				Litters			
n-Hexane (ppm)		0	200	1000	5000	0	200	1000	5000
Total examined (b)		325	287	319	255	27	27	28	25
Heads examined (c)		163	142	160	128	27	27	28	25
Skulls examined (d)		162	145	159	127	27	27	28	25
Variations									
Dilated Ureter	No.	0	0	1	0	0	0	1	0
	(%)	(0.0)	(0.0)	(0.3)	(0.0)	(0.0)	(0.0)	(3.6)	(0.0)
Supernumerary Rib	No.	30	27	40	37	11	10	12	13
	(%)	(9.2)	(9.4)	(12.5)	(14.5)	(40.7)	(37.0)	(42.9)	(52.0)
Fused Rib	No.	0	1	0	0	0	1	0	0
	(%)	(0.0)	(0.3)	(0.0)	(0.0)	(0.0)	(3.7)	(0.0)	(0.0)
Misaligned Sternabrae	No.	5	3	1	0	4	3	1	0
	(%)	(1.5)	(1.0)	(0.3)	(0.0)	(14.8)	(11.1)	(3.6)	(0.0)
Reduced Ossifications									
Sternebrae	No.	22	15	16	19	14	11	10	10
	(%)	(6.8)	(5.2)	(5.0)	(7.5)	(51.9)	(40.7)	(35.7)	(40.0)
Skull	No.	10	1	5	3	5	1	5	3
	(%)	(6.2)	(0.7)	(3.1)	(2.4)	(18.5)	(3.7)	(17.9)	(12.0)
Total Variations	No.	67	47	63	59	21	16	21	20
	(%)	(20.6)	(16.4)	(19.7)	(23.1)	(77.8)	(59.3)	(75.0)	(80.0)
Malformations									
Exencephaly	No.	0	0	0	1	0	0	0	1
	(%)	(0.0)	(0.0)	(0.0)	(0.4)	(0.0)	(0.0)	(0.0)	(4.0)
Limb Flexure	No.	7	2	0	0	4	2	0	0
	(%)	(2.2)	(0.7)	(0.0)	(0.0)	(14.8)	(7.4)	(0.0)	(0.0)
Total Malformations	No.	7	2	0	1	4	2	0	1
	(%)	(2.2)	(0.7)	(0.0)	(0.4)	(14.8)	(7.4)	(0.0)	(4.0)

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.

TABLE 8. Contemporary Control Data on Mouse Teratology Studies: Malformations and Variations.

		Fetuses (a) Number (Percent)	Litters Number (Percent)	Mean Percent per Litter (± SD)
Total examined (b)		975	83	---
Heads examined (c)		---	---	
Skulls examined (d)		---	---	
Variations				
Supernumerary Rib	No.	175	52	18.5 ± 24.4
	(%)	(17.9)	(62.7)	
Misaligned Sternabrae	No.	23	14	2.3 ± 6.3
	(%)	(2.4)	(16.9)	
Reduced Ossifications				
Sternebrae	No.	36	25	3.7 ± 6.4
	(%)	(3.7)	(30.1)	
Skull	No.	10	5	1.1 ± 4.8
	(%)	(1.0)	(6.0)	
Total Variations	No.	244	67	25.5 ± 26.1
	(%)	(25.0)	(80.7)	
Malformations				
Exencephaly	No.	1	1	0.1 ± 1.2
	(%)	(0.1)	(1.2)	
Folded Retina	No.	2	2	0.2 ± 1.5
	(%)	(0.2)	(2.4)	
Limb Flexure	No.	12	8	1.1 ± 3.8
	(%)	(1.2)	(9.6)	
Total Malformations	No.	15	10	1.5 ± 4.5
	(%)	(1.5)	(12.0)	

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.

TABLE 9. n–Hexane Mouse Teratology Study: Observed Variations and Abnormalities in Live Fetuses (Mean Percent per Litter Affected).

	n-Hexane Concentration (ppm)			
	0	200	1000	5000
Total litters examined	27	27	28	25
Variations:	% ± SD	% ± SD	% ± SD	% ± SD
Dilated Ureter	0 ± 0	0 ± 0	0.5 ± 2.7	0 f 0
Supernumerary Rib	9.3 ± 17.7	9.9 ± 18.4	12.2 ± 18.0	16.3 ± 20.3
Fused Rib	0 ± 0	0.4 ± 2.1	0 f 0	0 ± 0
Misaligned	1.4 ± 3.6	1.4 ± 4.5	0.3 ± 1.6	0 ± 0
Reduced Ossification:				
Sternebrae	6.8 ± 8.1	5.5 ± 7.6	5.1 ± 8.6	8.4 ± 14.5
Skull	3.3 ± 8.0	0.3 ± 1.5	1.6 ± 3.7	1.0 ± 2.8
Total Variations	20.8 ± 21.2	17.6 ± 22.9	19.8 ± 20.7	25.7 ± 27.9
Malformations:				
Exencephaly	0 ± 0	0 f 0	0 f 0	0.5 ± 2.5(a)
Limb Flexure	1.9 ± 5.2	0.7 ± 2.6	0 f 0	0 ± 0
Total Malformations:	1.9 ± 5.2	0.7 ± 2.6	0 f 0	0.5 ± 2.5

a) Significantly different from controls at $p<0.05$ following arcsin transformation of data and Tukey's t–test.

APPENDIX A

ANALYTICAL CHEMISTRY NARRATIVE AND DATA FOR N-HEXANE

ANALYTICAL CHEMISTRY NARRATIVE AND DATA FOR n-HEXANE

1. Test Material Receipt and Usage

n-Hexane, manufactured by Phillips Chemical Company, was received from Research Triangle Institute (RTI), P.O. Box 12194, Research Triangle Park, NC 27709-9981. The test material for this study (RTI Lot#H-222) was received on 5/19/86 and consisted of two 55-gallon drums containing ~102 gallons of n-hexane (Identified as BNW Lot 51436-58).

The bulk chemical was stored in its original shipping container at ~65°F in a flammable storage cabinet and maintained under a blanket of nitrogen. All transfers from the 55-gallon drum to the reservoir took place under a blanket of nitrogen to avoid the introduction of air into the bulk chemical. Approximately 12.5 kg of test material were required for each exposure day. The usage of n-hexane for the mouse teratology study is summarized in Table 1.

Table 1. Mouse Teratology Study with n-Hexane - Chemical Usage

Exposure Period	RTI Lot#	BNW Lot#	Test Material Used
3/18/87 - 4/2/87	H-222	51436-58 (Drums 1 & 2)	≈194 kg

2. Bulk Chemical Analysis

Bulk chemical analysis was performed using infrared spectroscopy and gas chromatography (GC) for identity and purity determinations. The gas chromatographic system used for purity analysis employed a 1.8m x 2mm glass column packed with 0.1% SP-1000 on 80/100 Carbopack C. BNW Lot 51436-58 was analyzed for bulk purity and found to be 99.2% pure relative to the frozen reference material BNW 51436-67-2.

3. Vapor Concentration Monitoring

A Hewlett-Packard 5840 gas chromatographic system (employing a 1/8" o.d. x 1.0 foot nickel column packed with 1% SP-1000 on 60/80 mesh Carbopack B; oven temperature was 120°C) was used to monitor animal exposures. This instrument was equipped with an 8-port stream select valve and measured n-hexane in the three exposed chambers, the control chamber, the exposure room, and the on-line standard.

a. Calibration of the On-Line Chamber Monitor

The calibration of the on-line chamber monitor was based on analysis of bubbler grab samples. Thus, the calibration of the on-line monitor was tied to gravimetrically prepared standard solutions in dodecane through a second directly calibrated GC which was off-line. The analysis depended upon quantitative preparation of gravimetric standards and careful grab sampling. The gravimetrically calibrated GC was used to measure the quantity of n-hexane collected from exposure chambers in dodecane filled bubblers. The relationship between the peak area observed with the on-line GC and the concentration of n-hexane in the chamber was then defined using chamber concentrations determined by the gravimetrically calibrated GC.

The analysis of bubbler grab samples was performed using a HP 5830 or HP 5840 GC with a 2 or 4 mm id x 1.8 m glass column packed with 3% OV-17 on 100/120 mesh Supelcoport. The temperature program was 40°C for 3 minutes to 150°C for 10 minutes at the rate of 15°C/minute. A set of three standards was run for each analysis session. The concentration range of the standards bracketed the concentration range of interest.

The calibration procedure required quantitatively prepared gravimetric standards and carefully collected grab samples of a measured volume. The collection efficiency of a single bubbler was less than 100%, some hexane broke through the primary bubbler. Breakthrough was typically 4-5%. Breakthrough was measured each time bubblers were collected by acquiring back-up bubblers for the high concentration chamber. The calculation for chamber concentration by the grab sampling method included a breakthrough correction.

b. Detection of Monitor Drift Using an On-Line Standard

An on-line standard was used to check instrument drift throughout the exposure day. The on-line standard was 1000 ppm n-hexane in nitrogen (MG Industries Scientific Gases, 11705 South Alameda St., Los Angeles, CA). The standard was checked before the start of any given exposure day, then monitored every 8th sample throughout the exposure period. The measured concentration for the standard had to be within ±10% of the assigned target value before any exposure could begin without consultation with the Exposure Control Task Leader. During the course of the exposure, if the on-line standard was within 5% of the target value, no change in calibration was required. If the on-line standard was between 5% and 10% of its assigned target, the calibration could be updated immediately by an Exposure or Chemistry Specialist. Such a correction was based upon the on-line standard. If the cumulative drift exceeded 15%, then the calibration was checked by quantitative analysis of grab samples.

c. Demonstration of Sensitivity and Specificity

The sensitivity of the GC was estimated from the decay profile for the highest concentration chamber. The minimum detectable limit (MDL) was estimated as 0.11 ppm. A measure of chromatographic specificity was defined by determination of the analytes partition coefficient. The retention time of methane, assumed to be non-retained was 0.13 min.; the retention time for n-hexane was 1.55 minutes. Thus, the partition ratio was about 11.0.

d. Precision, Linearity and Absolute Recovery Evaluation

Precision for the on-line GC was estimated from 8 consecutive measurements made on the 1000 ppm on-line certified standard using every active port on the 8 port stream select valve; a 0.2% coefficient of variation (CV) was observed (all values fell within ±3 ppm of the mean). Linearity of the on-line GC was assured by calibrating the on-line GC against a gravimetrically calibrated GC (also see comments in the "Calibration of the On-Line Chamber Monitor" section). This was accomplished by analyzing a series of bubbler grab samples acquired during exposure generation and then implementing the appropriate on-line GC calibration curve in the data acquisition and control system.

Achievement of linearity for the on-line monitor was therefore dependent upon defining a linear method for analysis of bubbler samples. The

calibration curve for this analysis showed good linearity over an extended range. Routine analysis of bubblers was performed using midrange, high and low level standards in order to assure linearity.

4. n-Hexane Degradation Studies

a. n-Hexane Stability in the Reservoir

Under the storage and generation conditions employed, decomposition of n-hexane was not anticipated. Prestart tests to confirm test material stability included analysis of an aged reservoir sample. n-Hexane (BNW Lot **50846-39)** was placed in the reservoir for generation of chamber atmospheres. At the end of **5** days, an aliquot of the test material was removed from the reservoir. Infrared spectroscopy and gas chromatography were used for identity and purity determinations. The bulk purity of the aged reservoir sample was **99.1%** relative to the reference material.

b. n-Hexane Degradation in Exposure Chambers

Studies of the degradation of n-hexane in the exposure chambers (with animals) were conducted on **3/28/87.** No evidence of impurities or degradation products was found. n-Hexane, BNW Lot **51436-58,** was the source of the test material. During exposure, samples of chamber atmospheres from the **5000** ppm and the **200** ppm chambers were taken by pulling a measured volume of gas through standard gas-sampling charcoal tubes. The sample size was adjusted to provide adequate sensitivity to detect impurities. Duplicate charcoal samples were taken at **4.6** and **27.6** liter collection volumes for the **5000** ppm and **200** ppm chambers. The charcoal tubes were desorbed using carbon disulfide. The GC conditions are summarized on the attached sample chromatograms.

Breakthrough was measured for each sample level and volume. Less than 5% breakthrough of total sample was observed for the **4.6** and **27.6** liter samples from the **5000** ppm and **200** ppm chambers. These determinations were made by analysis of the secondary charcoal bed within the tubes.

BULK CHEMICAL REANALYSIS

COMPOUND:	n-HEXANE
CAS#	110-54-3
LOT#	Phillips lot# H-222(BNW#51436-58-1)
APPEARANCE:	Clear liquid
RECEIPT DATE:	5/19/86
ANALYSIS PERIOD:	Subsequent
STORAGE TEMPERATURE:	**Room** Temperature
SAMPLE SUBMITTAL DATE:	3/5/87
SAMPLE ANALYSIS DATE:	3/5,6/87
ANALYSIS **PROCEDURE:**	Method #ØB-AC-3A15-ØØ
NOTEBOOK REFERENCE:	BNW 51436-85

ASSAY: Gas chromatography using a 1.8m x 2mm glass column packed with 0.1% SP-1000 on 801100 Carbopack C

Instrument: HP 5830A

RESULTS: % Purity

Date	Bulk
3/87	Reference Material RRF 0.5367 RSD ± 2.078 (BNW 51436-67-2)
	Test Material RRF 0.5326 RSD ± 1.41% (BNW 51436-58-1)
	Relative % Purity
	99.2

Retention Time of n-Hexane –2.5 minutes.
Retention **Time** of Internal **Standard** –6.9 minutes.

Test material sample was taken from drum BNW 51436-58-1

ASSAY: Gas chromatography using a 1.8m x 2mm glass column packed with 0.1 % SP-1000 on 80/100 Carbopack C

Instrument: HP 5830A

RESULTS: Impurity Profile

	Area %	
	Reference	Test
~RT	Material	Material
8.26	0.351	0.351
10.55	0.075	0.076
10.93	0.004	0.004
11.33	0.003	0.003

A major peak of 99.578 area **was** observed at a retention time of –12.6 minutes for both the reference and test material. Both the reference and test materials showed **4** impurity peaks, all ≥ 0.0038.

CONCLUSIONS: The basis of the analysis is quantitation of the major component of the bulk chemical by GC major peak comparison to a frozen reference material. Gas chromatography shows four impurity peaks similar in RT and **Area %** all ≥ 0.003%. Gas Chromatography also shows the test material to have a Relative Purity of 99.28 by area ratio of an internal standard.

Signature of Technician: S. A. Barraclough Date: 4-8-87

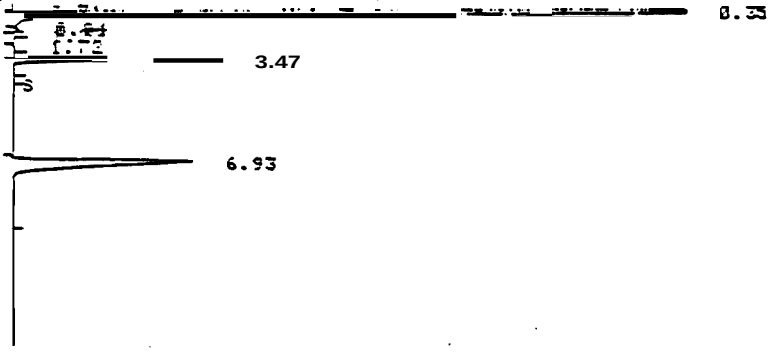
Signature of Chemist: [signature] Date: 4/18/87

```
TEMP:     400  150  150
TIME:      15.00
INJ TEMP 400  150  250
FID TEMP 400  275  275
TCD TEMP 400    0   45

CHT SPD     0.50
ZERO       10.2
ATTN 2^    14
FID SGNL    -5
SL? SENS    0.10
AREA REJ       0
FLOW  A     0.0   27.6
FLOW  B     0.0    4.4
```

Subsequent Purity Analysis of n-Hexane
Method: ØB-AC-3A15-ØØ
Column: 1.8 m x 2 mm I.D. glass,
0.1% SP-1000 on 80/100 Carbopack C
BNW 51436-80
GC: HP5840
Test Material: BNW 51436-58-1
Reference Material: BNW 51436-67-2
p. BNW 51436-85

```
DELETE CHANGE RUN 0
CHANGE RUN B 0
OPTN # 3 0
 INJ/STL,STROKE: 2 2 0
CHANGE RUN 1 4 STOP
START
```



RF: 0.5256

```
HP RUN #   1
BOTTLE  I
AREA %
```

Test Material: BNW 51436-58-1

RT	AREA	AREA %
0.31	156	6.000
0.35	2357000000	94.101
0.94	48140	0.016
1.01	66000	0.026
1.03	19960	0.008
1.72	7812	0.003
2.47	5045000	2.014
6.93	9590000	3.832

```
DIL FACTOR: 1.0000 E- 0
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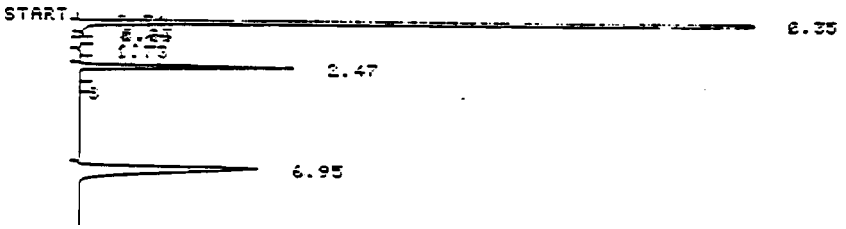



```
HP RUN #   8
BOTTLE  4
AREA %
```

Reference Material: BNW 51436-67-2

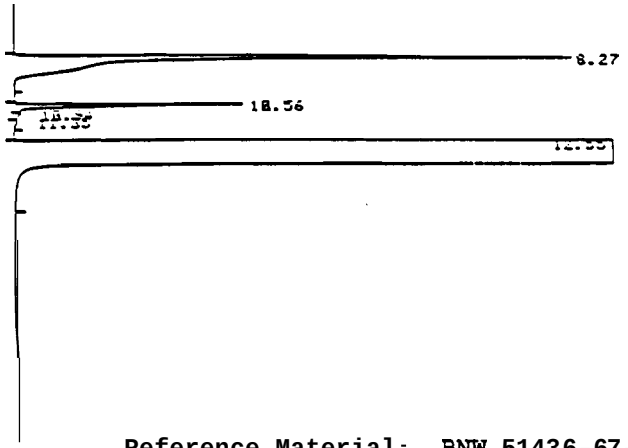
RT	AREA	AREA %
0.31	176	6.000
0.35	2412000000	94.130
0.93	48000	0.015
1.01	67000	0.027
1.03	14100	0.009
1.72	1100	0.000
2.47	5445000	2.000
6.93	9744000	3.719

RF: 0.5566

```
DIL FACTOR: 1.0000 E- 0
```

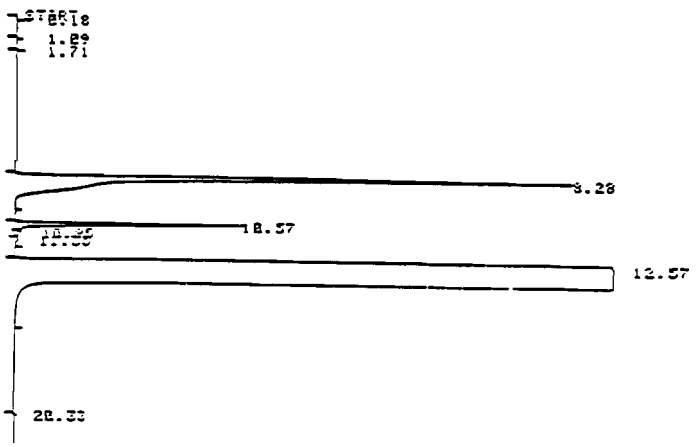
TEMP1	50	
TIME1	5.0	50
RATE	10.00	
TEMP2	225	
TIME2	5.0	
INJ TEMP	200	200
FID TEMP	250	250
OVEN MAX	400	
CHT SPD	0.50	
ATTN 2^	10	
FID SGNL	+0	
SLP SENS	0.10	
AREA REJ	1	
FLOW A	3	
FLOW B	84	
OPTN	21	

Impurity Profile of n-Hexane
Method: ØB-AC-3A15-ØØ
Column: 1.8 m X 2 mm I.D. glass,
0.1% SP-1000 on 80/100 Carbopack C
BNW 51436-80
GC: HP5840
Test Material: BNW 51436-58-1
Reference Material: BNW 51436-67-2
p. BNW 51436-85



BOTTLE 34 Reference Material: BNW 51436-67-2
** 5838A
AREA %

RT	AREA	AREA %
0.17	172	0.000
1.89	434	0.000
1.69	85	0.000
8.27	2887000	0.349
18.56	426200	0.074



BOTTLE 35 Test Material: BNW 51436-58-1
** 5838A
AREA %

RT	AREA	AREA %
0.10	167	0.000
1.89	157	0.000
1.71	36	0.000
8.28	1900000	0.350
18.57	420400	0.077
18.95	22500	0.004
11.35	14420	0.003
12.57	560000000	99.560
20.33		0.000

n-Hexane degradation in Exposure Chamber with Animals Present

Degradation Study

Studies of the degradation on hexane in the exposure chambers were conducted for the test run performed on March 28, 1987 Test material BNW Lot No. 51436-58 was used as the source of test material. The bulk purity using gas chromatography by major peak comparison was approximately 99.25 .

Samples were taken from the high (5000 ppm) and low (200 ppm) chambers were taken with animals present by pulling a measured volume of gas through standard gas sampling charcoal tubes. Sample size was adjusted to provide adequate sensitivity for impurities. Sample size was 4.6 liters for the 5000 ppm chamber and 27.6 liters for the 200 ppm chamber. Breakthrough was measured and found to be less than 5% for the 5000 ppm and 200 ppm samples by analysis of the secondary charcoal bed within the tubes. We assume that good trapping efficiency for impurities and degradation products will be achieved when good trapping efficiency is observed for hexane. Comparison of a hexane sample with a hexane sample desorbed from charcoal shows a good recovery ratio (-100%). The charcoal was transferred to GC autosampler vials and desorbed using carbon disulfide with approximately 1 minute of ultrasound treatment.

Samples were analyzed using an HP5890 chromatographic system with a DB-5, 30 m X 0.52 mm ID, 1.5 micron film thickness, fused silica megabore column and a temperature program of 35°C for 5 minutes to 250°C for 5 minutes at a rate of 20°C/minute.

Composition of Degradation Samples by GC Area %

RT (minutes)	Low Chamber	High Chamber	Bulk Hexane on Charcoal	Identity
2.2	-	0.10	0.11	unknown
2.4	99.58	99.51	04.50	n-hexane
2.8	0.41	0.38	0.39	unknown

An additional peak less than 0.004 % of total observed peak areas was observed for the high and low chamber charcoal samples at 14.5 minutes. This study shows no evidence for decomposition products exceeding 0.004% of the hexane concentration in the high and low chambers. The impurities at -2.2 and -2.8 minutes were found in equivalent amounts in a standard of bulk test material prepared with charcoal. Thus, these impurities are not formed by decomposition in the generator or chamber. The unknown peaks are probably other hexane isomers.

Technical Specialist: _____ Date: 5/7/87

Chemist: R.B. Westberg Date: 5/7/87

BULK CHEMICAL REANALYSIS

COMPOUND:	n-HEXANE
CAS#	110-54-3
LOT#	Phillips lot# H-222(BNW#51436-58-1&2)
APPEARANCE:	Clear liquid
RECEIPT DATE:	5/19/86
ANALYSIS PERIOD:	Initial
STORAGE TEMPERATURE:	Room Temperature
SAMPLE SUBMITTAL DATE:	6/6/86
SAMPLE ANALYSIS DATE:	6/6,10/86
ANALYSIS PROCEDURE:	Method #ØB-AC-3A15-ØØ
NOTEBOOK REFERENCE:	BNW 51436-70

IDENTITY: Infrared spectroscopy using a Nicolet FT-IR 60SX with 4mm NaCl windows and 0.1mm spacers.

RESULTS: The spectra was similar to that found in previous BNW analysis.

ASSAY: Gas chromatography using a a 1.8m x 4mm glass column packed with 0.1% SP-1000 on 80/100 Carbopack C.

Instrument: HP 5830A

RESULTS:

Date	% Purity Bulk		
6/86	Reference Material (BNW 50846-145-3)	RRF 0.5429	RSD ± 0.68%
	Test Material (BNW 51436-58-1)	RRF 0.5343	RSD ± 1.70

Relative % Purity

98.4

Retention Time of n-Hexane ~2.7 minutes.
Retention Time of Internal Standard ~ 7.0 minutes.
Minor impurity peaks were detected at ~ 1.4 and 2.0 minutes

Test material sample was taken from drum 1.

CONCLUSIONS: The basis of the analysis is quantitation of the major component of the bulk chemical by GC major peak comparison to 2 frozen reference material. S o reference material was provided. 5 x 10 ml portions of n-hexane were placed in glass septum vials, sealed with teflon lined septa and stored frozen for use as reference materials in future analyses. Infrared spectra was obtained between 4000cm-1 and 600cm-1. The spectra was similar to that provided by MRI.

Signature of Technician: _____ Date: 6-23-96

Signature of Chemist: _____ Date: 7/1/96

Initial Bulk (Re)analysis of Halane 59

Method: ØB-AC-3415-ØØ

GC: HP5830 N837630

Column: 1.8m x 2mm glass packed 80/100 Carbopack C / 0.1% SP1000 (BNW51436-33 KHK 4-22-86)

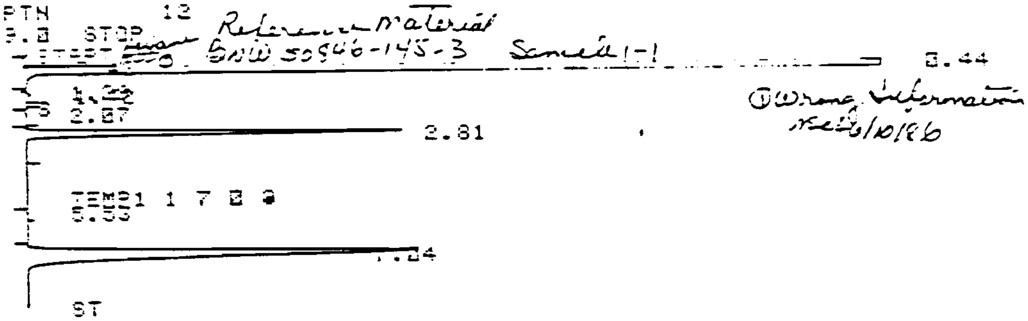
Bulk material: BNW51436-58-1

BNW51436-72 KHK 6/10/86

TEMP1	165	165
TIME1	15.0	
INJ TEMP	250	250
FID TEMP	275	275
OVEN MAX	400	

CHT SPD	0.50
ATTN 2↑	14
FID SGNL	-B
SLP SENS	0.10
AREA REJ	1
FLOW A	133
FLOW B	75
OPTN	12

9.0 STOP



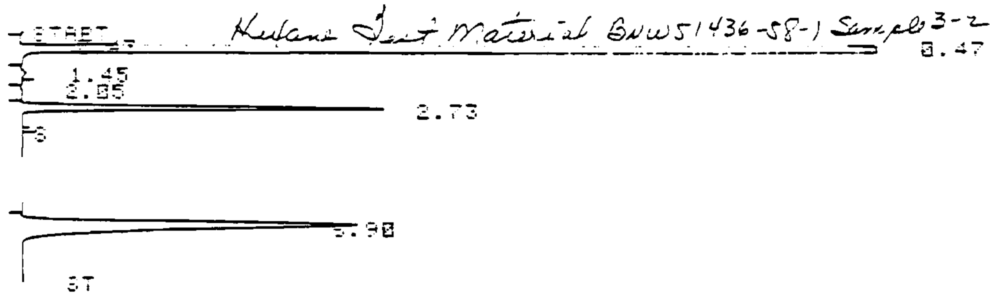
BOTTLE 22

** 5830A

NO METHOD

RT	AREA	AREA %
0.42	260700	0.057
0.44	429300000	94.403
1.29	5982	0.001
1.42	95120	0.021
2.07	6954	0.002
2.81	8762000	1.927
5.53	98	0.000
7.24	16320000	3.589

XF: 1.0000 E+ 0



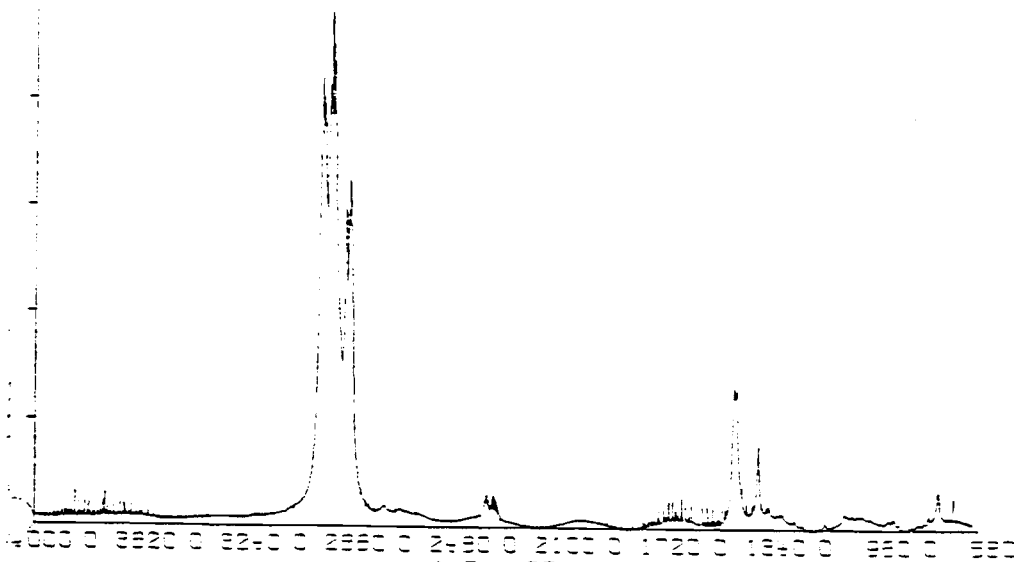
BOTTLE 33

** 5830A

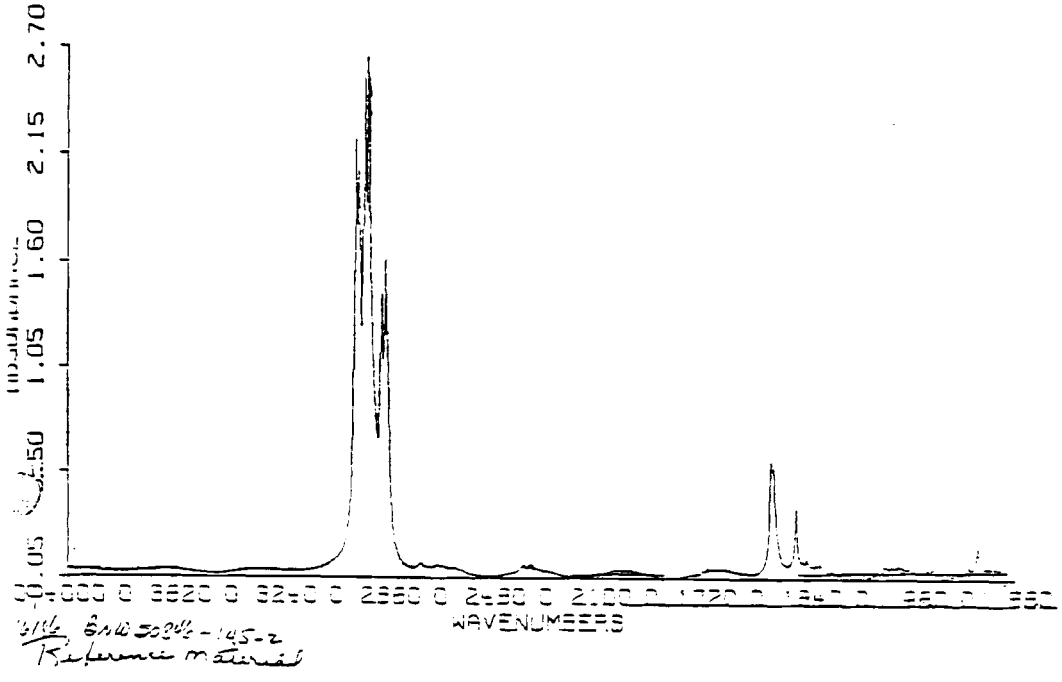
NO METHOD

RT	AREA	AREA %
0.43	3392000	1.632
0.47	447500000	93.045
1.45	121700	0.025
2.05	12070	0.003
2.73	8786000	1.827
5.98	16440000	3.418

Initial Bulk Analysis of n-H wane
Method: ØB-HC-3A1S-ØØ
Instrument: Nicolet FT-IR 60SX
Reference Material: BNW 51436-55-2
Bulk material: BNW 51436-55-1
BNW 51436-70 used 6-6/9-86



Initial Quick analysis of n-H room
Method: ΦB-HC-3A1S-ΦΦ
Instrument: Nicolet FT-IR 60SX
Reference Material: BNW 5036-145-2
Quick material: BNW ~~5036-~~ 51436-59-1
BNW 51436-70 used 6-6/9-86



APPENDIX B

EXPOSURE NARRATIVE AND DATA

FOR N-HEXANE

EXPOSURE DATA AND NARRATIVE FOR N-HEXANE

ANIMAL EXPOSURE CHAMBER

The Battelle-designed inhalation exposure chamber (commercially available from Harford Systems/Lab Products, Inc., Aberdeen, MD) ws used for the inhalation exposures. The 2.3 m^3 (1.7 m^3 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.

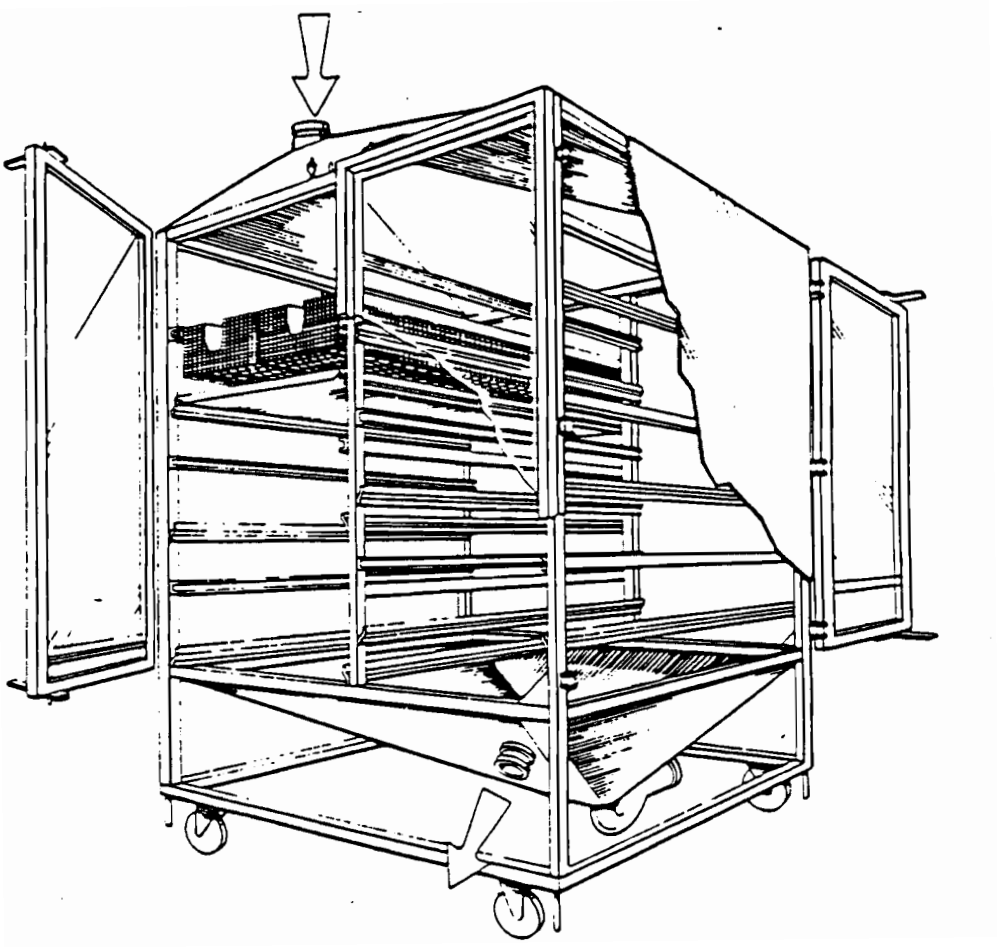
The catch pans, which remained in the chamber during exposure, were designed to aid in mixing to maintain uniform concentrations of aerosol, dust or vapors throughout the chamber. Incoming air was HEPA and charcoal filtered before addition of the test article. Incoming air containing a uniform mixture of the test article was diverted to flow 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 hexane 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 and 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 were stored in the exposure control center on separate micro-floppy diskettes. Data and comments from each exposure room were printed on separate printers. Data were printed and stored immediately upon completion of the measurement. At the end of the 24 hour period, the daily data were 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 ranges from audio/visual alert to automatic shutoff of the exposure generator. Alarm conditions which may have been a threat to the health of the animals alerted a building power operator who was on duty 24 hours per day.



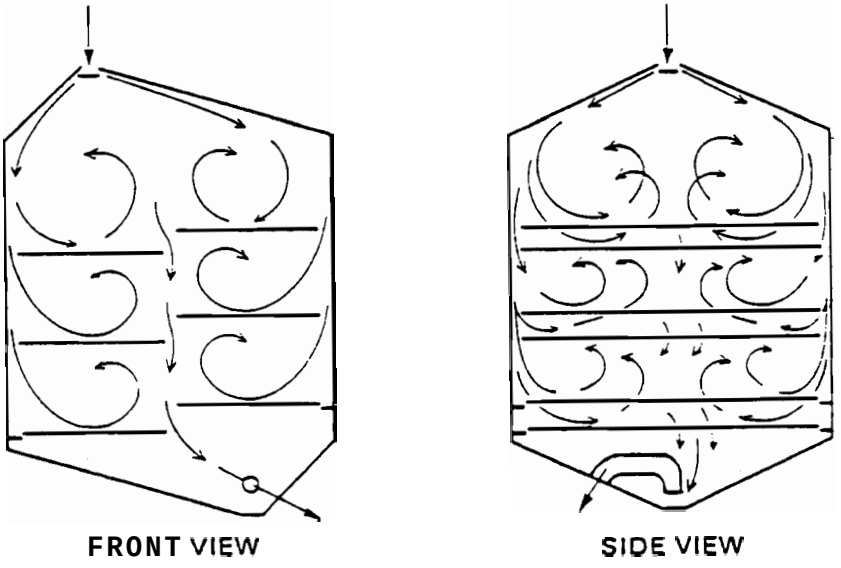


FIGURE B.1. n-Hexane Inhalation Exposure Chamber

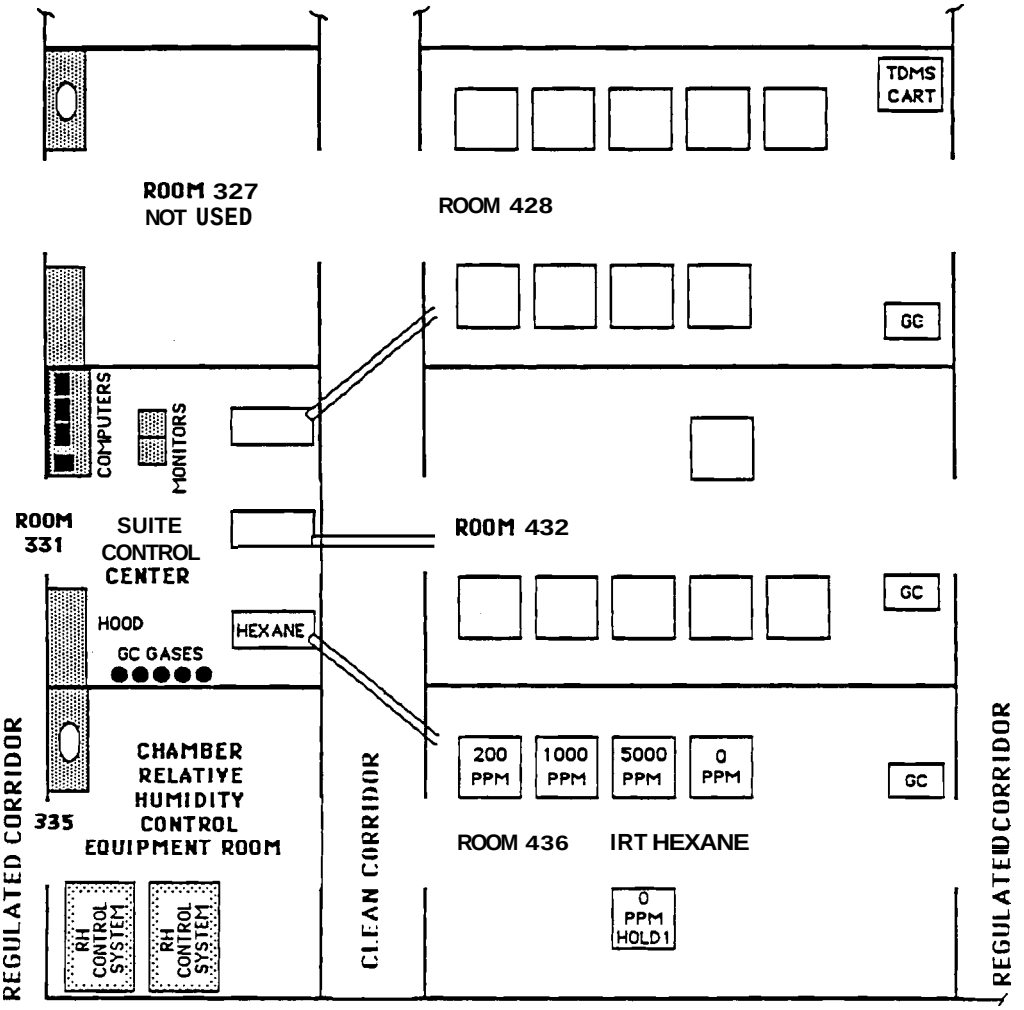


FIGURE B.2. n-Hexane Exposure Suite

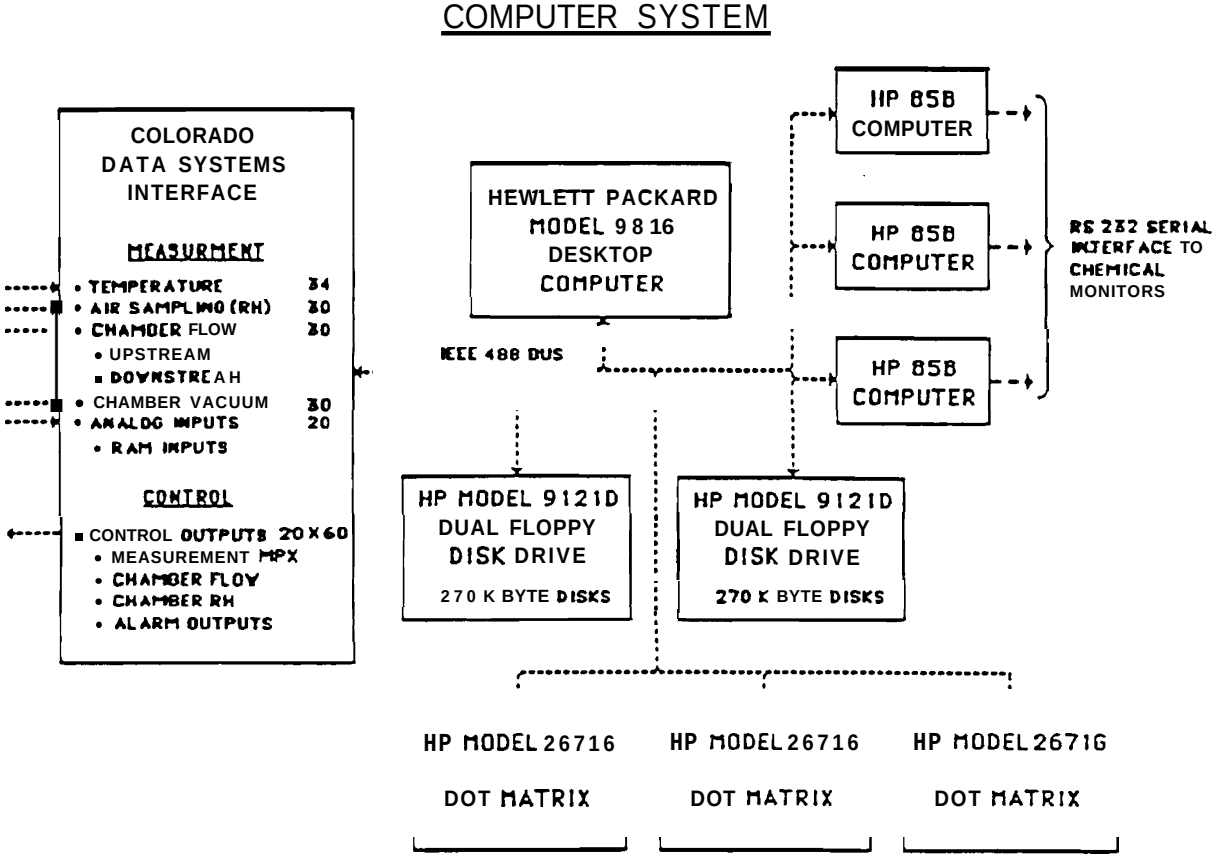


FIGURE B.3. **Data Acquisition System for n-Hexane Exposures**

Temperature was measured with an accuracy of approximately ± 0.5°F by Resistance Temperature Devices (RTD's) located at the measurement site. The RTD's 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.

Relative humidity (RH) was calculated with an accuracy of approximately ± 6% 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. 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 approximately ± 15 liters/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. Small 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 computer controlled pump in the exhaust line of each chamber.

Chamber vacuum, relative to the control center, was measured with an accuracy of approximately ± 0.2 cm H_2O using the same pressure transducer system which measured chamber air flows. Chamber vacuum was maintained at approximately (-)1" H_2O primarily by inlet resistance provided by the HEPA and charcoal filters.

HEXANE GENERATION SYSTEM

A schematic diagram of the Hexane generation and delivery system is shown in Figure B.4. Most of the generator was housed in a vented cabinet located in the Suite Control Center. The cabinet was vented to the building exhaust. The hexane to be vaporized was contained in a 19 liter stainless steel reservoir. This reservoir was filled daily from the original shipping container by the following method which was designed to prevent explosion during transfer. All oxygen in the reservoir was displaced with nitrogen through a purge port. The nitrogen pressure in the shipping container forced hexane through a filter and into the reservoir. The reservoir was on an electronic scale during filling so that the correct level was readily obtained. All metal containers were grounded. The filled reservoir was then transferred and installed into the generator cabinet.

During exposure the hexane was pumped from the reservoir through a stainless steel eductor tube and delivery tubes to vaporizers located at the fresh air inlet of each animal exposure chamber. Stable micrometering pumps with adjustable drift-free pump rates ranging from less than 1 x 10-3 to greater than 20 ml per minute were used.

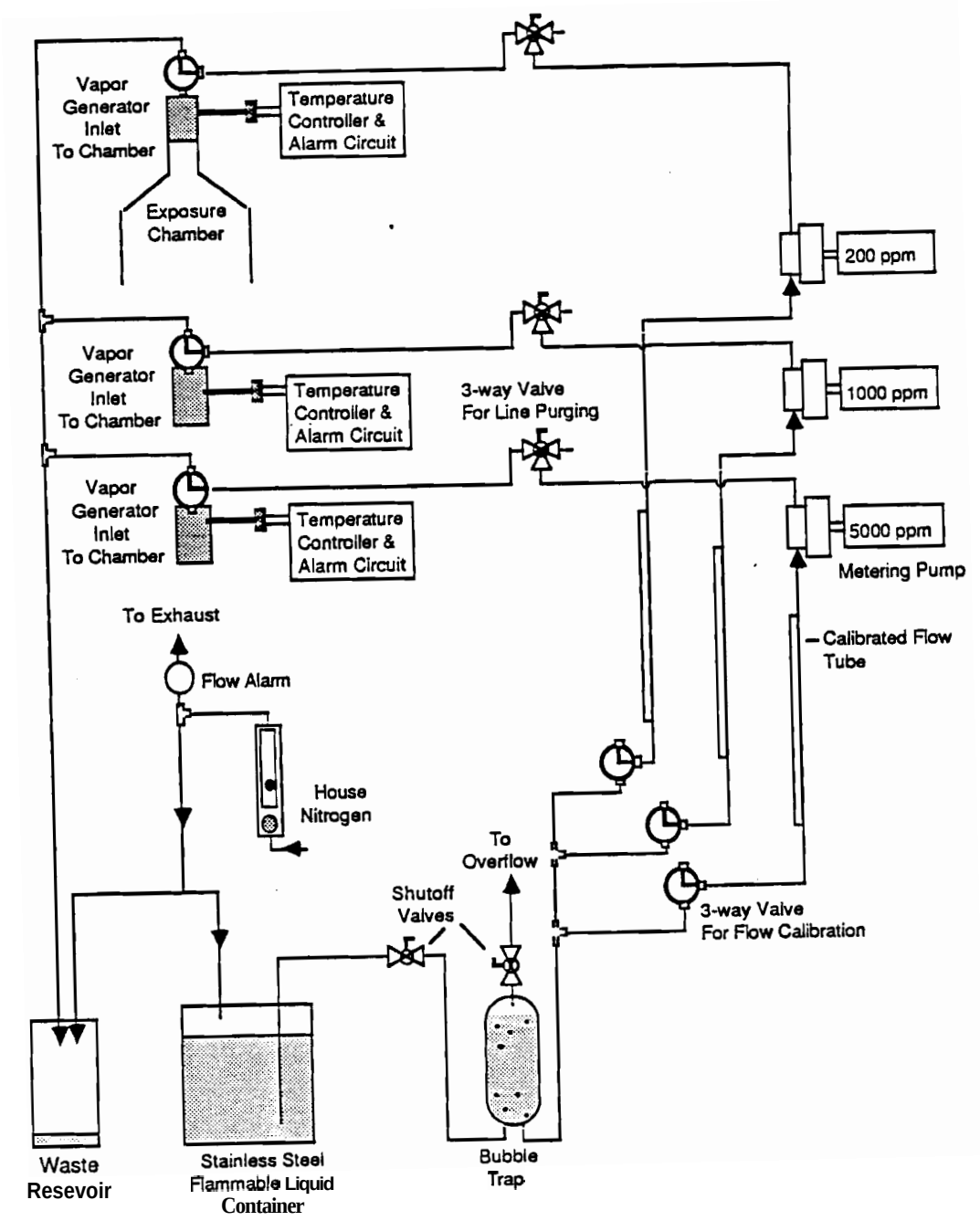


FIGURE B 4. n-Hexane Generation and Delivery System

The vaporizer (Figure B.4) comprised a stainless steel cylinder covered with a glass fiber wick from which the liquid was vaporized. The wick could be easily and inexpensively replaced if residue buildup occurred. An 80-watt heater and a temperature sensing element were incorporated within the cylinder and connected to a remotely located temperature controller. A second temperature monitor was incorporated in the vaporizer allowing the operating temperature to be recorded by the automated data acquisition system. The operating temperature of the vaporizer was maintained below 50°C (the boiling point of hexane is about 70°C). The cylindrical vaporizer was positioned in the fresh air duct leading directly to the inlet of the exposure chamber.

A clear Teflon® tube of measured volume, preceded by a three-way valve was attached downstream of the pump to facilitate measurement of the flow rate of the vapor generator. Measurement was accomplished by momentarily switching the three-way valve from the run position to the test position. A small bubble of air was pulled by the pump from the cabinet through the valve and into the clear tube. The progress of this bubble from one end of the tube to the other (calibrated volume) was timed with a stop watch. Flow rate was calculated by dividing the volume by the time. The concentration in the exposure chamber could be calculated from the flow measurements of liquid and dilution air and was used as a check on chamber concentrations in addition to GC measurements.

All generation equipment which came in contact with the hexane was stainless-steel, Teflon@ or Viton®. All equipment contained in the vented generator cabinet was explosion proof.

The exposure suite data acquisition and control computer automatically controlled the concentration of hexane in the animal exposure chambers by adjusting the flow rate of dilution air through the chamber over a narrowly limited flow range. This was accomplished by adjusting the dilution air flow pump which was mounted in the exhaust duct of the chamber. This air-multiplier-type pump was controlled by adjusting the control air pressure by a computer-controlled motor attached to the air pressure regulator.

Adjustments were made to the air flow only if the concentration was beyond the Non-Critical Limit (± 10% of target concentration). The concentration adjustment was limited to assure that the chamber dilution air flow was not adjusted beyond the non-critical flow limits (12 to 18 air changes per hour). If the allowed adjustment was not sufficient to bring the concentration back into the desired operating range, the computer made the maximum adjustment possible within the flow limits, then set the alarm and indicated to the operator that a manual adjustment of the generation system had to be made.

The following conditions for alarms and concentration adjustments were applied:

- Concentration ≤ Target + 10% and ≥ Target - 10%

  No action necessary

- Concentration > Target + 10% and ≤ Target + 20%
  or
  < Target - 10% and ≥ Target - 20%

  Set no alarms.
  Adjust chamber air flow rate to bring concentration as close to target as possible within air flow limits (12 to 18 air changes per hour).

- Concentration > Target + 20% and ≤ Target + 30%
  or
  < Target - 20% and ≥ Target - 30%

  Set audible alarm in control room and exposure room. If after normal working hours or if weekend, also set power operator alarm. Adjust chamber air flow rate to bring concentration as close to target as possible within air flow limits (12 to 18 air changes per hour).

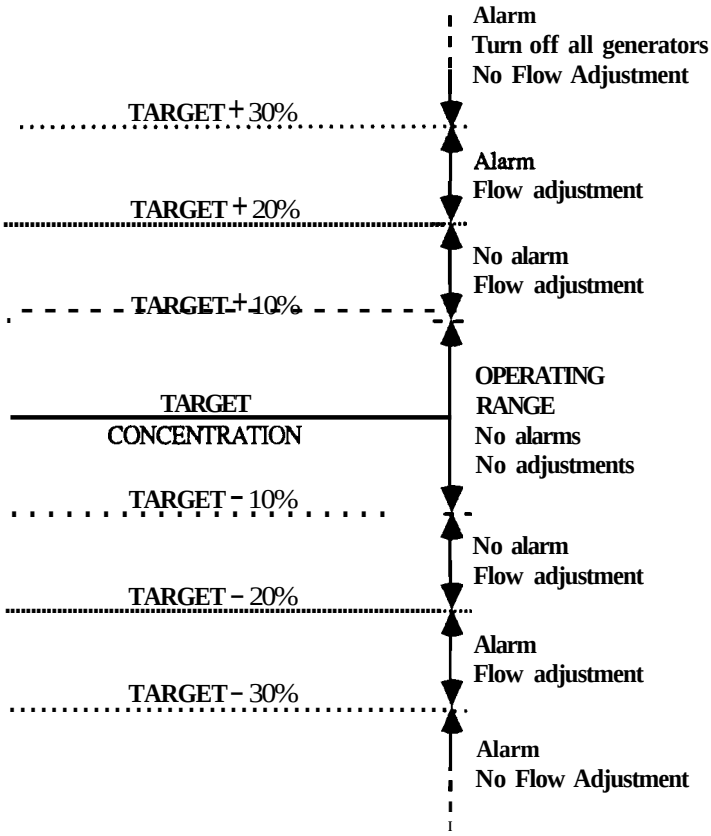
- Concentration > Target + 30%

  Turn off all generators.
  Set audible alarm in control room and exposure room. If after normal working hours or if weekend, also set power operator alarm. Make no adjustment of chamber air flow.

- Concentration < Target - 30%

  Set audible alarm in control room and exposure room. If after normal working hours or if weekend, also set power operator alarm. Make no adjustment of chamber air flow.

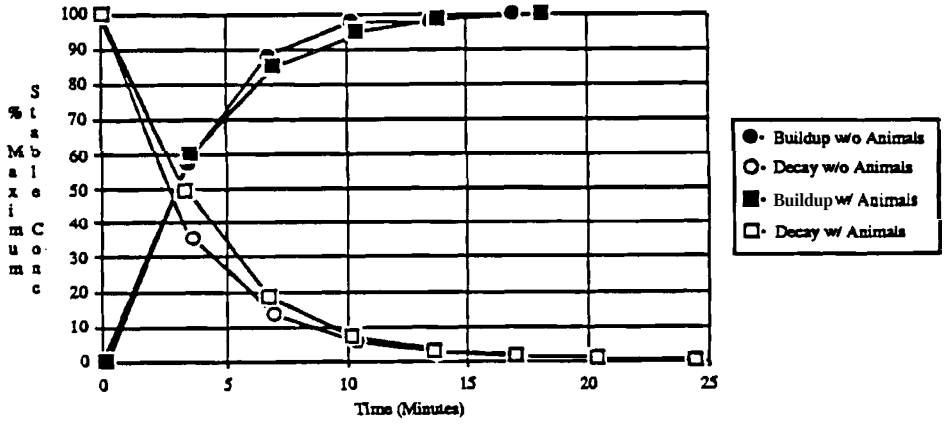
The following figure displays the above described alarms and the corresponding reactions:



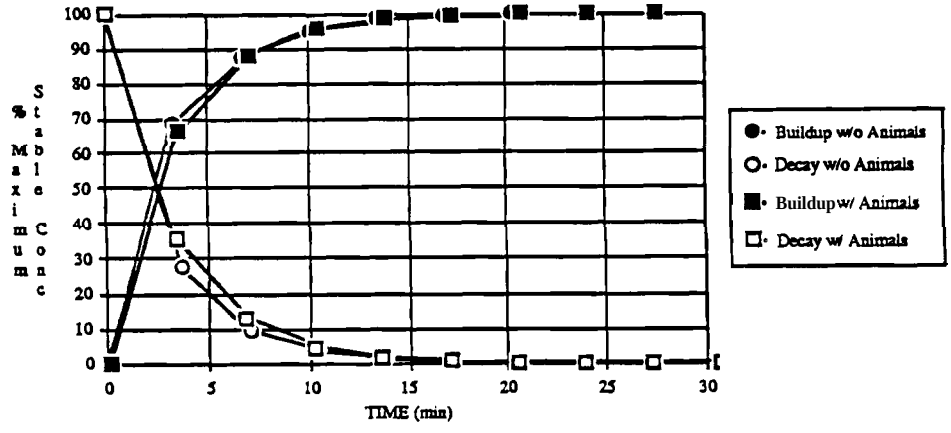
The time (T_{90}), following the start of generation, for the concentration to build up to 90% of the final stable concentration in the chamber and the time (T_{10}), following the stop of generation for the vapor concentration to decay to 10% of the stable concentration were determined before animals were placed in the chambers. The resulting curves for all chambers are shown in Figure B.5. The value of T_{90} was found to range from approximately 7 to 9 minutes. At a chamber air flow rate of 15 air changes per hour, the theoretical value for T_{90} is approximately 11 minutes. A T_{90} of 12 minutes was chosen for this study. The value of T_{10} also ranged from 7 to 9 minutes.

The buildup and decay of concentration with animals in the all chambers were checked during the first week of the study (Figure B.5). The values of T_{90} ranged from 8 to 9 minutes. The decay time, T_{10} with animals present ranged between 7 and 9 minutes.

IRT HEXANE - 200 ppm CHAMBER



IRT HEXANE - 1000 ppm Chamber



IRT HEXANE - 5000 ppm Chamber

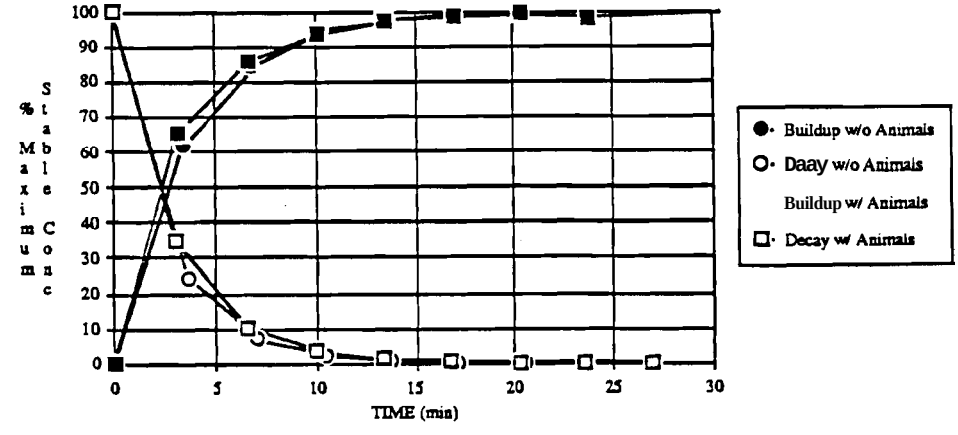


FIGURE B.5. Buildup and Decay Curves in Chambers With and Without Animals Present

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. Uniformity in all chambers was found to be acceptable. To provide easier interpretation of the results, the concentration readings at each port is also expressed as a percentage of the mean measurement at all ports measured. The possible variation of chemical concentration measured from one sample port to another during the chamber balance procedure is termed the Total Port Variablility (TPV). Three factors contribute to the TPV. The first, the Between Port Variablitiy (BPV), represents the variation of chemical distribution within the chamber. This factor is of interest because it is the measure of the uniformity of distribution of the chemical in the chamber. The second factor, the Within Port Variability (WPV), represents the fluctuation of the average chemical concentration within the chamber during the time the uniformity measurements are made. The third is the variability of the measurement instrument itself.

TABLE B.1. Teratology Study of Hexane in Mice - Summary of Chamber Uniformity Data Obtained Before Exposure (Prestart) and During Exposure (Poststart).

	TPV (%RSD)		WPV (%RSD)		BPV (%RSD)	
Chamber	Prestart	Poststart	Prestart	Poststart	Prestart	Poststart
200 ppm	1.0	0.2	1.1	0.3	0.0	0.0
1000 ppm	1.2	0.3	1.0	0.4	0.7	0.0
5000 ppm	0.6	0.5	0.4	0.1	0.4	0.4

Chamber Uniformity Limits

WPV ≤ 5% RSD

BPV ≤ 5% RSD

TPV ≤ 7% RSD

ENVIRONMENTAL DATA DURING EXPOSURE

Summations of chamber flow, temperature and relative humidity data for the study are shown in Table B.2. This table includes 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.

The mean value of temperature in all chambers for the entire study were between 72.8 and 76.3°F, all within the specified limits of 72 to 78°F. Temperature extremes ranged from 69.7 to 78.1°. The percent of temperature readings within the operating range for all chambers except Hold 1 were greater than 90%.

The mean values of relative humidity in all chambers for the study were between 47.6 and 52.1%, all within the specified limits of 40 to 70%. Relative humidity extremes (considering all chambers) ranged from 29 to 77%. The control chamber and 200 ppm chamber had 88% of readings within operating range, while the remaining chambers were above the 90% target for readings within operating range. Relative humidity in all chambers was generally lower than normal due to the extremely dry weather during this time of year.

The mean values of chamber flow in all chambers for the study were between 14.6 and 16.4 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 13.5 to 17.1 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 can be found later in this Appendix.

EXPOSURE DATA

Summaries of the concentration data for all chambers and the exposure room are included in Table B.3. The daily mean concentrations for all chambers were within ±7% of the target concentrations (the daily protocol required the daily means to be within ±10% of the target concentrations) except for the first day of exposure in the 200 ppm chamber. A delay in reaching T90 caused the daily mean for this chamber to be 83% of target. Standard deviations were outside the 10% protocol-defined limits on 2 days for the 200 ppm chamber, 1 day for the 1000 ppm chambers and 2 days for the 5000 ppm chamber. The percent of concentration readings within the operating range for the 200 ppm chamber was 94%, the other chambers were greater than 99%.

A complete discussion of all concentration excursions is included.

TABLE B.2. Inhalation Teratology Study of n-Hexane 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	72.8±0.8	101±1%	74.9	69.7	122	100
Hold 1 [1]	73.3±1.5	98±2%	77.4	71.2	37	86
200	76.3±1.8	102±1%	78.1	73.7	122	99
1000	76.2±0.8	102±1%	78.1	73.2	121	99
5000	74.3±9.9	99±1%	76.6	71.5	121	98

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	52.1±9.2	95±18%	77	33	115	88
Hold 1 [1]	49.3±5.9	90±12%	58	38	35	94
200	47.6±7.2	87±15%	63	29	116	88
1000	48.5±7.5	88±16%	65	31	115	90
5000	50.2±7.7	91±15%	70	32	115	90

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	14.9±0.2	99±1%	15.2	14.6	118	100
Hold 1 [1]	14.6±0.1	97±0%	14.7	14.5	36	100
200	16.4±9.8	109±5%	17.1	13.5	118	100
1000	15.5±1.2	103±1%	16.1	15.2	118	100
5000	15.3±0.2	102±1%	15.8	14.9	118	100

Dates Used for Analysis: 3/18/87-4/2/87 except [1] 3/17/87-3/21/87.

TABLE B 3. Inhalation Teratology Study of n-Hexane in Mice---Summation of Concentration Data. Acceptable Range Is Also Shown

Concentration (PPM)
Acceptable Range = Target ± 10%

Target Conc. (ppm)	Mean ± SD	Percent Target ± RSD	Maximum	Minimum	Number Samples	Number In Range	% Samples in Range
Room	0.00±0.02	———	0.4	0	683	*683	*100
0	0.00±0.00	———	0	0	681	*681	*100
Hold 1	0.00±0.00	———	0	0	166	*166	*100
200	203±20.9	101±10%	291	0	665	624	94
1000	1020±53	102±5%	1260	201	664	656	99
5000	5050±267	101±5%	5670	5	663	657	99
S t Gas	1030±3	103±0%	1040	1010	682	682	100

* Samples with concentration less than 4 ppm

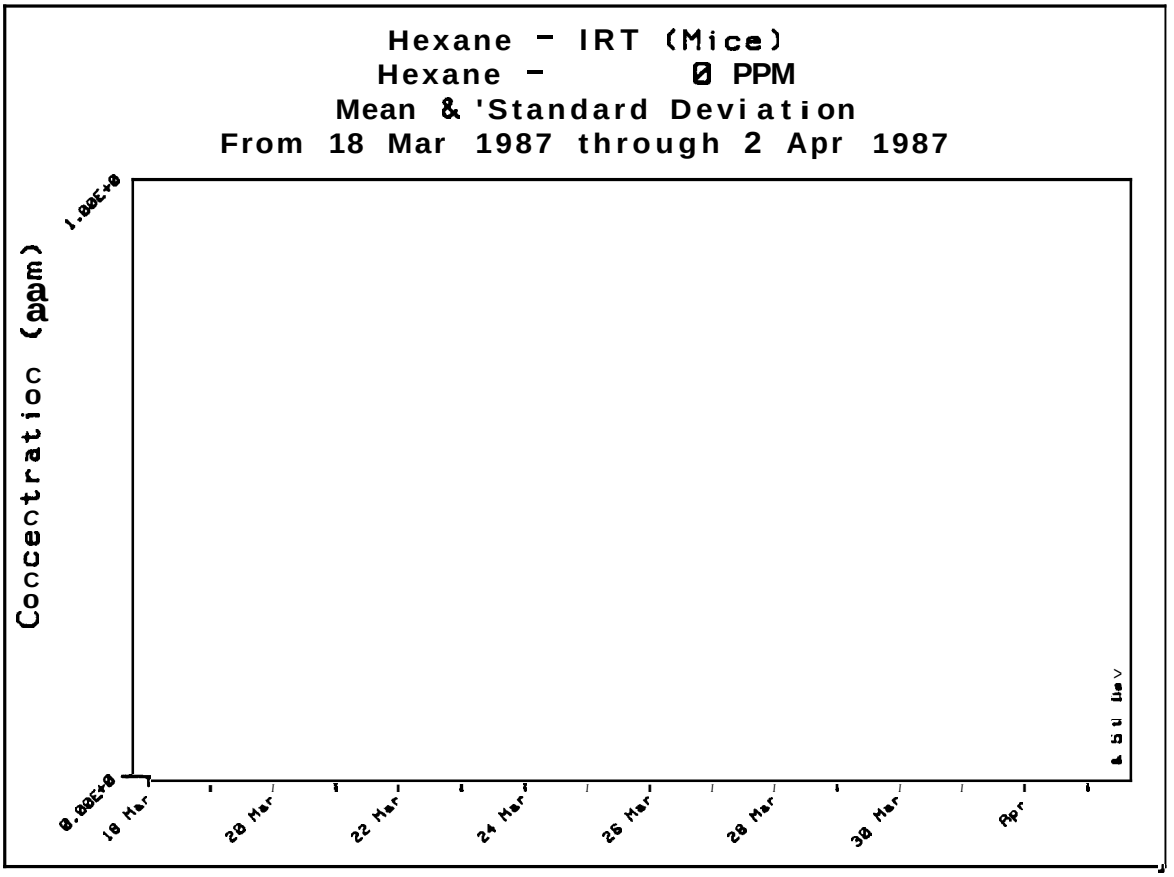
Dates Used for Analysis: 3/18/87 - 4/2/87 except 1 3/18/87 - 3/21/87.

Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 0 PPM/Concentration 0.00E+0 to 1.00E+0

Date	Mean	% Iaroct	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1907	0.00E+0	0%	0.000E+0	0%	0.0000	0.00E+0	13	43.	100%
19 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	4 1	11.	100%
20 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	37.	37.	100%
21 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	95.	100%
22 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	40.	40.	100%
23 Mar 1907	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
24 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	41.	41.	100%
25 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	43.	43.	100%
26 Mar 1907	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
27 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	92.	100%
28 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
29 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
30 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	12	42.	100%
31 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	41.	100%
1 Apr 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	9 4	100%
2 Apr 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%

Summary

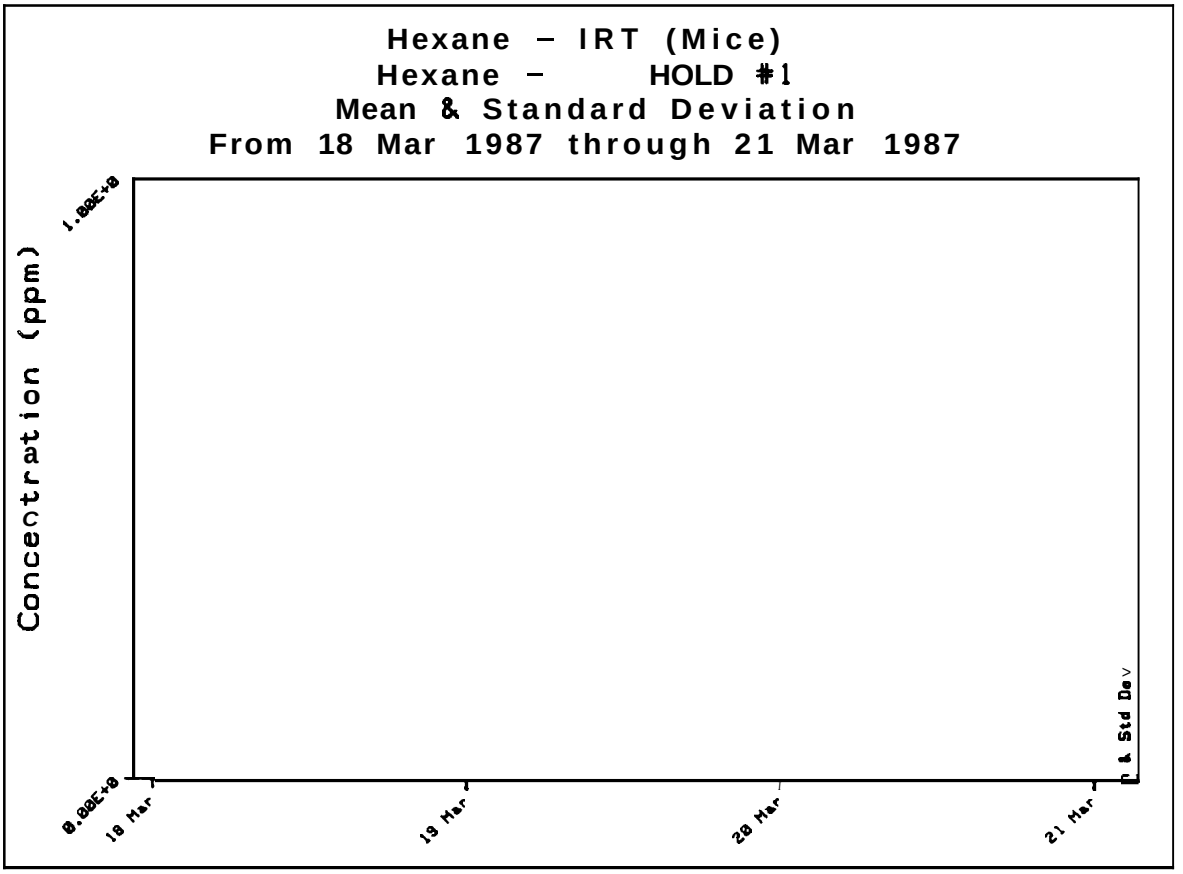


Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 21 Mar 1987

Summary Data for: Hexane - HOLD #1/Concentration 0.00E+0 to 1.00E+0

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	43.	43.	100%
19 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	11	11.	100%
20 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	37.	37.	100%
21 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%

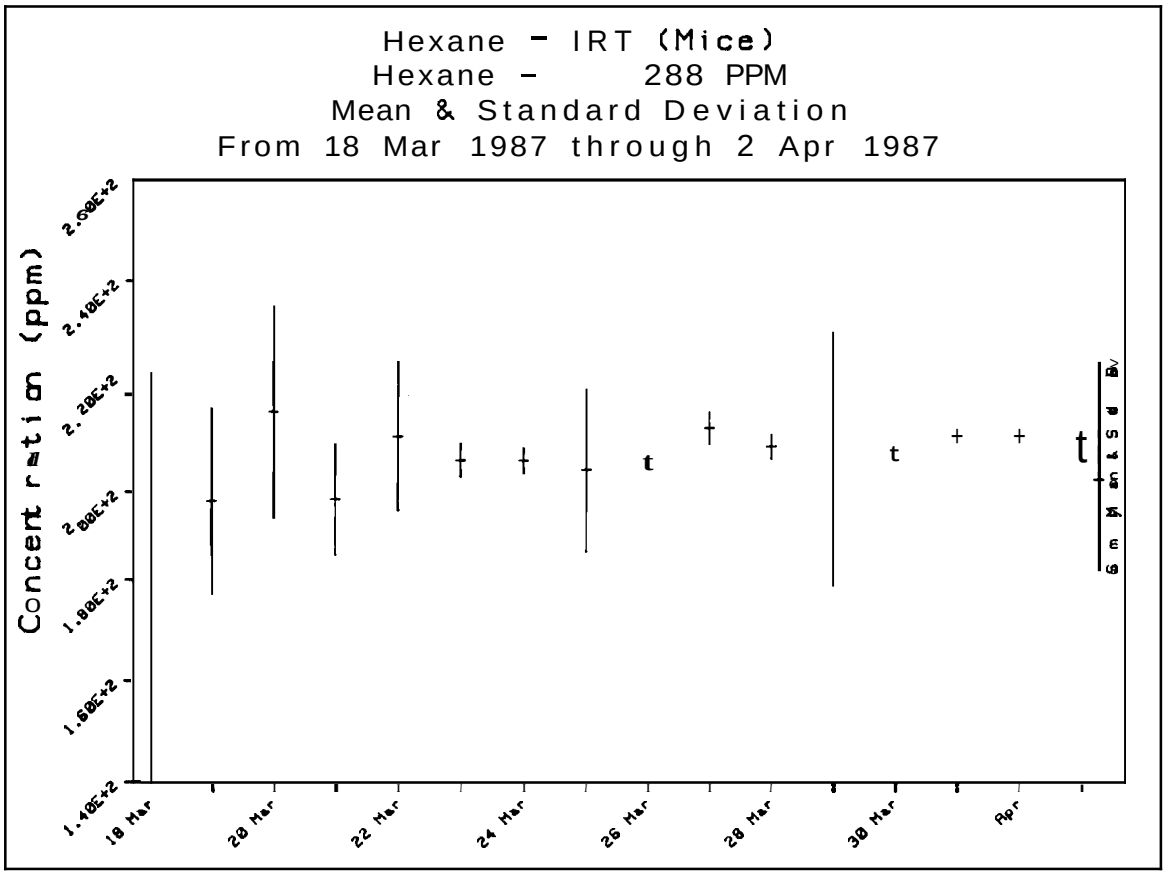
Summary



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 200 PPM/Concentration 1.80E+2 to 2.20E+2

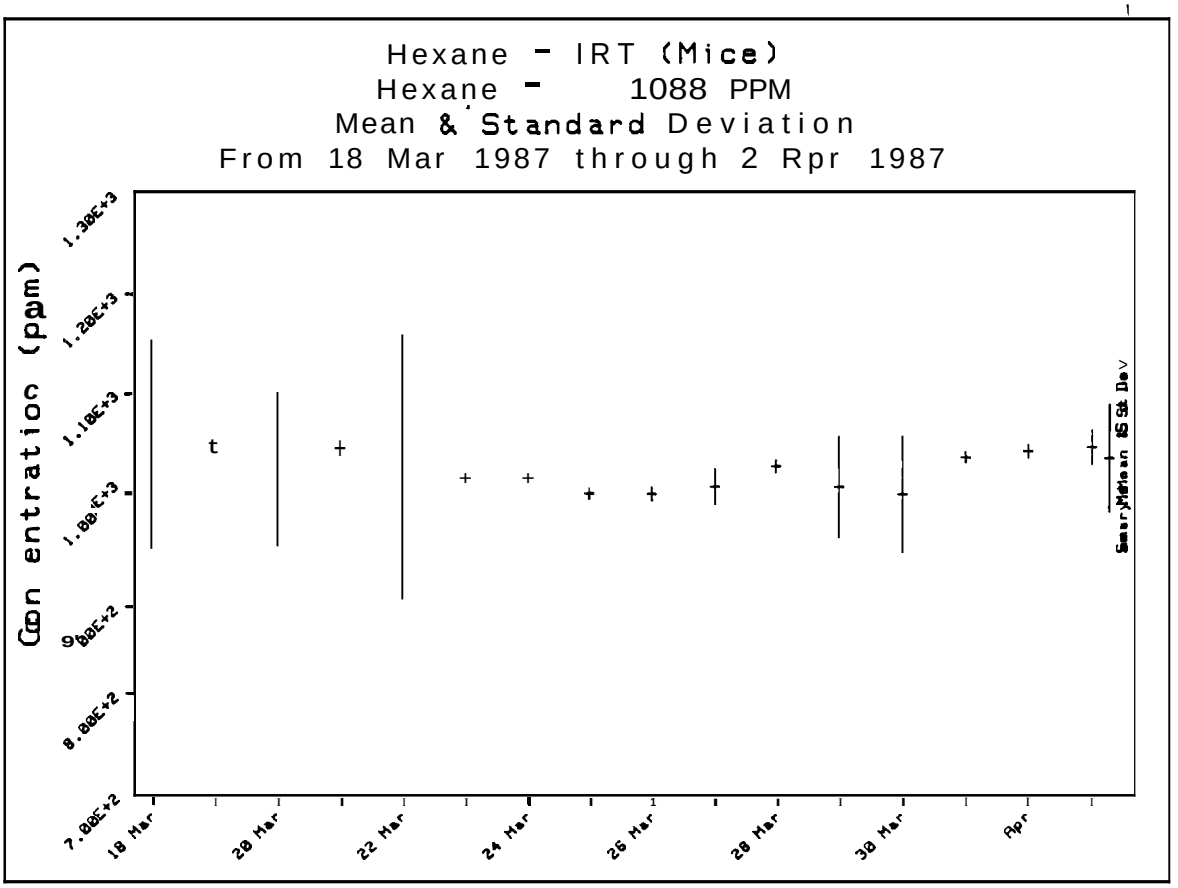
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	1.66E+2	83%	5.614E+1	34%	2.07E+2	0.00E+0	42.	24.	57%
19 Mar 1987	1.96E+2	98%	1.867E+1	10%	2.60E+2	1.69E+2	41.	29.	71%
20 Mar 1987	2.14E+2	107%	2.124E+1	10%	2.91E+2	1.63E+2	1	33.	80%
21 Mar 1987	1.96E+2	98%	1.113E+1	6%	2.11E+2	1.81E+2	43.	13.	100%
22 Mar 1987	2.09E+2	104%	1.494E+1	7%	2.15E+2	1.16E+2	41.	40.	98%
23 Mar 1987	2.04E+2	102%	3.354E+0	2%	2.15E+2	1.99E+2	41.	41.	100%
24 Mar 1987	2.04E+2	102%	2.559E+0	1%	2.10E+2	1.95E+2	41.	41.	100%
25 Mar 1987	2.02E+2	101%	1.635E+1	8%	2.07E+2	1.00E+2	41.	40.	98%
26 Mar 1987	2.04E+2	102%	1.486E+0	1%	2.07E+2	2.00E+2	41.	41.	100%
27 Mar 1987	2.11E+2	105%	3.176E+0	2%	2.14E+2	1.98E+2	41.	41.	100%
28 Mar 1987	2.07E+2	103%	2.392E+0	1%	2.14E+2	2.04E+2	42.	42.	100%
29 Mar 1987	2.04E+2	102%	2.536E+1	12%	2.12E+2	1.23E+1	43.	42.	98%
30 Mar 1987	2.05E+2	103%	1.200E+0	1%	2.07E+2	2.00E+2	40.	40.	100%
31 Mar 1987	2.08E+2	104%	9.251E-1	0%	2.10E+2	2.06E+2	12.	42.	100%
1 Apr 1987	2.09E+2	104%	1.341E+0	1%	2.13E+2	2.06E+2	42.	42.	100%
2 Apr 1987	2.07E+2	104%	3.191E+0	2%	2.16E+2	2.03E+2	43.	43.	100%
Summary	2.03E+2	101%	2.090E+1	10%	2.91E+2	0.00E+0	665.	624.	94%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 1000 PPM/Concentration 9.00E+2 to 1.10E+3

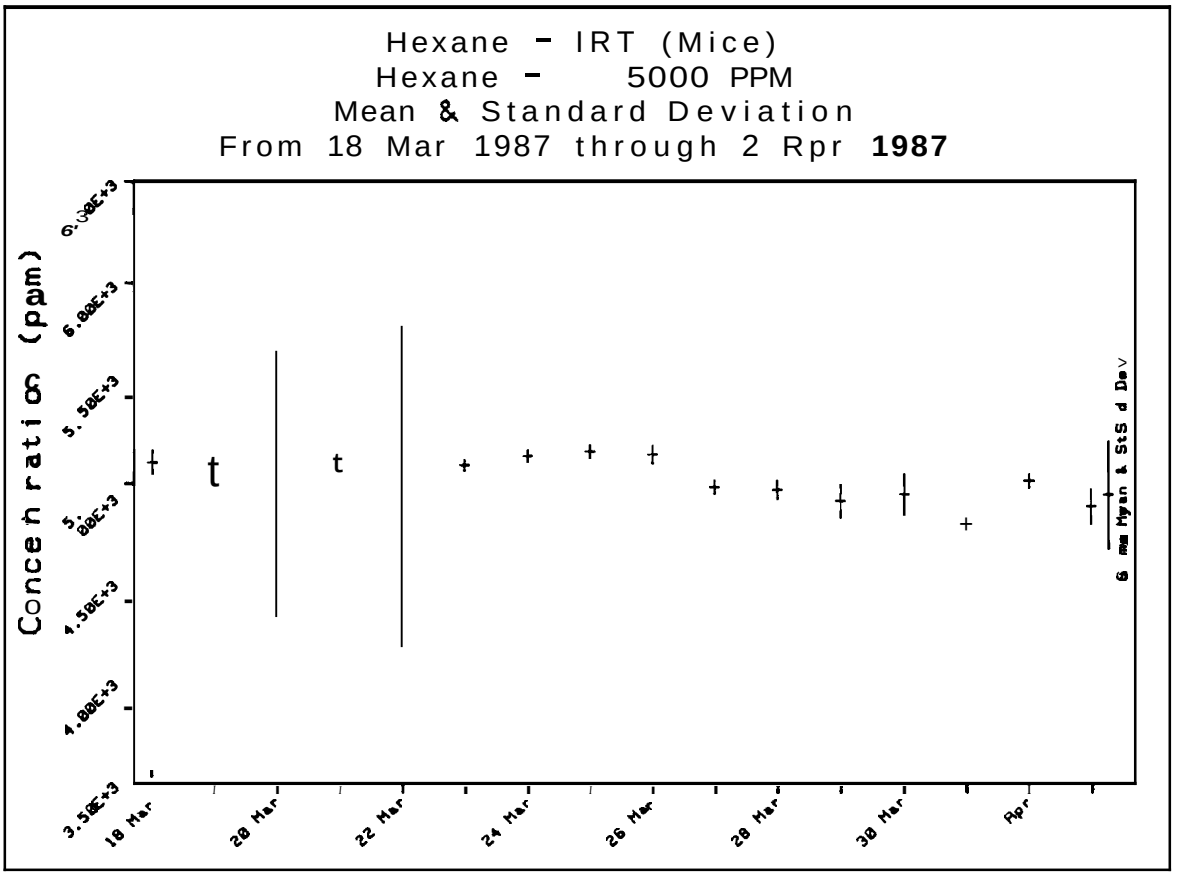
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	1.05E+3	105%	1.047E+2	10%	1.26E+3	4.18E+2	42.	40.	95%
19 Mar 1987	1.05E+3	105%	7.018E+0	1%	1.06E+3	1.01E+3	41.	41.	100%
20 ilar 1987	1.02E+3	102%	7.658E+1	7%	1.16E+3	6.71E+2	38.	35.	92%
21 ilar 1987	1.04E+3	104%	5.087E+0	0%	1.05E+3	1.03E+3	43.	43.	100%
22 ilar 1987	1.03E+3	103%	1.322E+2	13%	1.06E+3	2.01E+2	1	40.	98%
23 Mar 1987	1.02E+3	102%	7.565E+0	1%	1.04E+3	1.01E+3	42.	12.	100%
24 ilar 1987	1.02E+3	102%	4.279E+0	0%	1.02E+3	1.01E+3	42.	12.	100%
25 Mar 1987	1.00E+3	100%	5.327E+0	1%	1.01E+3	9.88E+2	41.	41.	100%
26 Mar 1987	1.00E+3	100%	6.548E+0	1%	1.01E+3	9.77E+2	41.	41.	100%
27 Mar 1987	1.01E+3	101%	1.682E+1	2%	1.03E+3	9.70E+2	41.	41.	100%
28 Mar 1987	1.01E+3	101%	6.192E+0	1%	1.03E+3	9.92E+2	42.	42.	100%
29 Mar 1987	9.91E+2	99%	5.021E+1	5%	1.02E+3	6.79E+2	43.	42.	98%
30 ilar 1987	9.83E+2	98%	5.760E+1	6%	1.02E+3	6.37E+2	10.	39.	97%
31 Mar 1987	1.02E+3	102%	5.320E+0	1%	1.03E+3	1.00E+3	42.	42.	100%
1 Apr 1987	1.03E+3	103%	6.711E+0	1%	1.04E+3	1.00E+3	42.	42.	100%
2 Apr 1987	1.03E+3	1033	1.695E+1	2%	1.05E+3	9.74E+2	43.	43.	100%
Summary	1.02E+3	102%	5.310E+1	5%	1.26E+3	2.01E+2	664.	656.	99%



Daily Summation Tar Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 5000 PPM/Concentration 4.50E+3 to 5.50E+3

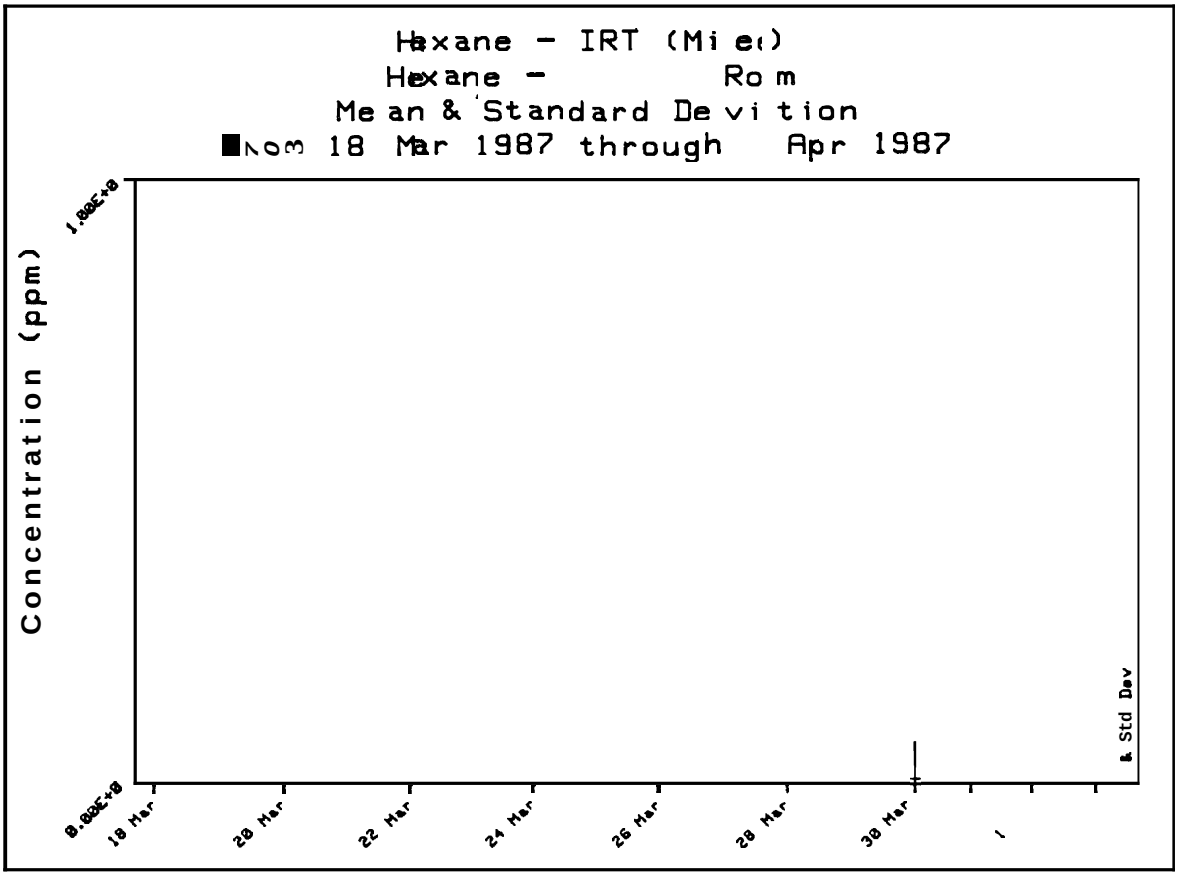
Date	Mean	% Target	Std Ow	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	5.11E+3	102%	5.766E+1	1%	5.23E+3	5.02E+3	42.	12.	100%
19 Mar 1987	5.07E+3	101%	7.356E+1	1%	5.25E+3	4.74E+3	11.	41.	100%
20 Mar 1987	5.00E+3	100%	6.619E+2	13%	5.67E+3	1.20E+3	37.	31.	92%
21 Mar 1987	5.10E+3	102%	3.681E+1	1%	5.17E+3	5.02E+3	43.	13.	100%
22 Mar 1987	4.98E+3	100%	7.978E+2	16%	5.18E+3	4.63E+0	11.	40.	98%
23 Mar 1987	5.09E+3	102%	2.924E+1	1%	5.16E+3	5.04E+3	12.	42.	100%
21 Par 1987	5.14E+3	103%	2.965E+1	1%	5.20E+3	5.08E+3	42.	12.	100%
25 Mar 1917	5.16E+3	1031	3.317E+1	1%	5.21E+3	5.08E+3	42.	42.	100%
26 Mar 1987	5.14E+3	103%	4.466E+1	1%	5.22E+3	4.99E+3	41.	41.	100%
27 Mar 1987	4.98E+3	100%	3.475E+1	1%	5.05E+3	4.91E+3	41.	41.	100%
28 Mar 1987	4.96E+3	99%	4.569E+1	1%	5.07E+3	4.78E+3	42.	42.	100%
29 Rr 1987	4.91E+3	98%	8.141E+1	2%	5.02E+3	4.49E+3	43.	12.	98%
30 Mar 1987	4.94E+3	99%	1.009E+2	2%	5.05E+3	4.38E+3	39.	38.	97%
31 Mar 1987	5.09E+3	102%	2.587E+1	1%	5.14E+3	5.04E+3	42.	42.	100%
1 Apr 1987	5.12E+3	102%	3.317E+1	1%	5.18E+3	5.01E+3	42.	42.	100%
2 Apr 1987	4.99E+3	100%	8.692E+1	2%	5.18E+3	4.87E+3	43.	43.	100%
Summary	5.05E+3	101%	2.666E+2	5%	5.67E+3	4.63E+0	663.	657.	99%



Daily Summation For Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - Room/Concentration 0.00E+0 to 1.00E+0

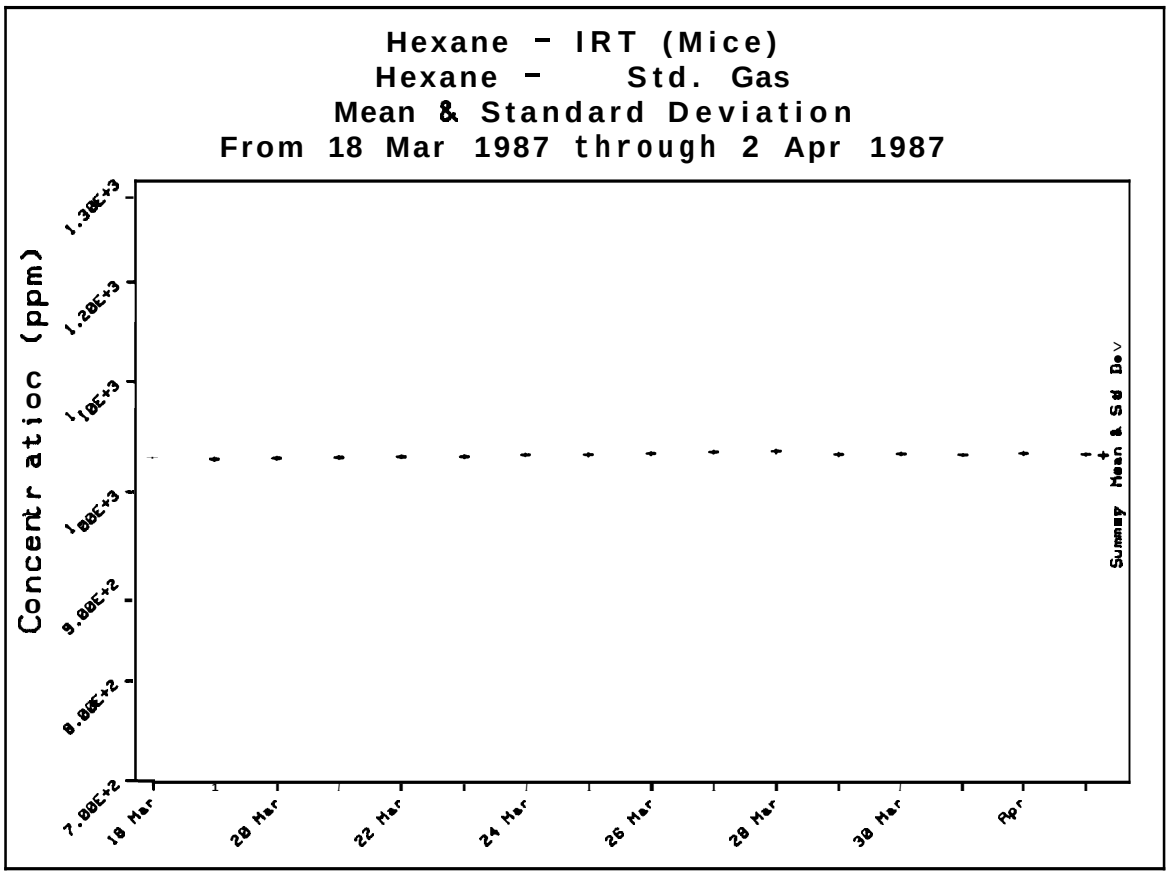
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	44.	100%
19 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	41.	41.	100%
20 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	38.	38.	100%
21 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	44.	100%
22 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	40.	40.	100%
23 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
24 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	41.	41.	100%
25 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	44.	100%
26 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
27 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
28 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
29 Mar 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
30 Mar 1987	9.25E-3	0%	5.993E-2	648%	3.88E-1	0.00E+0	42.	42.	100%
31 Mar 1987	6.67E-3	0%	4.423E-2	663%	2.93E-1	0.00E+0	44.	44.	100%
1 Apr 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	44.	100%
2 Apr 1987	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
Summary	9.98E-4	0%	1.861E-2	1865%	3.88E-1	0.00E+0	683.	683.	100%



Daily Summation For Hexane - IRT (Mice) From 10 Mar 1907 through 2 Apr 1987

Summary Data for: Hexane - Std. Gas/Concentration 9.00E+2 to 1.10E+3

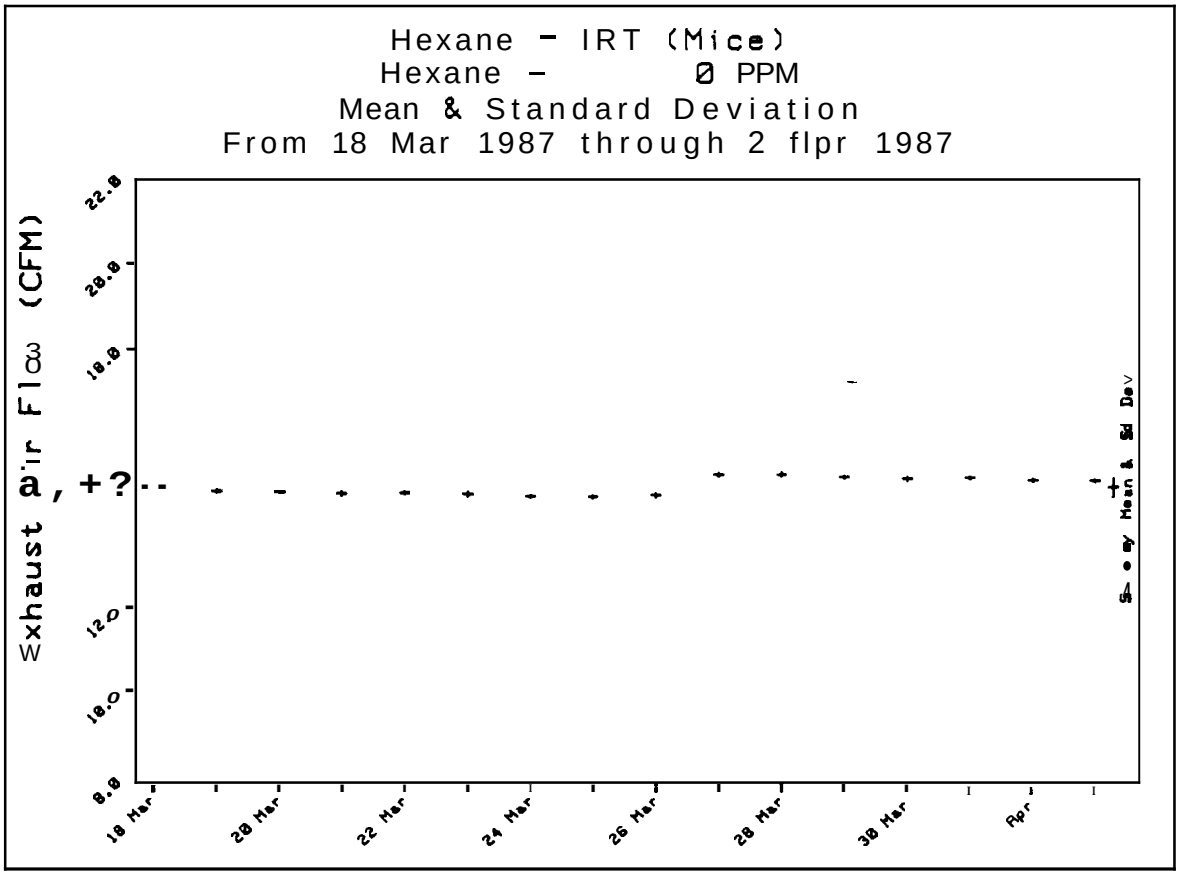
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	1.02E+3	102%	2.943E+0	0%	1.02E+3	1.01E+3	43.	43.	100%
19 Mar 1987	1.02E+3	102%	1.704E+0	0%	1.03E+3	1.02E+3	44.	44.	100%
20 hr 1987	1.02E+3	102%	1.347E+0	0%	1.03E+3	1.02E+3	40.	10.	100%
21 Mar 1987	1.03E+3	1031	1.351E+0	0%	1.03E+3	1.02E+3	41.	44.	100%
22 Mar 1907	1.03E+3	103%	9.945E-1	0%	1.03E+3	1.02E+3	41.	41.	100%
23 Mar 1987	1.03E+3	103%	1.170E+0	0%	1.03E+3	1.02E+3	12.	42.	100%
21 Mar 1987	1.03E+3	103%	1.343E+0	0%	1.03E+3	1.03E+3	42.	42.	100%
25 Mar 1987	1.03E+3	1031	1.794E+0	0%	1.03E+3	1.03E+3	42.	42.	100%
26 Mar 1987	1.03E+3	1031	1.530E+0	0%	1.03E+3	1.03E+3	43.	43.	100%
27 Mar 1987	1.03E+3	103%	1.608E+0	0%	1.03E+3	1.03E+3	42.	42.	100%
28 Mar 1987	1.03E+3	1031	1.978E+0	0%	1.04E+3	1.03E+3	44.	44.	100%
29 Mar 1987	1.03E+3	103%	1.620E+0	0%	1.03E+3	1.03E+3	44.	44.	100%
30 hr 1987	1.03E+3	1031	1.406E+0	0%	1.03E+3	1.03E+3	41.	41.	100%
31 Mar 1987	1.03E+3	1031	1.242E+0	0%	1.03E+3	1.03E+3	43.	43.	100%
1 Rpr 1987	1.03E+3	1031	1.737E+0	0%	1.03E+3	1.03E+3	13.	43	1001
2 Apr 1907	1.03E+3	1032	1.229E+0	0%	1.03E+3	1.03E+3	44.	41.	100%
Summary	1.03E+3	103%	3.241E+0	0%	1.04E+3	1.01E+3	682.	682.	100%



Daily Summation for Hexane - IRT (Mice) From 18 Par 1987 through 2 Apr 1987

Summary Data for: Hexane - 0 PPM/Exhaust Air flow 12.0 to 18.0

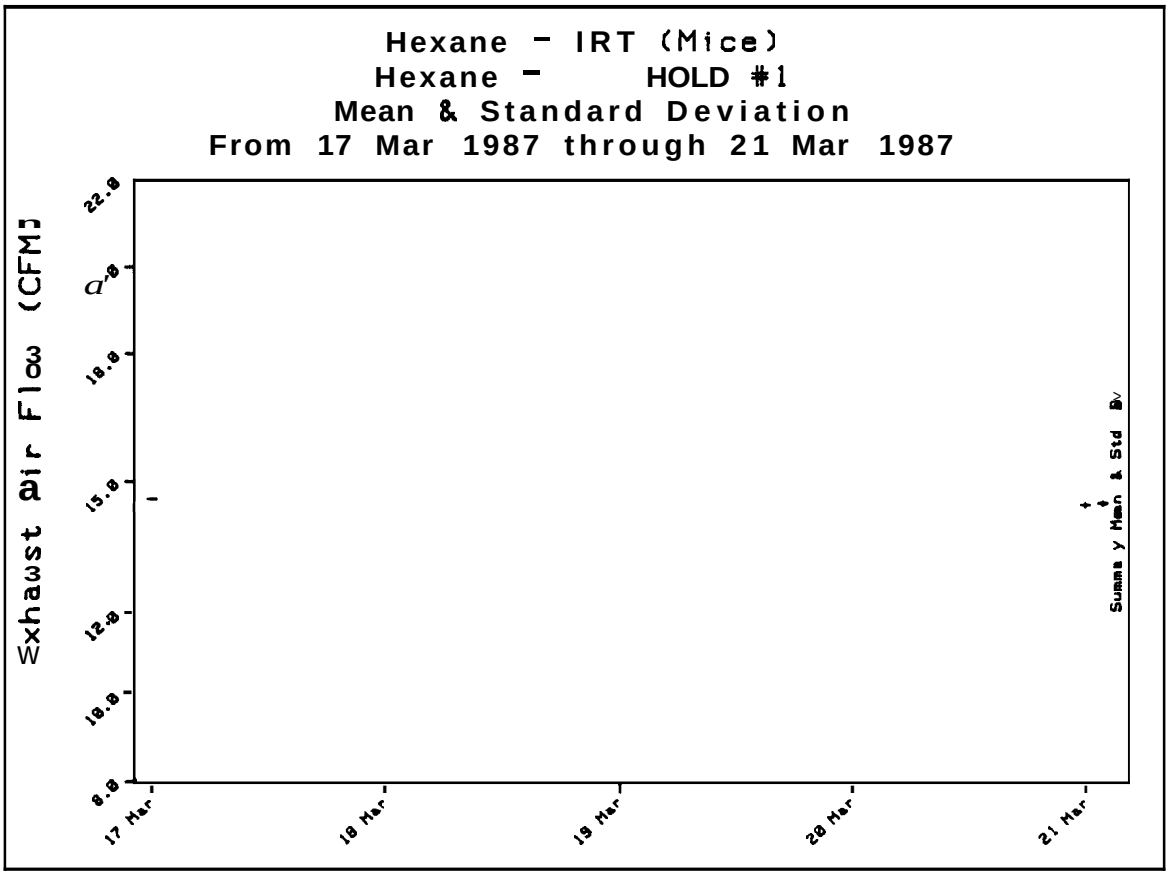
Date	Mean	% Target	Std Dev	Z RSD	Maximum	Minimum	N	Nin	% Nin
18 Mar 1987	14.7	98%	.05	OX	8	1.7	7.	7.	IOU
19 Mar 1987	14.7	98%	.04	0%	11.8	14.7	7.	7.	100%
20 Mar 1987	14.7	98%	0.00	OX	14.7	14.7	8	8	100%
21 Mar 1987	1.7	98%	.05	0X	11.7	11.6	7.	7.	100%
22 Mar 1987	14.7	98%	.01	OX	1	14.6	8	8	100%
23 Mar 1987	11.7	98%	.05	0%	11.7	14.6	7.	7.	100%
24 Mar 1987	14.6	97%	.04	0%	14.7	11.6	7.	7.	100%
25 Mar 1987	14.6	97%	.04	0%	7	11.6	7.	7.	100%
26 Mar 1987	1.7	98%	.05	OX	14.7	14.6	7.	7.	100%
27 Mar 1987	15.1	101%	.05	0%	15.2	15.1	8	8.	100%
28 Mar 1987	15.1	101%	.05	OX	15.2	15.1	8	8	100%
29 Mar 1987	15.1	101%	.01	0%	15.1	15.0	7.	7.	100%
30 Mar 1987	15.1	100%	.05	OX	15.1	15.0	7.	7.	100%
31 Mar 1987	15.1	101%	.04	0%	15.1	15.0	7.	7.	IOU'
1 Apr 1987	15.0	100%	.04	0%	15.1	15.0	8	8	100%
2 Apr 1987	15.0	100%	.04	OX	15.1	15.0	8	8	100%
Summary	4 .	99%	.21	1%	15.2	14.6	118.	118.	100%



Daily Summation For Hexane - E (Mice) From 17 Mar 1987 through 21 Mar 1987

Summary Data fa: Hexane - HOLD 01/Exhaust Rir Flow 12.0 to 18.0

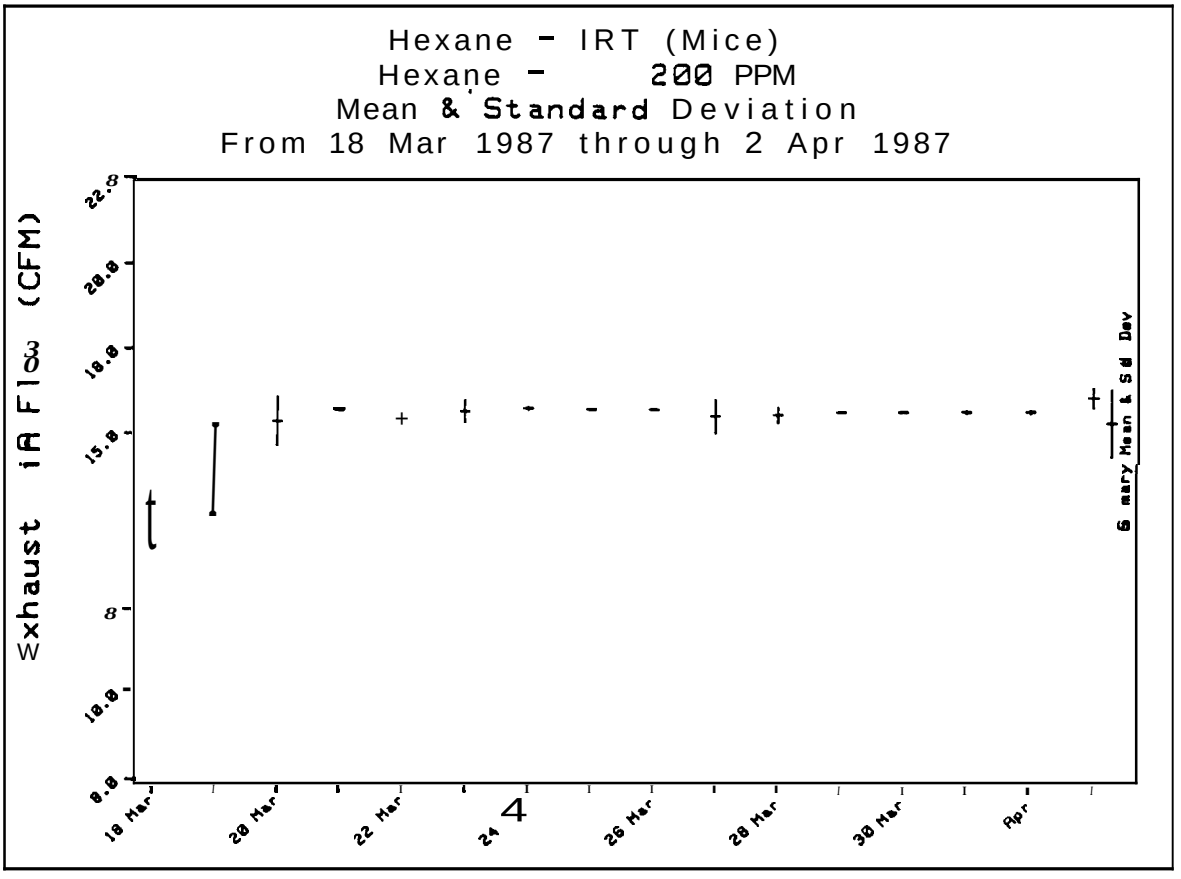
Date	Mean	% Target	Std Ctu	% RSD	Maximum	Minimum	N	N in	I N in
17 Mar 1987	11.6	97%	0.00	OX	I	14.6	7.	7.	100%
18 Mar 1987	14.6	98%	.05	0%	14.7	14.6	7.	7.	100%
19 Mar 1987	14.6	97%	.04	0%	14.7	14.6	7.	7.	100%
20 Mar 1987	14.6	97%	.04	0%	14.6	14.5	8.	8.	100%
21 Mar 1987	14.6	97%	.05	0%	14.6	14.5	7.	7.	100%
Summary	14.6	97%	.05	0%	14.7	14.5	36.	36.	100%



Daily Summation for Hexane - IRT (Mice) From 19 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 200 PPM/Exhaust Air Flow 12.0 to 18.0

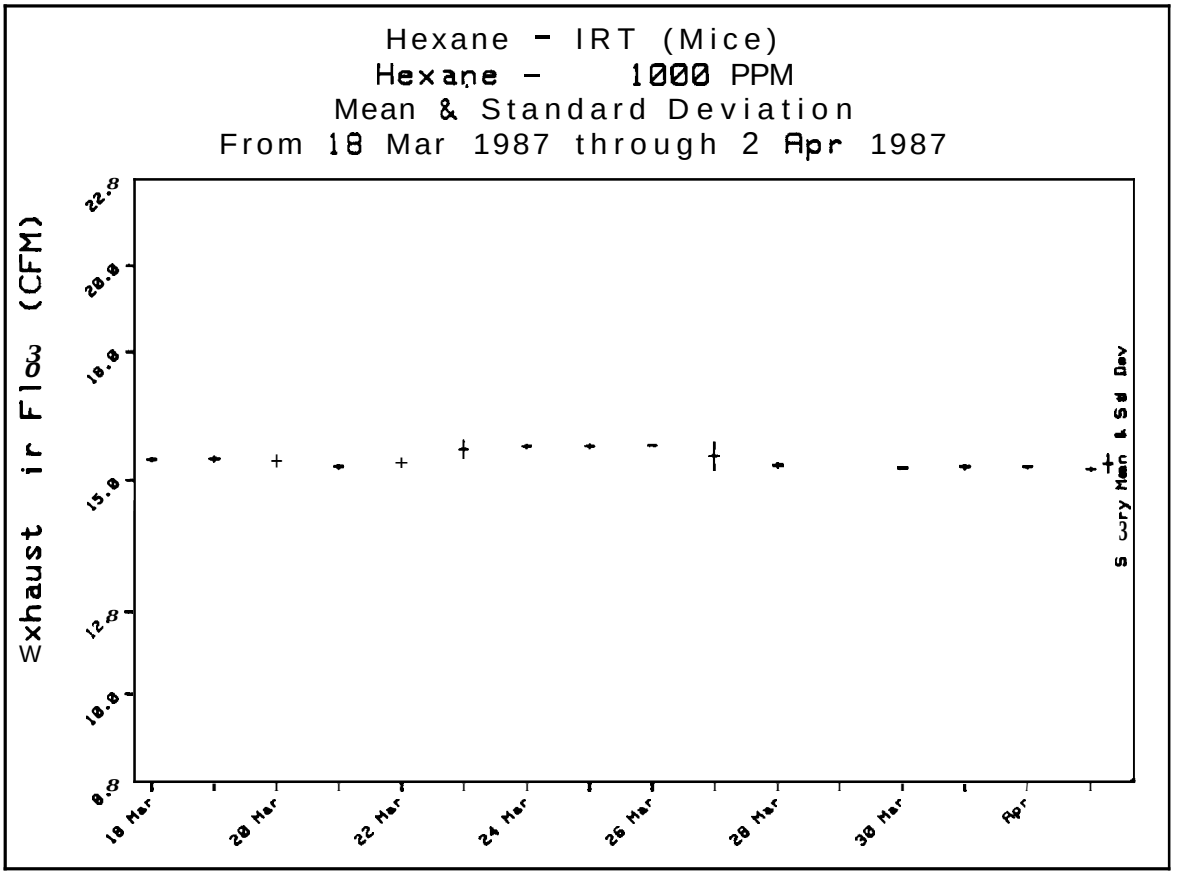
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	14.1	91%	.71	5%	15.1	13.5	7.	7.	100%
19 Mar 1987	15.2	101%	1.09	7%	6 .	13.5	7.	7.	100%
20 Mar 1987	153	109%	.57	4%	16.7	15.4	8.	8.	100%
21 Mar 1987	156	111%	0.00	OX	16.6	16.6	7.	7.	100%
22 Mar 1987	163	109%	.08	1%	16.5	16.2	8	8	100%
23 Mar 1987	167	112%	.24	1%	16.9	16.2	7.	7.	100%
24 Mar 1987	16.8	112%	.04	OX	16.9	16.8	7.	7.	100%
25 Mar 1987	15.8	112%	0.00	0%	16.0	16.8	7.	7.	100%
26 Mar 1987	16.8	112%	0.00	0X	16.8	16.8	7.	7.	100%
27 Mar 1987	155	110%	.38	2%	17.1	16.2	8	8	100%
28 Mar 1987	16.5	110%	.18	1%	16.7	16.2	8	8	100%
29 Mar 1987	155	111%	0.00	OX	16.6	16.6	7.	7.	100%
30 Mar 1987	16.6	111%	0.00	0X	16.6	16.6	7.	7.	100%
31 Mar 1987	16.6	111%	.04	0X	16.7	16.6	7.	7.	100%
1 Apr 1987	11.6	111%	.04	OX	16.7	16.5	8.	8.	100%
2 Apr 1987	16.9	113%	.24	1%	17.1	16.5	8.	8.	1001
Summary	16.4	109%	.78	5%	17.1	13.5	118.	118.	100%



Daily Summation For Hexane - IRT (Mice) Fro 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 1000 PPM/Exhaust Rir flow 12.0 to 18.0

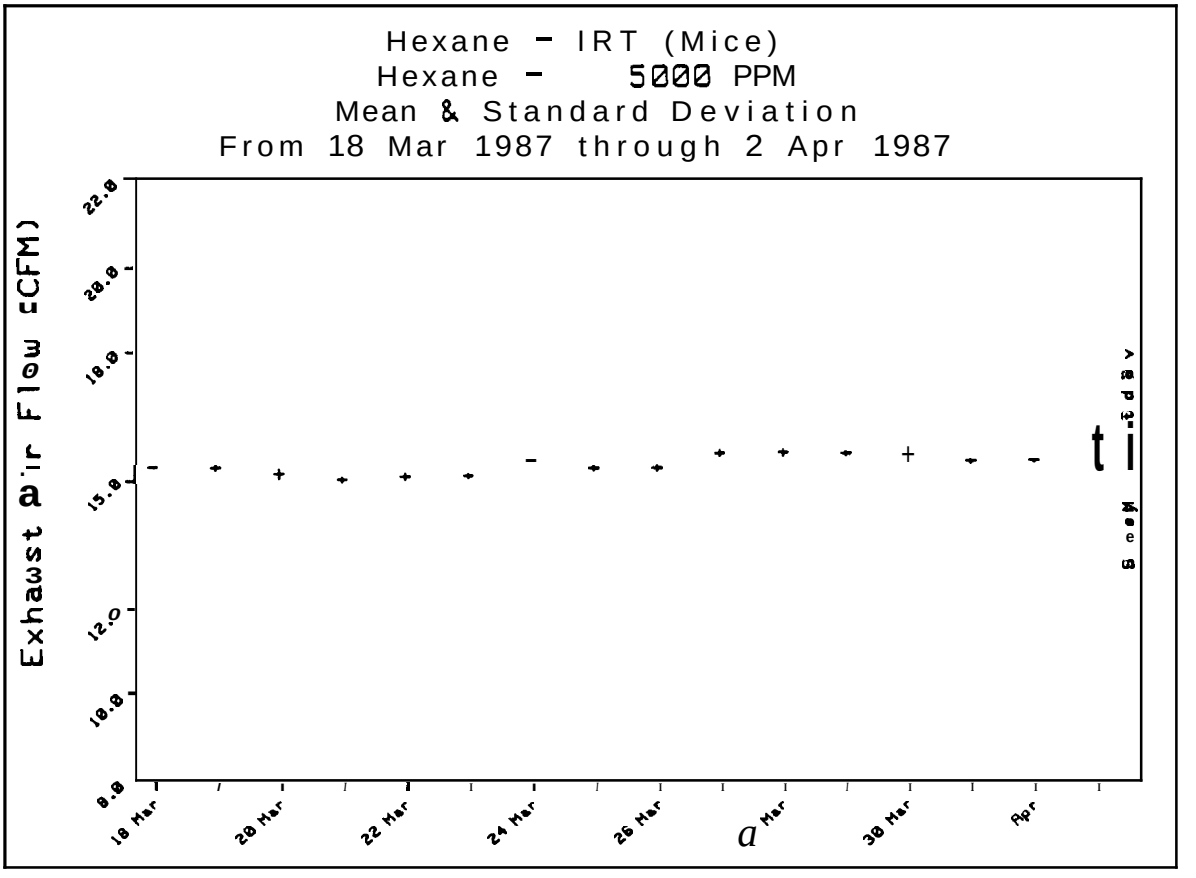
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	#	N in	% N in
18 Mar 1987	15.5	103%	.04	0%	15.5	15.4	7.	7.	100%
19 Mar 1987	15.5	103%	.06	0%	15.6	5	7.	7.	100%
20 Mar 1987	15.4	103%	.10	1%	15.5	15.3	8	8	100%
21 br 1987	15.3	102%	.04	0%	15.4	15.3	7.	7.	100%
22 Mar 1987	15.3	102%	.07	0%	15.4	15.2	8	8	100%
23 Mar 1987	15.7	105%	.19	1%	15.8	15.3	7.	7.	100%
24 Mar 1987	15.8	105%	.04	0%	15.8	15.7	7.	7.	100%
25 Par 1987	15.8	105%	.04	0%	15.8	15.7	7.	7.	100%
26 Mar 1987	15.8	105%	0.00	0%	15.8	15.8	7.	7.	100%
27 Mar 1987	15.7	105%	.31	2%	16.1	15.4	8.	8	100%
28 Mar 1987	15.5	103%	.05	0%	15.5	15.4	9.	8	100%
29 Mar 1987	15.4	103%	.04	0%	15.5	15.4	7.	7.	100%
30 Mar 1987	15.4	103%	0.00	0%	15.4	5 .	7.	7.	100%
31 Mar 1987	15.4	103%	.05	0%	15.5	15.4	7.	7.	100%
1 Apr 1987	15.4	1032	.03	0%	15.5	15.4	8	8	100%
2 Apr 1987	15.4	103%	.04	0%	15.5	15.3	8	8.	100%
Summary	15.5	103%	.19	1%	16.1	15.2	118.	118.	100%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 5000 PPM/Exhaust Air Flow 12.0 to 18.9

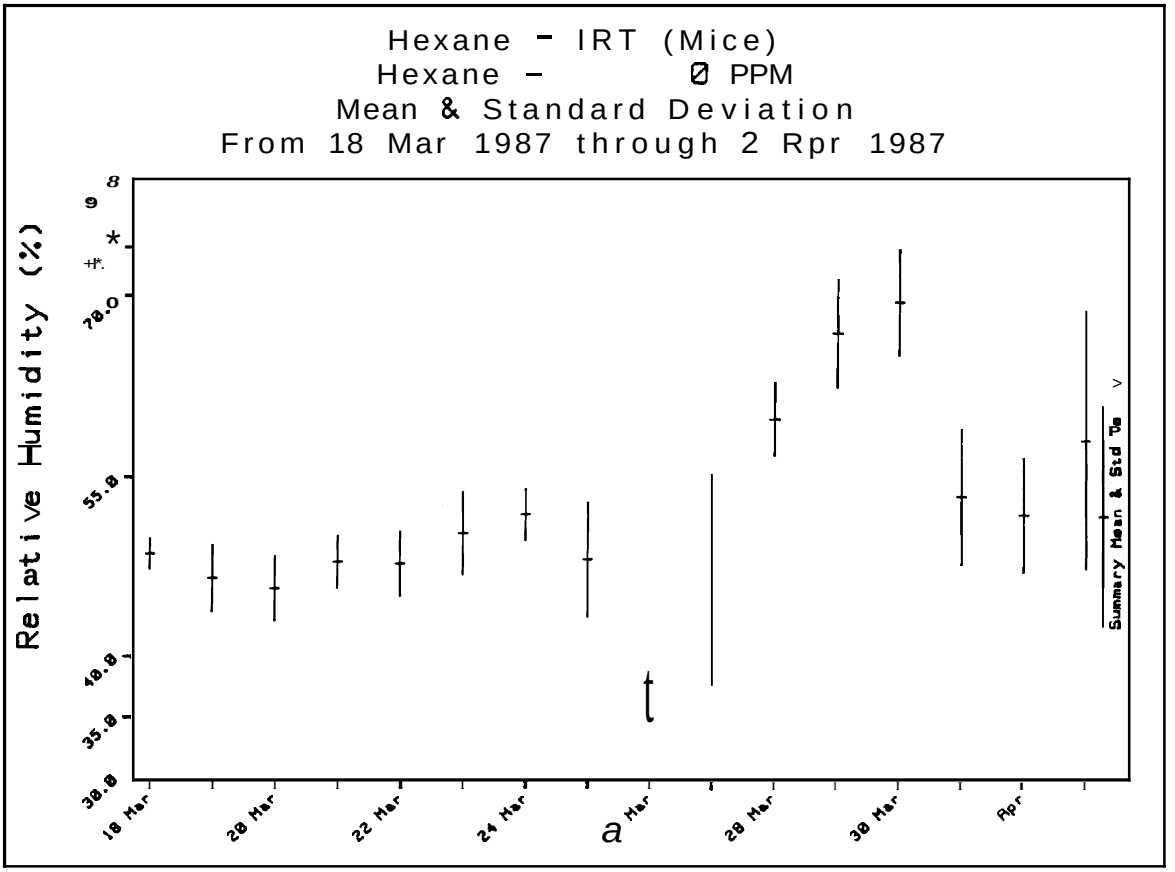
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	15.3	102%	0.00	0%	15.3	15.3	7.	7.	100%
19 Mar 1987	15.3	102%	.07	0%	15.1	15.2	7.	7.	100%
20 Mar 1987	15.1	101%	.11	1%	15.3	15.0	8.	8	100%
21 Mar 1987	15.0	100%	.06	0%	15.1	14.9	7.	7.	100%
22 Mar 1987	15.1	100%	.07	0%	15.1	14.9	8	8	100%
23 Mar 1987	15.1	100%	.05	0%	15.1	15.0	7.	7.	100%
24 Mar 1987	15.3	102%	0.00'	0%	15.3	15.3	7.	7.	100%
25 Mar 1987	15.2	102%	.05	0%	15.3	15.2	7.	7.	100%
26 Mar 1987	15.3	102%	.05	0%	15.3	15.2	7.	7,	100%
27 Mar 1987	15.6	104%	.06	0%	15.7	15.5	8	8	100%
28 Mar 1987	15.6	104%	.06	0%	15.7	15.5	8	8	100%
29 Mar 1987	15.6	104%	.05	01	15.6	15.5	7.	7.	100%
30 Mar 1987	15.4	103%	.11	1%	15.6	15.3	7.	7.	100%
31 Mar 1987	15.4	102%	.05	0%	5	15.3	7.	7.	100%
1 Apr 1987	15.4	102%	.05	0%	5 .	15.3	8.	8	100%
2 Apr 1987	15.7	105%	.21	1%	15.8	15.3	8.	8	100%
Summary	5.3	102%	.22	1%	15.8	11.9	118.	118.	100%



Daily Summation For Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 0 PPM/Relative Humidity 40.0 to 70.0

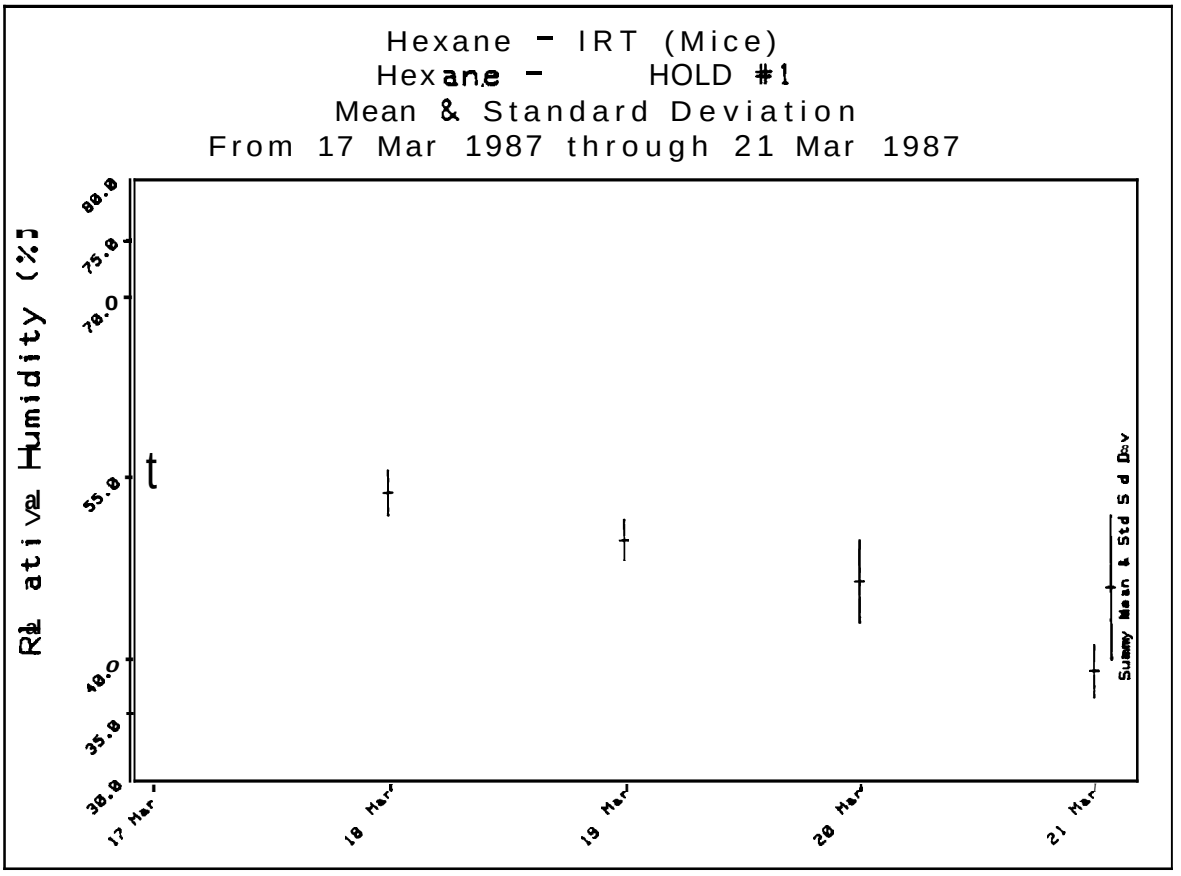
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% in
18 Mar 1987	48.6	88%	1.27	3%	50.0	47.0	7.	7.	100%
19 Mar 1987	46.6	85%	2.76	6%	50.0	43.0	7.	7.	100%
20 Mar 1987	6.8	83%	2.66	6%	19.0	42.0	8.	8	100%
21 Mar 1987	48.0	87%	2.16	5%	51.0	15.0	7.	7.	100%
22 Mar 1987	7.9	87%	2.67	6%	51.0	41.0	7.	7.	100%
23 Mar 1987	50.4	92%	3.46	7%	57.0	47.0	7.	7.	100%
21 Mar 1987	52.0	95%	2.16	4%	55.0	49.0	7.	7.	100%
25 Mar 1987	48.3	88%	4.75	10%	55.0	42.0	7.	7.	100%
26 Mar 1987	37.1	681	2.19	6%	39.0	33.0	7.	0.	0%
27 Mar 1987	46.7	85%	8.79	19%	60.0	37.9	7.	5.	71%
28 Mar 1987	60.1	109%	3.04	5%	63.0	55.0	8.	8	100%
29 Mar 1987	67.3	122%	4.45	7%	72.0	60.0	7.	5.	71%
30 Mar 1987	69.9	1272	4.34	6%	77.0	65.0	7.	4	57%
31 Mar 1987	53.7	98%	5.68	11%	57.0	41.0	7.	7.	100%
1 Apr 1987	52.1	95%	4.76	9%	61.0	47.0	8	8.	100%
2 Apr 1987	58.4	106%	10.74	18%	70.0	42.0	7.	7.	100%
Summary	52.1	95%	9.19	18%	77.0	33.0	115.	101.	88%



Daily Summation for Hexane - IRT (Mice) From 17 Mar 1987 through 21 Mar 1987

Summary Data for: Hexane - HOLD #1/Relative Humidity 90.0 to 70.3

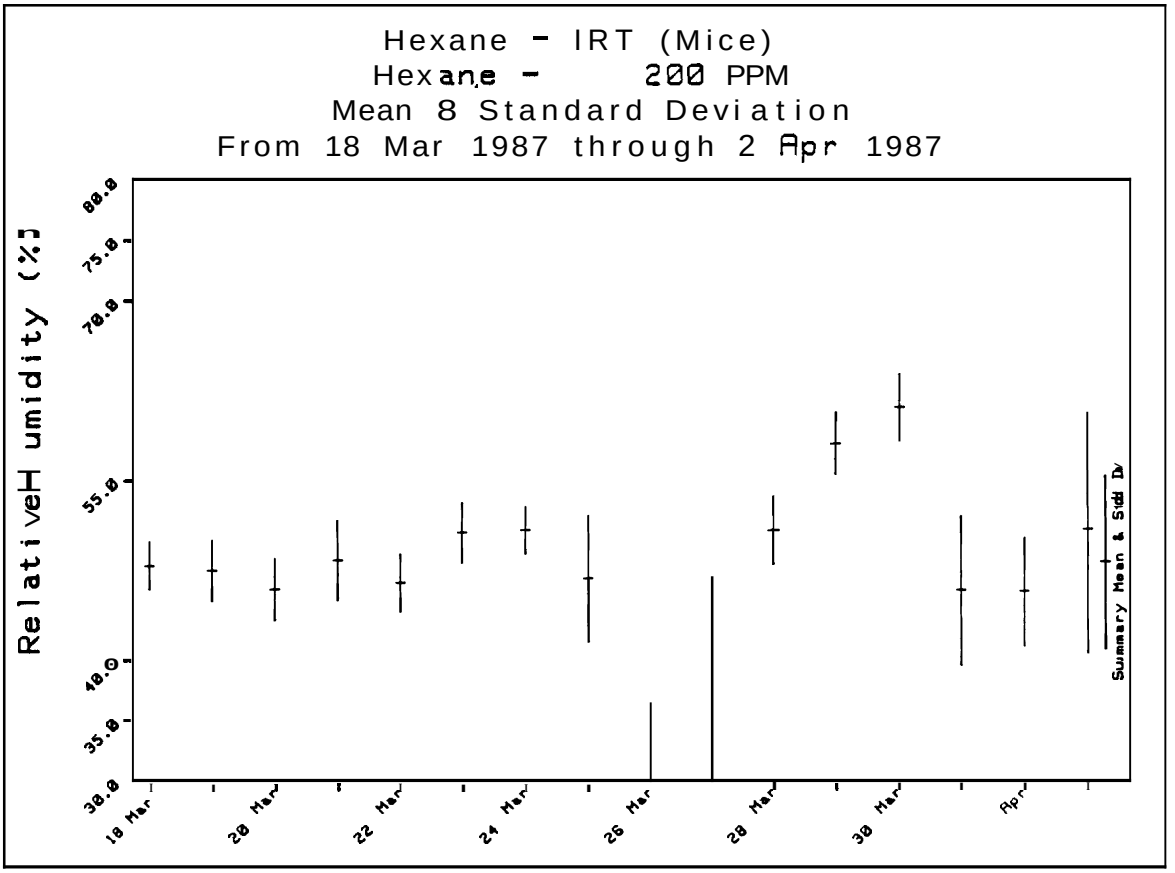
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	Min	% Min
17 Mar 1987	55.9	102%	1.46	3%	58.0	51.0	7.	7.	100%
18 Mar 1987	53.9	98%	1.86	3%	55.0	50.0	7.	7.	100%
19 Mar 1987	49.9	91%	1.68	32	53.0	18.0	7.	7.	100%
20 Mar 1987	46.4	84%	3.36	7%	50.0	42.0	7.	7.	100%
21 Mar 1987	40.5	74%	2.15	5%	44.0	38.0	7.	5.	71%
Summary	99.3	90%	5.90 ,	12%	58.0	38.0	35.	33.	94%



Daily Summation For Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 200 PPM/Relative Humidity 10.0 to 70.9

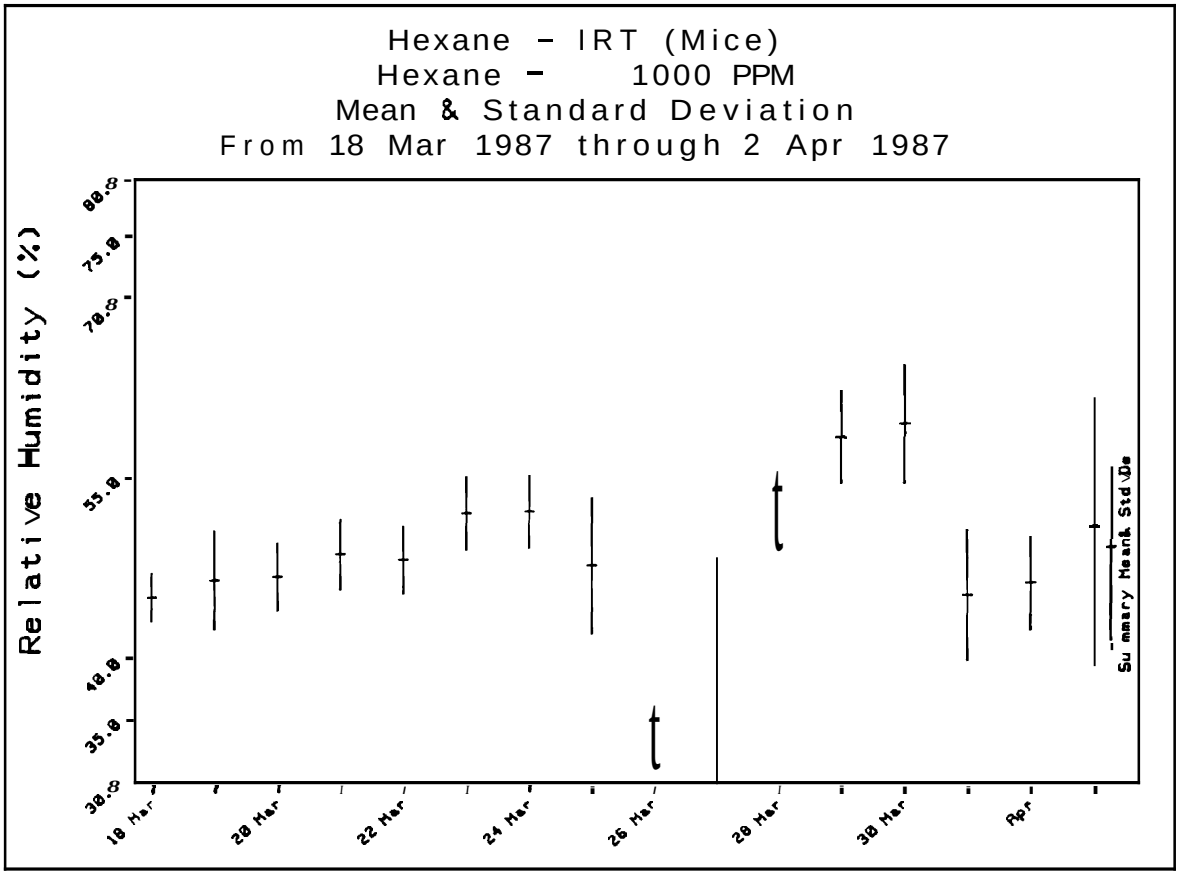
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	Min	% Min
18 Mar 1987	47.9	87%	1.95	4%	50.0	1	7.	7.	100%
19 Mar 1987	47.4	861	2.51	51	51.0	45.0	7.	7.	100%
20 Mar 1987	45.9	83%	2.53	6%	50.0	43.0	8.	8.	100%
21 Mar 1987	48.3	88%	3.30	7%	54.0	15.0	7.	7.	100%
22 Mar 1987	46.4	811	2.37	5%	19.0	43.0	7.	7.	100%
23 Mar 1987	50.6	92%	2.51	5%	55.0	47.0	7.	7.	100%
21 Mar 1987	50.7	921	1.98	4%	53.0	48.0	7.	7.	100%
25 Mar 1987	96.7	85%	5.22	11%	51.0	39.0	7.	6	861
26 Mar 1987	33.3	61%	3.15	9%	40.0	31.0	7.	1.	14%
27 Mar 1987	38.4	70%	8.38	22%	50.0	29.0	7.	3.	43%
28 Mar 1987	50.3	911	2.82	6%	53.0	46.0	8.	8.	100%
29 Mar 1987	56.1	102%	2.51	5%	59.0	52.0	7.	7.	100%
30 Mar 1987	59.1	108%	2.79	5%	63.0	55.0	7.	7.	100%
31 Mar 1987	15.3	82%	6.11	14%	53.0	33.0	8.	7.	88%
1 Apr 1987	45.1	821	4.45	10%	52.0	38.0	9	?.	88%
2 Apr 1987	50.3	91%	10.23	20%	60.0	33.0	7.	6.	86%
Summary	47.6	871	7.18	15%	63.0	29.0	116.	102.	88%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 1000 PPM/Relative Humidity 40.0 to 70.0

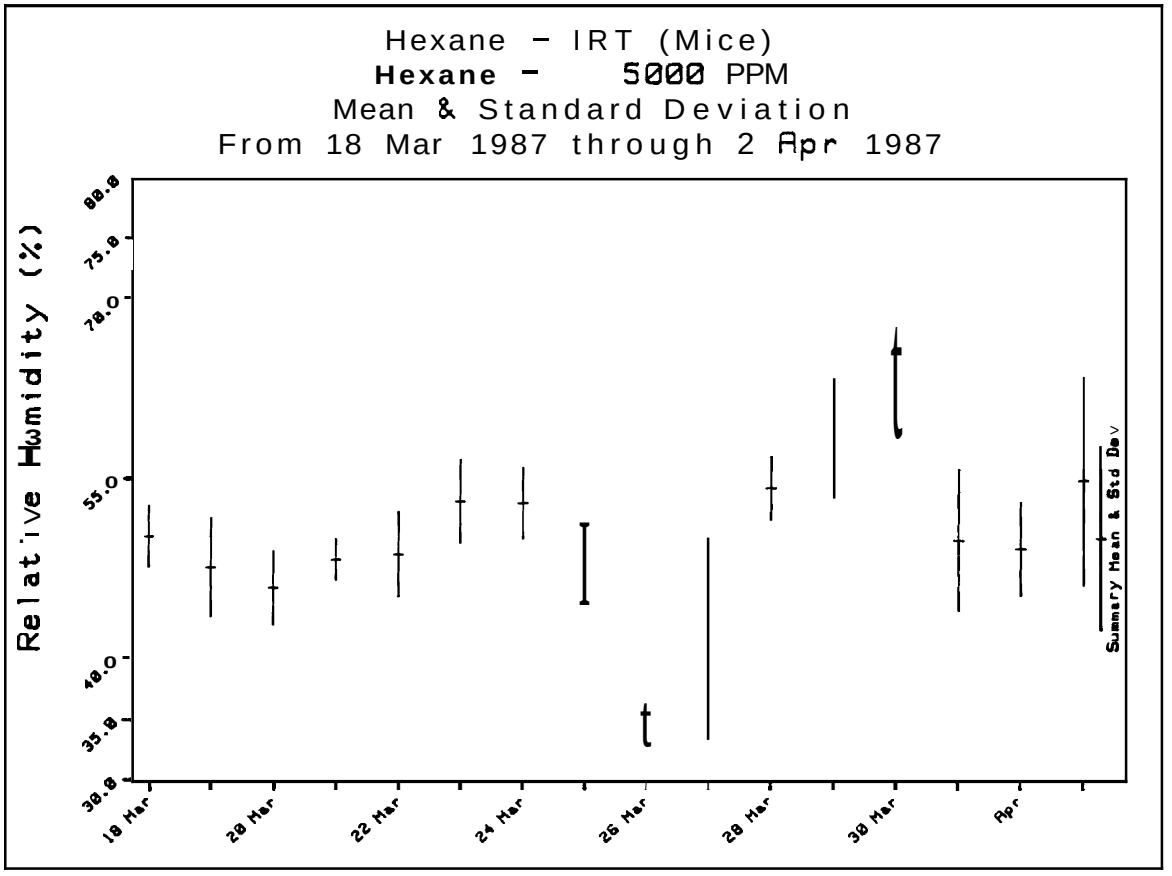
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	Min	% Min
18 Mar 1987	45.1	82%	1.95	4%	49.0	43.0	7.	7.	100%
19 Mar 1987	46.6	85%	1.01	9%	51.0	40.0	7.	7.	100%
20 Mar 1987	46.9	85%	2.75	5%	50.0	43.0	8.	8.	100%
21 Mar 1987	98.7	89%	2.97	6.1	54.0	46.0	7.	7.	100%
22 Mar 1987	18.3	88%	2.75	6%	52.0	15.0	7.	7.	100%
23 Mar 1987	52.1	951	3.02	6%	57.0	48.0	7.	7.	100%
24 Mar 1987	52.3	9 Y	3.04	6%	57.0	49.0	7.	7.	100%
25 Mar 1987	47.9	87%	5.58	12%	57.0	41.0	7.	7.	100%
26 Mar 1987	31.0	62%	2.71	81	40.0	32.0	7.	1.	14%
27 Mar 1987	40.4	74%	8.06	20%	53.0	31.0	7.	1	57%
28 Mar 1987	52.7	96%	3.49	7%	57.0	48.0	8.	8.	100%
29 Mar 1987	58.6	106%	3.82	7%	62.0	53.0	7.	7.	100%
30 Mar 1987	59.7	109%	1.92	8%	65.0	52.0	7.	7.	100%
31 Mar 1987	45.4	83%	5.29	12%	49.0	34.0	7.	6.	861
1 Apr 1987	46.4	84%	3.81	8%	54.0	42.0	8.	8.	100%
2 Apr 1987	50.7	92%	11.09	22%	61.0	34.0	7.	5.	71%
Summary	48.5	88%	7.52	16%	65.0	31.0	115.	103.	90%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 5000 PPM/Relative Humidity 40.0 to 70.0

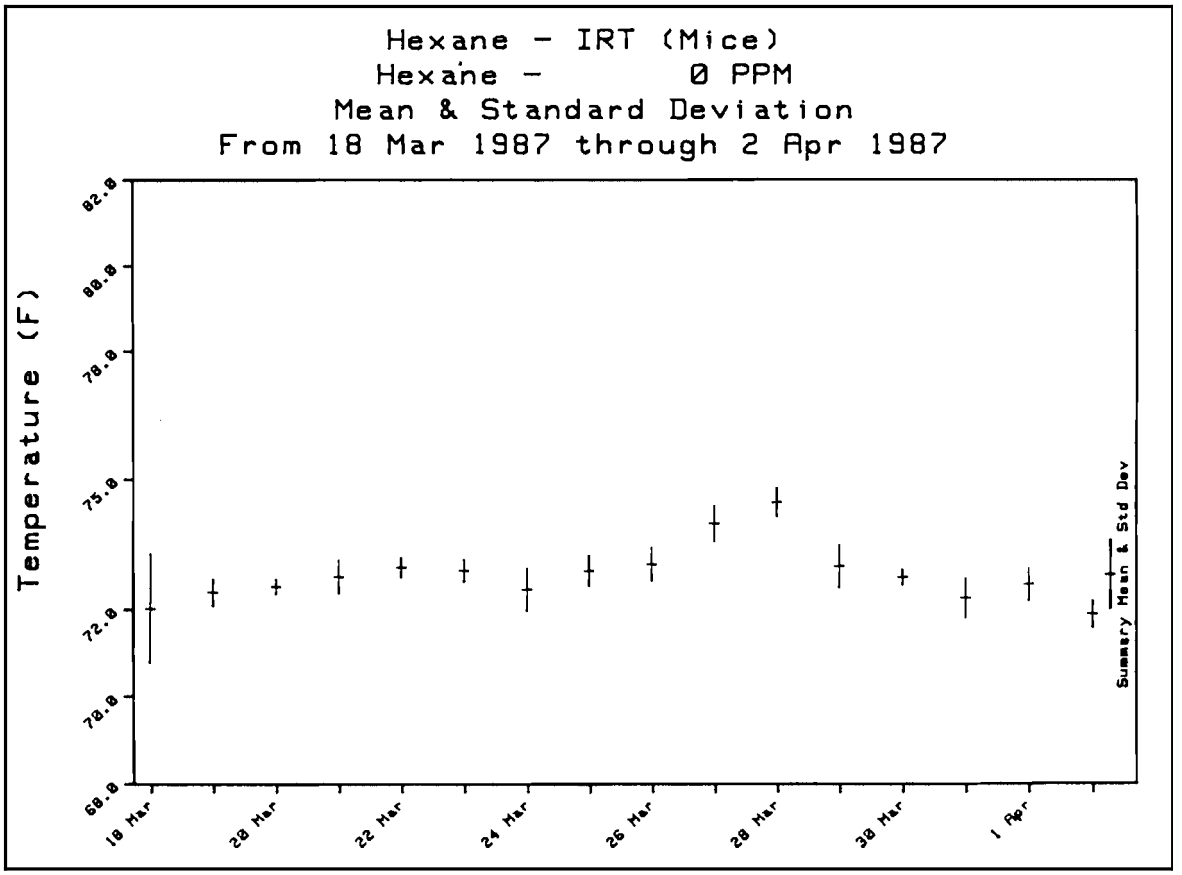
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	Min	% Min
18 Mar 1987	50.1	91%	2.51	5%	55.0	47.0	7.	7.	100%
19 Mar 1987	17.6	86%	4.12	9%	52.0	40.0	7.	7.	100%
20 Mar 1987	45.9	83%	3.09	7%	50.0	42.0	8.	8.	100%
21 Mar 1987	18.3	88%	1.70	4%	51.0	96.0	7.	7.	100%
22 Mar 1987	48.7	89%	3.55	7%	53.0	11.0	7.	7.	100%
23 Mar 1987	53.1	97%	3.41	6%	59.0	18.0	7.	7.	100%
24 Mar 1987	53.0	96%	2.94	6%	57.0	50.0	7.	7,	100%
25 Mar 1987	48.0	871	3.42	7%	52.0	43.0	7.	7.	100%
26 Mar 1987	34.9	63%	1.77	5%	37.0	33.0	7.	0.	0%
27 Mar 1987	11.9	761	8.31	20%	55.0	32.0	7.	4.	57%
28 Mar 1987	51.4	99%	2.56	5%	58.0	51.0	8	8	100%
29 Mar 1987	58.6	106%	4.96	8%	66.0	50.0	7.	7.	100%
30 Mar 1987	61.0	1162	4.83	8%	70.0	56.0	7.	7.	100%
31 Mar 1987	50.0	91%	5.89	12%	54.0	37.0	7.	6	861
1 Apr 1987	49.2	901	3.85	8%	56.0	15.0	8.	8.	100%
2 Apr 1987	55.0	100%	8.72	16%	65.0	41.0	7.	7.	100%
Summary	50.2	91%	7.66	15%	70.0	32.0	115.	104.	90%



Daily Summation For Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 0 PPM/Temperature 69.0 to 75.0

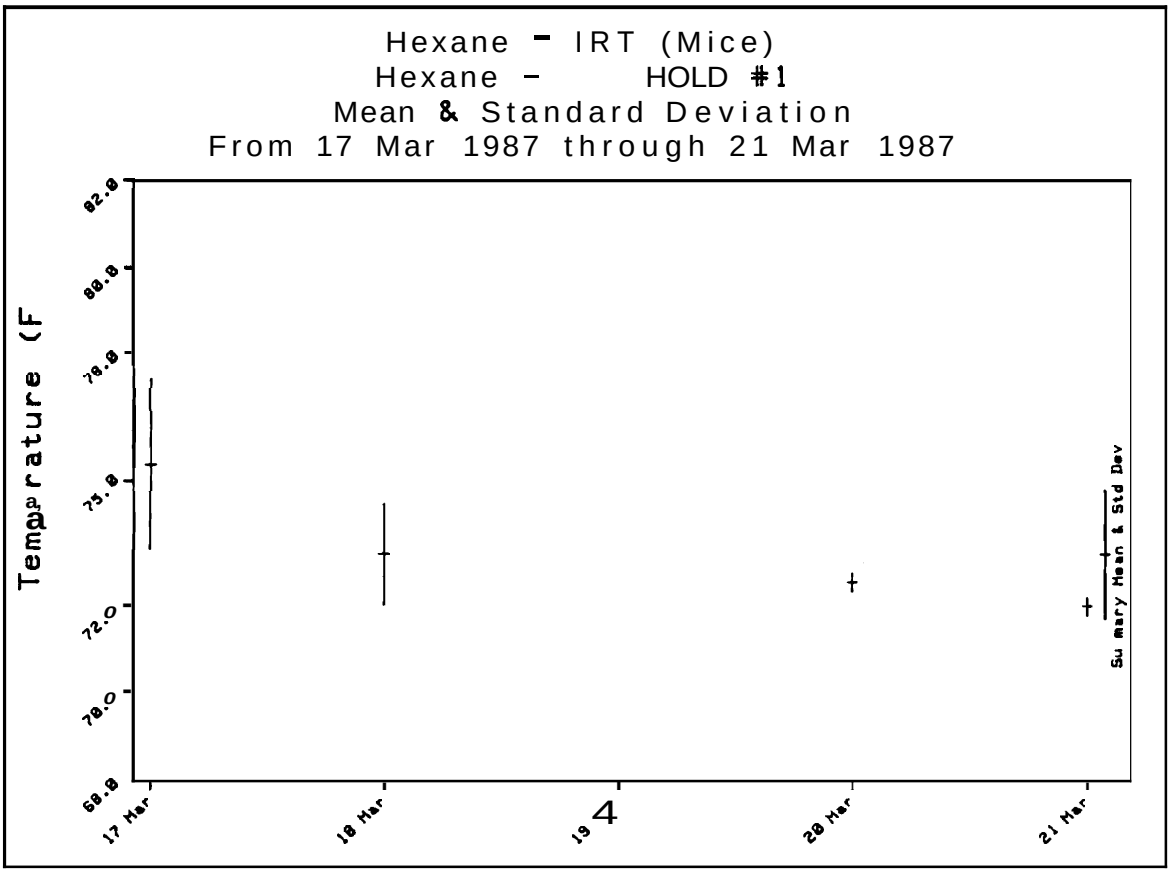
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	72.0	100%	1.25	2%	73.0	69.7	8.	8.	100%
19 Mar 1987	72.4	101%	.31	0%	72.8	71.9	7.	7.	100%
20 Mar 1987	72.5	101%	.18	0%	72.9	72.4	7.	7.	100%
21 Mar 1987	72.8	101%	.38	1%	73.2	72.2	7.	7.	100%
22 Mar 1987	73.0	101%	.23	0%	73.3	72.6	8.	8.	100%
23 Mar 1987	72.9	101%	.25	0%	73.3	72.6	7.	7.	100%
24 Mar 1987	72.5	101%	.50	1%	73.0	71.5	7.	7.	100%
25 Mar 1987	72.9	101%	.35	0%	73.3	72.4	8.	8.	100%
26 Mar 1987	73.1	101%	.38	1%	73.9	72.6	8.	8.	100%
27 Mar 1987	74.0	103%	.41	1%	74.4	73.4	8.	8.	100%
28 Mar 1987	74.5	103%	.34	0%	74.9	73.9	8.	8.	100%
29 Mar 1987	73.0	101%	.49	1%	74.0	72.3	8.	8.	100%
30 Mar 1987	72.8	101%	.18	0%	73.0	72.6	7.	7.	100%
31 Mar 1987	72.3	100%	.45	1%	72.8	71.3	8.	8.	100%
1 Apr 1987	72.6	101%	.37	1%	73.1	72.1	8.	8.	100%
2 Apr 1987	71.9	100%	.32	0%	72.2	71.4	8.	8.	100%
Summary	72.8	101%	.79	1%	74.9	69.7	122.	122.	100%



Daily Summation for Hexane - IRT (Mice) From 17 Mar 1987 through 21 Mar 1987

Summary Data for: Hexane - HOLD #1/Temperature 72.0 to 78.0

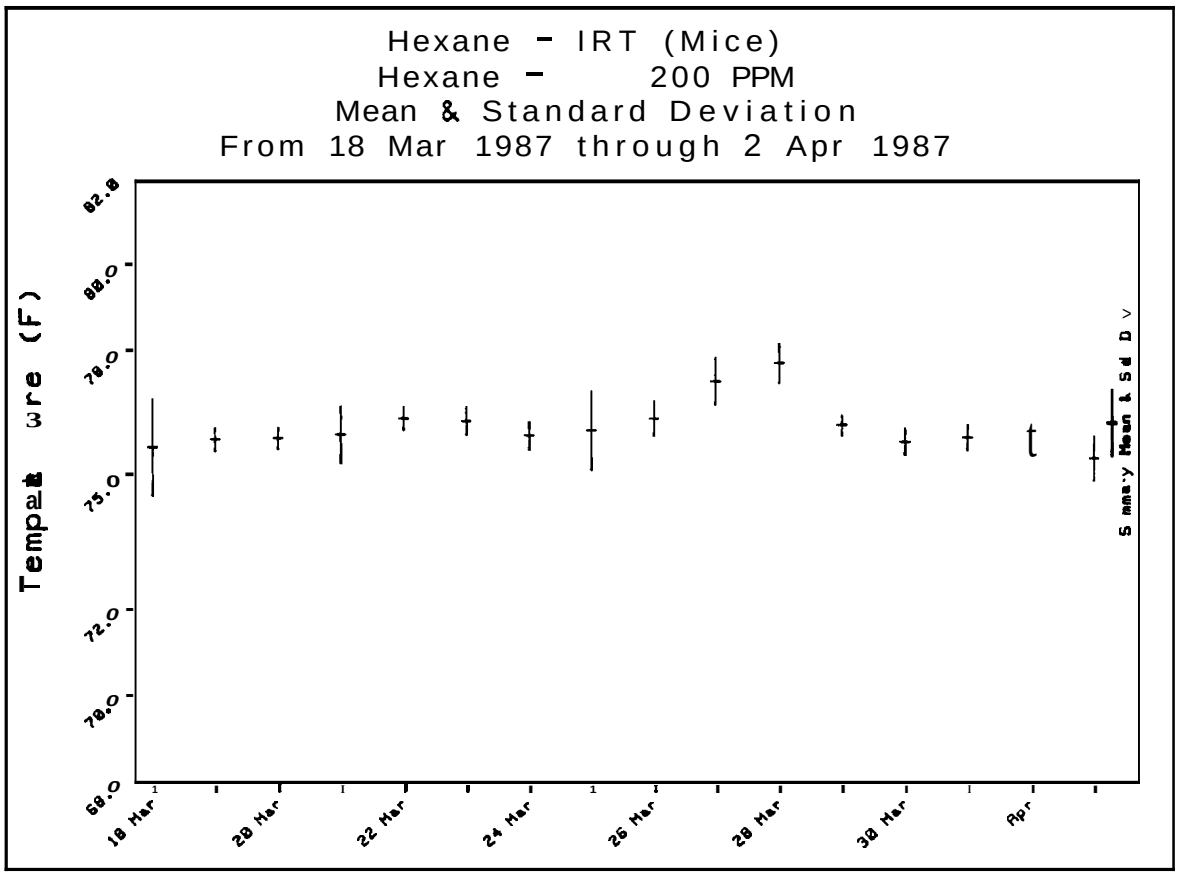
Date	Mean	% Target	Std Dev	RSD	Maximum	Minimum	N	N in	% N in
17 Mar 1987	75.4	101%	1.98	3%	77.4	72.5	7.	7.	100%
18 Mar 1987	73.3	98%	1.17	2%	74.2	71.2	8.	6.	75%
19 Mar 1987	73.1	97%	.31	0%	73.3	72.4	7.	7.	100%
20 Mar 1987	72.6	97%	.21	0%	73.0	72.3	8.	8.	100%
21 Mar 1987	72.1	96%	.21	0%	72.3	71.8	7.	4.	57%
Summary	73.3	98%	1.49	2%	77.4	71.2	37.	32.	86%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 throuah 2 Apr 1987

Summary Data for: Hexane - 200 PPM/Temperature 72.0 to 78.0

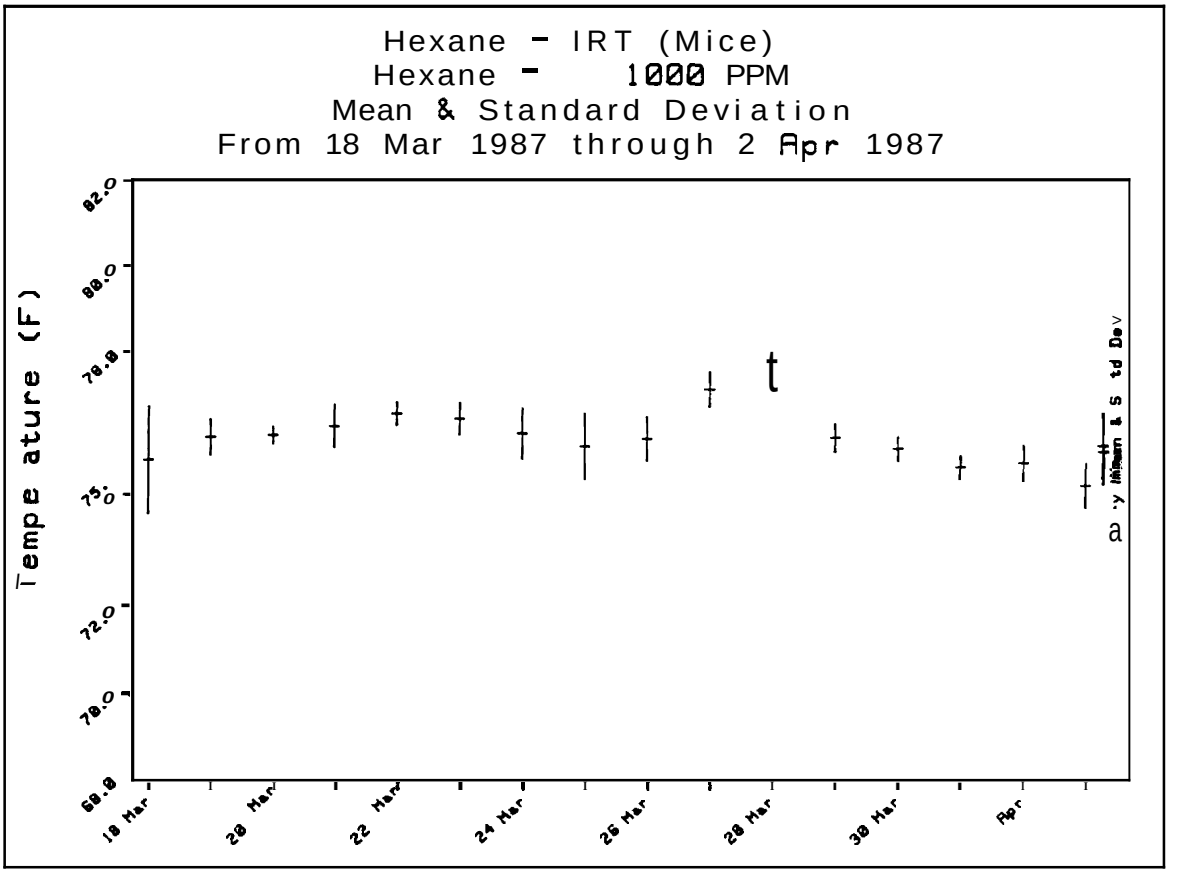
Date	Mean	% Target	Std Otu	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	75.8	101%	1.13	1%	76.7	73.7	8	8	100%
19 Mar 1987	76.0	101%	.27	OX	76.3	75.5	7.	7.	100%
20 Mar 1987	76.0	101%	.25	0%	76.3	75.7	7.	7.	100%
21 Mar 1987	76.1	101%	.66	1%	76.5	71.7	7.	7.	100%
22 Mar 1987	76.5	102%	.27	01	76.9	76.1	8	8	100%
23 Mar 1987	76.1	102%	.33 ,	0%	76.9	76.0	7.	7.	100%
24 Mar 1987	76.0	101%	.33	0% .	76.3	75.1	7.	7.	100%
25 Mar 1987	76.2	102%	.92	1%	76.7	73.9	8.	8.	100%
26 Mar 1987	76.4	102%	.41	1%	77.3	75.9	8.	8	100%
27 Mar 1987	77.3	103%	.54	1%	77.8	76.2	8.	8	100%
28 Mar 1987	77.7	104%	.45	1%	78.1	76.7	8.	7.	88%
29 Mar 1987	76.9	103%	.22	0%	77.1	76.5	8.	8	100%
30 Mar 1987	76.5	102%	.30	OX	76.9	76.0	7.	7.	100%
31 Mar 1987	76.0	101%	.29	0%	76.5	75.6	8	8.	100%
1 Apr 1987	76.0	101%	.39	11	76.5	75.3	8	8	100%
2 Apr 1987	75.6	101%	.51	1%	76.3	74.6	8	8.	100%
Summary	76.3	102%	.75	1%	78.1	73.7	122.	121.	99%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data for: Hexane - 1000 PPM/Temperature 72.0 to 78.0

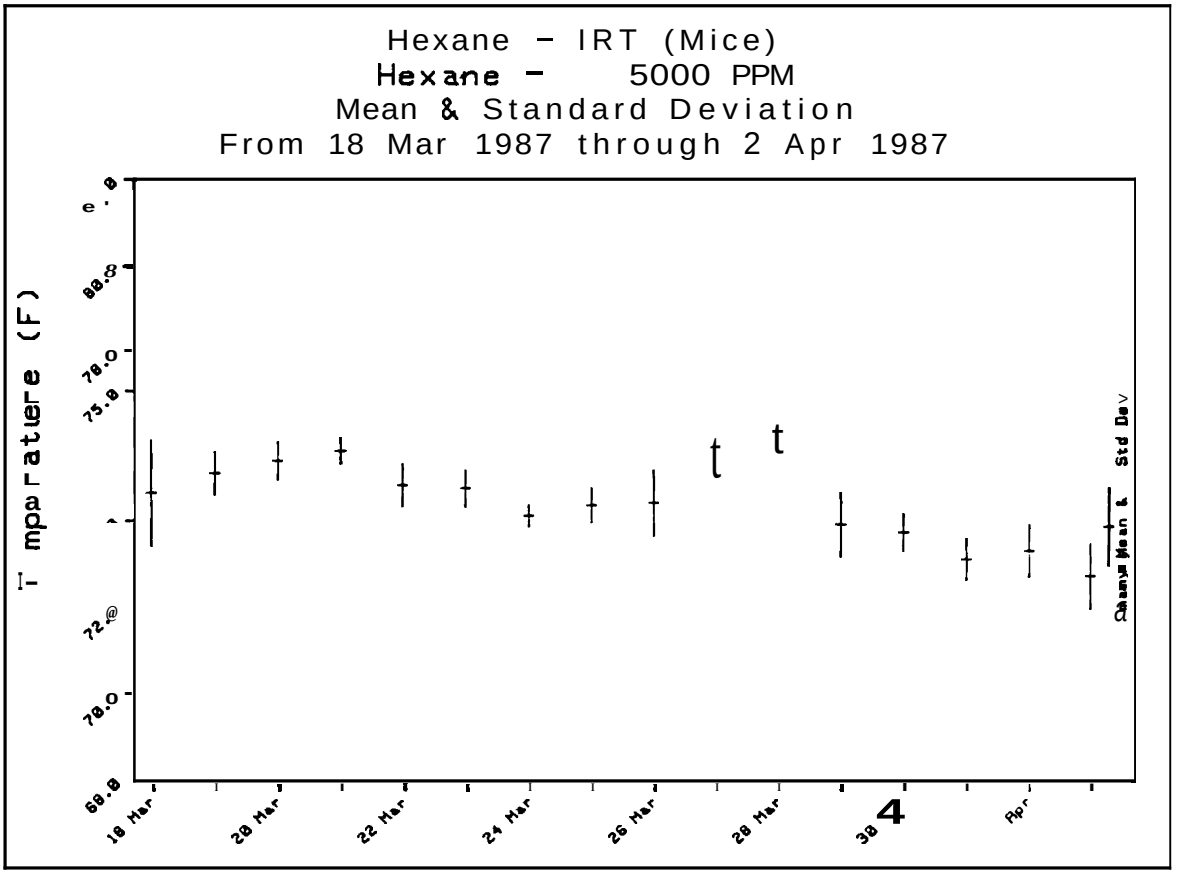
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
18 Mar 1987	75.5	101%	1.24	2%	76.5	73.2	8.	8	100%
19 Mar 1987	16.0	101%	.41	1%	76.5	75.4	7.	7.	100%
20 Mar 1987	76.0	101%	.20	0%	76.3	75.7	7.	7.	100%
21 Mar 1987	76.2	102%	.49	1%	76.8	75.3	7.	7.	100%
22 Mar 1987	76.5	102%	.26	0%	17.0	76.1	8.	8	100%
23 Mar 1987	76.1	102%	.37	0%	7	76.0	7.	7.	100%
24 Mar 1987	76.1	101%	.58	1%	76.7	74.9	7.	7.	100%
25 Mar 1987	75.0	101%	.75	1%	76.7	74.3	7.	7.	100%
26 Mar 1987	76.0	101%	.51	1%	76.9	75.1	8.	8.	100%
27 Mar 1987	77.2	103%	.41	1%	77.7	76.5	8.	8.	100%
28 Mar 1987	77.6	103%	.48	1%	78.1	76.7	8.	7.	88%
29 Mar 1987	76.5	102%	.32	0%	76.8	75.8	8.	8.	100%
30 Mar 1987	76.3	102%	.29	0%	76.7	75.8	7.	7.	100%
31 Mar 1987	75.9	101%	.27	0%	76.1	75.4	8.	8.	100%
1 Apr 1987	76.0	101%	.42	1%	76.6	75.3	8.	8.	100%
2 Apr 1987	75.4	101%	.53	1%	76.1	71.5	8.	8.	100%
Summary	76.2	102%	.75	1%	78.1	73.2	121.	120.	99%



Daily Summation for Hexane - IRT (Mice) From 18 Mar 1987 through 2 Apr 1987

Summary Data fw: Hexane - 5000 PPM/Temperature 72.0 to 78.0

Date	Mean	X Target	Std Dev	% RSD	Maximum	Minimum	N	Hin	% Nin
18 Mar 1987	73.5	981	1.21	2%	75.1	71.5	8	6	75%
19 Mar 1987	73.9	99%	.48	1%	71.7	73.3	7.	7.	100%
20 Mar 1987	71.2	991	.42	1%	75.1	73.9	7.	7.	100%
21 Mar 1987	71.5	99%	.30	0%	71.9	7 1 0	7.	7.	100%
22 Mar 1981	71.8	100%	.49	1%	75.5	71.1	8	8	100%
23 Mar 1987	71.8	100%	.43	1%	75.1	71.3	7.	7.	100%
21 Mar 1987	74.1	991	.25	0%	71.5	73.7	7.	7.	100%
25 Mar 1987	71.1	991	.39	1%	75.2	71.1	7.	7.	100%
26 Mar 1987	7 1 4	99%	.76	1%	75.7	73.6	8	8	100%
27 Mar 1987	75.5	101%	.47	1%	76.2	71.9	8	8.	100%
28 Mar 1987	76.0	101%	.34	0%	76.6	75.5	8	8.	100%
29 Mar 1987	71.1	99%	.73	1%	76.1	73.7	8	8	100%
30 Mar 1987	74.2	991	.42	1%	75.0	73.7	7.	7.	100%
31 Mar 1987	73.6	981	.46	1%	7 1 5	72.9	8	8	100%
1 Apr 1987	73.8	98%	.59	1%	74.7	72.7	8.	8	100%
2 Apr 1987	73.2	98%	.75	1%	74.6	72.2	8.	8.	100%
Summary	71.3	99%	.90	1%	76.6	71.5	121.	119.	99%



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: Hexane Mouse Teratology

REPORTING PERIOD: March 17 - April 2, 1987
NOTE: 24 Hour Data Collection **Period** extends from ~10:00 a.m. to ~10:00 a.m.

COMPILED BY: R. J. Weigel **DATE:** 4 / 15 / 87

CHAMBER CONCENTRATION

DATE	DISCUSSION OR EXPLANATION
3/18/87	At the start of the exposure **period** (10 minutes after T_{90}), the concentration in the 1000 pprn chamber (1 reading = 418 ppm) exceeded the lower critical alarm limit (800 pprn). Work on the chemical pump the preceding day had partially drained the delivery line, requiring additional time for chemical to reach the generator. Also during the exposure period, the concentration in the 1000 pprn chamber (1 reading = 1260 ppm) **exceeded** the upper critical alarm limit (1200 pprn). The chemical delivery pump rate was adjusted. Concentrations in the 200 pprn chamber did not reach operating levels until 13:52, 2:23 after the expiration of T_{90}. This was due to work on the 200 pprn chemical delivery pump the preceding day that drained the chemical delivery line. Exposure shutdown time was not changed so that exposure duration in the 200 pprn chamber was 17:33. During the exposure period (03:22 to 05:42), the concentration in the 200 pprn chamber (5 readings: 160, 159, 155, 156,154 ppm) exceeded the lower critical alarm **limit** (160 pprn). The **computer**-controlled exposure control function was not working during this **period.** The problem was corrected and normal operation resumed. **As** a result of the above problems, the mean exposure level and % relative standard deviation for the 200 pprn chamber exceeded the 10% limit.
3/19/87	During the exposure period, the concentration in the 200 ppm chamber (2 readings: 260,242 ppm) exceeded the upper critical alarm limit (240 pprn). The exhaust air flow was increased to lower the chamber concentration.
3/20/87	During the exposure period (14:14 to 15:28), the concentration in the 200 ppm chamber (6 readings: 291,258,248,248,246,253 ppm) exceeded the upper critical alarm limit (240 pprn). The exhaust air flow was increased to lower the chamber concentration. This was not a sufficient correction, so the chemical delivery pump rate was decreased. During the exposure period (19:17 to 21:31), the concentration in the 1000 pprn chamber (2 readings: 671,784 ppm) exceeded the lower critical alarm limit (800 pprn). The concentration control program was not functioning correctly, turning off the generator instead of adjusting exhaust flows. During the exposure period (19:21), the concentration in the 5000 pprn chamber (1 readings: 1200 ppm) exceeded the lower critical alarm limit (800 pprn). The concentration control program was not functioning correctly, turning off the generator instead of adjusting exhaust flows. Due to the large deviation from target concennation in the 5000 pprn chamber at 19:21, the daily % RSD for that chamber was 13%, which exceeded the 10% limit established in the protocol. The concentration mean for the 5000 chamber was 100% of target concentration.

3/22/87	At the start of the exposure period (30 minutes), the executive computer periodically shutdown exposure. Attributed to a faulty BCD card. Concentrations in the chambers above the T_{90} level were not recorded until 12:34. Exposures at target for all chambers lasted 19:15 hours. As a result, the daily % RSD for the 1000 chamber was 13%, which exceeded the 10% limit established in the protocol. The concentration mean for the 1000 chamber was 103% of target concentration. The daily % RSD for the 5000 chamber was 16%, which exceeded the 10% limit established in the protocol. The concentration mean for the 5000 chamber was 100% of target concentration. Concentration in the 200 ppm Chamber (1 reading: 116 ppm) exceeded the critical low operating limit of 160 pprn at 12:06. See comment above. Concentration in the 1000 ppm Chamber (1 reading: 201 ppm) exceeded the critical low operating limit of 800 ppm at 12:09. See comment above. Concentration in the 5000 ppm Chamber (1 reading: 5 ppm) exceeded the critical low operating limit of 4000 ppm at 12:13. See comment above.
3/25/87	During the exposure period, the concentration in the 200 ppm chamber (1 readings: 100 ppm) exceeded the lower critical alarm limit (160 pprn). Bubbles were removed from the pump.
3/29/87	During the exposure period, (13:30 to 13:49) the executive computer repeatedly turned off the generation process. The cause is unknown but noise in a line to the BCD card is suspected and is being checked. As a result, the concentration in the 200 ppm chamber (1 readings: 42.3 ppm) exceeded the lower critical alarm limit (160 ppm) at 13:38. The concentration in the 1000 ppm chamber (1 readings: 679 ppm) exceeded the lower critical alarm limit (800 ppm) at 13:41. The % RSD of the 200 pprn chamber (12%) exceeded the 10% limit specified in the protocol.
3/30/87	At the start of the exposure period (11:30), the executive computer turned off the generation process. The cause is still unknown but noise in a Iine to the BCD card is suspected As a result, the concentration in the 1000 ppm chamber (1 readings: 637 ppm) did not reach the target concentration until 12:08

TEMPERATURE & RELATIVE HUMIDITY

DATE	DISCUSSION OR EXPLANATION
3/26/87	Extremely dry outside air exceeded the capabilities of the building relative humidity system During this period: 6 readings (31% - 34%) in the 200 ppm chamber exceeded the lower critical alarm limit (35%). 6 readings (32% - 34%) in the 1000 ppm chamber exceeded the lower critical alarm limit (35%). 3 readings (33%) in the 5000 ppm chamber exceeded the lower critical alarm limit (35%) 1 readings (33%) in the 0 ppm (Control) chamber exceeded the lower critical alarm limit (35%) As a result, the mean relative humidity in the exposure chambers also exceeded the minimum operating limit of 35%. The mean %RH was 33.3% in the 200 ppm chamber, 34.0% in the 1000 ppm chamber and 34.9% in the 5000 ppm chamber.
3/27/87	Extremely dry outside air exceeded the capabilities of the building relative humidity system During this period: 3 readings (29% - 32%) in the 200 ppm chamber exceeded the lower critical alarm limit (35%). 2 readings (31% - 32%) in the 1000 ppm chamber exceeded the lower critical alarm limit (35%). 2 readings (32% - 34%) in the 5000 ppm chamber exceeded the lower critical alarm limit (35%):
3/31/87	Relative humidity in the 200 ppm chamber (1 reading: 33%) exceeded the lower critical alarm limit (35%). Operator made adjustment. Relative humidity in the 1000 ppm chamber (1 reading: 34%) exceeded the lower critical alarm limit (35%). Operator made adjustment.
4/2/87	Relative humidity in the 200 ppm chamber (1 reading: 33%) exceeded the lower critical alarm limit (35%). Operator made adjustment. Relative humidity in the 1000 ppm chamber (1 reading: 34%) exceeded the lower critical alarm limit (35%). Operator made adjustment.

CHAMBER FLOW **& VACUUM**

DATE	DISCUSSION OR EXPLANATION
	No problems or excursions during this reporting period.

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

n-Hexane Mouse Teratology Study: Body Weights (g) for Virgin Females

TMT=0 ppm n-Hexane

MATNO	Prestudy Wt	Exposure Day 1	Exposure Day 4	Exposure Day 7	Sacrifice Wt
3078	26.90	28.70	28.10	27.10	28.40
3122	29.60	30.60	29.90	30.20	30.70
3132	31.30	32.10	32.40	31.40	32.60
3133	28.70	29.00	28.70	27.90	28.30
3145	25.20	25.80	26.00	26.40	26.80
3218	27.40	28.80	29.20	27.30	27.10
3233	30.70	29.90	27.80	28.70	29.40
3247	31.80	32.40	32.00	33.30	33.20
3298	29.60	31.40	29.90	30.80	30.80
3321	28.30	28.60	29.30	29.10	27.50

n-Hexane Mouse Teratology Study: Body Weights (g) for Virgin Females

TMT=200 ppm n-Hexane

MATNO	Prestudy Wt	Exposure Day 1	Exposure Day 4	Exposure Day 7	Sacrifice Wt
3020	30.60	28.40	28.80	28.40	29.50
3064	24.70	26.30	26.20	26.70	25.30
3079	27.10	28.90	26.90	26.50	25.60
3082	28.80	28.10	27.50	26.80	28.20
3099	28.40	29.70	28.80	28.60	27.80
3128	27.70	26.40	27.10	27.00	26.50
3286	29.10	30.40	29.50	30.20	29.70
3302	29.50	31.70	31.50	31.80	30.40
3310	29.70	30.30	30.60	29.40	29.90
3355	31.30	28.80	27.60	28.10	27.10

n-Hexane Mouse Teratology Study: Body Weights (g) for Virgin Females

TMT=1000 ppm n-Hexane

MATNO	Prestudy Wt	Exposure Day 1	Exposure Day 4	Exposure Day 7	Sacrifice Wt
3001	31.50	30.40	30.80	30.50	30.80
3036	33.50	31.70	31.10	30.90	31.70
3051	28.30	28.10	28.20	28.10	28.50
3097	26.20	28.10	29.60	29.80	29.80
3120	28.10	28.20	28.10	28.30	29.30
3130	28.90	30.20	30.50	30.70	30.40
3169	28.70	27.70	28.70	27.20	27.00
3211	26.30	28.90	27.20	29.10	28.00
3220	30.70	31.10	32.00	32.10	32.70
3265	30.10	30.80	31.60	31.30	29.50

n-Hexane Mouse Teratology Study: Body Weights (g) for Virgin Females

TMT=5000 ppm n-Hexane

MATNO	Prestudy Wt	Exposure Day 1	Exposure Day 4	Exposure Day 7	Sacrifice Wt
3157	28.60	28.00	28.90	29.20	28.60
3197	26.40	27.20	28.70	28.90	29.60
3237	34.60	33.60	33.80	33.20	36.10
3241	30.80	29.20	31.00	30.60	31.10
3255	27.90	29.60	30.40	31.30	32.20
3257	26.20	26.40	26.80	26.30	28.60
3295	28.70	27.90	29.60	30.30	30.30
3300	30.30	29.40	29.00	30.30	30.10
3332	29.60	28.30	29.90	28.60	30.00
3350	29.70	28.00	28.60	28.30	28.90

n-Hexane Mouse Teratology Study: Body Weights (g) Top Plug-positive Females

0 ppm n-Hexane

MATNO	Prestudy Wt	0 dg Wt	6 dg Wt	9 dg Wt	12 dg wt	18 dg Wt	Uter Wt	Pregnant	NO. Sites	Live	Early Resorp	Late Resorp	DEAD
3019	28.30	26.60	30.60	31.90	34.70	45.50	12.50	1	7	6	1	0	0
3026	27.40	26.90	29.00	31.40	35.90	52.00	17.40	1	10	9	1	0	0
3034	28.70	30.30	29.80	31.10	34.10	48.70	16.90	1	12	10	2	0	0
3046	29.20	28.80	31.50	29.80	29.10	28.80	.	0	.	.	.	.	.
3050	28.20	28.00	32.30	35.70	43.10	63.30	22.80	1	13	13	0	0	0
3052	27.00	27.50	30.40	30.40	28.70	30.20	.	0	.	.	.	.	.
3069	27.70	27.70	29.60	28.90	29.50	28.60	.	0	.	.	.	.	.
3072	28.50	28.40	31.60	35.30	41.70	56.60	20.70	1	13	12	1	0	0
3077	29.00	27.60	31.20	34.10	39.20	60.50	24.60	1	15	15	0	0	0
3081	29.10	29.40	33.00	33.80	39.90	59.00	22.00	1	13	12	1	0	0
3113	31.00	32.00	32.60	33.90	39.20	61.00	25.00	1	15	15	0	0	0
3115	27.90	29.40	31.80	32.20	38.50	55.20	19.50	1	11	10	1	0	0
3116	28.00	28.30	31.90	34.50	40.20	58.90	22.60	1	14	13	1	0	0
3136	27.00	26.70	29.50	31.20	36.80	54.80	20.20	1	11	11	0	0	0
3140	28.90	27.80	30.90	31.90	35.90	47.60	13.40	1	6	6	0	0	0
3162	27.70	27.30	29.60	32.80	37.20	56.10	22.20	1	12	12	0	0	0
3166	26.80	26.10	26.80	25.90	25.80	25.60	.	0	.	.	.	.	.
3167	29.00	28.40	31.30	33.10	38.70	56.70	21.70	1	12	12	0	0	0
3178	27.50	25.60	25.60	28.90	27.70	27.80	.	0	.	.	.	.	.
3203	28.60	27.10	28.90	31.20	36.90	55.10	21.00	1	12	12	0	0	0
3213	31.20	31.60	35.50	38.00	42.30	59.40	20.40	1	15	13	1	1	0
3215	29.80	29.80	33.20	34.30	42.80	58.50	20.20	1	11	11	0	0	0
3225	28.30	28.00	30.20	33.40	39.10	57.10	23.90	1	16	14	2	0	0
3234	27.80	27.50	28.70	29.30	29.30	29.50	.	0	.	.	.	.	.
3236	29.20	29.10	31.40	33.20	37.70	58.50	23.10	1	15	15	0	0	0
3239	29.00	28.10	30.30	32.10	38.10	55.40	22.20	1	13	12	1	0	0
3246	30.10	30.30	32.60	35.70	42.60	62.70	23.70	1	13	13	0	0	0
3251	29.60	28.90	32.70	34.80	42.80	64.30	26.40	1	14	14	0	0	0
3270	28.10	27.60	31.20	31.00	37.50	57.50	23.20	1	13	13	0	0	0
3303	29.50	29.00	31.50	33.70	38.90	54.20	18.10	1	11	10	1	0	0
3311	30.60	30.60	34.50	35.90	42.40	64.60	26.30	1	16	15	1	0	0
3318	26.40	26.50	29.50	31.40	36.00	51.80	18.20	1	10	10	0	0	0
3359	29.50	29.00	33.20	35.60	40.80	64.20	29.50	1	17	17	0	0	0

200 ppm n-Hexane

MATNO	Preatudy Wt	0 dg Wt	6 dg Wt	9 dg wt	12 dg wt	18 dg Wt	Uter Wt	Pregnant	No. Sites	Live	Early Resorp	Late Resorp	DEAD
3004	28.30	26.90	29.20	29.90	35.60	52.30	19.70	1	11	11	0	0	0
3013	28.20	28.70	32.20	35.90	40.80	59.10	22.50	1	14	13	0	1	0
3015	31.00	30.90	33.90	35.70	39.90	58.10	22.20	1	13	13	0	0	0
3043	30.40	28.30	30.40	32.90	39.00	55.60	18.40	1	11	9	1	1	0
3057	26.60	26.70	29.10	30.20	30.90	31.30	.	0	.	.	.	.	.
3063	28.80	27.90	31.10	32.80	36.80	55.20	20.80	1	15	13	1	1	0
3065	26.30	26.50	29.40	28.10	27.40	27.30	.	0	.	.	.	.	.
3071	28.60	27.50	28.40	31.20	32.90	47.90	16.00	1	10	10	0	0	0
3085	28.20	28.60	31.80	34.50	39.00	58.10	20.60	1	13	12	1	0	0
3089	26.70	26.90	29.10	30.90	37.40	56.00	19.80	1	12	9	0	3	0
3095	30.50	30.10	33.20	32.90	34.70	32.30	.	0	.	.	.	.	.
3110	26.80	26.70	29.80	30.90	34.90	51.30	16.70	1	11	9	1	1	0
3112	30.90	28.90	32.20	35.00	40.10	58.00	21.90	1	13	12	1	0	0
3159	30.00	29.20	30.70	31.60	33.30	46.60	13.10	1	8	7	1	0	0
3163	30.50	30.30	34.10	34.70	38.10	47.40	11.30	1	7	5	2	0	0
3182	23.20	24.00	24.90	25.10	23.30	24.00	.	0	.	.	.	.	.
3187	28.30	28.00	31.80	34.30	39.80	58.80	22.80	1	14	13	1	0	0
3190	28.30	27.70	30.70	32.10	37.10	54.10	17.60	1	10	10	0	0	0
3193	27.10	27.10	28.40	32.20	37.20	55.80	21.40	1	12	12	0	0	0
3202	27.50	28.30	30.90	33.00	38.50	57.50	19.00	1	13	11	2	0	0
3240	28.90	30.40	32.70	35.90	39.60	48.70	11.30	1	14	6	7	1	0
3262	29.80	29.40	33.10	36.70	41.00	59.90	23.70	1	16	12	3	1	0
3269	28.90	30.60	33.00	36.20	42.20	59.30	23.40	1	14	13	1	0	0
3273	28.10	29.20	29.70	31.30	31.30	32.50	.	0	.	.	.	.	.
3279	28.60	28.20	31.30	33.20	36.60	52.70	18.90	1	11	10	1	0	0
3280	29.00	27.80	29.50	30.80	30.00	30.00	.	0	.	.	.	.	.
3297	29.50	27.90	31.00	33.40	36.40	52.00	19.00	1	13	11	2	0	0
3307	28.90	29.60	31.30	33.00	37.00	51.20	16.60	1	11	9	2	0	0
3319	27.40	28.20	31.60	34.20	37.40	54.00	17.90	1	10	9	1	0	0
3327	25.00	26.90	31.70	32.90	39.30	59.00	22.10	1	14	12	2	0	0
3328	30.40	30.80	32.20	36.50	38.80	58.00	19.80	1	12	11	1	0	0
3338	27.40	28.80	31.40	34.50	39.00	56.70	19.60	1	14	11	0	3	0
3352	27.40	27.40	27.30	27.50	27.50	27.20	.	0	.	.	.	.	.
3357	27.80	27.20	30.30	31.80	37.70	55.00	22.90	1	14	14	0	0	0

1000 ppm n-Hexane

MATNO	Prestudy Wt	0 dg Wt	6 dg Wt	9 dg wt	12 dg wt	18 dg Wt	Uter Wt	Pregnant	No. Sites	Live	Early Resorp	Late Resorp	DEAD
3009	29.70	29.30	32.10	34.50	39.10	57.00	18.60	1	11	10	1	0	0
3014	29.60	28.20	30.40	32.00	36.10	53.10	18.80	1	11	11	0	0	0
3022	28.20	27.50	30.60	28.10	28.90	27.30	.	0	.	.	.	.	.
3025	27.10	27.00	29.90	31.80	35.70	51.70	16.70	1	10	9	0	1	0
3031	30.40	28.90	30.90	33.50	36.80	51.50	18.60	1	10	9	0	1	0
3038	25.90	25.80	28.00	28.30	27.40	26.70	.	0	.	.	.	.	.
3058	28.80	28.30	30.20	32.10	37.30	55.70	18.90	1	10	10	0	0	0
3062	27.50	26.70	29.50	31.90	36.40	53.80	20.20	1	12	11	1	0	0
3064	29.00	29.90	32.00	33.30	37.40	49.00	13.50	1	7	7	0	0	0
3067	29.70	28.00	31.70	33.00	38.60	57.90	22.40	1	14	12	1	1	0
3068	29.10	30.50	29.80	30.50	30.70	30.00	.	0	.	.	.	.	.
3075	29.50	29.50	31.90	33.60	40.20	56.50	20.40	1	13	12	1	0	0
3083	29.40	30.80	33.10	36.00	39.70	59.50	20.40	1	13	11	0	2	0
3088	27.90	29.00	31.80	35.70	42.10	61.90	23.30	1	13	13	0	0	0
3138	29.60	28.40	30.90	33.30	37.50	51.90	15.30	1	9	8	1	0	0
3164	28.90	28.00	31.70	34.10	39.60	58.70	22.90	1	14	14	0	0	0
3199	26.10	26.30	31.10	32.30	38.70	57.00	22.30	1	15	15	0	0	0
3204	32.90	31.50	34.00	32.00	32.50	33.20	.	0	.	.	.	.	.
3207	27.80	28.10	28.20	29.50	29.20	29.20	.	0	.	.	.	.	.
3216	32.00	30.10	32.10	33.90	39.10	61.40	25.20	1	15	15	0	0	0
3217	28.80	27.30	32.40	34.30	40.70	53.30	16.30	1	13	9	3	1	0
3219	27.70	28.50	33.10	36.20	40.00	63.60	24.00	1	16	16	0	0	0
3226	30.10	30.50	33.80	37.50	45.40	69.60	29.30	1	16	16	0	0	0
3248	29.10	29.50	31.60	34.20	37.20	51.00	15.60	1	9	9	0	0	0
3261	27.50	27.80	29.10	33.10	39.40	56.70	23.00	1	14	13	0	1	0
3267	26.20	26.00	25.90	25.50	25.80	25.40	.	0	.	.	.	.	.
3289	26.90	27.60	30.40	34.60	41.90	61.50	24.60	1	13	12	0	1	0
3293	28.00	28.20	31.30	31.40	35.30	55.60	20.90	1	11	11	0	0	0
3308	25.00	25.50	28.40	30.50	32.80	51.50	19.10	1	13	11	1	1	0
3322	28.60	27.40	30.30	32.40	37.20	53.70	19.30	1	11	10	0	1	0
3323	27.10	29.10	31.10	31.90	36.60	55.50	20.20	1	13	12	1	0	0
3341	29.60	28.80	29.90	30.40	33.60	46.30	15.40	1	10	9	1	0	0
3343	27.40	27.30	29.20	32.20	37.80	53.10	20.60	1	14	13	1	0	0
3356	26.80	27.50	29.50	30.00	33.90	52.10	19.00	1	11	11	0	0	0

5000 ppm n-Hexane

MATNO	Prestudy Wt	0 dg Wt	6 dg Wt	9 dg Wt	12 dg wt	18 dg Wt	Uter Wt	Pregnant	No. Sites	Live	Early Resorp	Late Resorp	DEAD
3008	28.60	29.10	29.30	29.30	31.40	30.90	.	0		.		.	
3030	27.60	28.40	30.90	33.90	37.10	66.10	19.60	1	11	10	0	1	0
3036	26.60	27.20	29.00	30.10	30.80	38.90	.	0	.	.			
3040	27.40	27.10	30.00	31.90	33.20	42.20	8.40	1	5	5	0	0	0
3042	28.80	28.30	29.70	29.80	30.20	30.80		0		.			
3047	27.60	27.30	28.60	31.00	36.10	62.00	19.20	1	12	11	0	0	0
3066	30.10	30.50	32.30	36.50	41.30	64.90	18.10	1	14	11	0	3	0
3098	28.00	29.00	31.10	34.30	39.10	66.60	21.20	1	14	14	0	0	0
3109	28.70	28.90	31.70	35.60	41.00	68.10	19.60	1	12	10	1	1	0
3118	28.90	29.70	32.60	36.40	41.70	64.20	17.60	1	13	10	3	0	0
3121	27.80	26.70	28.40	31.30	35.80	49.20	14.90	1	12	8	3	1	0
3129	27.60	28.00	30.40	29.50	30.70	29.30		0	.	.	.		
3131	29.60	28.80	32.30	35.40	39.70	62.60	16.20	1	9	8	1	0	0
3137	28.80	27.40	29.40	32.60	37.20	62.30	16.60	1	8	8	0	0	0
3139	27.20	27.90	30.00	31.20	36.30	61.90	17.60	1	11	9	0	2	0
3186	30.90	30.00	32.10	32.50	40.00	67.40	20.60	1	13	13	0	0	0
3206	28.60	26.50	30.60	29.20	30.90	30.30		0	.				
3209	27.90	27.90	32.50	36.20	38.40	68.00	19.30	1	11	11	0	0	0
3223	28.00	26.90	30.00	34.20	41.10	66.80	21.80	1	13	13	0	0	0
3230	31.40	29.30	34.50	36.90	42.70	62.20	22.00	1	12	12	0	0	0
3243	28.80	30.50	32.70	33.60	44.10	69.00	22.90	1	17	16	0	1	0
3264	24.80	26.60	30.20	32.80	38.00	61.90	19.10	1	11	11	0	0	0
3259	26.90	27.60	29.30	31.70	37.10	61.20	14.60	1	11	9	1	1	0
3266	26.20	25.80	28.50	30.30	35.70	63.20	16.80	1	11	10	1	0	0
3276	30.00	27.90	28.60	30.40	31.40	32.90	.	0	.				
3286	30.00	31.00	33.60	34.70	40.70	66.80	18.60	1	12	10	1	0	0
3291	30.20	29.60	30.60	31.60	32.80	31.00	.	0	.	.			
3294	28.70	28.60	31.30	35.10	40.90	67.60	20.90	1	12	11	0	1	0
3301	26.90	27.20	30.40	31.40	34.60	49.00	16.20	1	10	9	1	0	0
3304	28.70	27.90	30.70	30.90	35.80	43.30	6.40	1	6	3	2	1	0
3306	30.80	29.90	30.70	32.10	34.00	61.60	17.90	1	9	9	0	0	0
3312	28.90	28.70	31.70	34.10	39.70	68.30	22.00	1	14	13	0	1	0
3329	27.90	28.10	28.00	29.20	30.20	28.20		0					
3333	28.90	28.90	28.30	28.90	30.10	28.80		0					

0 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3019	1	1	2	1.46	0.11			
3019	2	1	1	1.62	0.11			
3019	3	2	.	.	.			
3019	4	1	2	1.48	0.11			
3019	5	1	1	1.50	0.11			
3019	6	1	1	1.69	0.12	SURB		
3019	7	1	2	1.65	0.11			
3026	1	1	2	1.49	0.14			
3026	2	1	2	1.41	0.10			
3026	3	1	1	1.49	0.12			
3026	4	1	2	1.50	0.12			
3026	5	1	1	1.41	0.13			
3026	6	1	2	1.43	0.13			
3026	7	1	2	1.42	0.12			
3026	8	2	.	.	.			
3026	9	1	1	1.46	0.13	ROST		
3026	10	1	2	1.29	0.10			
3034	1	1	2	1.46	0.09	SURB		
3034	2	1	2	1.39	0.09	SURB	ROSK	
3034	3	2	.	.	.			
3034	4	1	1	1.37	0.10	SURB		
3034	5	1	1	1.33	0.09	ROSK		
3034	6	1	1	1.38	0.10	ROST		
3034	7	1	1	1.29	0.07			
3034	8	1	2	1.29	0.09			
3034	9	1	2	1.35	0.08			
3034	10	2	.	.	.			
3034	11	1	1	1.13	0.08			
3034	12	1	2	1.27	0.10			
3050	1	1	2	1.33	0.08			
3050	2	1	1	1.49	0.11			
3050	3	1	1	1.39	0.10			
3050	4	1	1	1.47	0.10			
3050	5	1	1	1.42	0.10	ROST		
3050	6	1	1	1.37	0.10			
3050	7	1	2	1.52	0.10	ROST		
3050	8	1	2	1.49	0.11			
3050	9	1	2	1.42	0.10	ROSK		
3050	10	1	2	1.37	0.10			
3050	11	1	1	1.38	0.10	ROSK		
3050	12	1	2	1.42	0.07			
3050	13	1	2	1.37	0.05	ROSK		
3072	1	1	2	1.38	0.07			
3072	2	1	2	1.29	0.08			
3072	3	1	2	1.32	0.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

---------- Ø ppm n-Hexane ----------

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3072	4	2	.	.	.			
3072	5	1	1	1.40	Ø.08			
3072	6	1	1	1.38	Ø.09			
3072	7	1	1	1.31	Ø.07			
3072	8	1	1	1.32	Ø.08			
3072	9	1	2	1.39	Ø.06			
3072	10	1	2	1.43	Ø.08			
3072	11	1	1	1.52	Ø.09			
3072	12	1	1	1.48	Ø.08			
3072	13	1	1	1.47	Ø.09			
3077	1	1	2	1.38	Ø.09			
3077	2	1	2	1.26	0.08			
3077	3	1	1	1.38	0.09	SURB		
3077	4	1	2	1.39	0.07			
3077	5	1	2	1.33	0.08			
3077	6	1	1	1.23	0.09	SCST		
3077	7	1	1	1.42	0.07			
3077	8	1	1	1.34	0.08			
3077	9	1	2	1.17	0.09			
3077	10	1	2	1.36	0.08			
3077	11	1	1	1.24	0.10			
3077	12	1	1	1.36	0.09			
3077	13	1	1	1.35	0.08			
3077	14	1	1	1.26	0.09			
3077	15	1	2	1.42	Ø.10			
3081	1	1	1	1.41	Ø.11			
3081	2	1	1	1.38	0.09			
3081	3	1	2	1.39	0.10			
3081	4	1	1	1.45	0.10			
3081	5	1	2	1.40	0.09	SURB		
3081	6	1	2	1.36	0.10	ROST		
3081	7	2	.	.	.			
3081	8	1	1	1.49	Ø.11	SURB		
3081	9	1	1	1.57	0.09	SURB		
3081	10	1	1	1.47	0.09			
3081	11	1	1	1.53	Ø.11			
3081	12	1	1	1.34	0.09			
3081	13	1	2	1.46	0.12	SURB		
3113	1	1	1	1.50	0.08			
3113	2	1	2	1.29	0.09			
3113	3	1	2	1.33	0.08			
3113	4	1	2	1.35	0.08			
3113	5	1	2	1.28	0.08			
3113	6	1	1	1.35	0.10			
3113	7	1	2	1.36	0.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

Ø ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3113	8	1	1	1.46	Ø.1Ø			
3113	9	1	1	1.43	Ø.1Ø			
3113	1Ø	1	2	1.35	Ø.Ø8			
3113	11	1	2	1.24	Ø.Ø9			
3113	12	1	1	1.42	Ø.11			
3113	13	1	1	1.31	Ø.1Ø			
3113	14	1	2	1.29	Ø.1Ø			
3113	15	1	1	1.35	Ø.Ø9			
3115	1	1	2	1.54	Ø.1Ø	ROSK		
3115	2	1	2	1.56	Ø.12			
3115	3	1	1	1.58	Ø.13	ROSK	ROST	
3115	4	1	2	1.49	Ø.Ø7	ROST		
3115	5	1	1	1.56	Ø.12			
3115	6	2			.			
3115	7	1	1	1.38	Ø.1Ø			
3115	8	1	2	1.53	Ø.11	ROSK		
3115	9	1	1	1.64	Ø.12			
3115	1Ø	1	1	1.54	Ø.Ø9	ROST		
3115	11	1	1	1.63	Ø.1Ø			
3116	1	1	2	1.36	Ø.Ø7			
3116	2	1	1	1.38	Ø.1Ø			
3116	3	1	1	1.41	Ø.1Ø			
3116	4	1	1	1.48	Ø.1Ø			
3116	5	1	2	1.31	Ø.Ø7			
3116	6	1	2	1.32	Ø.Ø8			
3116	7	1	1	1.41	Ø.Ø9			
3116	8	1	2	1.42	Ø.Ø7			
3116	9	1	1	1.52	Ø.Ø9	ROST		
3116	1Ø	2			.			
3116	11	1	2	1.3Ø	Ø.Ø8			
3116	12	1	2	1.44	Ø.Ø9			
3116	13	1	2	1.37	Ø.Ø7			
3116	14	1	2	1.38	Ø.Ø8			
3136	1	1	1	1.6Ø	Ø.Ø9	SURB		
3136	2	1	1	1.58	Ø.1Ø	SURB		
3136	3	1	2	1.55	Ø.1Ø	SURB		
3136	4	1	1	1.5Ø	Ø.12	SURB		
3136	5	1	1	1.2Ø	Ø.Ø9	SURB		
3136	6	1	2	1.38	Ø.Ø8	SURB		
3136	7	1	2	1.42	Ø.Ø9	SURB		
3136	8	1	2	1.4Ø	Ø.Ø9	SURB		
3136	9	1	1	1.52	Ø.Ø9			
3136	1Ø	1	2	1.38	Ø.Ø9	SURB		
3136	11	1	1	1.48	Ø.Ø9			
3140	1	1	1	1.81	Ø.12			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

---------- Ø ppm n-Hexane ----------

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3140	2	1	2	1.31	0.12			
3140	3	1	1	1.78	0.12			
3140	4	1	2	1.66	0.10			
3140	5	1	1	1.78	0.12			
3140	6	1	1	1.85	0.11			
3162	1	1	2	1.51	0.09			
3162	2	1	2	1.57	0.10			
3162	3	1	2	1.56	0.10			
3162	4	1	2	1.47	0.08			
3162	5	1	1	1.54	0.09			
3162	6	1	1	1.57	Ø.11			
3162	7	1	2	1.44	0.08			
3162	8	1	1	1.48	0.09			
3162	9	1	1	1.50	Ø.08			
3162	10	1	2	1.40	0.08			
3162	11	1	2	1.48	0.09			
3162	12	1	1	1.56	0.11			
3167	1	1	2	1.49	0.07			
3167	2	1	1	1.38	0.10			
3167	3	1	2	1.38	0.07			
3167	4	1	2	1.48	0.09			
3167	5	1	2	1.48	0.07			
3167	6	1	2	1.40	0.09			
3167	7	1	1	1.50	0.10			
3167	8	1	1	1.57	0.08			
3167	9	1	1	1.45	0.09			
3167	10	1	2	1.44	0.08			
3167	11	1	1	1.50	0.10			
3167	12	1	1	1.55	0.09			
3203	1	1	2	1.30	0.09			
3203	2	1	2	1.30	0.09	ROSK		
3203	3	1	1	1.46	0.10	ROST	MAST	
3203	4	1	2	1.46	0.11			
3203	5	1	1	1.47	0.14			
3203	6	1	1	1.36	0.12			
3203	7	1	2	1.31	0.08			
3203	8	1	1	1.30	0.09			
3203	9	1	1	1.43	0.09			
3203	10	1	2	1.41	0.08	ROST		
3203	11	1	1	1.38	0.09			
3203	12	1	1	1.40	0.10			
3213	1	1	1	1.09	0.08			
3213	2	1	1	1.22	0.12			
3213	3	1	1	1.10	0.09			
3213	4	1	1	1.20	0.10			

Status: **1** = Live; **2** = Early Resorption; **4** = Late Resorption
Sex: Male = **1;** Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities **[ABNn]**

0 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3213	5	2	.	.	.			
3213	6	4	.	.	.			
3213	7	1	2	1.22	0.10			
3213	8	1	2	1.14	0.11	ROSK		
3213	9	1	2	1.12	0.08			
3213	10	1	2	1.11	0.10	ROST		
3213	11	1	2	1.01	0.09			
3213	12	1	2	1.06	0.08			
3213	13	1	1	1.20	0.09			
3213	14	1	2	1.06	0.11			
3213	15	1	1	1.11	0.08			
3215	1	1	1	1.42	0.10			
3215	2	1	2	1.50	0.09			
3215	3	1	2	1.45	0.09	ROST		
3215	4	1	1	1.55	0.11			
3215	5	1	2	1.50	0.09			
3215	6	1	2	1.34	0.09	SURB		
3215	7	1	1	1.47	0.11			
3215	8	1	1	1.54	0.10	ROST		
3215	9	1	2	1.45	0.10			
3215	10	1	2	1.49	0.08			
3215	11	1	2	1.52	0.10			
3225	1	1	2	1.17	0.07	ROST		
3225	2	1	I	1.37	0.09			
3225	3	1	2	1.30	0.08	ROST	MAST	
3225	4	1	2	1.16	0.09			
3225	5	1	I	1.35	0.07			
3225	6	1	1	1.37	0.08	LMFL		
3225	7	1	I	1.37	0.10			
3225	8	1	2	1.35	0.08			
3225	9	1	2	1.30	0.09			
3225	10	1	I	1.40	0.08			
3225	11	2	.	.	.			
3225	12	1	2	1.40	.	MAST		
3225	13	1	1	1.56	0.09			
3225	14	1	2	1.47	0.08			
3225	15	2	.	.	.			
3225	16	1	2	1.50	0.07			
3236	1	1	I	1.26	0.07			
[illegible]	2	1	I	1.29	0.11			
3236	3	1	2	1.17	0.07	ROST		
3236	4	1	I	1.14	0.09			
3236	6	1	1	1.31	0.09			
3236	8	1	2	1.18	0.08	ROST		
[illegible]	7	1	2	1.19	0.05			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

---------- 0 ppm n-Hexane ----------

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3236	8	1	2	1.22	0.09	SURB		
3236	9	1	2	1.10	0.06	ROST		
3236	10	1	2	1.16	0.07			
3236	11	1	2	1.22	0.08			
3236	12	1	1	1.28	0.08	SURB		
3236	13	1	2	1.24	0.09			
3236	14	1	1	1.32	0.10			
3236	15	1	2	1.18	0.07			
3239	1	1	2	1.49	0.10			
3239	2	1	2	1.52	0.09	MAST		
3239	3	1	2	1.52	0.09			
3239	4	1	2	1.46	0.06			
3239	5	1	2	1.35	0.07			
3239	6	1	2	1.39	0.09			
3239	7	1	1	1.54	0.11			
3239	8	1	2	1.51	0.10			
3239	9	1	2	1.50	0.07			
3239	10	2	.	.				
3239	11	1	1	1.44	0.09			
3239	12	1	2	1.56	0.10			
3239	13	1	1	1.53	0.08			
3246	1	1	2	1.50	0.07			
3246	2	1	1	1.41	0.06	ROST		
3246	3	1	1	1.48	0.09			
3246	4	1	2	1.50	0.08			
3246	5	1	1	1.56	0.09			
3246	6	1	2	1.32	0.07			
3246	7	1	2	1.43	0.09			
3246	8	1	1	1.53	0.10			
3246	9	1	2	1.39	0.07			
3246	10	1	1	1.50	0.09			
3246	11	1	1	1.41	0.08			
3246	12	1	2	1.40	0.09			
3246	13	1	2	1.37	0.09			
3251	1	1	2	1.35	0.10	LMFL		
3251	2	1	1	1.53	0.10			
3251	3	1	1	1.56	0.14	LMFL		
3251	4	1	1	1.50	0.11	LMFL		
3251	5	1	2	1.49	0.06			
3251	6	1	2	1.45	.			
3251	7	1	2	1.53	0.11			
3251	8	1	2	1.42	0.08			
3251	9	1	1	1.46	0.10			
3251	10	1	2	1.45	0.10			
3251	11	1	2	1.57	0.06			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

Ø ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3251	12	1	2	1.57	0.09			
3251	13	1	2	1.49	0.11			
3251	14	1	1	1.49	0.09			
3270	1	1	2	1.46	0.08			
3270	2	1	2	1.41	0.08	LMFL		
3270	3	1	2	1.37	0.08			
3270	4	1	2	1.47	0.10			
3270	5	1	2	1.44	0.10			
3270	6	1	2	1.41	0.10			
3270	7	1	2	1.41	0.10			
3270	8	1	1	1.52	0.10			
3270	9	1	1	1.49	0.12	LMFL		
3270	10	1	1	1.42	0.10			
3270	11	1	2	1.42	0.09			
3270	12	1	1	1.44	0.11	SURB		
3270	13	1	1	1.41	0.10	SURB		
3303	1	2	.	.	.			
3303	2	1	2	1.43	0.09			
3303	3	1	2	1.49	0.09	ROST		
3303	4	1	1	1.33	0.09			
3303	5	1	2	1.45	0.10			
3303	6	1	2	1.41	0.08			
3303	7	1	1	1.42	0.08			
3303	8	1	1	1.49	0.09			
3303	9	1	2	1.40	0.10			
3303	10	1	1	1.45	0.09			
3303	11	1	2	1.38	0.08			
3311	1	2	.	.	.			
3311	2	1	1	1.44	0.11			
3311	3	1	2	1.43	0.10			
3311	4	1	2	1.43	0.09	ROST		
3311	5	1	2	1.39	0.09			
3311	6	1	2	1.44	0.11			
3311	7	1	2	1.39	0.09			
3311	8	1	2	1.35	0.09			
3311	9	1	1	1.41	0.10	LMFL		
3311	10	1	2	1.39	0.09			
3311	11	1	2	1.31	0.09			
3311	12	1	1	1.37	0.10			
3311	13	1	1	1.49	0.11	SURB		
3311	14	1	2	1.38	0.09			
3311	15	1	2	1.40	0.09			
3311	16	1	2	1.45	0.10			
3318	1	1	1	1.44	0.09	SURB		
3318	2	1	1	1.47	0.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

---------- Ø ppm n-Hexane ----------

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3318	3	1	1	1.37	0.10			
3318	4	1	1	1.52	0.10			
3318	5	1	1	1.34	Ø.11			
3318	6	1	2	1.53	0.10			
3318	7	1	1	1.47	0.08			
3318	8	1	1	1.49	0.08			
3318	9	1	2	1.05	0.09			
3318	10	1	1	1.49	0.07			
3359	1	1	2	1.37	0.07			
3359	2	1	2	1.50	0.11			
3359	3	1	1	1.53	0.10			
3359	4	1	1	1.43	Ø.10	SURB		
3359	5	1	1	1.44	0.09			
3359	6	1	2	1.46	0.08	SURB		
3359	7	1	2	1.37	0.08			
3359	8	1	1	1.44	0.09			
3359	9	1	2	1.28	0.08	SURB		
3359	10	1	2	1.32	0.08			
3359	11	1	2	1.33	0.08			
3359	12	1	2	1.28	0.06	SURB		
3359	13	1	2	1.36	0.07			
3359	14	1	2	1.48	0.08			
3359	15	1	2	1.42	0.08			
3359	16	1	2	1.44	Ø.08	SURB		
3359	17	1	2	1.29	Ø.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3004	1	1	1	1.50	0.12			
3004	2	1	2	1.40	0.09			
3004	3	1	2	1.44	0.09			
3004	4	1	2	1.42	0.11			
3004	5	1	1	1.42	0.08			
3004	6	1	2	1.41	0.09			
3004	7	1	2	1.38	0.09	ROST	MAST	
3004	8	1	1	1.35	0.08			
3004	9	1	2	1.41	0.10	ROST		
3004	10	1	1	1.50	0.09			
3004	11	1	1	1.46	0.11			
3013	1	1	1	1.21	0.12			
3013	2	1	2	1.32	0.11	ROST		
3013	3	1	2	1.27	0.10	ROSK		
3013	4	1	2	1.36	0.10			
3013	5	1	1	1.29	0.11			
3013	6	1	1	1.44	0.09			
3013	7	1	2	1.44	0.12			
3013	8	1	1	1.45	0.11			
3013	9	1	1	1.39	0.13			
3013	10	1	1	1.48	0.13			
3013	11	1	1	1.39	0.10			
3013	12	1	2	1.46	0.13			
3013	13	1	2	1.37	0.09			
3013	14	4	.	.	.			
3015	1	1	2	1.46	0.09			
3015	2	1	2	1.44	0.09			
3015	3	1	1	1.48	0.11			
3015	4	1	2	1.34	0.08			
3015	5	1	2	1.32	0.11			
3015	6	1	1	1.40	0.09			
3015	7	1	1	1.35	0.09			
3015	8	1	1	1.40	0.09			
3015	9	1	1	1.43	0.09			
3015	10	1	2	1.29	0.09			
3015	11	1	2	1.26	0.10			
3015	12	1	2	1.20	0.08			
3015	13	1	1	1.31	0.07			
3043	1	2	.	.	.			
3043	2	4	.	.	.			
3043	3	1	1	1.48	0.10	FURB		
3043	4	1	2	1.45	0.10	SURB		
3043	5	1	2	1.56	0.10	ROST		
3043	6	1	2	1.44	0.09		SURB	
3043	7	1	2	1.41	0.10			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3043	8	1	1	1.54	0.11			
3043	9	1	2	1.20	0.12			
3043	10	1	2	1.39	0.09		SURB	
3043	11	1	2	1.52	0.11			
3063	1	2	.	.				
3063	2	1	1	1.42	0.07			
3063	3	4	.	.				
3063	4	1	2	1.09	0.06			
3063	5	1	2	1.20	0.06			
3063	6	1	2	1.32	0.06			
3063	7	1	2	1.24	0.06			
3063	8	1	1	1.34	0.08			
3063	9	1	2	1.34	0.06			
3063	10	1	1	1.39	0.08			
3063	11	1	1	1.31	0.07			
3063	12	1	1	1.29	0.07			
3063	13	1	2	1.23	0.06			
3063	14	1	1	1.14	0.06			
3063	15	1	1	1.31	0.07			
3071	1	1	1	1.30	0.10			
3071	2	1	1	1.25	0.11			
3071	3	1	1	1.19	0.09			
3071	4	1	1	1.22	0.09			
3071	5	1	2	1.20	0.09			
3071	6	1	1	1.23	0.08			
3071	7	1	1	1.18	0.08			
3071	8	1	2	1.11	0.07			
3071	9	1	1	1.20	0.08			
3071	10	1	2	1.14	0.08			
3085	1	1	1	1.44	0.09			
3085	2	1	1	1.41	0.09			
3085	3	1	2	1.34	0.10			
3085	4	1	1	1.44	0.12			
3085	5	1	2	1.23	0.08			
3085	6	1	2	1.32	0.10			
3085	7	1	1	1.48	0.10			
3085	8	1	2	1.33	0.10			
3085	9	1	1	1.39	0.10			
3085	10	1	1	1.48	0.12			
3085	11	1	2	1.28	0.06			
3085	12	1	1	1.33	0.09			
3085	13	2	.	.	.			
3089	1	1	1	1.64	0.12			
3089	2	1	1	1.56	0.11			
3089	3	1	1	1.56	0.10			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3089	4	1	2	1.54	0.10			
3089	5	1	2	1.41	0.09			
3089	6	4	.	.	.			
3089	7	4	.	.	.			
3089	8	4	.	.	.			
3089	9	1	2	1.53	0.10			
3089	10	1	2	1.49	0.09	SURB		
3089	11	1	2	1.43	0.08			
3089	12	1	2	1.51	0.11	SURB		
3110	1	1	2	1.32	0.10			
3110	2	1	1	1.27	0.08			
3110	3	4	.	.	.			
3110	4	1	1	1.39	0.13			
3110	5	1	1	1.33	0.10			
3110	6	1	2	1.21	0.07	LMFL		
3110	7	1	2	1.13	0.10	SURB		
3110	8	2	.	.	.			
3110	9	1	1	1.13	0.09	ROST		
3110	10	1	1	1.37	0.11			
3110	11	1	1	1.39	0.09			
3112	1	1	2	1.42	0.09	SURB		
3112	2	1	2	1.32	0.09	SURB		
3112	3	1	1	1.27	0.12	SURB	ROST	
3112	4	1	1	1.43	0.11	SURB		
3112	5	1	2	1.42	0.10	SURB	ROST	
3112	6	1	2	1.34	0.09			
3112	7	1	1	1.40	0.12	SURB		
3112	8	1	2	1.41	0.09	SURB		
3112	9	1	1	1.40	0.12	SURB		
3112	10	2	.	.	.	SURB		
3112	11	1	1	1.46	0.12	SURB		
3112	12	1	1	1.47	0.11	SURB		
3112	13	1	1	1.44	0.12			
3159	1	1	1	1.38	0.07			
3159	2	1	2	1.47	0.09			
3159	3	2	.	.	.			
3159	4	1	1	1.46	0.11			
3159	5	1	1	1.47	0.08			
3159	6	1	1	1.39	0.10			
3159	7	1	2	1.35	0.11			
3159	8	1	1	1.43	0.12			
3163	1	2	.	.				
3163	2	1	2	1.83	0.11			
3163	3	1	2	1.69	0.10			
3163	4	1	2	1.49	0.13	ROST	MAST	

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3163	5	1	1	2.17	0.13			
3163	6	2	.	.	.			
3163	7	1	2	1.45	0.09			
3187	1	1	2	1.28	0.09			
3187	2	1	1	1.40	0.09	LMFL		
3187	3	1	2	1.42	0.06			
3187	4	1	2	1.38	0.08			
3187	5	1	1	1.43	0.07	SURB		
3187	6	1	1	1.38	0.09			
3187	7	1	1	1.41	0.09			
3187	8	1	2	1.35	0.07			
3187	9	2	.	.	.			
3187	10	1	1	1.41	0.10			
3187	11	1	2	1.41	0.08			
3187	12	1	2	1.40	0.09			
3187	13	1	1	1.41	0.09			
3187	14	1	1	1.50	0.10			
3190	1	1	1	1.48	0.09			
3190	2	1	1	1.48	0.09			
3190	3	1	1	1.48	0.12			
3190	4	1	1	1.39	0.08			
3190	5	1	2	1.46	0.09			
3190	6	1	1	1.42	0.09			
3190	7	1	2	1.25	0.08			
3190	8	1	2	1.29	0.09			
3190	9	1	2	1.23	0.12			
3190	10	1	1	1.44	0.09			
3193	1	1	2	1.47	0.10			
3193	2	1	1	1.46	0.11			
3193	3	1	2	1.43	0.08			
3193	4	1	1	1.45	0.10			
3193	5	1	1	1.41	0.09	SURB		
3193	6	1	1	1.50	0.09			
3193	7	1	1	1.46	0.09			
3193	8	1	2	1.40	0.09	SURB		
3193	9	1	1	1.41	0.09	SURB		
3193	10	1	2	1.41	0.09	ROST		
3193	11	1	1	1.37	0.08			
3193	12	1	2	1.37	0.07			
3202	1	1	2	1.36	0.08			
3202	2	1	2	1.44	0.10			
3202	3	2	.	.				
3202	4	1	2	1.39	0.08			
3202	5	1	2	1.35	0.09	SURB		
3202	6	1	2	1.33	0.09			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3202	7	1	2	1.30	0.09			
3202	8	1	2	1.33	0.08			
3202	9	1	1	1.38	0.09			
3202	10	2	.		.			
3202	11	1	2	1.33	0.10			
3202	12	1	2	1.29	0.10			
3202	13	1	2	1.28	0.07			
3240	1	2	.	.	.			
3240	2	1	1	1.50	0.10			
3240	3	2	.	.	.			
3240	4	2	.	.	.			
3240	5	1	2	1.35	0.09			
3240	6	2						
3240	7	4						
3240	8	1	2	1.47	0,09		SURB	
3240	9	2						
3240	10	1	2	1.44	0,09			
3240	11	1	1	1.48	0.10			
3240	12	1	1	1.37	0.10	SURB		
3240	13	2			.			
3240	14	2	.	.	.			
3262	1	1	1	1.40	0.11			
3262	2	2	.	.	.			
3262	3	1	1	1.48	0.08			
3262	4	4	.	.	.			
3262	5	1	2	1.39	0.09			
3262	6	1	1	1.46	0.12			
3262	7	1	1	1.43	0.10			
3262	8	1	1	1.52	0.11			
3262	9	2	.	.	.			
3262	10	1	2	1.45	0.10			
3262	11	1	2	1.35	0.10			
3262	12	2			.			
3262	13	1	1	1.54	0.10			
3262	14	1	1	1.47	0.08			
3262	15	1	2	1.49	0.09			
3262	16	1	1	1.38	0.08			
3269	1	1	1	1.52	0.12			
3269	2	1	1	1.50	0.10			
3269	3	1	2	1.37	0.09			
3269	4	1	1	1.44	0.09			
3269	5	2			.			
3269	6	1	2	1.31	0.09			
3269	7	1	2	1.31	0.08			
3269	8	1	2	1.38	0.09	ROST		

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3269	9	1	2	1.51	0.10			
3269	10	1	2	1.42	0.08			
3269	11	1	2	1.46	0.08			
3269	12	1	2	1.44	0.09			
3269	13	1	2	1.30	0.09			
3269	14	1	2	1.41	0.10			
3279	1	1	1	1.56	0.10			
3279	2	1	2	1.55	0.12			
3279	3	1	2	1.08	0.07	ROST	MAST	
3279	4	1	2	1.57	0.10			
3279	5	1	1	1.61	0.11			
3279	6	1	2	1.60	0.10			
3279	7	1	1	1.54	0.13			
3279	8	2	.	.				
3279	9	1	1	1.61	0.11	SURB		
3279	10	1	2	1.39	0.10			
3279	11	1	1	1.58	0.10		SURB	
3297	1	1	1	1.38	0.11			
3297	2	1	1	1.44	0.11			
3297	3	2	.	.	.			
3297	4	1	1	1.45	0.09			
3297	5	1	2	1.32	0.12			
3297	6	1	2	1.20	0.07			
3297	7	1	2	1.18	0.11			
3297	8	1	2	1.12	0.09			
3297	9	2	.	.	.			
3297	10	1	1	1.33	0.07			
3297	11	1	2	1.19	0.10			
3297	12	1	2	1.32	0.10			
3297	13	1	2	1.21	0.08			
3307	1	1	1	1.47	0.11			
3307	2	1	2	1.38	0.11			
3307	3	1	1	1.52	0.13	ROST		
3307	4	1	1	1.40	0.10			
3307	5	2	.	.				
3307	6	1	2	1.39	0.09	ROST		
3307	7	1	2	1.35	0.09			
3307	8	1	1	1.36	0.08			
3307	9	2	.	.	.			
3307	10	1	1	1.42	0.08			
3307	11	1	2	1.47	0.10			
3319	1	1	1	1.57	0.10			
3319	2	2	.	.	.			
3319	3	1	2	1.53	0.11			
3319	4	1	2	1.47	0.12			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3319	5	1	1	1.42	0.10	SURB		
3319	6	1	1	1.43	0.12			
3319	7	1	1	1.54	0.08	SURB		
3319	8	1	1	1.52	0.10			
3319	9	1	1	1.49	0.13			
3319	10	1	1	1.58	0.13			
3327	1	1	2	1.49	0.08			
3327	2	1	2	1.49	0.09			
3327	3	2	.	.	.			
3327	4	1	2	1.38	0.07			
3327	5	1	2	1.49	0.10	ROST		
3327	6	1	2	1.34	0.07			
3327	7	1	1	1.42	0.08			
3327	8	1	2	1.38	0.08			
3327	9	1	1	1.61	0.09	ROST		
3327	10	1	2	1.54	0.10			
3327	11	1	2	1.59	0.08			
3327	12	1	2	1.49	0.09			
3327	13	2	.	.	.			
3327	14	1	1	1.45	0.10			
3328	1	1	1	1.49	0.09			
3328	2	1	1	1.52	0.11			
3328	3	1	1	1.53	0.11			
3328	4	1	2	1.40	0.10			
3328	5	1	2	1.31	0.07			
3328	6	1	2	1.28	0.08			
3328	7	1	1	1.46	0.13			
3328	8	1	2	1.35	0.08			
3328	9	1	1	1.45	0.11			
3328	10	1	2	1.36	0.08			
3328	11	2	.	.	.			
3328	12	1	2	1.40	0.09			
3338	1	1	1	1.44	0.10			
3338	2	1	2	1.25	0.10			
3338	3	1	2	1.22	0.08			
3338	4	4	.	.	.			
3338	5	4	.	.	.			
3338	6	1	2	1.26	0.07			
3338	7	1	2	1.29	0.08			
3338	8	4	.	.	.			
3338	9	1	2	1.27	0.06			
3338	10	1	2	1.27	0.09			
3338	11	1	2	1.26	0.07			
3338	12	1	2	1.26	0.08			
3338	13	1	1	1.33	0.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

200 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3338	14	1	1	1.22	0.07			
3357	1	1	2	1.31	0.10			
3357	2	1	2	1.36	0.09			
3357	3	1	1	1.33	0.07			
3357	4	1	1	1.37	0.09			
3357	5	1	2	1.28	0.09			
3357	6	1	1	1.27	0.06			
3357	7	1	1	1.38	0.10			
3357	8	1	1	1.23	0.07			
3357	9	1	2	1.35	0.08			
3357	10	1	2	1.38	0.08			
3357	11	1	1	1.47	0.10			
3357	12	1	1	1.43	0.08			
3357	13	1	2	1.21	0.05			
3357	14	1	1	1.30	0.09			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3009	1	1	1	1.52	0.13			
3009	2	1	1	1.39	0.10			
3009	3	1	1	1.47	0.11			
3009	4	1	1	1.53	0.12			
3009	5	2	.	.				
3009	6	1	2	1.40	0.10			
3009	7	1	2	1.35	0.09			
3009	8	1	2	1.44	0.10	ROST		
3009	9	1	1	1.52	.0.12	ROST		
3009	10	1	2	1.42	0.11	ROST		
3009	11	1	1	1.47	0.13			
3014	1	1	2	1.30	0.11			
3014	2	1	1	1.34	0.10			
3014	3	1	1	1.36	0.14			
3014	4	1	1	1.40	0.11			
3014	5	1	1	1.34	0.16			
3014	6	1	1	1.35	0.16			
3014	7	1	1	1.22	0.12	ROSK		
3014	8	1	1	1.36	0.12			
3014	9	1	2	1.30	0.12			
3014	10	1	1	1.29	0.11			
3014	11	1	2	1.27	0.09			
3025	1	1	1	1.51	0.11			
3025	2	4	.	.	.			
3025	3	1	1	1.43	0.16			
3025	4	1	1	1.49	0.16			
3025	5	1	1	1.40	0.12			
3025	6	1	1	1.33	0.11	ROST		
3025	7	1	2	1.35	0.09			
3025	8	1	1	1.37	0.13			
3025	9	1	2	1.22	0.11			
3025	10	1	1	1.44	0.11			
3031	1	1	2	1.45	0.08			
3031	2	1	2	1.43	0.09			
3031	3	1	2	1.47	0.10			
3031	4	1	2	1.49	0.10	SURB		
3031	5	4	.	.				
3031	6	1	2	1.44	0.10			
3031	7	1	1	1.58	0.10			
3031	8	1	1	1.59	0.10			
3031	9	1	1	1.54	0.09			
3031	10	1	1	1.55	0.09			
3058	1	1	2	1.43	0.10			
3058	2	1	1	1.45	0.10			
3058	3	1	1	1.49	0.11			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3058	4	1	2	1.42	0.09			
3058	5	1	2	1.44	0.09			
3058	6	1	2	1.47	0.09			
3058	7	1	1	1.49	0.12			
3058	8	1	2	1.46	0.08			
3058	9	1	1	1.58	0.10			
3058	10	1	1	1.49	0.10			
3062	1	1	1	1.52	0.07			
3062	2	1	2	1.46	0.07			
3062	3	1	1	1.65	0.09	SURB		
3062	4	1	1	1.55	0.08			
3062	5	2	.	.	.			
3062	6	1	1	1.55	0.08			
3062	7	1	2	1.40	0.08			
3062	8	1	1	1.40	0.09			
3062	9	1	1	1.41	0.09			
3062	10	1	1	1.44	0.08			
3062	11	1	2	1.58	0.08			
3062	12	1	1	1.51	0.09			
3064	1	1	2	1.47	0.11			
3064	2	1	2	1.53	0.10			
3064	3	1	1	1.64	0.11	ROSK	SURB	DIUR
3064	4	1	2	1.41	0.11			
3064	5	1	2	1.51	0.10	SURB		
3064	6	1	2	1.44	0.10			
3064	7	1	2	1.54	0.13			
3067	1	1	2	1.39	0.08	ROST		
3067	2	1	2	1.36	0.08			
3067	3	2	.	.	.			
3067	4	1	1	1.49	0.09			
3067	5	1	1	1.44	0.09			
3067	6	1	1	1.41	0.09			
3067	7	1	1	1.36	0.07			
3067	8	1	2	1.22	0.06			
3067	9	1	2	1.24	0.08			
3067	10	4	.	.	.			
3067	11	1	1	1.38	0.09			
3067	12	1	1	1.40	0.08	SURB		
3067	13	1	2	1.27	0.07			
3067	14	1	1	1.41	0.07			
3075	1	1	2	1.49	0.10	SURB		
3075	2	1	1	1.37	0.09	SURB		
3075	3	1	2	1.33	0.10			
3075	4	1	2	1.25	0.11	SURB		
3075	5	2	.	.				

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3076	6	1	2	1.36	0.09			
3076	7	1	1	1.30	0.09			
3076	8	1	1	1.26	0.11			
3076	9	1	2	1.26	0.10	SURB		
3076	10	1	1	1.31	0.11			
3076	11	1	2	1.37	0.12			
3076	12	1	2	1.19	0.12	ROST	MAST	
3076	13	1	2	1.36	0.11	SURB		
3083	1	1	1	1.23	0.10			
3083	2	4	.	.				
3083	3	1	1	1.24	0.09			
3083	4	1	2	1.16	0.09			
3083	5	1	2	1.25	0.10			
3083	6	1	2	1.30	0.11			
3083	7	1	1	1.21	0.08			
3083	8	1	1	1.25	0.11			
3083	9	4	.	.	.			
3083	10	1	2	1.22	Ø.11			
3083	11	1	2	1.22	Ø.11			
3083	12	1	2	1.28	0.09			
3083	13	1	1	1.27	0.07			
3088	1	1	2	1.46	.			
3088	2	1	1	1.50	Ø.11			
3088	3	1	2	1.39	0.10			
3088	4	1	2	1.39	0.09			
3088	5	1	2	1.41	0.09			
3088	6	1	1	1.47	0.10			
3088	7	1	1	1.38	0.10	SURB		
3088	8	1	2	1.40	0.09			
3088	9	1	1	1.43	0.10			
3088	10	1	1	1.45	0.10			
3088	11	1	1	1.40	0.10			
3088	12	1	2	1.43	0.09			
3088	13	1	2	1.37	0.07			
3138	1	1	2	1.49	0.12			
3138	2	1	2	1.47	0.11			
3138	3	1	1	1.50	0.10			
3138	4	1	1	1.64	Ø.11			
3138	5	2	.	.	.			
3138	6	1	1	1.51	Ø.10			
3138	7	1	1	1.48	Ø.09			
3138	8	1	2	1.55	Ø.08			
3138	9	1	2	1.48	Ø.10			
3164	1	1	2	1.39	Ø.10			
3164	2	1	1	1.38	Ø.09			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3164	3	1	1	1.47	0.09			
3164	4	1	1	1.43	0.09	ROSK		
3164	5	1	1	1.31	0.08			
3164	6	1	2	1.18	0.06			
3164	7	1	1	1.29	0.07			
3164	8	1	1	1.32	0.07			
3164	9	1	2	1.38	0.06			
3164	10	1	1	1.36	0.08			
3164	11	1	1	1.36	0.09			
3164	12	1	2	1.32	0.07			
3164	13	1	2	1.34	0.09			
3164	14	1	2	1.26	0.06			
3199	1	1	1	1.23	0.06			
3199	2	1	2	1.24	0.06			
3199	3	1	1	1.30	0.08			
3199	4	1	1	1.25	0.07			
3199	5	1	2	1.19	0.06			
3199	6	1	1	1.24	0.07			
3199	7	1	2	1.17	0.07	ROST		
3199	8	1	1	1.17	0.07	ROST		
3199	9	1	1	1.11	0.07	ROST		
3199	10	1	2	1.01	0.06	ROST		
3199	11	1	1	1.17	0.06			
3199	12	1	2	1.25	0.07			
3199	13	1	2	1.26	0.07			
3199	14	1	2	1.22	0.06			
3199	15	1	2	1.09	0.08			
3216	1	1	1	1.43	0.08			
3216	2	1	2	1.47	0.03			
3216	3	1	1	1.32	0.07			
3216	4	1	2	1.32	0.11			
3216	5	1	2	1.41	0.09			
3216	6	1	2	1.42	0.09			
3216	7	1	1	1.30	0.10			
3216	8	1	2	1.03	0.07			
3216	9	1	2	1.39	0.07			
3216	10	1	2	1.46	0.09			
3216	11	1	2	1.29	0.08			
3216	12	1	2	1.37	0.09			
3216	13	1	1	1.34	0.10			
3216	14	1	2	1.34	0.09			
3216	15	1	2	1.36	0.07			
3217	1	1	1	1.41	0.09			
3217	2	1	2	1.36	0.06			
3217	3	2						

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3217	4	1	2	1.39	0.08			
3217	5	1	1	1.43	0.11			
3217	6	1	1	1.46	0.10			
3217	7	4	.	.	.			
3217	8	1	2	1.28	0.08			
3217	9	1	1	1.37	0.08			
3217	10	2	.	.	.			
3217	11	1	2	1.36	0.09			
3217	12	1	1	1.39	0.07			
3217	13	2	.	.	.			
3219	1	1	2	1.14	0.08			
3219	2	1	2	1.06	0.09			
3219	3	1	1	1.18	0.10			
3219	4	1	1	1.20	0.09			
3219	5	1	2	1.17	0.08			
3219	6	1	1	1.11	0.09			
3219	7	1	2	1.09	0.09	ROSK		
3219	8	1	2	1.19	0.09			
3219	9	1	1	1.17	0.08			
3219	10	1	1	0.69	0.08			
3219	11	1	2	1.15	0.09			
3219	12	1	1	1.14	0.09			
3219	13	1	2	1.09	0.09			
3219	14	1	2	1.07	0.07			
3219	15	1	2	1.06	0.08			
3219	16	1	1	1.17	0.10			
3226	1	1	2	1.49	0.08	SURB		
3226	2	1	2	1.41	0.07			
3226	3	1	1	1.54	0.10			
3226	4	1	1	1.52	0.09	SURB		
3226	5	1	2	1.47	0.09	SURE		
3226	6	1	1	1.43	0.08	SURE		
3226	7	1	2	1.49	0.08			
3226	8	1	2	1.41	0.08			
3226	9	1	2	1.43	0.16			
3226	10	1	2	1.45	0.07			
3226	11	1	1	1.61	0.11	SURB		
3226	12	1	2	1.46	0.07			
3226	13	1	2	1.46	0.07			
3226	14	1	2	1.40	0.09			
3226	15	1	1	1.57	0.09			
3226	16	1	1	1.54	0.10			
3248	1	1	1	1.35	0.12			
3248	2	1	1	1.39	0.10			
3248	3	1	1	1.43	0.12	ROST		

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3248	4	1	2	1.01	0.08			
3248	5	1	1	1.41	0.10			
3248	6	1	1	1.41	0.12			
3248	7	1	2	1.39	0.10			
3248	8	1	2	1.37	0.11			
3248	9	1	2	1.40	0.12			
3261	1	1	2	1.48	0.08			
3261	2	1	2	1.33	0.06			
3261	3	1	2	1.45	0.09	SURB		
3261	4	1	1	1.40	0.07	SURB		
3261	5	1	2	1.24	0.06			
3261	6	1	1	1.45	0.09	SURB		
3261	7	1	1	1.35	0.07	SURB		
3261	8	1	1	1.43	0.07			
3261	9	1	1	1.33	0.06			
3261	10	1	1	1.37	0.07			
3261	11	1	1	1.38	0.08	SURB		
3261	12	4	.	.	.			
3261	13	1	1	1.38	0.08	SURB		
3261	14	1	1	1.34	0.08		SURB	
3289	1	1	1	1.62	0.09			
3289	2	1	2	1.49	0.08			
3289	3	4	.	.				
3289	4	1	2	1.54	0.07			
3289	5	1	1	1.50	0.09			
3289	6	1	2	1.48	0.08			
3289	7	1	1	1.47	0.10			
3289	8	1	1	1.54	0.09			
3289	9	1	2	1.41	0.09			
3289	10	1	2	1.35	0.08			
3289	11	1	2	1.52	0.07			
3289	12	1	1	1.43	0.07	ROST		
3289	13	1	1	1.47	0.09			
3293	1	1	1	1.49	0.10			
3293	2	1	2	1.46	0.10	SURB		
3293	3	1	1	1.49	0.04	SURB		
3293	4	1	2	1.42	0.10			
3293	5	1	1	1.51	0.11	SURB		
3293	6	1	1	1.50	0.07			
3293	7	1	1	1.54	0.12	SURB		
3293	8	1	2	1.45	0.12			
3293	9	1	1	1.48	0.17	SURB		
3293	10	1	1	1.57	0.11	SURB		
3293	11	1	1	1.43	0.16			
3308	1	1	1	1.29	0.08			

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

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

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3308	2	2	.		.			
3308	3	1	2	1.26	0.08			
3308	4	1	2	1.28	0.08			
3308	5	1	1	1.38	0.06			
3308	6	1	1	1.31	0.08			
3308	7	4	.					
3308	8	1	1	1.30	0.08			
3308	9	1	1	1.31	0.10			
3308	10	1	1	1.19	0.09	ROST		
3308	11	1	1	1.22	0.08			
3308	12	1	2	1.30	0.07			
3308	13	1	2	1.30	0.08			
3322	1	1	1	1.41	0.07			
3322	2	1	2	1.35	0.08			
3322	3	1	1	1.17	0.08			
3322	4	1	1	1.31	0.10			
3322	5	1	2	1.31	0.09			
3322	6	1	2	1.38	0.08			
3322	7	1	1	1.48	0.09			
3322	8	4	.	.				
3322	9	1	1	1.39	0.09			
3322	10	1	1	1.35	0.09			
3322	11	1	1	1.50	0.10			
3323	1	1	2	1.31	0.08			
3323	2	1	2	1.42	0.12			
3323	3	1	1	1.35	0.10			
3323	4	2	.	.				
3323	5	1	1	1.09	0.08	ROSK	SURB	ROST
3323	6	1	2	1.26	0.02			
3323	7	1	2	1.31	0.09			
3323	8	1	1	1.40	0.11			
3323	9	1	1	1.32	0.10	SURB		
3323	10	1	1	1.30	0.08	SURB		
3323	11	1	2	1.24	0.08			
3323	12	1	1	1.42	0.09			
3323	13	1	2	1.32	0.11			
3341	1	1	1	1.21	0.09	ROST		
3341	2	1	2	1.38	0.09	SURB	ROST	
3341	3	1	2	1.36	0.07	SURB		
3341	4	2	.	.				
3341	5	1	2	1.40	0.10			
3341	6	1	1	1.38	0.11			
3341	7	1	2	1.38	0.10			
3341	8	1	2	1.31	0.09			
3341	9	1	1	1.41	0.10			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3341	10	1	1	1.38	0.10	SURB		
3343	1	1	1	1.31	0.11	SURB		
3343	2	1	2	1.26	0.10			
3343	3	1	1	1.38	0.09			
3343	4	1	1	1.26	0.09			
3343	5	1	1	1.20	0.09	SURB		
3343	6	1	2	1.30	0.10			
3343	7	1	1	1.38	0.09			
3343	8	1	2	1.19	0.08	SURB		
3343	9	2	.	.	.			
3343	10	1	2	1.27	0.09			
3343	11	1	1	1.02	0.07	SURB		
3343	12	1	1	1.29	0.08			
3343	13	1	2	1.24	0.10			
3343	14	1	1	1.36	0.10	SURB		
3356	1	1	1	1.40	0.12			
3356	2	1	1	1.33	0.10			
3356	3	1	1	1.44	0.09			
3356	4	1	2	1.29	0.08			
3356	5	1	2	1.20	0.06			
3356	6	1	1	1.47	0.09			
3356	7	1	1	1.38	0.11			
3356	8	1	1	1.42	0.09			
3356	9	1	1	1.39	.			
3356	10	1	2	1.24	0.11			
3356	11	1	2	1.43	0.09			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3030	1	1	1	1.41	0.11			
3030	2	1	2	1.40	0.12			
3030	3	1	2	1.43	0.12			
3030	4	1	1	1.51	0.14	SURB		
3030	5	4	.	.	.			
3030	6	1	2	1.28	0.10			
3030	7	1	2	1.49	0.10			
3030	8	1	2	1.29	0.08			
3030	9	1	1	1.47	0.11			
3030	10	1	2	1.35	0.11	SURB		
3030	11	1	1	1.40	0.11		SURB	
3040	1	1	2	1.32	0.13			
3040	2	1	2	1.04	0.10	ROST	SURB	
3040	3	1	2	1.01	0.11	ROST		
3040	4	1	1	1.19	0.13	SURB		
3040	5	1	2	1.47	0.11	ROST		
3047	1	1	1	1.28	0.09			
3047	2	1	1	1.23	0.09			
3047	3	1	2	1.20	0.08			
3047	4	1	2	1.27	0.07			
3047	5	1	1	1.29	0.06			
3047	6	1	1	1.29	0.07			
3047	7	1	1	1.29	0.10			
3047	8	1	2	1.32	0.10			
3047	9	1	2	1.29	0.09			
3047	10	1	1	1.40	0.08	ROST		
3047	11	1	2	1.28	0.10			
3047	12	1	1	1.37	0.10	ROSK		
3066	1	1	2	1.31	0.09			
3066	2	1	2	1.32	0.10			
3066	3	1	1	1.34	0.10			
3066	4	1	1	1.34	0.08			
3066	5	1	1	1.24	0.11			
3066	6	1	1	1.27	0.12			
3066	7	4	.	.	.			
3066	8	1	2	1.16	0.10			
3066	9	1	2	1.09	0.08			
3066	10	1	2	1.36	0.10			
3066	11	1	1	1.46	0.10			
3066	12	4	.	.	.			
3066	13	1	2	1.13	0.09			
3066	14	4	.	.	.			
3098	1	1	1	1.27	0.06	SURB	ROST	
3098	2	1	1	1.33	0.07	SURB		
3098	3	1	1	1.33	0.08			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3098	4	1	2	1.12	0.08	SURB		
3098	5	1	1	1.14	0.08	SURB		
3098	6	1	2	1.06	0.06	SURB		
3098	7	1	1	1.13	0.08			
3098	8	1	2	1.12	0.06			
3098	9	1	1	1.31	0.07	SURB		
3098	10	1	1	1.22	0.09	SURB		
3098	11	1	2	1.16	0.06	SURB		
3098	12	1	2	1.23	0.06	ROST		
3098	13	1	2	1.27	0.07			
3098	14	1	2	1.21	0.06			
3109	1	1	1	1.49	0.12			
3109	2	4	.	.	.			
3109	3	1	2	1.45	0.10			
3109	4	1	1	1.39	0.10			
3109	5	1	2	1.31	0.08			
3109	6	2	.	.	.			
3109	7	1	1	1.50	0.10			
3109	8	1	1	1.46	0.12			
3109	9	1	2	1.36	0.12	SURB		
3109	10	1	1	1.50	0.12			
3109	11	1	1	1.59	0.11			
3109	12	1	2	1.37	0.11			
3118	1	1	2	1.39	0.10			
3118	2	1	1	1.40	0.10			
3118	3	2	.	.	.			
3118	4	1	2	1.33	0.08			
3118	5	1	2	1.32	0.09			
3118	6	1	1	1.49	0.11			
3118	7	1	1	1.39	0.07			
3118	8	1	1	1.36	0.08			
3118	9	1	1	1.37	0.09			
3118	10	1	2	1.34	0.10			
3118	11	2	.	.	.			
3118	12	1	2	1.10	0.08			
3118	13	2	.	.	.			
3121	1	1	2	1.34	0.12	ROST		
3121	2	1	1	1.41	0.09			
3121	3	4	.	.	.			
3121	4	2	.	.	.			
3121	5	1	1	1.59	0.11			
3121	6	1	1	1.44	0.08			
3121	7	2	.	.	.			
3121	8	1	2	1.21	0.10			
3121	9	1	2	1.44	0.09			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3121	10	1	2	1.38	0.09			
3121	11	1	2	1.40	0.09	ROST		
3121	12	2						
3131	1	2	.	.	.			
3131	2	1	2	1.55	0.11			
3131	3	1	1	1.62	0.12			
3131	4	1	1	1.58	0.11			
3131	5	1	2	1.57	0.10			
3131	6	1	1	1.61	0.10			
3131	7	1	1	1.63	0.12			
3131	8	1	2	1.52	0.09			
3131	9	1	1	1.63	0.10			
3137	1	1	1	1.62	0.11			
3137	2	1	2	1.40	0.08	SURB		
3137	3	1	2	1.49	0.09			
3137	4	1	1	1.43	0.11			
3137	5	1	2	1.31	0.10			
3137	6	1	2	1.12	0.08	EXCE		
3137	7	1	2	1.50	0.07			
3137	8	1	2	1.51	0.09			
3139	1	1	2	1.32	0.09		SURB	
3139	2	1	1	1.41	0.09	ROST		
3139	3	1	1	1.39	0.08			
3139	4	4	.	.	.			
3139	5	1	2	1.35	0.08			
3139	6	1	2	1.27	0.06			
3139	7	1	2	1.31	0.07	ROST		
3139	8	4	.	.	.			
3139	9	1	2	1.23	0.09	SURB		
3139	10	1	2	1.31	0.08			
3139	11	1	1	1.26	.	SURB		
3185	1	1	1	1.33	0.08			
3185	2	1	2	1.21	0.07			
3185	3	1	1	1.31	0.09	SURB		
3185	4	1	1	1.30	0.09	SURB		
3185	5	1	1	1.25	0.08			
3185	6	1	1	1.30	0.09			
3185	7	1	1	1.30	0.08			
3185	8	1	2	1.19	0.07			
3185	9	1	1	1.31	0.09			
3185	10	1	1	1.21	0.08	SURB		
3185	11	1	2	1.17	0.07			
3185	12	1	2	1.17	0.08			
3185	13	1	1	1.25	0.07			
3209	1	1	2	1.45	0.08			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3209	2	1	2	1.50	0.09			
3209	3	1	2	1.36	0.11			
3209	4	1	2	1.37	0.09			
3209	5	1	2	1.37	0.08			
3209	6	1	1	1.42	0.10	ROSK		
3209	7	1	2	1.45	0.10			
3209	8	1	1	1.49	0.09			
3209	9	1	2	1.29	0.09			
3209	10	1	1	1.39	0.12			
3209	11	1	1	1.41	0.08			
3223	1	1	2	1.41	0.08			
3223	2	1	1	1.49	0.08			
3223	3	1	1	1.46	0.08			
3223	4	1	2	1.32	0.06			
3223	5	1	2	0.78	0.06			
3223	6	1	1	1.46	0.09			
3223	7	1	1	1.41	0.07			
3223	8	1	1	1.51	0.08			
3223	9	1	1	1.50	0.08			
3223	10	1	2	1.40	0.07			
3223	11	1	1	1.42	0.09			
3223	12	1	1	0.92	0.06			
3223	13	1	1	1.42	0.08			
3230	1	1	1	1.58	0.12			
3230	2	1	2	1.42	0.11			
3230	3	1	2	1.36	0.10			
3230	4	1	2	1.38	0.10			
3230	5	1	2	1.27	0.08			
3230	6	1	2	1.47	0.11			
3230	7	1	1	1.46	0.11			
3230	8	1	2	1.41	0.12			
3230	9	1	1	1.51	0.09	SURB		
3230	10	1	1	1.50	0.11			
3230	11	1	2	1.39	0.11			
3230	12	1	1	1.47	0.09	SURB		
3243	1	1	1	1.20	0.06			
3243	2	1	1	1.12	0.06			
3243	3	1	2	0.64	0.09			
3243	4	1	1	1.13	0.07			
3243	5	1	1	1.19	0.08			
3243	6	1	2	1.05	0.04			
3243	7	1	1	1.24	0.08			
3243	8	1	2	1.14	0.06			
3243	9	1	1	1.03	0.08			
3243	10	1	1	1.17	0.09	ROST		

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3243	**11**	**1**	**2**	**1.21**	**0.08**			
3243	**12**	**4**	.	.	.			
3243	**13**	**1**	**1**	**1.10**	**0.07**			
3243	**14**	**1**	**1**	**1.01**	**0.07**			
3243	**15**	**1**	**2**	**1.07**	**0.09**			
3243	**16**	**1**	**2**	**1.02**	**0.08**			
3243	**17**	**1**	**1**	**1.14**	**0.10**			
3254	**1**	**1**	**2**	**1.36**	**0.07**			
3254	**2**	**1**	**1**	**1.54**	**0.08**	ROST		
3254	**3**	**1**	**1**	**1.54**	**0.10**			
3254	**4**	**1**	**2**	**1.41**	**0.08**	ROST		
3254	**5**	**1**	**2**	**1.48**	**0.08**	SURB		
3254	**6**	**1**	**2**	**1.23**	**0.07**	SURB		
3254	**7**	**1**	**2**	**1.03**	**0.07**	SURB		
3254	**8**	**1**	**1**	**1.49**	**0.08**	**SURB**		
3254	**9**	**1**	**2**	**1.15**	**0.09**		SURB	ROST
3254	**10**	**1**	**1**	**1.46**	**0.10**			
3254	**11**	**1**	**1**	**1.37**	**0.08**	ROST		
3259	**1**	**1**	**2**	**1.26**	**0.12**			
3259	**2**	**2**	.	.	.			
3259	**3**	**1**	**2**	**1.24**	**0.11**	SURB		
3259	**4**	**1**	**2**	**1.16**	**0.08**	SURB		
3259	**5**	**4**	.	.	.			
3259	**6**	**1**	**2**	**1.23**	**0.08**			
3259	**7**	**1**	**1**	**1.25**	0.08			
3259	**8**	**1**	**2**	**1.22**	0.10			
3259	**9**	**1**	**2**	**1.16**	0.08			
3259	**10**	**1**	**2**	**1.19**	0.09	SURB		
3259	**11**	**1**	**2**	**1.18**	0.09			
3266	**1**	**1**	**2**	**1.41**	0.07			
3266	**2**	**1**	**2**	**1.38**	0.07			
3266	**3**	**1**	**2**	**1.40**	0.08			
3266	**4**	**1**	**2**	**1.33**	0.07			
3266	**5**	**2**	.	.	.			
3266	**6**	**1**	**2**	**1.21**	**0.08**			
3266	**7**	**1**	**1**	**1.37**	0.07			
3266	**8**	**1**	**2**	**1.36**	0.06			
3266	**9**	**1**	**2**	**1.30**	0.07	ROST		
3266	**10**	**1**	**2**	**1.35**	0.07			
3266	**11**	**1**	**1**	**1.41**	0.09			
3285	**1**	**1**	**2**	**1.46**	0.09	SURB		
3285	**2**	**1**	**2**	**1.43**	0.09			
3285	**3**	**2**	.	.				
3285	**4**	**1**	**2**	**1.42**	0.09	SURB		
3285	**5**	**1**	**1**	**1.48**	**0.11**			

Status: **1** = Live; 2 = **Early** Resorption; 4 = Late Resorption
Sex: **Male** = 1; **Female** = 2 See Code Sheet (pg 32 this Appendix) for identification of **abnormalities [ABNn]**

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3285	6	1	2	1.43	0.09			
3285	7	1	2	1.47	0.09			
3285	8	1	1	1.52	0.10			
3285	9	1	1	1.50	0.11	SURB		
3285	10	2	.	.				
3285	11	1	1	1.55	0.09			
3285	12	1	1	1.45	0.11			
3294	1	1	1	1.54	0.10			
3294	2	1	1	1.50	0.10	SURB		
3294	3	1	2	1.36	0.09			
3294	4	1	1	1.48	0.16			
3294	5	4	.	.	.			
3294	6	1	2	1.42	0.09			
3294	7	1	1	1.59	0.11			
3294	8	1	2	1.45	0.10			
3294	9	1	2	1.35	0.09			
3294	10	1	2	1.40	0.09			
3294	11	1	1	1.51	0.10			
3294	12	1	2	1.40	0.08			
3301	1	1	1	1.50	0.10			
3301	2	1	2	1.39	0.10			
3301	3	1	2	1.24	0.08			
3301	4	1	2	1.21	0.07			
3301	5	1	2	1.31	0.11			
3301	6	2	.	.				
3301	7	1	2	1.27	0.08			
3301	8	1	2	1.26	0.10			
3301	9	1	2	1.32	0.09	ROST		
3301	10	1	1	1.22	0.08			
3304	1	1	2	1.46	0.12	SURB		
3304	2	2	.	.				
3304	3	4	.	.	.			
3304	4	1	1	1.38	0.12	SURB		
3304	5	1	2	1.29	0.16			
3304	6	2	.	.	.			
3305	1	1	1	1.62	0.13			
3305	2	1	1	1.64	0.14			
3305	3	1	2	1.47	0.10			
3305	4	1	2	1.55	0.12			
3305	5	1	2	1.46	0.12			
3305	6	1	2	1.51	0.08			
3305	7	1	1	1.50	0.09			
3305	8	1	1	1.23	0.10			
3305	9	1	1	1.56	0.10			
3312	1	1	2	1.44	0.07			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

5000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt	Placenta Wt	ABN1	ABN2	ABN3
3312	2	1	1	1.29	0.07			
3312	3	1	2	1.29	0.07			
3312	4	1	2	1.23	0.07			
3312	6	1	1	1.31	0.08			
3312	6	1	2	1.20	0.08	ROST		
ƎƎ12	7	1	2	1.26	0.09			
3312	8	1	1	1.26	0.09	ROST		
3312	9	4	.	.	.			
3312	10	1	1	1.39	0.08			
3312	11	1	2	1.20	0.07			
3312	12	I	2	1.45	0.07			
3312	I3	1	1	1.49	0.09	ROSK		
3312	14	1	1	1.49	0.08			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption
Sex: Male = 1; Female = 2 See Code Sheet (pg 32 this Appendix) for identification of abnormalities [ABNn]

Code Sheet for Fetal Abnormalities

DIUR	Dilated Ureter
EXCE	Exencephaly
FURB	Fused Ribs
LMFL	Limb Flexure
MAST	Misaligned Sternebrae
ROSK	Reduced Ossification - Skull
ROST	Reduced Ossification - Sternebrae
SCST	Scrambled Sternebrae
SURB	Supernumerary Rib

n-Hexane Mouse Teratology Study: Calendar of Events

Exposure levels; Treatments1-4	0, 200, 1000 5000 ppm n-hexane
Animals ordered	1-27-87
Animals received (ARC# 870028)	2/18/87
Eartagging and pre-study weights	3/3/87
Initial health screen 5M, 5F	3/4/87
Virgins weighed, randomized and selected	3/6/87
Animals released for study, but are to remain on quarantine	3/9/87
Additional health screen 5M, 5F	3/17/87
Detection of copulation (0 dg), randomized, weighed, individually caged	(A) 3-12-87 (15) (B) 3-13-87 (17) (C) 3-14-87 (74) (D) 3-15-87 (52) (E) 3-16-87 (19)
Study mice moved to exposure room	3/17/87
Exposure (20 hours/day; 6-17 dg):	(A) 3-18-87 to 3-29-87 (15) females (B) 3-19-87 to 3-30-87 (17) females (C) 3-20-87 to 3-31-87 (45) females (D) 3-21-87 to 4-1-87 (44) females (E) 3-22-87 to 4-2-87 (19) females
Weighed (6dg) start exposure	(A-E) 3/18 to 3/22/87
Weighed (9dg)	(A-E) 3/21 to 3/25/87
Weighed (12dg)	(A-E) 3/24 to 3/28/87
Sacrifice (18dg):	(A) 3/30/87 (B) 3/31/87 Terminal serology (C) 4/1/87 (D) 4/2/87 (E) 4/3/87
Virgins- expose 12 days concurrent with Grp A	3/18 TO 3/29/87
Weighed, exposure day 1	3/18/87
Weighed exposure day 4	3/21/87
Weighed exposure day 7	3/24/87
Sacrifice, one day post-exposure	3/30/87
Fetal exams completed	4/30/87

n-HEXANE MOUSE TERATOLOGY STUDY DISPOSITION

Exposure Group	Treatment	Plug-positive Female Mice On Study(a)	Removed From Study	Plug-positive Female Mice for Sacrifice	Virgins	Litters Examined
Control (0 ppm)	1	35	2(b)	33	10	27
200 ppm	2	35	1(b)	34	10	27
1000 ppm	3	35	1(b)	34	10	28
5000 ppm	4	35	1(c)	34	10	25

(a) The study protocol requires a minimum of 33 plug-positive females (to obtain 20 pregnant females).
(b) Premature delivery of litter - not treatment related.
(c) Injured and sacrificed prior to the scheduled sacrifice.

APPENDIX D

ANIMAL HEALTH SCREEN

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: Hexane Teratology
building: LSL II
Room: 433
Date initiated: 3/4/87

Lab no: P-39
Animal/Shipment no: 870028
Date rc'd: 2/18/87
Source: CR Kingston K96
Species/Strain: Mice/CD1
Sex: M/F Age: ED **12/25/66**

Status: Received 5 male (#1-5) and 5 female (#6-10) mice for pre-exposure health screen including gross necropsy, parasite examination, histopathology and serology.

Endoparasite/Ectoparasite exam
0/10 * Anal tspe exam (Syphacia sp.)
0/10 Cooi pelt exam (Ectoparasites)

*Number positive/number examined

Gross Necroosv
1/10 *Left hind foot amputated below tibia (#7)

*Number affected/number examined

Serology: Mouse
0/10 * Mycoplasma pulmonis
0/10 Sendai virus
0/10 Pneumonia virus of mice
0/10 Mouse hepatitis virus (1/10 tested indeterminate #9)
0/10 GD VII virus

*Number of positive tests/number tested

Nasopharyngeal culture
6/10 * Beta hemolytic Streptococcus (Group C, not S. zooepidemicus)
0/10 Bordetella bronchiseptica
0/10 Citrobacter freundii
6/10 Coagulase positive Staphylococcus
0/10 Klebsiella oxytoca
0/10 Klebsiella pneumoniae
0/10 Pasteurella multocida
0/10 Pseudomonas aeruginosa
0/10 Streptococcus pneumoniae

*Number of positive cultures/number cultured

Histopathology

1/10*	Liver	Occasional tiny focus of inflammation in hepatic parenchyma (#7)
1/10	Liver	Occasional slignt perivascular inflammation (#7)

*Number affected/number examined

Correlation/Summary

Serologic tests for viral antibodies were done on ten additional mice (ARC Lab #P-35) because of the equivocal MHV test in one mouse and the presence of a few minimal liver lesions in another mouse. These findings are not of particular concern but the addtional tests will provide confirmation of the viral free status of these mice.

The Group C Streptococcus, while not Streptococcus zooepidemicus, may have some potential far causing secondary infections in mice and other rodents. However, it is not expected to have any effect on mice as they are used in this study. These animals are being held in quarantine status to prevent transmission of the Group C Strep into other animal rooms and its possible establishment in other populations in the facility.

Released for Study on 3/9/87.

They will be held on Quarantine for the duration of the study due to the presence of Group C Streptococcus.

A E Farrell 4/6/87
Technologist

Veterinarian 4/1/87

RODENT HEALTH SCREEN
HISTOPATHOLOGY

Lab Number 90-30
STUDY/Species Hexane Teratology - Mouse
Histo Number 287-123

ANIMAL NUMBER	1	2	3	4	5	6	7	8	9	10
Luna	1	1	1	1	1	1	1	1		1
Trachea	1	1	1	1	1	1	X	1	1	X
Ileum	1	1	1	1	1	1	1	1	1	1
Colon	1	1	1		1	1	1	1	1	1
Harderran Gland (rat)										
Salivary Gland (rat)										
Submand Lymph Node (rat)										
Heart	1	1	1	1	1	1	1	1	1	1
Liver	1	1	1	1	1	1	2,3	1	1	1
Kidnov	1	1	1	1	1	1	1	1	1	1

OBSERVATIONS:

X Not examined (tissue no: submitted or lost in processing)

1 N3 significant lesions

2 Occasional tiny focus of inflammation in hepatic parenchyma

3 Occasional slight perivascular inflammation SS 3/19/87

These animals were verbally released for study by notification from Teresa Mast on 3/9/87. These will be held on quarantine status for the remainder of the study because of the presence of a Group C Streptococcus. SS 3/19/87

Ref: ØS-AR-3FØ2
10/2/86

RODENT HEALTH SCREEN
GROSS NECROPSY

Lab Number P30

STUDY/Species Hexane/mice

Date Performed 3/4/87

ANIMAL NUMBER	1M	2M	3M	4M	5M	6F	7F	8F	9F	10F
Haircoat/Skin	1	1	1	1	1	1	2	1	1	1
Ventral Neck Area	1	1	1	1	1	1	1	1	1	1
Abdominal Viscera	1	1	1	1	1	1	1	1	1	1
Thoracic Viscera	1	1	1	1	1	1	1	1	1	1
Middle Ear	1	1	1	1	1	1	1	1	1	1
Eyes/Conjunctiva	1	1	1	1	1	1	1	1	1	1
Harderian Gland (rat)	1	1	1	1	1	1	1	1	1	1
Brain	1	1	1	1	1	1	1	1	1	1
Tissues saved in 10% NBF**	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
Anal tape	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Coat/feet exam										
ear tag	–	–	–	–	–	3155	3126	3263	3210	3315

aEJ 3/4/87

OBSERVATIONS:

X Not examined

1 N3 significant lesions

2 Left ~~front~~ hind tibia missing

** Tissues saved: lungs with trachea, heart, salivary gland, right kidney, brain, ileum, colon, liver, spleen, testis/ovary turbinates, eyes with harderian gland (rats), other

Ref: CB-AR-3FD2
9/8/86

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: Hexane Teratology
Building: LSL II
Room: 433
Date initiated: 3/17/87

Lab no: P-35
knimal/Shipment no: 870028
Date rc'a: 2/18/87
Source: CR Kingston K96
Species/Strain: Mice/CD1
Sex: M/F Age: ED 12/25/57

Status: Ten mice(5 male and 5 female) received for follow-up study of P-30

Gross Necropsy
No significant lesions

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

Correlation/Summary
All serologic tests were negative indicating these mice aid not have antibodies to any of the above pathogens and presumably that all animals from this shipment were free of infection by the same pathogens.

RE Isaacs 4/6/87
Technologist

4/1/87
Veterinarian

RODENT HEALTH SCREEN
GROSS NECROPSY

Lab Number P35

STUDY/Species Mart Kevane

Date Performed 3/17/87

ANIMAL NUMBER	1M	2M	3M	4M	5M	6F	7F	8F	9F	10F
Haircoat/Skin	/	/	/	/	/	/	/	/	/	/
Ventral Neck Area										
Abdominal Viscera										
Thoracic Viscera										
Middle Ear										
Eyes/Conjunctiva										
Harderian Gland (rat)										
Brain	↓	↓	↓	↓	↓	↓		↓	↓	↓
Tissues saved in 10% NBF**	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ear tag number						3141	3249	3271	3235	3292

OBSERVATIONS:

X Not examined

1 No significant lesions

<

** Tissues saved: lungs with trachea, heart, salivary gland, right kidney, brain, ileum, colon, liver, spleen, testis/ovary turbinates, eyes with harderian gland (rats), other _____

Ref: OS-AR-3F02
9/8/86

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: Hexane Teratology
Building: LSL II
Room: 436
Date initiated: 3/31/07

Lab no: P-44
Animal/Shipment no: 870038
Date rc'd: 2/18/87
Source: CR Kingston K96
Species/Strain: Mice/Cd1
Sex: M/F Age: BD 12/25/87

Status: Eight mouse blood samples received for terminal sacrifice serology

Serology: Mouse

*	
0/8	Mycoplasma pulmonis
0/8	Sendai virus
0/8	Pneumonia virus of mice
0/8	Mouse hepatitis virus
0/8	GD VII virus

*Number of positive tests/number tested

Correlation/Summary

All seroiogic tests were negative indicating these mice did not have antibodies to any of the above pathogens.

AE Farrell 4/27/87
Technologist

Stephen C Rowe 4/27/87
Veterinarian

ARC RODENT HEALTH SCREEN REPORT

Investigator: Mast
Study: Hexane Teratology
Building: LSL II
Room: 436
Date initiated: 4/3/87

Lab no: P-46
Animal/Shipment no: 870038
Date rc'd: 2/18/87
Source: CR Kingston K96
Species/Strain: Mice/Cd1
Sex: M/F Age: **BD** 12/25/07

Status: Two mouse blood samples received for terminal sacrifice serology as a supplement. to ARC Lab No. P-44

Serology: Mouse

*	
0/2	Mycoplasma pulmonis
0/2	Sendai virus
0/2	Pneumonia virus of mice
0/2	Mouse hepatitis virus
0/2	GD VII virus

*Number of positive tests/number tested

Correlation/Summary

All serologic tests were negative indicating these nice did not have antibodies to any of the above pathogens.

A E Jarrell 4/27/87
Technologist

Stephen E. Clarke 4/27/87
Veterinarian

APPENDIX E

QUALITY ASSURANCE STATEMENT

TERATOLOGY STUDY OF n-HEXANE IN MICE

Quality Assurance Statement

Listed below are the phases and/or procedures included in the study described in this report which were reviewed by the Quality Assurance Unit during the period, 2/1/87 - 5/1/87, specifically for this study and the dates the reviews were performed and findings reported to management. (Findings were reported to the study director or her designee at the time of the review.)

Phase/Procedure Reviewed	Review Date	Date Findings Submitted in Writing to Study Director/Management
Animal Receipt	2/26/87	3/4/87
Body Weights	3/3/87*	3/4/87
Animal Identification	3/3/87*	3/4/87
Health Screen	3/4/87*	3/9/87
Mating	3/16/87	3/23/87
Body Weights	3/16/87	3/23/87
Dosing	3/27/87*	3/31/87
Teratology Examinations	3/31/87*	3/31/87
Necropsy	3/31/87	3/31/87
Data	9/23 &10/1/87*	3/29/88
Data	2/3-5/88*	3/29/88
Draft Final Report	2/25&28/88	3/29/88
Final Report	6/7&22/88	6/22/88

*Reviewed specifically for this study

R A Heilman
Quality Assurance Specialist

6/22/88
Date

APPENDIX F

PROTOCOL AND CAGE *MAPS*

INHALATION REPRODUCTIVE TOXICOLOGY STUDY PROTOCOL
n-HEXANE

I. TITLE: Teratology Study of n-Hexane in Mice

II. PURPOSE OF STUDY

The straight-chain hydrocarbon, n-hexane, is commonly used as a solvent for the extraction of oil seeds, as a reaction medium in the production of polyolefins, elastomers and pharmaceuticals, and as a component of quick-drying cements, lacquers and adhesives. The production of n-hexane, which was estimated to be four billion pounds per year in 1979, utilizes stocks of straight-run gasoline and higher boiling liquid products stripped from natural gas or paraffinic fractions of refinery streams. It is also found as a minor component of gasoline and its combustion products, hence petroleum products are a major source of environmental hexane contamination. Due to the large-scale production and widespread use of hexane, including teaching laboratories, the opportunity for industrial, incidental environmental, or volitional (glue-sniffing) exposure to hexane vapors is significant. The studies described herein are proposed as a result of a concern that this exposure may result in a negative impact on human reproductive function.

Several excellent reviews concerning hexacarbon toxicity and metabolism are available in Experimental and Clinical Neurotoxicology (edited by Spencer and Schaumburg, 1980) and in CRC Critical Reviews in Toxicology (Spencer, Schaumburg, Sabri, and Veronesi, 198Ø). In summary, polyneuropathies have been reported following exposure of workers to n-hexane contained in adhesives or used as an industrial solvent as well as following repeated volitional exposure by glue sniffing. A metabolite, 2,5-hexanedione, has been shown to be responsible for most, if not all, of the neurotoxicity. Younger rats appear to be less sensitive to n-hexane neurotoxicity than are older animals. It has been suggested that this difference may be due to their having shorter axons with smaller diameters, or to a Greater rate of growth and repair in peripheral nerves compared to that of adults (Howd et al., 1983; Kimura et al., 1971). Likewise, Graham and Gottfried (1984) hypothesized that mice are less sensitive than rats to gamma-diketones, such as 2,5-hexanedione, because myelinated axons in mice are shorter and have smaller diameters than the corresponding axons in larger species.

Pharmacokinetic and distribution studies in rats of inhaled n-hexane have indicated that the hexane saturation concentration of organs is directly proportional to their lipid content, and that blood contains more hexane in relation to its lipid content than do organs (knaersen, 1981; Bohlen et al., 1973). Baker and Rickert (1981) found that the metabolism and elimination of n-hexane were dependent upon exposure concentration, but that the tissue concentration of the metabolite, 2,5-hexanedione, was not directly related to n-hexane exposure concentration. Bus et al. (1982), using ^{14}C-labeled n-hexane in 6-hour exposures, found that the distribution of radioactivity was dose-dependent.

In studies designed to address the possiblity that exposure to hexane may affect prenatai development Bus et al. (1979) also determined the

distribution and half-lives of n-hexane ($t_{1/2}$= 1.2 hr) and 2,5-hexanedione ($t_{1/2}$=3.9 hr) in maternal organs and fetuses exposed to n-hexane during gestation. Concentrations of n-hexane and its metabolites in fetuses were approximately equal to those in maternal blood. Nevertheless, they observed no statistically significant effects on intrauterine mortality, fetal body weights or the incidence of fetal anomalies following 6-hour daily inhalation exposures to 1000 ppm of n-hexane from 8-12, 12-16, or 8-16 dg. Growth of pups was impaired for the first 3 postnatal weeks in the group exposed from 8-16 dcj, but the possibilities of maternally-mediated effects or postnatal exposure via milk were not examined.

Other developmental studies include that of Marks et al. (1981) who found that oral administration of n-hexane (2.2 g/kg) daily from 6 through 15 dg in mice produced one maternal death, but no fetal effects. When they administered 2.8, 7.9 or 9.9 g/kg/day of n-hexane as 3 daily doses, maternal mortality was increased in a dose-related manner and fetal weight was reduced at the two higher dose levels, but no fetal malformations were observed.

Exposure of female rats for 7 hours per day to hexane vapor at concentrations up to 10,000 ppm for 15 days prior to conception and through 18 dg produced neither signs of neuropathy nor indications of effects on postnatal maturation and growth of the pups (Howell and Cooper, 1981; Howell, 1979). No effects on the visual (VER) or interhemispheric (IHR) evoked response of anesthesized offspring were found in one series of experiments; however, in a second experiment, there was an increased amplitude of the VER peaks in unanesthesized 45-day old pups of the high-concentration group.

These studies are rather convincing relative to the absence of morphologic effects (despite the low exposure concentration of 1000 ppm in one rat study). Although the altered VER may suggest functional impairment of the fetal/neonatal nervous system, the more likely explanation - maternal toxicity - has not been addressed. While it is tempting to conclude that fetal and neonatal rats and mice are relatively resistant to the effects of n-hexane exposure, these conclusions are based on incomplete evidence. In order to provide more definitive information regarding the teratogenic potential (or lack thereof) of n-hexane the following study will be performed with the goal of maximizing maternal exposures.

Since it appears that toxicity is a product of concentration-time factors, an adequate assessment of the teratologic potential requires evaluaticns after prolonqed exposures at high concentrations in several species. To accomplish this, the study in mice defined in this protocol will employ multiple levels ranging up to the maximum practicable concentration—5000 ppm—for 20 hour per day. These exposures will extend throughout the late implantation, organogenic, and fetal development stages (i.e., 6 through 17 dg), with aetaiied teratologic evaluations performed at 18 dg. A similar study will be subsequently performed with rats to obtain comparative data in another species. To examine the potential for neurotoxicity, other subsequent studies in rats will be performed using the same prenatal exposure regimen in addition to a postnatal exposure, in which primary emphasis would be placed on evaluation of postnatal growth, deveiopment,

and sensory-motor functions.

Reported effects on lipid metabolism have suggested the possibility that the ovaries or ovulation may be affected by inhalation exposure. Although the limited data of Howell and Cooper (1981) regarding preconception and preimplantation exposure suggest that the ovary is not a target organ for n-hexane toxicity, the lack of information on the uptake of n-hexane or its metabolites into the ovary is disturbing. Since the need for a specific study is not immediately justified, the ovaries from the pregnant animals in this study will be preserved at necropsy and provided to another laboratory (designated by the sponsor) for oocyte enumerations. An additional group of animals will be exposed concurrently to determine the effect of n-hexane exposure on virgin females.

III. SPONSOR AND SPONSOR'S REPRESENTATIVE

A. Sponsor:
National Institute of Environmental Health and Safety
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
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.)

A. Prestart audit for GLP compliance: 3/16/87
B. Animals arrive: week of 2/16/87
C. Quarantine, health evaluation and identification of females: 2/16/87 - 3/12/87
D. Initiation of breeding procedures and randomization of animals into treatment groups: 3/12/87
E. Initiation of exposure:3/18/87
F. Initiation of necropsies: 3/30/87
G. Evaluation of fetal specimens and data:4/6/87-7/1/87
H. Completion of draft report:8/1/87
I. Completion of final report:10/1/87

VI. TEST SYSTEM

A. Species: mouse
B. Strain: CrI:CD-1(ICR)BR

C. Number of Animals and Supplier: 350 female and 75 male animals will be purchased from the Charles River Breeding Laboratories, Kingston, N.Y.

D. Age Of Animals Upon Arrival: 7-8 weeks

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

F. Number of Animals in Study: A minimum of 33 plug-positive females (to obtain 20 pregnant females) will comprise each of the four treatment groups; the minimum number of plug-positive females to be exposed will be 132.

G. Test Systen Justification: The use of mice as a test system was specified by the sponsor. Differences in sensitivity to induced neuropathies following exposure to the hexane metabolite, 2,5-hexanedione have been reported for rats and mice. In particular, data from this study will be compared with the results from a teratology study in rats which has been performed using an identical exposure regimen.

VII. TEST SYSTEM HOUSING, HANDLING AND ENVIRONMENTAL CONDITIONS

A. Quarantine and Acclimation:

1. Upon arrival at PNL, the animals will be quarantined (ØB-AR-3FØ3) for 3-4 weeks in the LSL-II Building.

2. Temperatures in all rooms will be maintained at 73 ± 3 °F and relative humidities at 50 ± 15% during the quarantine, acclimation and exposure periods. These values will be measured and recorded twice daily.

3. During the quarantine period the animals will be housed by sex, approximately 10 mice per cage in wire cages. The cage space will meet the requirements stated in the Guide for Use of Laboratory Animals.

4. During the breeding period the animals will be housed in the quarantine room.

5. Plug-positive females will be acclimated from Ø to 6 ag 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.

B. Feed. NIH-Ø7 Open Formula Diet (pellets) will be provided ad libitum during the acclimation and experimental period. Feed will remain in place during the exposure period and will be changed dally.

C. Randomization: Virgin females will be randomly chosen and assigned to dose groups based on the first weighing. Their weights will be ranked

from lightest to heaviest and each animal randomly assigned to a treatment group by means of a computer-assisted randomization program which is based on a single blocking factor, body weight (ØB-DT-3BØB). On the day of plug detection (0 dg), the mated mice will be weighed and assigned to dose groups as above.

E. Identification:

1. All female mice will be individually identified by metal ear tags during the first weighing session (ØB-DT-3BØ1).

2. Cage maps (ØB-DT-3BØ3) showing placement of individual animals in each cage unit of the exposure chamber will be prepared and updated daily. Each exposure chamber will be identified by chamber number and exposure level. The proposed arrangement of the exposure chambers is included in Attachment 2.

G. Animal Disease Screening Program (ØB-AR-3FØ2): Approximately 2-3 weeks after receipt of the animals, five females and five males will be examined for internal and external parasites and bacterial pathogens; their sera will be tested for antibodies to selected pathogens and histopathologic examinations of lung, liver, kidney, ileum, colon and heart will be performed. At necropsy, serum from 5 animals in the control group and 5 from the high dose group will be tested for antibodies to selected pathogens.

VIII TEST ARTICLE

A. Chemical name: n-Hexane
B. Formula: $CH_3CH_2CH_2CH_2CH_2CH_3$
C. Manufacturer: Phillips Chemical Company
D. Source: Research Triangle Institute, Research Triangle Park, NC
E. CAS No.: 110-54-3
F. NTP No.: 10189-N
G. LOT No.: RTI log number: 4911-100-01
BNW LOT No.: 51436-58
H. The vehicle control will be filtered air.
I. Storage conditions: A ready reserve is maintained in a flammable storage cabinet located in room 315 of the LSII Building. The remaining inventory is in a chemical storage facility adjacent to the Research Technology Laboratory. Both locations are maintained to approximately 72 °F.

J. Analytical Chemistry

1. Upon receipt, identity and gross purity analyses of the bulk chemical were performed by infrared spectroscopy; gas chromatography (GC) was used to determine purity by major peak comparison and also to qenerate an impurity profile (ØB-AC-3A15). Subsequent bulk assays, upon completion of the animal exposures, will use GC to determine test material purity and an impurity profile.

2. n-Hexane concentrations within the exposure chambers will be monitored (ØB-AC-3B1P) using an HP-584Ø aas chromatograph calibrated by the method detailed in ØB-AC-3CØW (see Attachment 2).

IX. 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.

X. EXPERIMENTAL DESIGN AND **DOSE** LEVELS

A. Experimental Design: Four groups of animals, consisting of at least 33 plug-positive mice in each group, will be exposed to the test chemical on 12 consecutive days (6 dg through **17** dg). The animals will be necropsied on 18 dg for maternal and fetal evaluations.

In addition, 10 virgin females will be added to the control and to each dose group for the purpose of obtaining ovaries to be used for quantitative ovarian follicle counts. These animals will be exposed for 12 consecutive days concurrently with the plug-positive animals and sacrificed the day of cessation of exposure.

B. Exposure Regimen: Chamber atmospheric concentrations of n-hexane will be Ø (filtered air), 200, 1000 and 5000 ppm. Plug-positive mice and the virgin females will be exposed for 20 hrs/day for 12 consecutive days. Control mice (0 ppm) will be housed in an exposure chamber in the same room, and will be handled in the same manner as the mice that are exposed to the test chemical. The exposure chamber doors will be closed throughout the exposure and nonexposure periods, except during animal care procedures. Exposure chamber temperatures will be maintained at 75 ± 3°F and relative humidities at 55 ± 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: The maximum exposure chamber atmospheric concentration **of** hexane, 5000 ppm, is 50% of the LEL (lower explosion limit). In order to maximize maternal exposure the exposure time is extended to 20 hr/day for all doses; exposure concentrations were approved by the Sponsor.

XI. EXPERIMENTAL OBSERVATIONS

A. Clinical Observations: The animals will be observed daily for mortality, morbidity, and signs of toxicity. The date and time of death or euthanasia of moribund animals will be recorded and the animals will be necropsied according to (ØB-DT-3BØF).

B. Body Weights: All female mice will be weighed during the week prior to mating. Virgin females (10/group) will be randomly selected at this time (see Randomization, pg. 4). After breeding plug-positive females will be weighed again on Ø, 6, 9, 12, and 18 dg (ØB-DT-3BCC). Virgin females will be weighed on tne 1st, 6th and last day of exposure. The body weight on Θ dg (for mated females) will be used for randomization of plug-positive animals (ØB-DT-3BØB) into four exposure groups.

C. Scheduled Necropsy: The mice are scheduled to be euthanized with CO_2 on 18 dg. At necropsy (ØB-DT-3BØG) maternal animals will be weighed and

examined for gross tissue abnormalities. 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. The gravid uterus will be removed and weighed, and the number, position and status of implants will be recorded. The placentas will be weighed and examined. 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, their sex will be determined and they will be weighed. Visceral examination (Staples, 1977; [ØB-DT-3BØG]) and examination of skeletons (prepared by the method of Kimmel, C., personal communication, 1985 and Hendrickx, A.G., personal communication, 1985; [ØB-DT-3BØG]) will be performed on all live fetuses; approximately 50% of the fetal heads will be examined by razor-blade sectioning of fixed preparations (Wilson, 1965; [ØB-DT-3BØI]). Records of morphologic lesions observed in gross and visceral examinations will include photographs (ØB-DT-3BØJ) of 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.

D. Indices of Effects: The following parameters, expressed as mean ± SE, 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 weight on Θ, 6, 9, 12, and 18 dg
- Weight of gravid uterus
- Extragestational weight and weight gain
- Number of implantation sites/litter
- Number of litters with live fetuses
- Number and percent sf live fetuses/litter
- Eody weight of live fetuses/litter
- Body weight of male and female fetuses/litter
- Placental weights from live fetuses/litter
- Sex ratio of fetuses/litter
- Number an5 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
- 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 listed in Table I. Further statistical analyses may be performed at discretion of sponsor.

XIII. STORAGE OF STUDY MATERIALS

All raw data and study records will be retained in the Project Office (room 1328) with the exception of exposure and monitoring data which will be stored in room 1229; all tissues and fetal specimens will be temporarily stored in the Teratology Laboratory (room 1428). All of these rooms are located in Life Science Laboratory II, Battelle, Pacific Northwest Laboratory. All tissue specimens will be shipped to the NTP Archives. Records generated in the conduct of the study will be microfiched. Computer tapes of biological data, the original and one copy of the microfiche, and the microfiche index will be sent to Dr. Schwetz (NIEHS) for storage in the NTP Archives. Bound PNL laboratory notebooks, which are required to remain at PNL, will be placed in storage in PNL Files. The Quality Assurance Unit at PNL will retain the following materials:

- QAU master schedule and audit records.
- Personnel training and experience records and job descriptions (a list of people who participated in the study is sent to NTP archives).
- Maintenance and calibration records of equipment used on the study. (Exception - if the equipment is government-owned, the records would accompany the equipment.)

XIV. RECORDS RETENTION

The following records, generated during the course of the study, will be maintained at PNL until they are shipped to the NTP archives. Some of these records may be presented in the protocol or in study reports.

A. Personnel Records:

1. Current professional resume and job description for each person recording data.

2. Safety Training records, including respirator and hazardous material, and specific-task training records.

3. Accident/injury reports for personnel in contact with the test material cr test system.

4. Record of removal of any individual, because of illness, from direct contact with the test system.

B. Study Protocol:

1. Study protocol prepared prior to tne initiation of the study and approved by the PNL Study Director, the PNL QAU Officer and tne NTP Project Officer(s).

TABLE 1. PROPOSED STATISTICAL METHODS

INDICES	SUMMARY STATISTICS*	ARCSIN TRANS-FORMATION	ANOVA with MULTIPLE COMPARISONS
MATERNAL:			
Number/percent dead			
Body weight			
Weight of gravid uterus			
Extragestational weight			
REPRODUCTIVE:			
Number/percent pregnant			
Number of implantation sites/litter			
Number/percent resorptions/litter			
Number/percent litters with resorptions			
Percent resorptions in litters with resorptions			
Number/percent live fetuses/litter			
Number/percent non-live (resorptions + dead fetuses/litter)			
Placental weight			
FETAL:			
Body weight			
Sex ratio			
Number/percent of litters with malformed fetuses			
Number/percent of malformed fetuses			
Number/percent of malformed fetuses/litter			

* Mean, standard deviation, and range
Analysis of variance (Steel arid Torrie, 1980)

2. All amendments to the study protocol resulting from modifications in the study or time schedule..

3. A record of any deviations from the protocol and corrective actions that could affect the integrity of the study.

C. Equipment Records:

1. Name(s) of person(s) assigned to clean, inspect, and maintain equipment.

2. Schedule for cleaning, calibrating, inspecting and maintaining equipment.

3. Documentation of routine cleaning, inspection, calibration, and maintenance of equipment.

4. Documentation of any nonroutine maintenance
   a. Description of malfunction.
   b. Description of remedial action taken.

D. Test Materials Records:

1. Test materials identity records including manufacturer, quantity, lot number(s) and purity grade.

2. Records from NTP analytical contractor concerning characterization, bulk stability and shipment.

3. PNL records for receipt and storage of material, including storage conditions.

4. PNL records for bulk analysis and degradation.

5. PNL records of inventory, usage and shipment of unused test materiai to the NTP repository.

E. Delivery System for Test Material:

1. Detailed descriptions of systems fcr exposure control, test material generation, animal exposure and data acquisition.

2. Chamber concentration monitoring records including chamber uniformity and equilibrium tests and test system exposure records.

3. Chamber environmental data (temperature and humidity), chamber vacuum and airfiow aaca.

F. Animal Records:

1. Animal receiving records including supplier, species, strain, birth week, sex, number of animals cf each sex, receiving date and condition upon receipt.

2. Health evaluation records of findings, written release from quarantine/acclimation or rezsons for rejection for use in the studv and results of serologic examination at sacrifice.

3. Housing records for quarantine, acclimation, mating and exposure to the test material, including room location, temperature, relative humidity, lighting cycle, caging type, number of animals per cage, location of chambers within the exposure room, cage assignment of individual animals within the exposure chamber and sanitation procedures (frequency and methods of cage and room cleaning/sterilization).

4. Feed records of commercial source and product information (feed tags, lot numbers and milling dates), analyses and mode and frequency of feeding.

5. Records of mode and frequency of watering, annual analysis and weekly water hardness tests (records are maintained in offices of the building engineer or building manager).

6. Animal disposition records.

G. Study Implementation and Conduct Records:

1. Mating records and assignment of animals to treatment groups.

2. Body weights.

3. Dates of exposure intervals for individual animals.

4. Daily observations.

5. Time of deathleuthanasia of animals occurring prior to schedclec sacrifice and results of gross necropsy.

6. At scheduled sacrifice, gross necropsy findings in maternal animals; number and placement of implantation and resorption sites; number and placement of live and dead fetuses; placental weights;fetal body weights and sexes; results from external, visceral, head and skeletal examinations; photographs of representative fetal morphologic alterations.

H. All relevant correspondence.

I. Reports:

1. Literature Survey and Recommendations for Studies

2. Monthly Progress Reports

3. Draft Final and Final Reports

J. Internal Computer Generated Forms and Tables:

1. Study data and statistical analyses.

2. Analytical data.

3. Exposure suite control center computer printouts.

K. Standard Operating Procedures: The list of SOP's to be used in this study appears in Attachment I. A file of these SOP's is maintained in the QAU office.

L. Health and Safety Records:

1. NTP safety and toxicity package.

2. PNL Biohazard Protocol and Health and Safety Plan.

3. Personnel respirator and hazardous material training records; accident/injury reports.

4. Monitoring records of ventilation system, hoods and exhaust systems used in this study.

5. Relevant sections of the Health and Safety Monthly Progress Reports

6. NTP site visit reports, attention items and related correspondence concerning health and safety.

XV. 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).

B. This Protocol will be the controlling document in case of discrepancies between the Protocol and SOPs. If discrepancies are noted, the Study Director is to be notified immediately to resoive and document the variance between the Protocol and SOP.

XVI. HEALTH AND SAFETY

PNL's Health and Safety Plan, which has been submitted for NTP approval, is detailed in ØB-HS-3S1C. In addition, a respiratory program is outlined in ØB-HS-3S1B. This is supplemented by an SOP (ØB-HS-3S19) which covers the use of supplied-air respirators which will be worn by personnel during periods of animal care while the chambers are open, and by an SOP (ØB-HS-3S1A) which covers the use of a self-contained breathing apparatus for use when entering a rocm under emergency conditions following an accidental release of the chemical.

Personnel Training, protective equipment and facilities are designed to conform with DOE health and safety requirements and with Health and Safety Minimum Requirements for Laboratories under Contract to the NTP Systemic Toxicology Branch, dated November 19, 1984 and consisting of a basic document of eight pages, Appendix I cf ten pages and Appendix II of two pages.

XVII. APPROVAL BY PNL

Terry J. Mast
Study Director

Date: 3/2/87

R.A. Heinen
Quality Assurance Auditor

Date: 3/6/87

XVIII. APPROVAL BY NTP

BA Schwetz
Co-Study Officer

Date: 3 Mar 87

Richard E. Morrissey
Co-Study Officer

Date: 3 March 87

XIX. REFERENCES

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ATTACHMENT 1

STANDARD OPERATING PROCEDURES FOR INHALATION

REPRODUCTIVE TOXICOLOGY STUDIES

STANDARD OPERATING PROCEDURES FOR INHALATION
REPRODUCTIVE TOXICOLOGY STUDIES

EXPOSURE SYSTEM

Inhalation Exposure Chamber Balance	ØB-BE-3B24
Model 1 Chamber Leak Tester	ØB-BE-3DØ6
Calibration and Check of Chamber Airflow Using Digital Anemometer	ØB-BE-3CØV
Filling Out Data Sheets	ØB-BE-3BØ7
EG&G Hygrometer: Operation, Maintenance and Calibration	ØB-BE-3CØJ
Relative Humidity Determination Via Use of Dewpoint Hygrometer	ØB-BE-3B1X
Exposure Suite Data Analysis Program Operation	ØB-BE-3EØB
Exposure Suite Routine Computer Operation	ØB-BE-3GØ4
Software Change Protocol	ØB-BE-5EØ2
Study Protocol Entry into Exposure Suite Computers	ØB-BE-3EØ9
Exposure Suite QC, Maintenance and Calibration	ØB-BE-3DØE
General FGD Calibration - Exposure Chamber and Generator Cabinets	ØB-BE-3C13
Hexane Exposure System Daily Operating Procedure	ØB-BE-3B2Y
Hexane Exposure System Quality Control, Maintenance and Calibration	ØB-BE-3DØM

ANALYTICAL CHEMISTRY AND MONITORING

Operation of HP584Ø Gas Chromatograph for Monitoring n-Hexane in Inhalation Chamber	ØB-AC-3B1P
Calibration of n-Hexane Inhalation Chamber Monitor	ØB-AC-3CØW
Bulk Chemical Analysis of n-Hexane	ØB-AC-3A15

ANIMAL RESOURCE CENTER

Sarrier Procedures for LSL II Animal Facility	ØB-AR-3BØG
Moving Animals from LSL II Animal Resources Center	ØB-AR-3BØN
Management of Animal Feed	ØB-AR-3FØ5
Sanitizing Operations Monitoring	ØB-AR-3HØA
Pre-exposure Health Screening for Rodents	ØB-AR-3FØ2
Quarantine of Animals	ØB-AR-3FØ3
Daily Care of Animals and Cleaning of Exposure Rooms	ØB-AR-3FØA
Handling Escaped Small Animals	ØB-AR-3BØ8
Selection and Notification Procedures, Moribund Sacrifice Animals and Animals Found Dead	ØB-AR-3FØB
Weighing Rodents with Toledo Semi-Automatic Weighting System using the 733 ASR Terminal	ØB-AR-3GØH

REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY

Identification of Animals	ØB-DT-3BØ1
Cage Location Maps and Daily Observations	ØB-DT-3BØ3
Randomization of Animals	ØB-DT-3BØB
Animal Body Weights	ØB-DT-3BØC
Rodent Mating Procedures	ØB-DT-3BØD
Necropsies for Health Evaluation and Dead and	

Moribund Animals	ØB-DT-3BØF
Necropsy and Developmental Evaluations for Teratology Studies--Rodents and Rabbits	ØB-DT-3BØG
Examination of Fetal Heads Fixed in Bouin's Solution	ØB-DT-3BØI
Photography	ØB-DT-3BØJ
Data Acquistion and Transfer with a Microcomputer	ØB-DT-3BØK
Examination of Fetal Skeletons Stained with Alcian Blue/Alizarin Red	ØB-DT-3BØY

HEALTH AND SAFETY

Biohazard Protocol n-Hexane	ØB-HS-3S1S
Bioassay Studies: Health and Safety Plan	ØB-HS-3S1C
The 3M Brand W-2869 Hardcap, Continuous-Flow Air-line Respirator	ØB-HS-3S19
Respiratory Protection Program	ØB-HS-3S1B

ATTACHMENT 2

DESCRIPTION OF THE EXPOSURE SYSTEM FOR INHALATION REPRODUCTIVE TOXICOLOGY STUDIES

CONTENTS

EXPOSURE SYSTEM DESCRIPTION

I. ANIMAL EXPOSURE CHAMBER

The Battelle-designed stainless steel chamber (U.S. Patent #4,216,741) available from Hazleton Systems, Inc., Aberdeen, MD, is used for inhalation exposures (Figure 1A). The total volume of the chamber is 2.3 m^3, the chamber has an active mixing volume of 1.7 m^3, the remainder being the non-mixing inlet and exhaust volumes. 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 collection of urine and feces are suspended below each cage unit. Catch pans are left in position during each exposure period. Instructions for maintenance of these chambers is detailed in SOP# ØB-BE-3DØ6.

The chamber was designed so that uniform aerosol or vapor concentrations can be maintained throughout the chamber when the catch pans are 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. Waves 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 wall. Tests have shown that aerosol or vapor concentrations uniform to within 8% throughout the chamber can be obtained repeatedly provided the aerosol or vapor is uniformly mixed before passing through the chamber inlet.

Rats and mice are exposed in individual cages with automatic watering. The floor area of an individual mouse cage is 106 cm^2 and of a rat cage 270 cm^2 (representing dimensions 14.0 cm by 7.6 cm with height 15.0 cm, and 27.9 cm by 9.7 cm with height 20.0 cm, respectively). There are 60 mice or 24 rat individual cages per cage unit. Up to six cage units can fit in a chamber.

II EXPOSURE SUITE CONTROL CENTER

A computer located in the Suite Control Center interfaces with system monitors and controls the basic functions of chamber air flow, test chemical concentration, vacuum, temperature and relative humidity in each of three exposure rooms (Figure 2). The arrangement of computer control and interface instrumentation is shown in Figure 3. The executive computer is an Hewlett Packard Model 9816. All data acquisition and automated 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 gas chromatographic (GC) data is collected and preconditioned by Hewlett Packard Model 85B computers, one for each of the exposure rooms. Conditioned data is transferred to the executive computer for analysis, storage, printing and concentration control. Up to two GCs can be attached to each HP85B computer. Data from all monitoring equipment other than the GCs are inputted through a Colorado Data Systems (CDS) Model 53A-IBX Intelligent Interface System.

System control is provided from the computer by means of control relays in the CDS Intelligent Interface System. These relays control such devices as valves, drive motors, audible alarms, indicator lamps, etc.

A complete description of the software for this system is contained in document ØB-BE-5EØ1. Maintenance of the system is detailed in SOP #ØB-BE-3DØE. Routine operation of the computer system is detailed in SOP #ØB-BE-3GØ4. Routine daily operation of the system hardware is detailed in SOP #ØB-BE-3B2Y.

C. TEST ARTICLE GENERATION, MONITORING

1. Hexane Vapor Generation System

A Schematic diagram of the hexane vapor generation and delivery system is shown in Figure 4. Most of the hexane generator system will be enclosed within a vented cabinet locatd in the Exposure Suite Control Center. The hexane to be vaporized will be contained in an 19 liter stainless steel reservoir. This reservoir will be filled daily from the original shipping container by the following method which is designed to prevent explosion during transfer. All oxygen in the reservoir will be displaced with nitrogen. A vacuum will be applied to the reservoir to suck hexane through an eductor tube placed in the shipping container into the reservoir. All metal containers will be properly grounded. Transfer will take place in a vented vapor hood and the filled reservoir will then be transferred and installed into the generator cabinet.

During exposure the hexane will be pumped from the reservoir through a stainless steel eductor tube and delivery tubes to vaporizers located at the fresh air inlet of each animal exposure chamber. Stable micrometering pumps with adjustable drift-free pump rates ranging from less than 1×10^{-3} to greater than 20 ml per minute will be used.

The vaporizer (Figure 5) comprises a stainless steel cylinder covered with a glass fiber wick from which the liquid is vaporized. The wick can be easily and inexpensively replaced if necessitated by residue buildup. An 80-watt heater and a temperature sensing element are incorporated within the cylinder and connected to a remotely located temperature controller. A second temperature monitor is incorporated in the vaporizer allowing the operating temperature to be recorded by the automated data acquisition system. The operating temperature of the vaporizer will be maintained below 50°C (the boiling point of hexane is about 70°C). The cylindrical vaporizer will be positioned in the fresh air duct leading directly to the inlet of the exposure chamber.

A clear teflon® tube of measured volume, preceded by a three-way valve will be attached just upstream of the pump to facilitate measurement of the liquid flow rate of the vapor generator. Measurement will be accomplished by momentarily switching the three-way valve from the run position to the test position. A small bubble of air will be pulled by the pump from the cabinet through the valve and into the clear tube. The progress of this bubble from one end to the other of the tube (calibrated volume) will be timed with a stop watch. Flow rate will be calculated by dividing the volume by the time. The concentration in the exposure chamber can be calculated from the flow measurements of liquid and dilution of air.

All generation equipment which comes in contact with the hexane will be stainless-steel, teflon® or viton®. All equipment contained in the vented generator cabinet will be explosion proof.

Detailed operating instructions for this system are contained in SOP's ØB-BE-3B2Y and ØB-BE-3DØM.

2. Test Article Concentration Monitoring

An HP Model 5840 gas chromatograph with a flame ionization detector (FID) will be used to monitor the exposure chambers, the control chamber, the exposure room and a hexane standard gas. Sampling from multiple positions will be accomplished by means of an automated multiplexed eight-port sampling valve. The sampling system (Figure 6) is incorporated into the relative humidity (RH) sampling system. Samples of the atmosphere from each sample location are continuously drawn by a vacuum pump through polytetrafluoroethylene-lined, stainless-steel sample lines to a location near the input to the eight-port sample valve. This assures fresh samples at the monitor. The sample lines, which continue from the point where they "T" off to the eight-port valve to the dew point monitor, are polytetrafluoro-ethylene.

Sample values are accumulated and printed by an HP model 85B computer until samples from all eight ports of the sample valve have been measured. These values are then sent to the executive computer for printing and storage. As each value is sent to the HP 85B, it 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 then take the appropriate action as follows:

- Concentration ≥ non-critical low limit and ≤ non-critical high limit:

  No action

- Concentration < non-critical low limit but ≥ critical low limit:

  Increase concentration by decreasing chamber air flow.

- Concentration < critical low limit:

  Increase concentration by decreasing chamber air flow and activate audible alarm.

- Concentration > non-critical high limit but ≤ critical high limit:

  Decrease concentration by increasing chamber air flow.

- Concentration > critical high limit:

  Turn off generation system and activate audible alarm.

The monitor will be calibrated by quantitative analysis of grab samples. Additionally, the operation of the chamber-monitoring gas chromatograph will be checked daily against an on-line standard. This check provides a measure of day-to-day instrument drift. Additional calibration checks with grab samples will be performed to check the monitor calibration when drift of the on-line standard response factor is detected. Under normal circumstances, the calibration check will be performed once monthly (SOP #ØB-AC-3CØW).

Daily operating procedures for the concentration monitoring system are contained in SOP #ØB-AC-3B1P. Routine maintenance of the gas chromatograph is covered in SOP #ØB-AC-3DØ2.

The uniformity of the distribution of test chemicals in the chamber will be checked before the start of the study following SOP #ØB-BE-3B24.

3. Explosive-Level Detector

Figure 6 shows the explosive-level detection system. Sample lines from all chambers containing test chemicals "T" off from the chamber sample stream to the dewpoint hygrometer. Equal sample rates from each of these lines are controlled by flow meters incorporating five metering valves. Sample flow from each line is mixed in a plenum containing the explosive-level detector head. The detector will be set to alarm if the level in any one chamber reaches 20% of the lower explosive limit while the level in all other chambers is zero (SOP #ØB-BE-3CØU) and ØB-BE-3CØB). An alarm condition will automatically shut off the flow of test compound to all chambers.

D. ENVIRONMENTAL MONITORING

1. Temper Measureme

Temperatures of the exposure chambers, exposure rooms and, if necessary, test chemical generators, are measured by Resistance Temperature Devices (RTDs). The RTDs will be placed in a representative location in each chamber (a top sample port on the back side). Each RTD can be connected to an Omega Model 412B

digital thermometer by a manual select switch or by computer controlled scanner relays in the CDS IIS (Figure 7). This allows temperature to be read manually or to be recorded automatically. All temperature measurement equipment except the RTDs will be located in the Suite Control Center. Temperatures will be automatically recorded at regular periods during each 24-hour day.

The RTD will be calibrated at least once every 2 months (SOP #ØB-BE-3CØD and ØB-BE-3CØL). Calibration will generate values for offset and slope, which will be entered into the computer for each RTD. Calibration data will be included as part of the study archives.

2. Relative Humidity Measurements

Relative humidity (RH) will be measured using a EG&G Model 910 chilled-mirror dewpoint hygrometer located in the Suite Control Center. Samples of the air from each measurement location will be pulled through individual polytetrafluoroethylene sample lines to a central location in the Suite Control Center (Figure 6). This assures a fresh sample of the air at the point of measurement. Air from exposure chambers will be sampled from a representative location (a top port on the back side). Sample air from a particular location passes through a three-way valve to the system exhaust. When the RH is to be measured at that location, the three-way valve is switched to divert the flow to the dewpoint hygrometer. The valve can be controlled by either a manual switch or by a computer-controlled relay in the CDS IIS. This allows RH to be measured manually or automatically. Once the dewpoint has been determined by the hygrometer, the RH is automatically calculated by the executive computer using the dewpoint value (T_1) and the drybulb temperature (T_2), measured simultaneously at that measurement location.

The following equation is used for this calculation:

$$\% \text{ RH} = \frac{10^{\left(9.91 - \frac{2714.55}{(5/9)(T_1-32)+293.3}\right)}}{10^{\left(9.91 - \frac{2714.55}{(5/9)(T_2-32)+293.3}\right)}} \times 100$$

where: T_1 = dewpoint temperature, °F
T_2 = drybulb temperature, °F

Calibration of the dewpoint hygrometer will be checked before the start of the study and at least once every two months thereafter (ØB-BE-3CØJ and ØB-BE-3B1X). The procedure requires comparison of the RH calculated by the system monitor to measurements made by calibrated dewpoint hygrometer at the sample location. Calibration of the system monitor can be accomplished by inserting a value for offset and slope in the computer for each measurement location. Calibration data will be included as part of the study archive. RH will be recorded at regular periods during each 24-hour day.

3. Chamber Air-Flow Measurements

Chamber air flow is measured by a multiplexed orifice-meter system (Figure 8). Calibrated flow orifices are installed at the inlet and exhaust of each chamber. The desired flow orifice is attached to a Validyne Model DP-45 pressure transducer and CD-18 carrier demodulator pressure-measurement system through Tygon® tubes by means of solenoid valves. The valves can be operated either by a manual switch or by computer activated relays in the CDS IIS. This allows flow to be measured either manually or automatically. Pressure is read manually on a Validyne Model PM-12 voltmeter. Usually chamber flow will be measured using the exhaust flow orifice; however, after closing of the chamber doors, both inlet and exhaust flow measurements will be made and compared to determine if there are leaks in the chamber. If leaks are present, the executive computer will notify the operator and will not allow exposures to proceed until the leak is repaired.

All flow measurement equipment, except the multiplexed solenoid valves, is located in the Suite Control Center. Flow will be automatically recorded at regular intervals during the 24-hour day. The Validyne pressure transducer will be calibrated once each week (ØB-BE-3CØW and ØB-BE-3CØX). Calibration of the flow orifices will be checked once every two months (SOPs #ØB-BE-3CØS and ØB-BE-3CØV). Calibration of each orifice will generate coefficients that will be inserted into the computer flow equation for each orifice. Calibration data will be included as part of the study archive.

4. Chamber Vacuum Measurements

The same Validyne pressure transducer system used to measure chamber flows will be used to measure chamber vacuum (Figure 8). Vacuum in the chamber will be measured relative to atmospheric pressure in the Suite Control Room. Vacuum will be automatically recorded at regular intervals during the 24-hour day.

Vacuum will also be continuously monitored by a pressure switch mounted near each chamber. If the chamber should develop a leak (for example, a door inadvertently opened or a sample port stopper jarred loose), the pressure switch will immediately shut off the flow of compound to the chamber and alert the executive computer of the condition. The computer will activate an audio alarm and print and display a comment for the operator.

E. ENVIRONMENTAL CONTROLS

1. Animal Facility Air Handling System

Supply air enters the building through two identical parallel air handling systems (Figure 9). 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 - which includes 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.

2. Animal Room Air Handling System

The air from the two building air handling systems is then mixed together by an air mixing unit and is divided into two ducts which feed the rooms on East and West sides of the animal quarters. If necessary, steam is injected into the air in these ducts to maintain the RH of the room at between 35% and 65%.

3. Chamber Relative Humidity (RH) Control

Figure 10 shows a schematic diagram of the system used to control the relative humidity in the exposure chambers. Equipment located in the RH Control Equipment Room (Room 335) provides separate ducts of dry and moist air to each exposure chamber. A mixing valve, controlled by the computer, mixes the proper proportions of the moist and dry air to maintain the proper RH in each chamber.

Filtered air with a maximum dewpoint of about 53°F is supplied to the RH control equipment by the building air handling system. This air is evenly delivered to two ducts. Air from the first duct passes into a plenum where steam is injected to bring the air to a dewpoint of about 65°F. This provides moist air to the mixing valves. Steam is generated from city tap water with no additional additives. The air from the second duct passes through a refrigeration coil which reduces the moisture content of the air to a dewpoint of about 38°F. This provides "dry" air to the mixing valves.

Chamber RH is measured by the multiplexed dewpoint hygrometer. If the RH is found to be beyond the RH control range, the computer will calculate and make the appropriate adjustment to the mixing valve to bring the chamber RH to the desired target value.

4. Chamber Air-Flow Coctrol

Flow of air through the chamber is maintained by an AIR-VAC Engineering Model TDRH 1000 air- multiplier pump located in the exhaust duct of the chamber (Figure 11). This air-pressure-driven pump is stable, contains no moving parts, and is very reliable. Exhaust air from the chamber is HEPA-filtered before passing through this pump to remove particles which may reduce pump reliability. The pressure regulator, which controls the pump race, is operated by a motor drive system. The motor drive can be controlled by a manual switch or automatically by the computer through a relay in the CDS IIS. Fine control of exposure concentration will be accomplished by automatically adjusting the chamber air flow within the allowable flow limits. Gross

adjustments of concentration must be done manually by adjustment of the generation system. Maintenance of the chamber air flow control system is covered in SOP #ØB-BE-3DØE.

Exhaust from all chambers is collected into a central chamber exhaust duct within the exposure room. The exhaust from the chamber pump is rigidly attached to the central chamber exhaust duct. This rigid attachment prevents the possible escape of test compound into the room. The vacuum level in the central duct is regulated by a motor-driven feedback damper to prevent variations in building exhaust pressure from affecting chamber air-flow rates.

The air-flow rate in the central chamber exhaust duct is continuously monitored and alarmed. If the flow in this duct falls below 50% of the normal flow, the monitor trips the alarm which immediately shuts off the test compound generator system. Maintenance and calibration of the exhaust duct monitor is covered in SOP #ØB-BE-3DØE.

5. Chamber Temperature Control

Nearly all of the heat load contributed to the exposure chamber by the animals is dissipated from the chamber by radiation through the chamber walls (Bernstein and Drew, 1980). Consequently, temperature of the air supplied to the chamber has little effect on the temperature of the chamber while, on the other hand, the temperature of the room housing the chamber has a great deal of effect. For this reason, the major method of chamber temperature will be control of the room temperature. However, some cooling of chambers full of animals will be affected by the cool incoming air from the chamber's RH control system. Typically, a chamber full of animals will require the addition of dry air to maintain the proper RH. The dry air from the RH control system is cooler than room temperature. On the other hand, some warming of a chamber containing few animals will be affected by the warm air from the chamber's RH control system. Typically, a chamber with few animals will require the addition of wet air to maintain the proper chamber RH. The wet air is equal to or warmer than the room temperature.

F. CHAMBER EXHAUST WASTE TREATMENT

The exhaust from the central chamber exhaust duct is mixed with the exhaust from the entire animal facility (75,000 cfm) prior to being exhausted from the building stack. Dilution of chamber exhaust with building exhaust results In an acceptable stack concentration of less than 10% of the threshold limit value (TLV) for the test article.

G. DATA HANDLING

Data from each exposure room are stored in the Exposure Suite Control Center on separate magnetic diskettes by Hewlett Packard Model 9121 micro-floppy disk drives. Data and comments from each exposure room are printed on separate thermal dot-matrix printers (Hewlett

Packard Model 2171G). Data are printed and stored immediately upon completion of the measurement to a Daily Log (example, Figure 12). At the end of the day (24-hour period), the daily data are analyzed and a summary is printed (Figure 13). This summary includes the mean, standard deviation, maximum, minimum and target values for each set of data for the 24-hour period. A second printout (Figure 14) provides a list of outliers (i.e., all data points which were beyond the defined critical limits). This printout will allow quick review of the data.

Data handling and analysis procedures are described in the SOPs ØB-BE-5EØ3, ØB-BE-3EØA, and ØB-BE-3EØB.

H. EQUIPMENT OR POWER FAILURE PROTECTION SYSTEMS

In the event of equipment failure, or of a short-term power failure, two parameters must be considered most important to the well-being of the animals - temperature and air flow. To understand the factors protecting against either of these two parameters becoming life-threatening to the animals, one must understand both the emergency power system and the emergency air handling equipment.

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 LSL-II through two types of motor control centers. One type can switch power to the equipment from either city power or emergency 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 equpiment supplied by the motor control center.

All equipment critical to the well-being of the animals is connected to the emergency-power-type motor control centers. A list of this equipment is as follows:

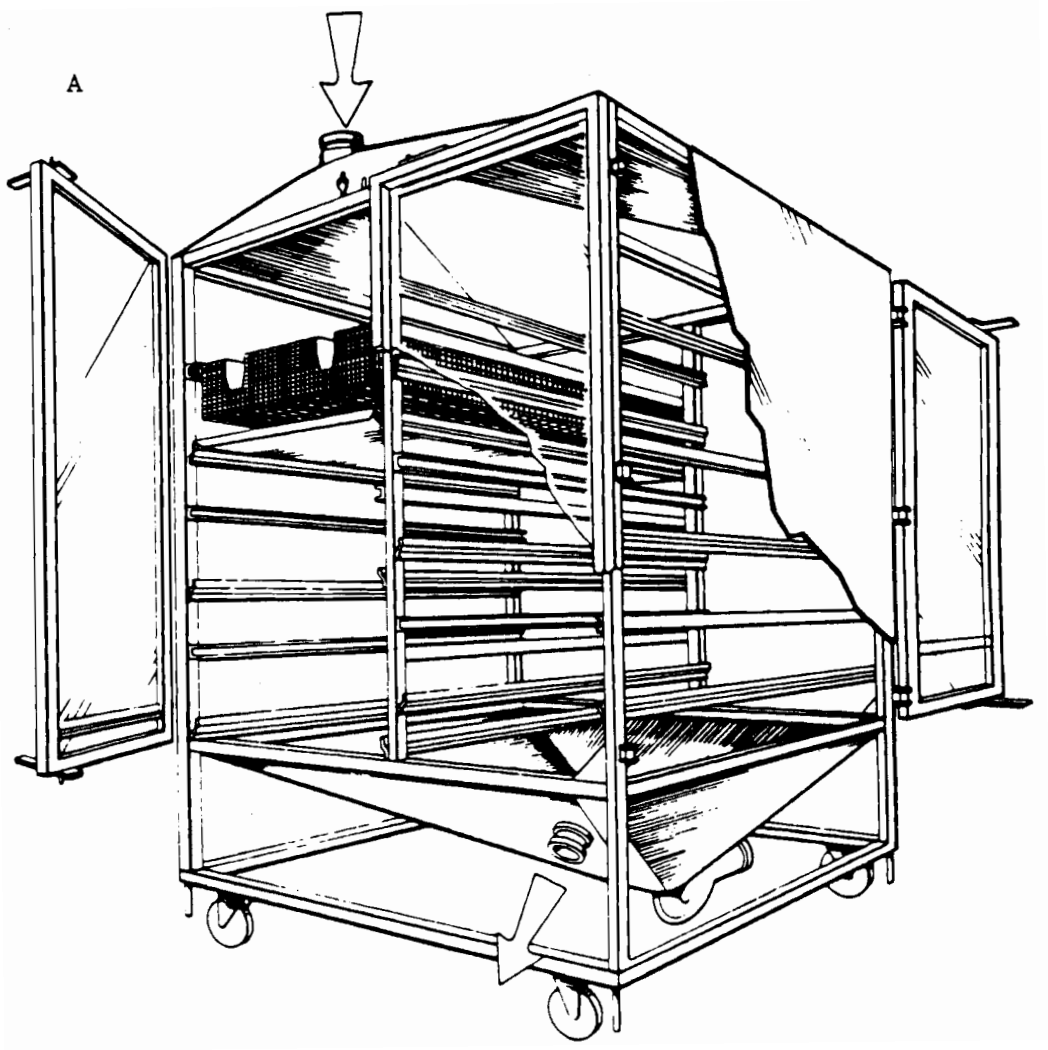
- Emergency lighting and electrical outlets
- Chillers #1 and #2
- Boiler and feedwater pump systems #1 and 82
- Air compressors #1 and #2
- Air supply fans #1 and #2
- Air exhaust fans #1 and #2

It should be noted that there are two identical units of all of the 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 operste one of the two identical units. If, during a power outage, the unit of equipment that is on emergency power should happen to fail, the other unit of identical equipment can be manually switched to run on emergency power.

All building or chamber systems which are essential to the survivial 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, including the Task Leader(s) or the Principal Investigator(s) of the program(s) affected.

References

1. Rernstein, D.M. and R.T. Drew. 1980. The major parameters affecting temperature inside inhalation chambers. AIHAJ, (41) 6/80, pp. 420-426.



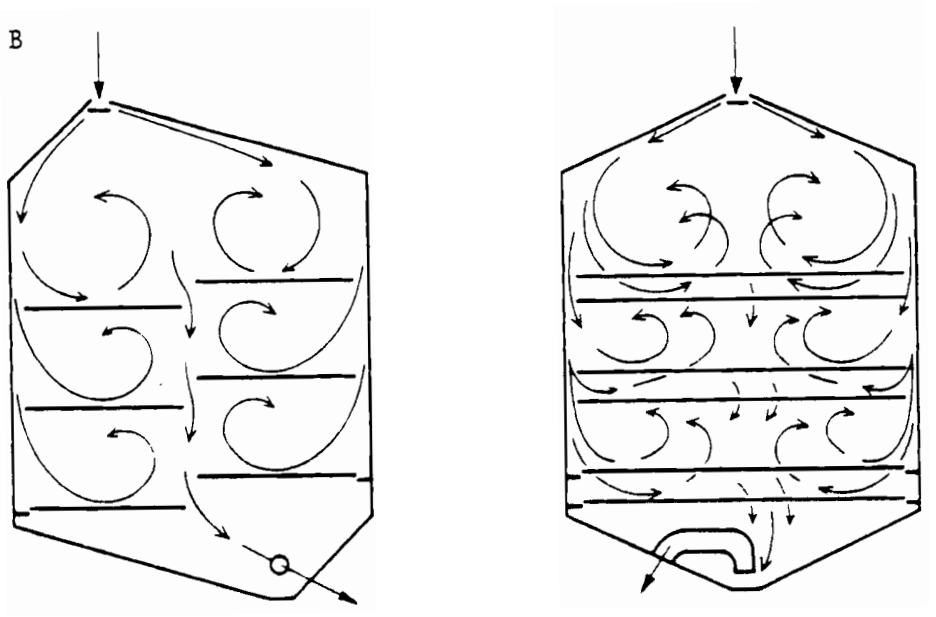


FIGURE 1. Inhalation Exposure Chamber Designed at BNW (A. Oblique cutaway view of the chamber; B. Airflow patterns)

EXPOSURE SUITE #1

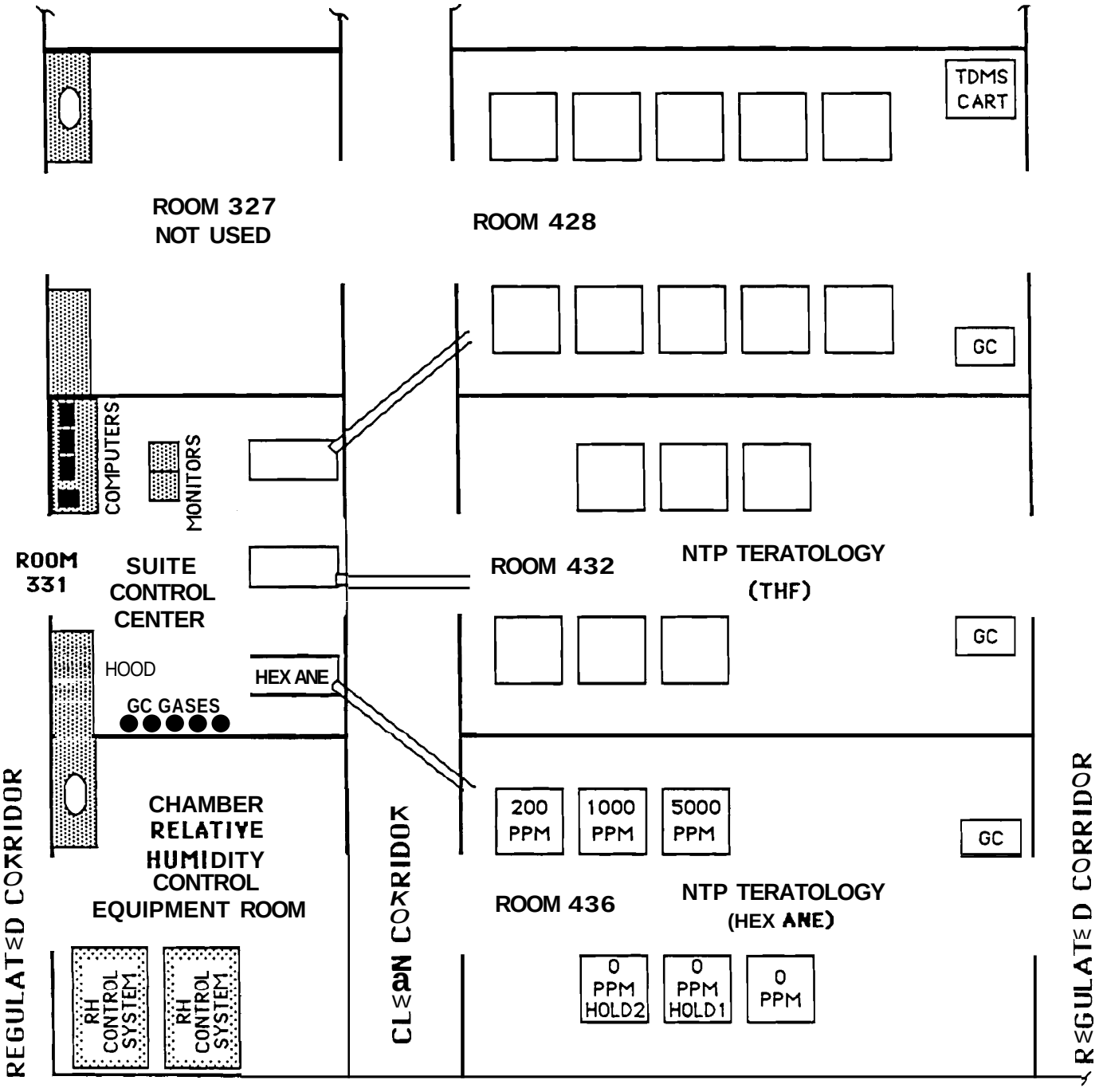


FIGURE 2. Schematic Diagram of the Three Exposure Rooms in the Automated Inhalation Exposure Suite.

COMPUTER SYSTEM

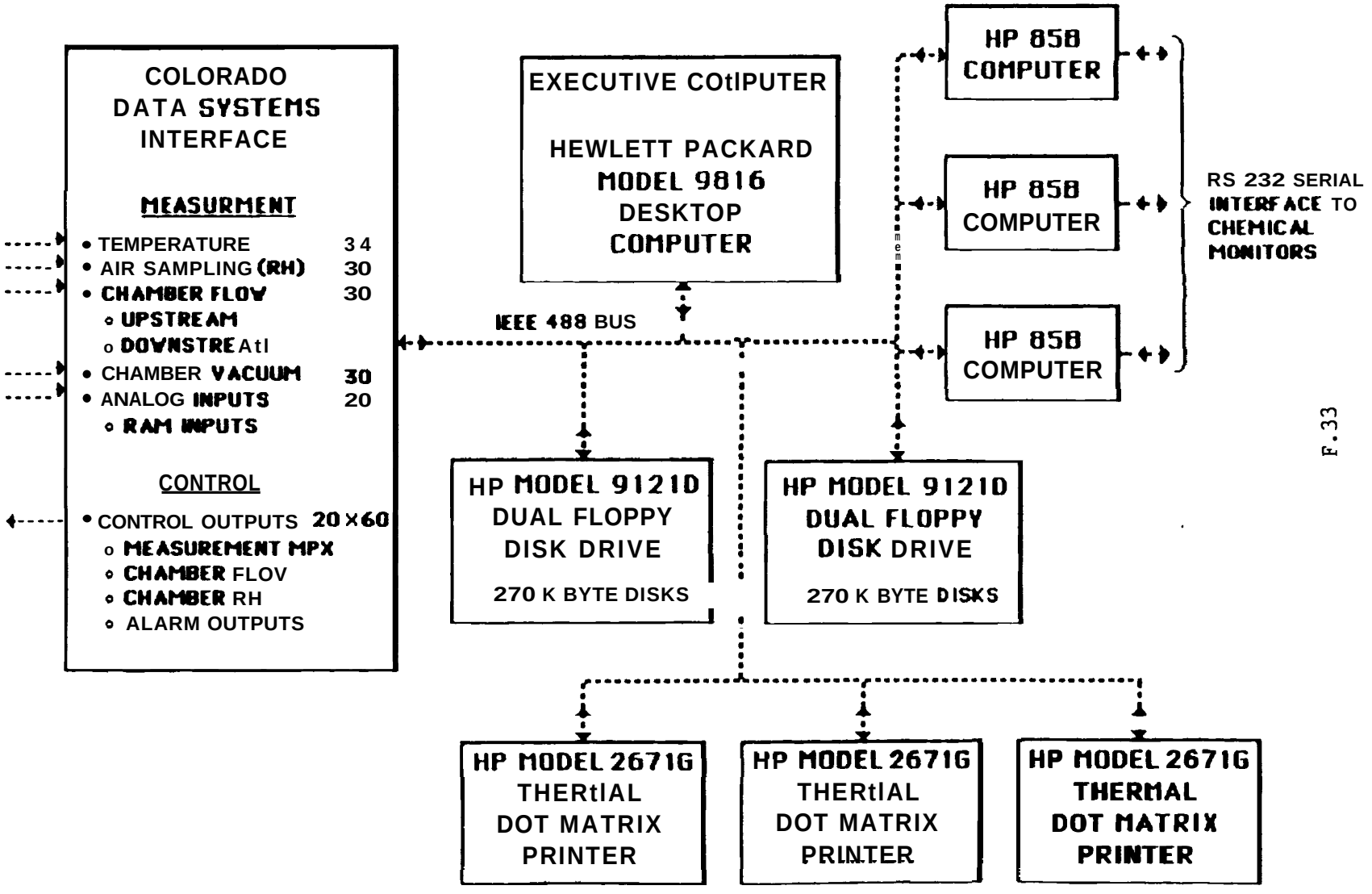


FIGURE 3. Block Diagram of Data Acquisition andControl Computers and Interface Instrumentation

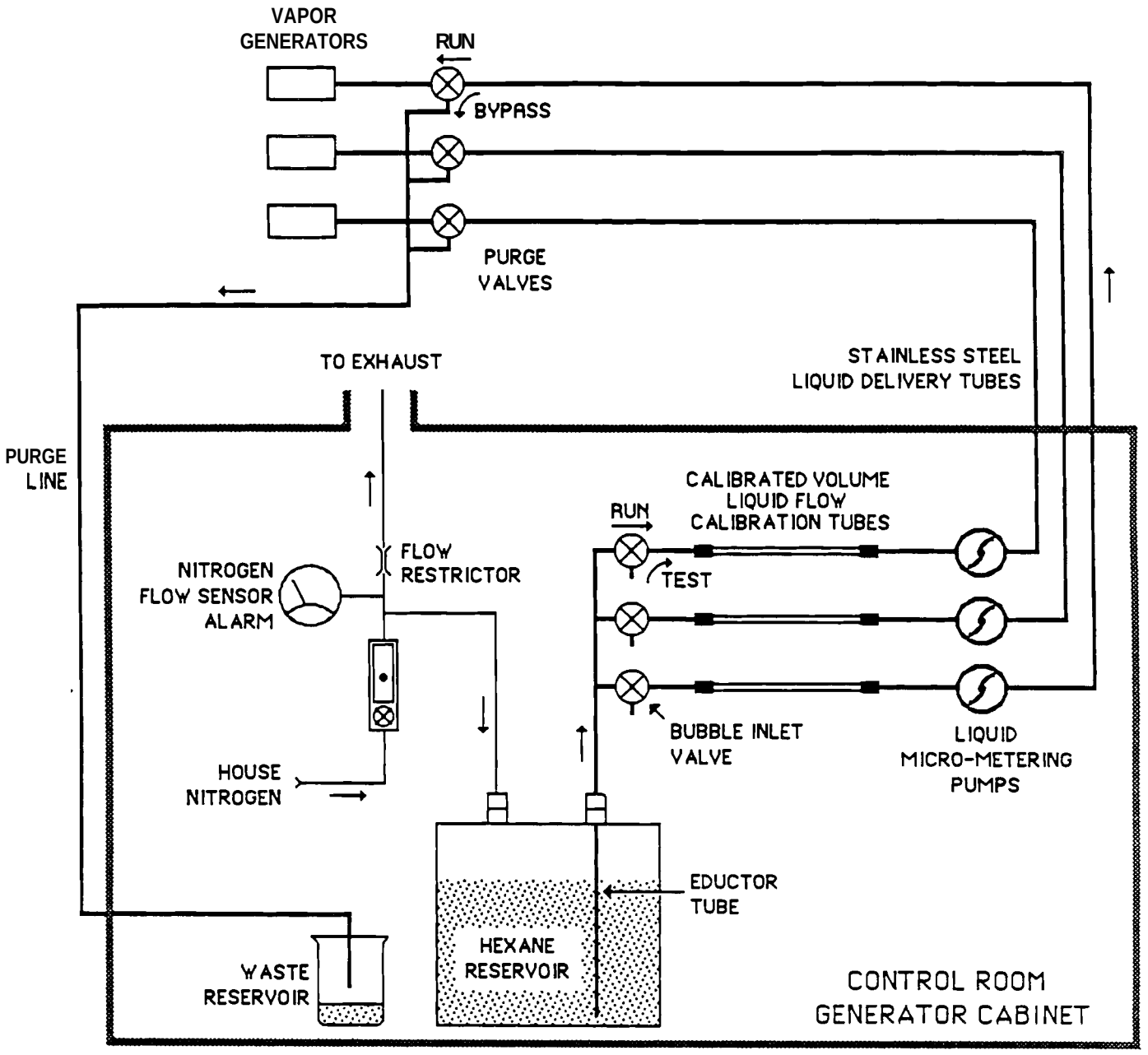


FIGURE 4. Schematic Diagram of the Hexane Vapor Generation System.

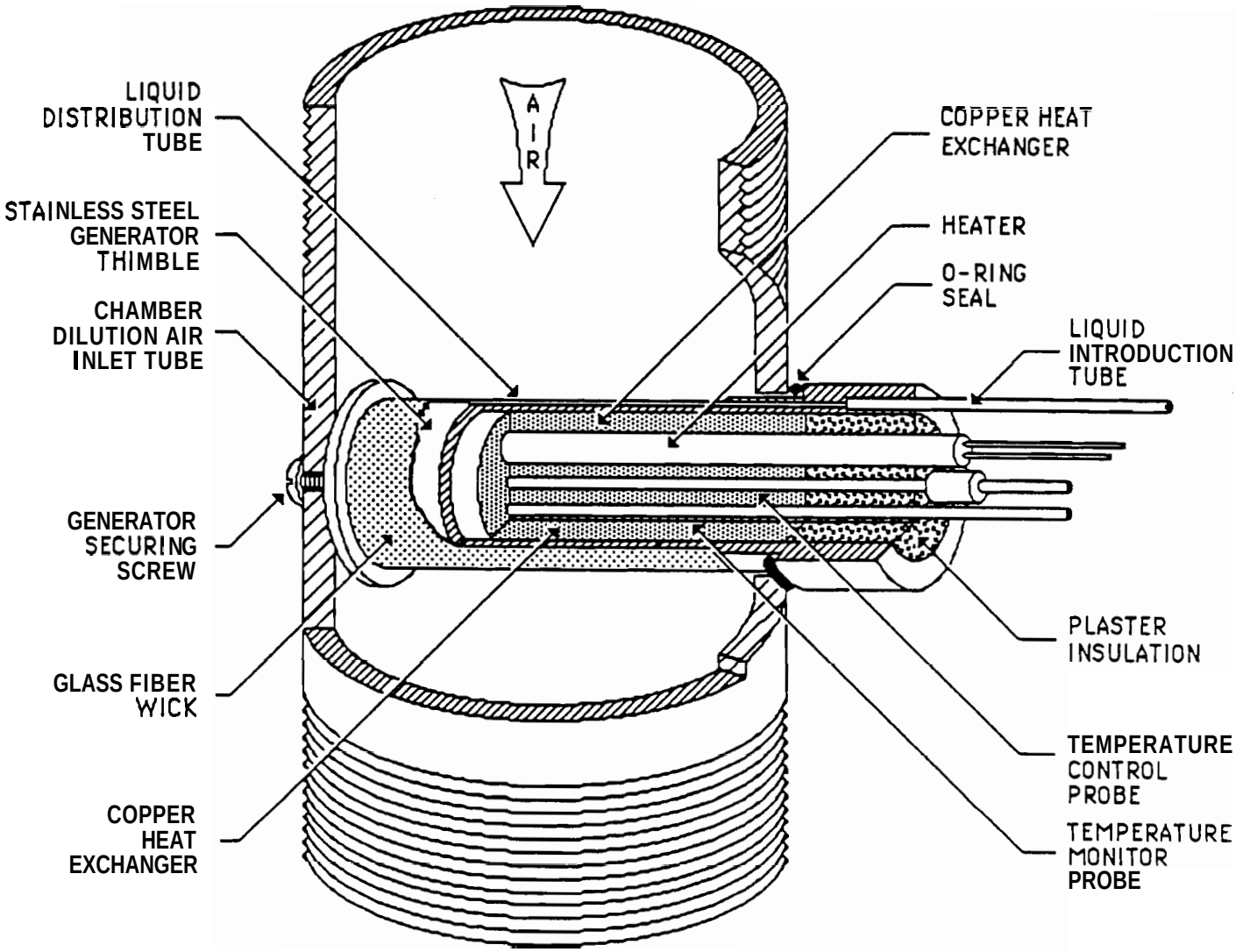


FIGURE 5. Cutaway Drawing of the Hexane Vapor Generator Located in the Fresh-Air Inlet Tube of the Exposure Chamber.

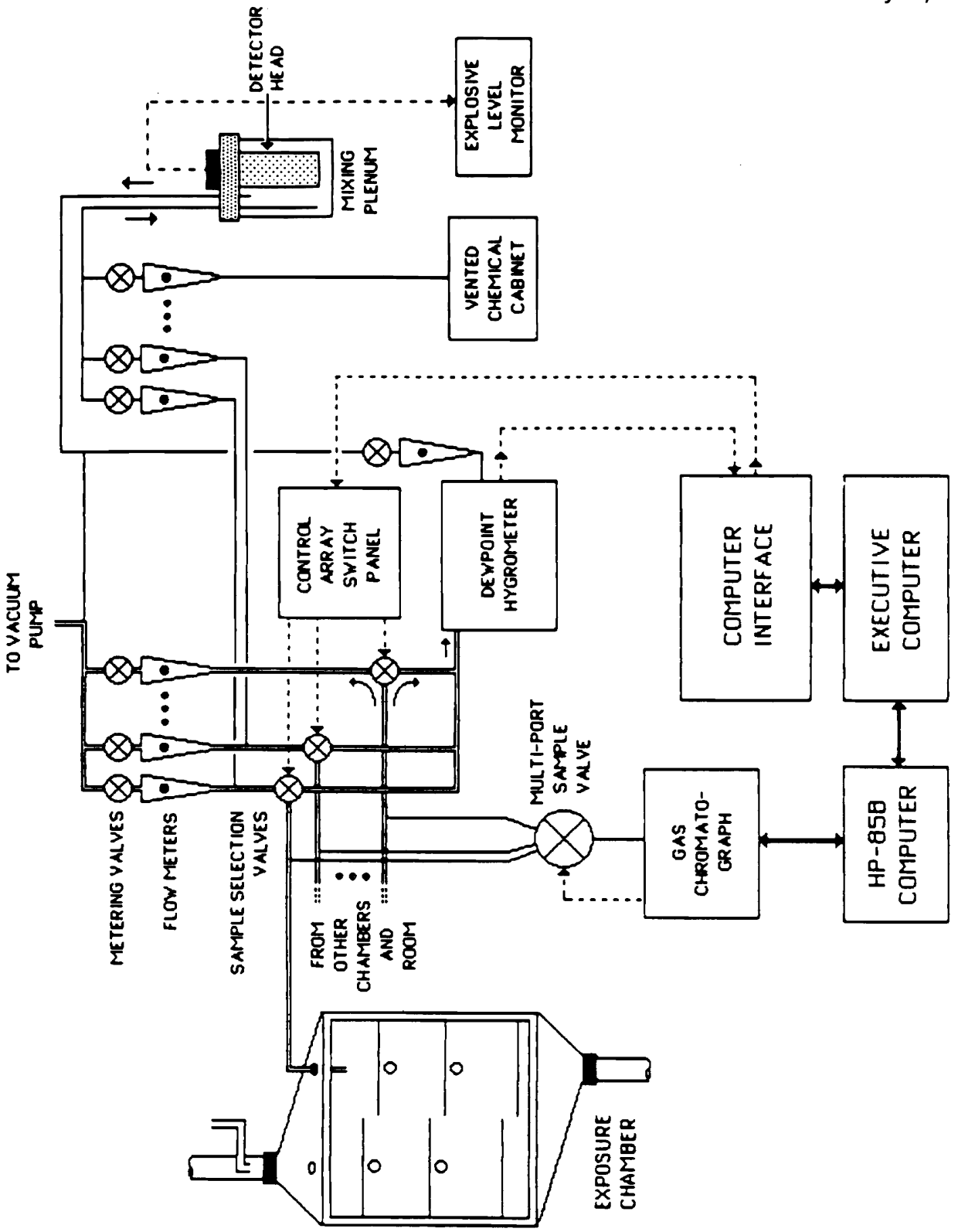


FIGURE 6. Schematic Diagram of the Dewpoint, Chemical Concentration, and Explosive Level Monitoring Systems

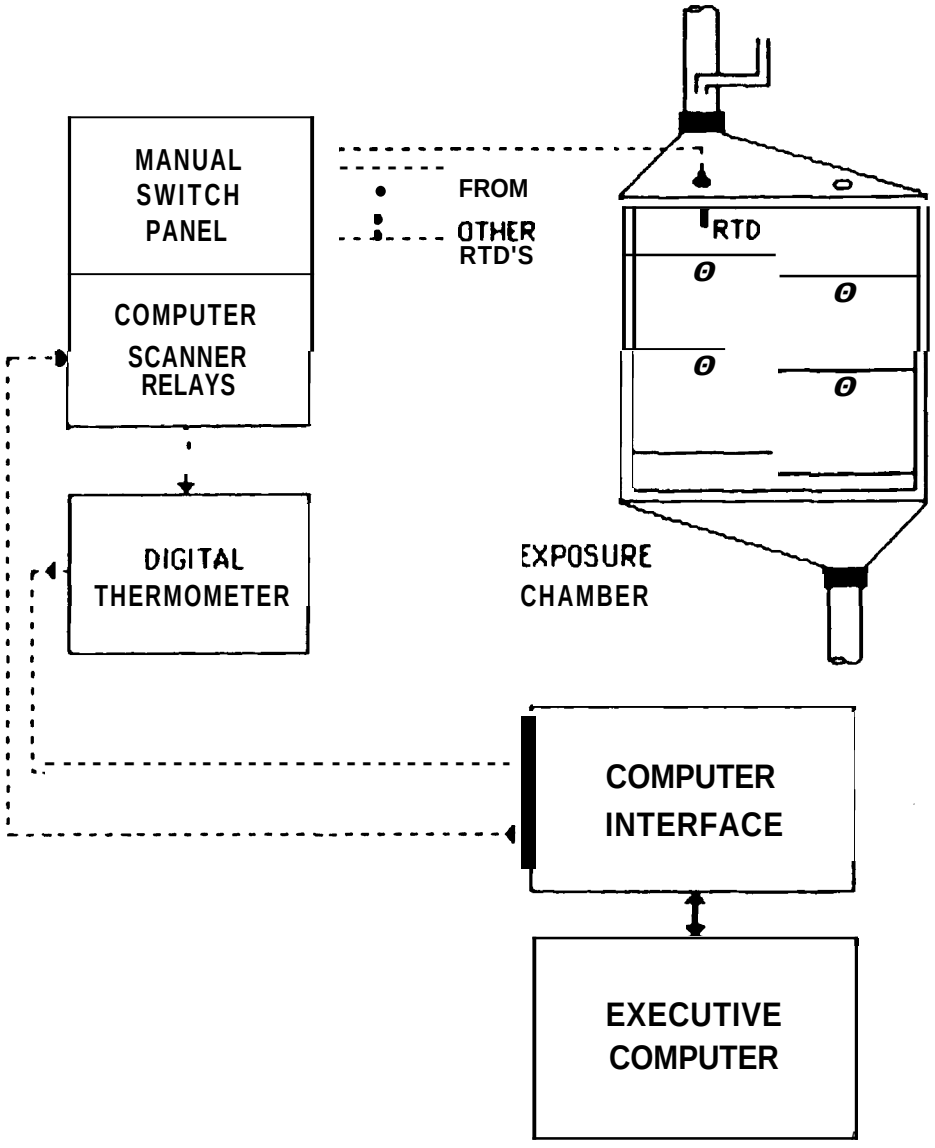


FIGURE 7. **Schematic Diagram of Temperature Monitoring System**

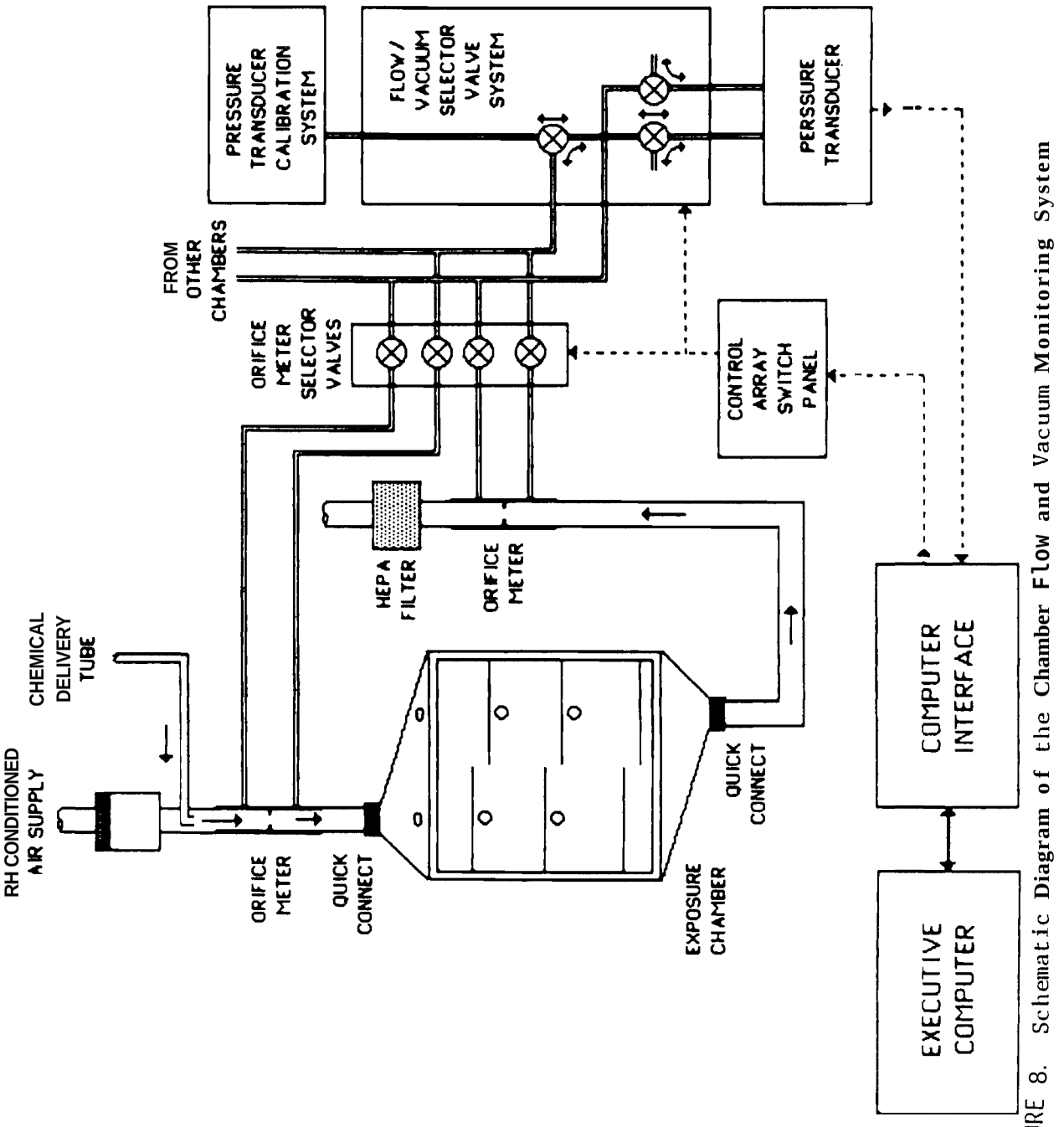


FIGURE 8. Schematic Diagram of the Chamber Flow and Vacuum Monitoring System

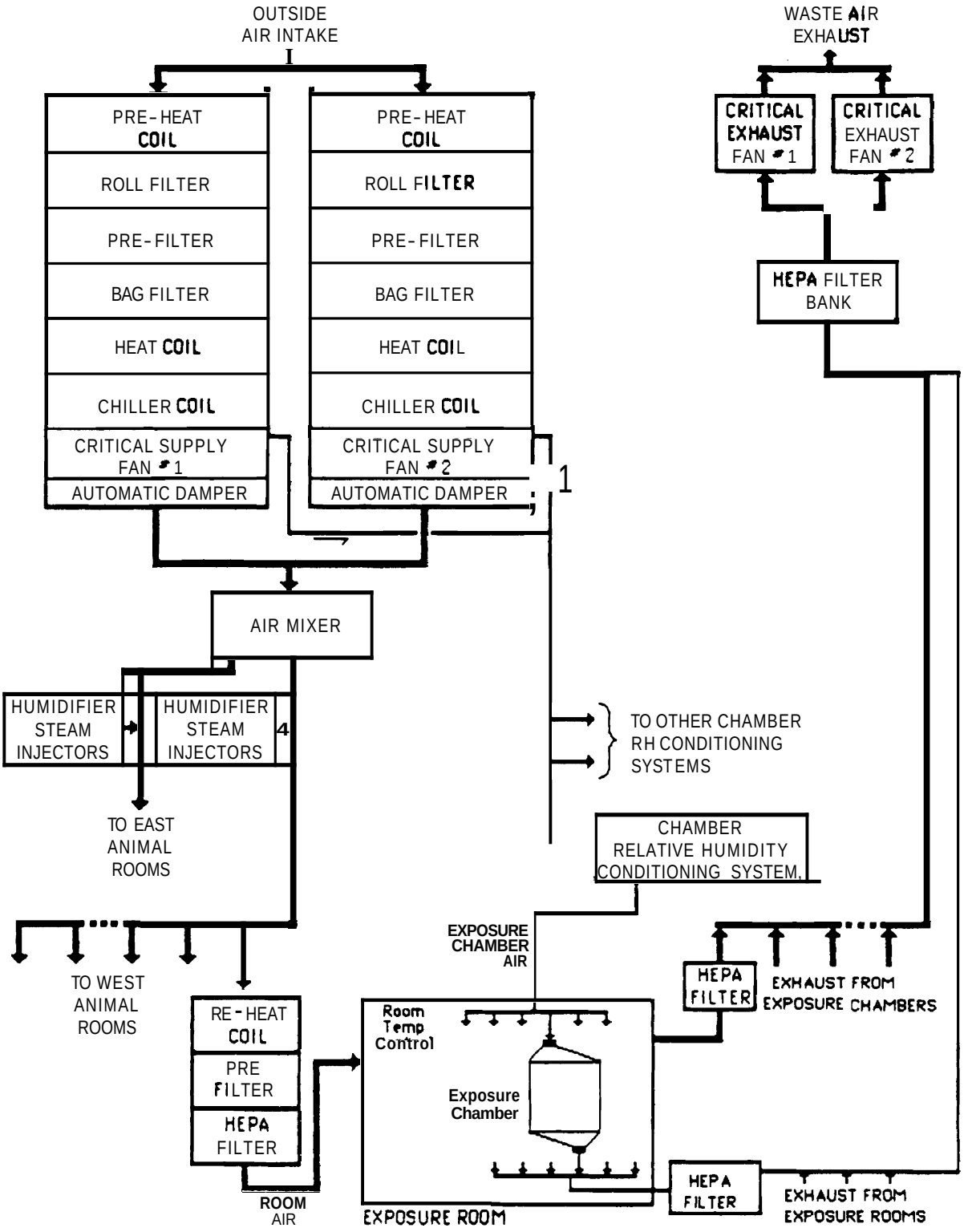


FIGURE 9. Air Handling System for Animal Rooms of Life Sciences II Building

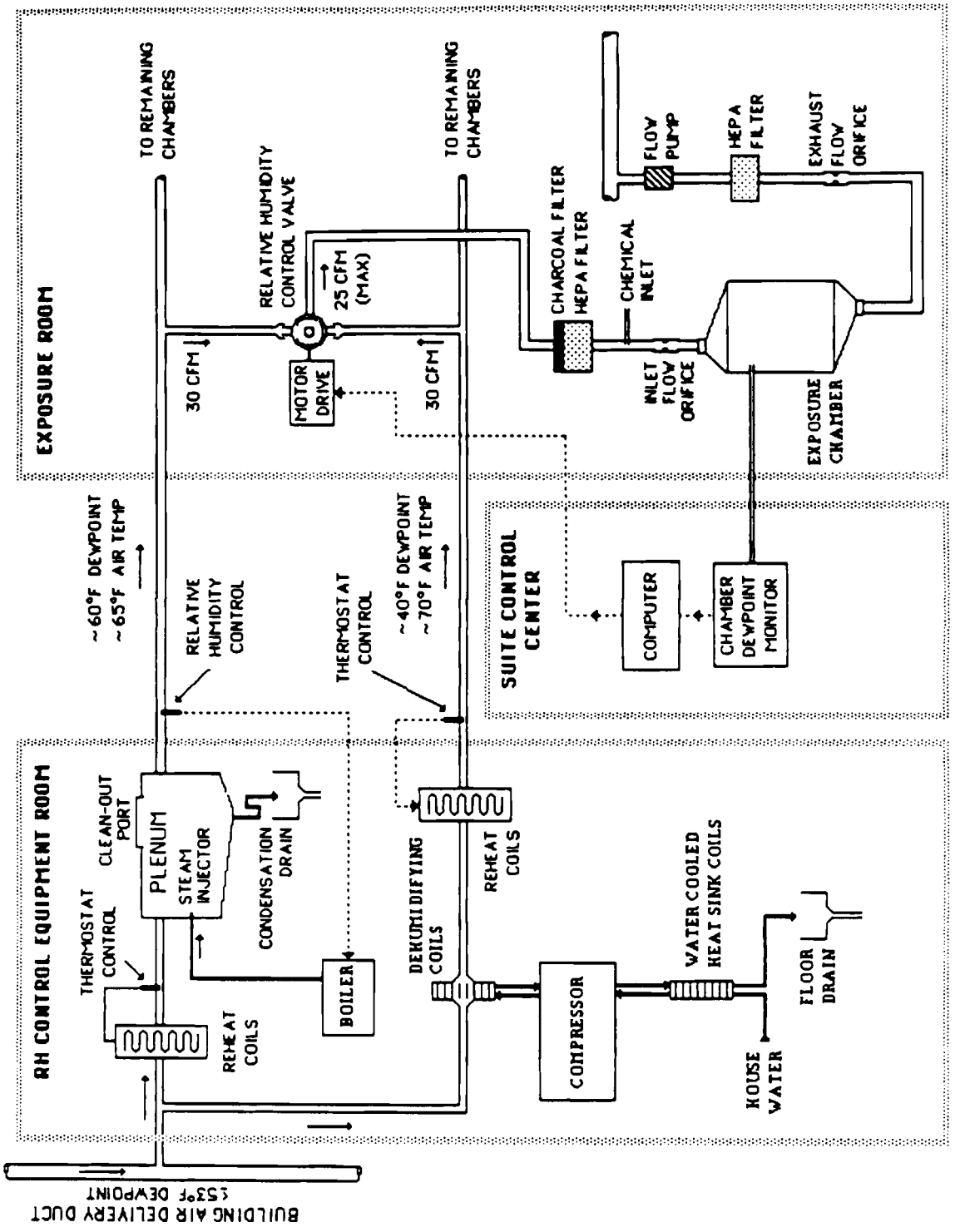


FIGURE 10. Schematic Diagram of Chamber Relative Humidity Control System

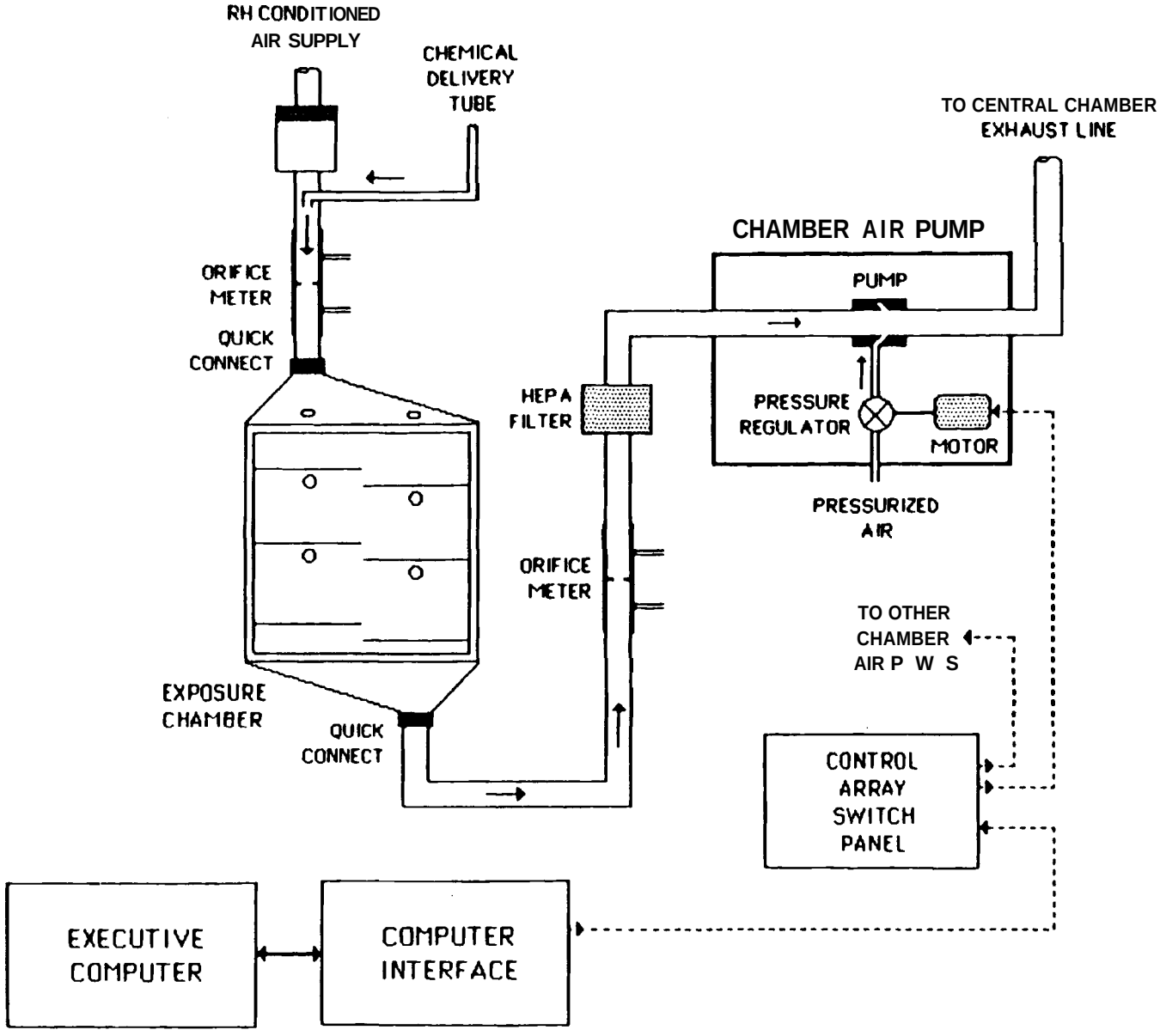


FIGURE 11. **Schematic Diagram of the Chamber Air Flow Pump and Air Flow Control System**

Exp #1: Demonstration Program: **85.01** **24** July 1985

Time	Location	Function	Data		
21:01	Ch #1 -- Room **324**	Temperature	(BSI	**79.1**	F
21:02	Ch #2 -- Room **324**	Relatrve Humidity	**OKI**	**40.**	%
21:03	Ch #3 -- Room **324**	Flow	OKI	**16.3**	CFM
21:06	Ch #2 -- Room **436**	Relative Humidity	(**BSE**	**65.**	%
21:07	Ch #2 -- Room **436**	Vacuum	<OKE	**1.5**	**HOH**
21:08	Ch #1 -- Room **324**	Vacuum	<BSI	.8	**HOH**
21:10	Ch #2 -- Room **324**	Relatrve Humidity	<OKI	**35.**	%
21:13	Ch #3 -- Room **324**	Concentration	OKI	5.000E+1	PPM
21:16	Ch #2 -- Room **436**	Relative Humidity	(BSE	**65.**	%
21:16	Ch #2 -- Room **436**	Vacuum	<OKE	**5**	**HOH**
21:17	Ch #1 -- Room **324**	Temperature	<BSI	**81.1**	F
21:18	Ch #2 -- Room **324**	Relative Humidity	**OKI**	**46.**	%
21:18	Ch #3 -- Room **324**	Flow	OKI	**16.3**	CFM
21:19	Ch #2 -- Room **436**	Relative Humidity	(BSE	**65.**	%
21:20	Ch #2 -- Room **436**	Vacuum	OKE	**1.4**	**HOH**
21:21	Ch #1 -- Room 324	Vacuum	<BSI	.8	HOH
21:25	Ch #2 -- Room 324	Relative Humidity	<OKI	**35.**	%
21:26	Ch #3 -- Room 324	Concentration	OKI	5.000E+1	PPM
21:26	Ch #2 -- Room 436	Relative Humidity	(**BSE**	**65.**	%
21:26	Ch #2 -- Room 436	Vacuum	<OKE	**1.3**	HOH
21:27	LJF This is a demonstration of the comment routrne. This routine is available from every menu.				
21:40	Ch #2 -- Room 436	Relative Humidity	(BSE	**65.**	%
21:46	Ch #2 -- Room 436	Vacuum	<OKE	.8	HOH
21:48	Ch #1 -- Room **324**		<**BSI**	.8	**HOH**
21:50	Ch #2 -- Room **324**	e Humidity	<OKI	**35.**	%
21:**53**	Ch #3 -- Room **324**		OKI	5.000E+1	PPM
21:56	Ch #2 -- Room 436	Relative Humidity	(BSE	**65,**	%
21:06	Ch #2 -- Room **436**	Concentration	OKE	1.5	HOH
		Relative Humi			
		Vacuum			

FIGURE 12. Example of "Daily Log" Printout from Data Acquisition and Control Computer. See following page for explanation of columns.

DESCRIPTION COMPUTER "LOG BOOK" OUTPUT

The exposure number, exposure name, program version and exposure date will be printed at the top of every report page.

Time--This is the far left column. This is the time that the measurement was taken.

Location--This identifies where the data came from. Also referred to in the menus as "Location". This column allows for 20 characters.

Function--This identifies which function was used to take the reading. This column allows for 20 characters.

Data--This is the raw data. This column includes an alarm code, a status code, the data value and a units label.

Alarm code--"(" means that the data has exceeded non-critical alarm limits.
"<" means that the data has exceeded critical alarm limits.

Status code--OK1 - Okay and calibrated. Data is included in summary.
OKE - Okay and calibrated. Data is not included in summary.
BS1 - Beyond service time. Data is included in summary.
BSE - Beyond service time. Data is not included in summary.

Data format--Data will be expressed as four significant digits with non significant zeros suppressed. Number of decimal points was determined in the menus. (Function Assignments Menu.)
Examples: DDDD.
DDD.D
DD.DD
D.DDD
.DDDD
D.DDDESZ

Units label--This column allows 9 characters. Examples: ppm, °F, °C, HOH.

NOTE: At almost any time during the exposure day, a comment can be entered from the keyboard. Because our report is generated as events occur, comments can appear in the middle of the logbook printout. This first line will show only the time and the operator's full name. The next lines will contain the body of the comment.

FIGURE 12. (Continued)

Summation for the File: 23 July 1985 Exposure: Demonstration

Temperature	Mean	% Tam	Std Dev	% RSD	Maximum	Minimum	N	Target
Ch #01	73.20	101	.125	1	74.6	70.7	10	72.0
Ch #02	74.30	103	.128	7	78.3	72.7	15	72.0
Ch #03	73.20	101	.134	3	75.3	70.7	15	72.0
Ch #04	68.20	95	.131	2	75.5	65.7	15	72.0
Ch #05	73.20	101	.131	2	76.3	68.7	15	72.0
Ch #06	73.40	102	.139	2	75.3	72.7	15	72.0
Ch #07	69.40	96	.150	1	74.3	68.7	10	72.0
Ch #08	70.20	98	.130	2	75.3	72.7	15	72.0
Room	74.20	103	.130	2	75.3	72.7	15	72.0
Flow	**Mean**	**% Tarc**	**Std Dev**	**% RSD**	**Maximum**	**Minimum**	**N**	**Target**
Ch #01	14.10	94		3	17.0	12.0	a	15.0
Ch #02	17.80	118	.500	4	19.0	14.0	12	15.0
Ch #03	15.80	105	.400	3	17.0	12.0	15	15.0
Ch #04	13.80	92	.300	2	15.0	12.0	16	15.0
Ch #05	10.50	72	.200	3	12.0	8.0	10	15.0
Ch #06	14.80	99	.400	3	17.0	12.0	15	15.0
Ch #07	16.80	112	.300	4	10.0	14.0	14	15.0
Ch #08	14.3	91	.400	3	17.0	12.0	15	15.0
Relative Humidity	**Mean**	**% Tam**	**Std Dev**	**% RSD**	**Maximum**	**Minimum**	**N**	**Tamet**
Ch #01	51.0	102	5.10	10	70.	41.	14	50.
Ch #02	48.0	96	5.20	11	55.	45.	14	50.
Ch #03	52.0	106	5.30	10	70.	45.	14	50.
Ch #04	51.0	102	5.10	10	70.	41.	14	50.
Ch #05	48.0	96	5.20	11	55.	45.	14	50.
Ch #06	52.0	106	5.30	10	70.	45.	14	50.
Ch #07	51.0	102	5.10	10	70.	41.	14	50.
Ch #08	48.0	96	5.20	11	55.	45.	14	50.
Room	52.0	106	5.30	10	70.	45.	14	50.

FIGURE 13. Example of 24-Hour Data "Summation" Printout from Data Acquisition and Control Computer. Data are organized by data type.

Outlier Table for the File : 24 July 185 Exposure: Demonstration

Date	Origin	Function	Time	Data	Lower	Target	Higher
23 Jul	Temperature	Ch #01	16:45	69.3	70.0	72.0	74.0
23 Jul			16:48	59.2	70.0	72.0	74.0
23 Jul			16:51	69.0	70.0	72.0	74.0
23 Jul			16:55	69.1	70.0	72.0	74.0
23 Jul			16:59	69.3	70.0	72.0	74.0
23 Jul		Ch #02	16:47	68.1	7015	72.0	74.0
23 Jul			16:49	68.3	70.0	72.0	74.0
23 Jul		Ch #03	16:40	69.0	70.0	72.0	74.0
23 Jul			16:59	75.1	70.0	72.0	74.0
23 Jul		Ch #04	17:09	74.8	70.0	72.0	74.0
23 Jul		Ch #05	14:59	74.3	70.0	72.0	74.0
23 Jul		Ch #08	16:01	57.1	70.0	72.0	74.0
23 Jul			16:20	68.1	70.0	72.0	74.0
23 Jul		Room	16:23	69.0	70.0	72.0	74.0
23 Jul			16:41	69.8	70.0	72.0	74.0
23 Jul	Flow	Ch #01	12:45	11.2	12.3	15.0	17.0
23 Jul			15:23	19.1	12.0	15.0	17.0
23 Jul		Ch #05	15:33	0.1	12.0	15.0	17.0
23 Jul		Ch #08	10:23	20.1	12.0	15.0	17.0
23 Jul			16:41	20.2	12.0	15.0	17.0
23 Jul	Concentration	Ch #03	10:45	4.560E+0	5.000E+0	7.500E+0	1.000E+1
23 Jul			10:50	4.350E+0	5.000E+0	7.500E+0	1.000E+1
23 Jul			11:01	4.200E+0	5.000E+0	7.500E+0	1.000E+1
23 Jul			11:14	4.130E+0	5.000E+0	7.500E+0	1.000E+1
23 Jul			11:28	4.580E+0	5.000E+0	7.500E+0	1.000E+1
23 Jul		Ch	9:06	1.143E+1	5.000E+0	7.500E+0	1.000E+1
23 Jul			9:21	1.194E+1	5.000E+0	7.500E+0	1.000E+1
23 Jul			9:46	1.053E+1	5.000E+0	7.500E+0	1.000E+1
23 Jul		Ch	11:46	1.001E+1	5.000E+0	7.500E+0	1.000E+1
23 Jul			12:07	1.003E+1	5.000E+0	7.500E+0	1.000E+1

FIGURE 14. Example of 24-Hour Data "Outlier Table" Printout from Data Acquisition and Control Computer. Table shows data which were beyond the defined operating limits.

March 23, 1988

n-Hexane Mouse Teratology Study
Protocol ØB-DT-1FØJ-ØØ-Ø176

NOTE TO THE **FILE:** Deviation from Protocol During the Study

Virgin Body Weights

Due to scheduling problems the virgins were weighed on exposure days 1, 4, and 7, rather than on expsoure days 1, 3, and 6 as specified in the protocol.

Terryl J. Mast, Study Director

SPONSER: NTP – IRT

STUDY: MOUSE TERATOLOGY

ROOM: **436**

DATE: **3-22-87** BOW

CHEMICAL: n-HEXANE

CHAMBER: TREATMENT 1

CONCENTRATION: ϕ ppm

LEVEL 3

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26		41		56	
10	3321	25		40		55	
9	3296	24		39		54	
8	3247	23		38		53	
7	3233	22		37		52	
6	3218	21		36		51	
5	3145	20		35		50	
4	3133	19		34		49	3166
3	3132	18		33		48	3113
2	3122	17		32		47	3052
1	3078	16		31		46	3034
	VIRGINS						GES GRP A

LEVEL 4

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27	3359	42		57	
11		26	3318	41	3311	56	
10		25	3239	40	3270	55	
9		24	3225	39	3251	54	
8		23	3151	38	3246	53	
7		22	3140	37	3236	52	
6		21	3136	36	3215	51	
5		20	3116	35	3162	50	
4	3303	19	3081	34	3069	49	3351
3	3234	18	3077	33	3050	48	3203
2	3213	17	3072	32	3026	47	3167
1	3178	16	3046	31	3019	46	3115
	GES GRP B		GES GRP C		GES GRP D		GES GRP E

SPONSER: NTP-IRT

STUDY: MOUSE TERATOLOGY

ROOM: 436

DATE: 3-22-87 BSW

CHEMICAL: n-HEXANE

CHAMBER: TREATMENT 2

CONCENTRATION: 200 ppm

LEVEL 3

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26		41		56	
10	3355	25		40		55	
9	3310	24		39		54	
8	3302	23		38		53	
7	3286	22		37		52	
6	3128	21		36		51	
5	3099	20		35		50	
4	3082	19		34		49	3163
3	3079	18		33		48	3057
2	3054	17		32		47	3015
1	3020	16		31		46	3013
	VIRGINS						GES GRP A

LEVEL 4

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26	3357	41	3352	56	
10		25	3279	40	3307	55	
9		24	3262	39	3297	54	
8		23	3187	38	3280	53	
7		22	3159	37	3273	52	
6		21	3112	36	3240	51	
5		20	3089	35	3193	50	3338
4	3327	19	3085	34	3110	49	3328
3	3269	18	3065	33	3095	48	3319
2	3202	17	3063	32	3043	47	3182
1	3190	16	3060	31	3004	46	3071
	GES GRP B		GES GRP C		GES GRP D		GES GRP E

SPONSER: NTP-IRT
CHEMICAL: n-HEXANE
STUDY: MOUSE TERATOLOGY
CHAMBER: TREATMENT 3
ROOM: 436
CONCENTRATION: 1000 ppm
DATE: 3-22-87

BSW

LEVEL 3

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26		41		56	
10	3265	25		40		55	
9	3220	24		39		54	
8	3211	23		38		53	
7	3169	22		37		52	
6	3130	21		36		51	
5	3120	20		35		50	
4	3097	19		34		49	3068
3	3051	18		33		48	3064
2	3036	17		32		47	3038
1	3001	16		31		46	3022
	VIRGINS						GES GRP A

LEVEL 4

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26	3343	41	3289	56	
10		25	3341	40	3267	55	
9		24	3164	39	3261	54	
8		23	3138	38	3248	53	
7		22	3075	37	3226	52	
6		21	3067	36	3217	51	
5		20	3062	35	3216	50	3356
4	3322	19	3058	34	3207	49	3323
3	3219	18	3031	33	3171	48	3308
2	3204	17	3025	32	3088	47	3293
1	3199	16	3009	31	3014	46	3083
	GES GRP B		GES GRP C		GES GRP D		GES GRP E

SPONSER: NTP–IRT

STUDY: MOUSE TERATOLOGY

ROOM: 436

DATE: 3-22-87

BSW

CHEMICAL: n–HEXANE

CHAMBER: TREATMENT 4

CONCENTRATION: 5000 ppm

LEVEL **3**

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26		41		56	
10	3350	25		40		55	
9	3332	24		39		54	
8	3300	23		38		53	
7	3295	22		37		52	
6	3257	21		36		51	
5	3255	20		35		50	
4	3241	19		34		49	
3	3237	18		33		48	3098
2	3197	17		32		47	3066
1	3157	16		31		46	3047
	VIRGINS						GES GRP A

4

LEVEL **4**

Cage		Cage		Cage		Cage	
15		30		45		60	
14		29		44		59	
13		28		43		58	
12		27		42		57	
11		26	3139	41	3329	56	
10		25	3137	40	3294	55	
9		24	3131	39	3291	54	
8		23	3129	38	3276	53	
7		22	3121	37	3272	52	
6		21	3118	36	3254	51	
5	3312	20	3109	35	3243	50	3333
4	3301	19	3042	34	3230	49	3305
3	3285	18	3040	33	3223	48	3304
2	3266	17	3030	32	3185	47	3259
1	3209	16	3008	31	3035	46	3206
	GES GRP B		GES GRP C		GES GRP D		GES GRP E

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