

**Final Report**

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**Inhalation Developmental  
Toxicology Studies:  
Teratology Study of  
N-Hexane in Rats**

**T. J. Mast**

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**December 1987**

**Prepared for the  
National Institute of Environmental  
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INHALATION DEVELOPMENTAL TOXICOLOGY  
STUDIES: TERATOLOGY STUDY OF N-HEXANE  
IN RATS

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No. NIH-YO1-ES-70153

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## ABSTRACT

The straight chain hydrocarbon, n-hexane, is a volatile, ubiquitous solvent used in industrial, academic, and smaller **commercial** environments. The significant opportunity for women of child-bearing age to be exposed to this chemical prompted the undertaking of a study to assess the developmental toxicity of n-hexane in an animal model. Timed-pregnant (30 animals per group) and virgin (10 animals per group) Sprague-Dawley rats were exposed to 0 (filtered air), 200, 1000, and 5000 ppm n-hexane (99.9% purity) vapor in inhalation chambers for 20 h/day for a period of 14 consecutive days. Sperm-positive females were exposed for 6-19 days of gestation (dg) and virgins were exposed concurrently for 14 consecutive days. The day of sperm detection was designated as 0 dg for mated females. Adult female body weights were monitored prior to, throughout the exposure period, and at sacrifice. Uterine, placental, and fetal body weights were obtained for gravid females at sacrifice. Implants were enumerated and their status recorded as live fetus, early or late resorption, or dead. Live fetuses were sexed and examined for gross, visceral, skeletal, and soft-tissue craniofacial defects.

Maternal toxicity manifested as a reduction in extra-gestational maternal weight gain was observed at all exposure levels, and was statistically significant for the 5000 ppm exposure group. Extra-gestational maternal weight gain (calculated from 0 dg to 20 dg) relative to control animals was reduced by 20, 23, and 45% for the 200, 1000, and 5000 ppm exposure groups, respectively. Cumulative weight gain (CWG) for dams in the 1000 and 5000 ppm exposure groups was significantly reduced with respect to controls by 20 dg. The CWG for the 5000 ppm was also significantly reduced with respect to controls by 13 dg.

Comparison of n-hexane exposed groups with the control group (0 ppm) indicated that gestational exposure to n-hexane did not result in an increase in the incidence of intrauterine deaths or in the incidence of fetal malformations. A statistically significant reduction in fetal body weight relative to controls was observed for males at the 1000 and 5000 ppm exposure levels (7 and 15% reduction, respectively). Female weights were also reduced with respect to controls for these exposure levels (3 and 14% reduction, respectively), but the reduction was statistically significant for only the 5000 ppm group. Gravid uterine weight was also significantly less than controls for

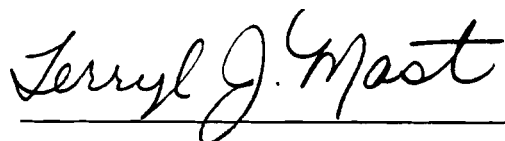
the 5000 ppm exposure groups. A statistically significant increase in the mean percent incidence per litter of reduced ossification of sternebrae 1-4 was observed for the 5000 ppm group, and was positively correlated with exposure concentration. This increased incidence of reduced ossification in the sternebrae, and the reduction in fetal body weight at the 5000 ppm level, may have been inter-related manifestations of a slight growth retardation.

No major abnormalities were found in any of the fetuses. Variations observed included dilated ureter, renal pelvic cavitation, supernumerary ribs, and reduced skeletal ossifications at several sites. The increase in mean percent incidence per litter of reduced ossification of sternebrae 1-4 was statistically significant for the highest exposure concentration, and the increase was positively correlated with increasing exposure concentration. The lowest n-hexane exposure concentration, 200 ppm, proved to be a no observable effect level for developmental toxicity.

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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 performed due to concern that exposure to n-hexane vapors may result in a negative impact on **human** reproductive function and/or fetal development.

An excellent review concerning hexacarbon toxicity and metabolism is available in Experimental and Clinical Neurotoxicology (edited by Spencer and Schaumburg, 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 **neurotox-**icity 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 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 <sup>14</sup>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 response 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 of the high-concentration group.

These studies are rather convincing relative to the absence of **morpho-**logic effects following gestational exposure to n-hexane vapors (despite the low exposure concentration of **1000** ppm 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 potential developmental toxicity of n-hexane, the following study was performed with the goal of maximizing maternal exposure during gestation.

Since it appears that toxicity is a function of concentration vs. duration of exposure over certain concentration ranges for most chemicals, an adequate assessment of the teratologic potential of n-hexane requires evaluations after exposure to a series of concentrations, the highest of which causes some maternal toxicity. To achieve this goal, this study in rats employed multiple exposure levels ranging up to 5000 ppm for 20 **h/day**. (The maximum exposure concentration was limited by safety considerations to 50% of the lower explosion limit, **≈10,000** ppm, for n-hexane [NIOSH, 1981].) These exposures extended throughout the late implantation, organogenic, and fetal developmental stages (**i.e.**, 6-19 dg). Fetal evaluations were performed on 20 dg. A similar study was performed with mice to obtain comparative data in another species, and will be reported elsewhere.

Reported effects on lipid metabolism suggest 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 is disturbing. 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 **sperm-positive** females to determine the effect of n-hexane exposure on the ovaries of non-pregnant rats. Results from this segment of the study 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 Sprague-Dawley rats (Charles River, Raleigh, NC), each consisting of 30 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 14 consecutive days for 20 h/day. Sperm-positive females were exposed on 6-19 days of gestation (dg). The day of a sperm-positive vaginal smear was designated as 0 dg. Exposures commenced at 12 NOON On 6 dg and continued for 20 hours until 8 A.M. on the following morning. The last day of exposure began at 12 NOON on 19 dg and ended at 8 A.M. on the morning of 20 dg. Control animals (0 ppm) were housed in an exposure chamber in the same room, and were handled in the same manner as the rats 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 lower explosion limit, which is  $\approx 11,000$  ppm (NIOSH, 1981).

**Exposure** Bulk chemical purity analyses were performed on the single lot of n-hexane used for rat 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 299.5% (Research Triangle Institute [RTI] lot no. H-201).

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, distribution line, 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, 994 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<sup>3</sup> (1.7 m<sup>3</sup> 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 (HEPA and charcoal filtered before addition of the test article) flowed through the chamber at approximately 15 air changes per hour.

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 5-gallon reservoir which was renewed daily. The test material was delivered 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, with and without animals in the chambers, were checked during the first week of the study, Figure 1. The time required to reach 90% of the target concentration ( $T_{90}$ ) ranged from 11.0 - 11.5 min. The decay time (the time required to reach 10% of the target concentration [ $T_{10}$ ]) with animals present ranged from 10.0 - 11.0 min. Uniformity of vapor concentration in the exposure chambers was measured prior to the start of, and once during the study. Uniformity in all chamber was found acceptable (e.g.  $\pm 10\%$ ).

**Animal Husbandry** Upon receipt, all animals were housed in a quarantine room for 20 days prior to the start of the study. Males and females were caged separately on wire racks equipped with automatic waterers (five animals per cage). At the end of the quarantine period five females and five males were killed and examined for internal and external parasites and bacterial pathogens. Serum from each animal was tested for antibodies to selected pathogens, and histopathologic examinations of lung, liver, kidney, ileum, colon, heart and Harderian gland were performed (Appendix D). Another check for antibodies to selected viral pathogens was performed on five females from the control group and five females from the 5000 ppm group on serum obtained at the final 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 house. Due to the long daily duration of the exposures, 20 h, food was left in place during the exposures and replaced daily. 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  $73\pm 3^{\circ}\text{F}$  and humidity was maintained  $50\pm 15\%$ .

During the exposure period all chambers were maintained within the limits of  $75\pm 3^{\circ}\text{F}$ . Actual temperature means were between 74.2 and  $76.8^{\circ}\text{F}$ , all within the specified limits. Mean relative humidity in all exposure chambers was between 52.5 and 57.7%; these values were within the specified limits of  $55\pm 15\%$ . The average air flow in all chambers for the study was between 14.3 and 15.3 CFM (1 CFM = 1 air change per hour), all flows were within the speci-

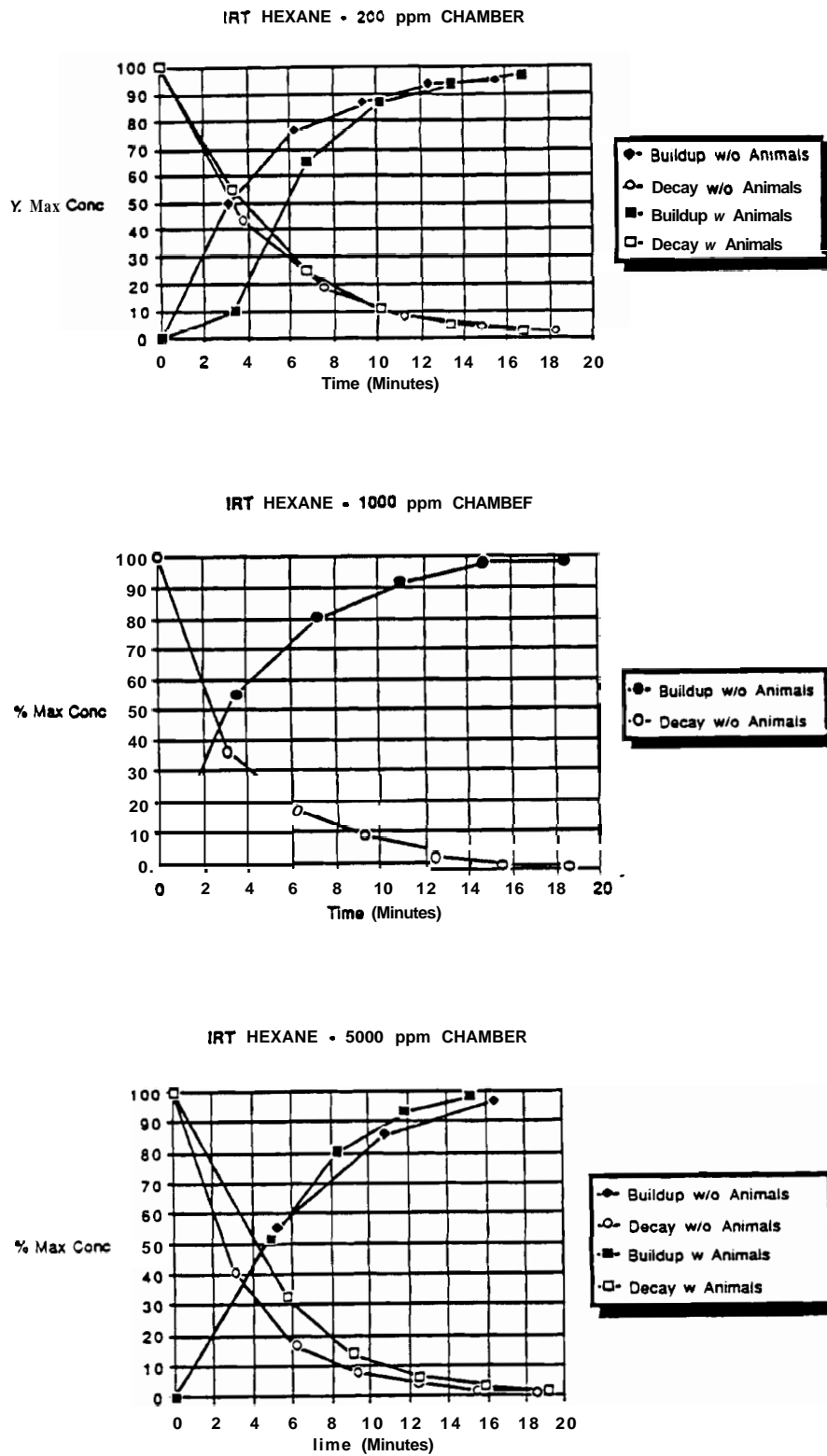


Figure 1. Buildup and decay of vapor concentrations in the 200 and 5000 ppm chambers (with and without animals present), and in the 1000 ppm chamber (without animals present).

fied 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 rats 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 a microscopic examination of vaginal lavage fluid for sperm; if positive, this day was designated as 0 dg. At this time, the **sperm-positive** females were weighed and randomly assigned to exposure groups, again using body weight as the blocking variable. Mating was conducted for four successive nights to obtain the desired number of sperm-positive females. Three days prior to the start of the exposure, virgins and sperm-positive females were placed in a holding chamber for acclimatization.

Sperm-positive females were weighed on 0, 6, 13, and 20 dg and virgins were weighed 14 days prior to the start of exposure, on exposure days 1 and 8, and at the time of sacrifice. The pregnant females were removed from the exposure chambers on the morning of 20 dg, weighed and euthanized with CO<sub>2</sub> after which their uteri were removed and weighed. Virgins were killed on the day after their last day of exposure. At the time of sacrifice, animals were examined grossly for signs of toxicity.

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, examined for gross defects, and their sex was determined. All live fetuses were examined for visceral defects and their sex was confirmed at this time. Visceral exams were performed on fetuses euthanized with an injection of **Nembutal®** (sodium pentobarbital). 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

for examination of 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. Duncan's multiple-range test (two-tailed) was used to assess statistically significant differences between control and exposed groups. 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 a basis for analysis of fetal variables.

## **RESULTS**

Summaries of the concentration data for all chambers are shown in Table 1. The daily **mean** concentrations for all chambers were within 8% of the target concentrations. More detailed summaries of concentration data as well as summaries of environmental data are included in Appendix B along with graphic illustrations of the daily mean and standard deviation for each chamber.

Although decomposition of n-hexane was not anticipated under the storage and generation conditions employed, test material stability for a reservoir sample aged five days was confirmed. Purity analyses were performed on samples collected from the high and low chambers before and during animal exposures. 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. No evidence of impurities or degradation products were found in samples from the exposure chambers.

Each exposure group consisted of 30 sperm-positive female rats and 10 virgin female rats. All animals were killed following the 14<sup>th</sup> day of expo

Table 1. N-Hexane Rat 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
17	0	0	0%	0	0
Summary	0	0	0%	0	0

200 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	191	36	19%	1	205
2	202	5	2%	189	208
3	201	18	9%	173	276
4	203	11	5%	173	234
5	196	3	2%	188	202
6	204	4	2%	195	209
7	199	3	2%	195	211
8	197	2	1%	191	202
9	205	3	2%	199	220
10	198	6	3%	186	212
11	204	7	3%	194	232
12	203	4	2%	196	212
13	201	5	2%	188	211
14	201	3	1%	196	208
15	198	40	20%	16	218
16	194	35	18%	5	209
17	200	6	3%	188	216
Summary	200	16	8%	1	276

1000 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	1020	100	10%	814	1290
2	1010	106	11%	880	1310
3	1000	91	9%	868	1240
4	993	53	5%	902	1090
5	1020	85	8%	913	1320
6	1000	49	5%	898	1170
7	996	57	6%	916	1240
8	988	51	5%	918	1170
9	1010	53	5%	897	1150
10	998	42	4%	898	1100
11	1010	45	4%	906	1110
12	999	52	5%	878	1120
13	976	91	9%	603	1130
14	999	53	5%	873	1140
15	925	198	21%	468	1470
16	942	169	18%	27	1110
17	1010	58	6%	818	1160
Summary	994	89	9%	27	1470

5000 ppm n-Hexane					
Exposure Day	Mean	Std Dev	%RSD	Min	Max
1	5030	204	4%	4670	5490
2	5040	270	5%	4170	5340
3	5000	148	3%	4720	5260
4	4960	176	4%	4670	5470
5	4900	55	1%	4740	4990
6	4980	144	3%	4600	5240
7	5030	96	2%	4740	5270
8	4980	100	2%	4770	5120
9	4980	143	3%	4700	5230
10	4900	119	2%	4750	5300
11	5040	115	2%	4710	5280
12	5060	82	2%	4870	5210
13	5050	189	4%	4480	5260
14	5140	73	1%	4970	5260
15	4870	954	20%	735	5380
16	4810	835	17%	17	5220
17	4960	95	2%	4750	5130
Summary	4990	312	6%	17	5490

sure, 86% of the sperm-positive females were found to be pregnant at the time of sacrifice. Exposure to n-hexane vapors on 6-19 dg had no effect on the number of implantations, the mean percent of live pups per litter, the mean percent of resorptions per litter, or on the fetal sex ratio, Tables 2 and 3. There were no maternal deaths and no clinical signs of toxicity were noted; however, two pregnant dams (5000 ppm group), one non-pregnant female (200 ppm group), and one virgin (5000 ppm group) were found to have ulceration sites in the cardiac region of the stomach and no food in the digestive tract at the time of sacrifice.

The mean body weight of virgin females exposed to 5000 ppm n-hexane vapor for 14 consecutive days, Table 4, was significantly less than the mean weight for virgin control animals by exposure day 8, and remained so at the time of sacrifice. Mean body weights of virgin females in the other two exposure levels, 200 and 1000 ppm, were not affected at any time during the exposure period or at the time of sacrifice.

Pregnant females exposed to 5000 ppm n-hexane showed a significant decrease in mean body weight by 13 dg when compared to that of control animals and an even greater reduction by 20 dg, Table 5. A decrease in body weight was observed by 13 dg for both the 200 and 1000 ppm with a further reduction by 20 dg; however, these decreases were not statistically significant. Mean cumulative weight gains for pregnant ~~rats~~ **exposed** to n-hexane vapors and that for control animals are shown graphically in Figure 2. There was an exposure-related decrease in the cumulative **body** weight gain of the pregnant females. This reduction relative to control animals was statistically significant for the 1000 ppm group at 20 dg, and for the 5000 ppm group at 13 and 20 dg.

The mean gravid uterine weight at the time of sacrifice was reduced for all treatment groups as compared to controls; however, the difference was significant only in the 5000 ppm group, Table 5. The extra-gestational weight gain (EGWG; body weight at the time of sacrifice minus the gravid uterine weight) was also reduced for all treatment groups when compared to controls, and again, the difference was only significant for the 5000 ppm group. The mean ratio of uterine weight to extra-gestational weight gain for the 5000 ppm group was significantly greater than the mean ratio for the control group, Figure 3.

Table 2. N-Hexane Rat Teratology Study: Reproductive measures for female rats (mean  $\pm$  std).

	n-Hexane Chamber Concentration (ppm)			
	0	200	1000	5000
<b>NUMBER OF:</b>				
Sperm-positive Rats Exposed (a)	30	30	30	30
Number pregnant rats	24	24	27	28
Pregnant rats (%)	80.0	80.0	90.0	93.3
Litters with live fetuses	23 (b)	24	27	28
Implantations/dam	15.8 $\pm$ 2.3	15.3 $\pm$ 2.4	15.5 $\pm$ 3.0	15.4 $\pm$ 2.7
Live fetuses/litter	14.7 $\pm$ 2.8	14.6 $\pm$ 2.4	14.5 $\pm$ 3.3	14.6 $\pm$ 2.8
Resorptions/litter	1.1 $\pm$ 0.8	0.7 $\pm$ 1.1	1.0 $\pm$ 1.2	0.8 $\pm$ 1.0
Early	0.9 $\pm$ 0.9	0.6 $\pm$ 1.0	0.8 $\pm$ 1.1	0.6 $\pm$ 0.9
Late	0.2 $\pm$ 0.4	0.1 $\pm$ 0.4	0.2 $\pm$ 0.4	0.1 $\pm$ 0.4
Dead fetuses/litter	0	0	0	0
<b>PERCENT OF:</b>				
Live fetuses/litter	92.6 $\pm$ 6.0	95.6 $\pm$ 6.5	92.2 $\pm$ 11.5	94.9 $\pm$ 6.3
Resorptions/litter	7.4 $\pm$ 6.0	4.4 $\pm$ 6.5	7.8 $\pm$ 11.5	5.2 $\pm$ 6.3
Early	6.2 $\pm$ 6.3	3.9 $\pm$ 6.2	5.9 $\pm$ 8.3	4.3 $\pm$ 6.2
Late	1.1 $\pm$ 2.5	0.6 $\pm$ 2.7	1.9 $\pm$ 5.3	0.8 $\pm$ 2.1

(a) Does not include 10 virgin females per exposure group.

(b) One pregnant animal dropped from study because of broken tooth; only 23 litters examined.

Table 3. Average fetal and placental weights (g) for rat litters exposed to n-hexane vapors in utero (mean  $\pm$  std).

	n-Hexane Chamber Concentration (ppm)			
	0	200	1000	5000
Litters Examined	23	24	27	28
Fetuses examined	339	350	392	408
Heads examined	170	157	186	205
Sex Ratio (M/F)	0.53 $\pm$ 0.14	0.48 $\pm$ 0.11	0.46 $\pm$ 0.17	0.54 $\pm$ 0.14
Fetal weight	3.48 $\pm$ 0.37	3.54 $\pm$ 0.36	3.27 $\pm$ 0.32 (a)	2.97 $\pm$ 0.38 (b)
Placental weight	0.44 $\pm$ 0.05	0.42 $\pm$ 0.05	0.41 $\pm$ 0.06	0.38 $\pm$ 0.05 (b)
Fetal weight:				
Male	3.60 $\pm$ 0.39	3.66 $\pm$ 0.39	3.33 $\pm$ 0.33 (b)	3.05 $\pm$ 0.41 (b)
Female	3.33 $\pm$ 0.37	3.43 $\pm$ 0.37	3.23 $\pm$ 0.32	2.86 $\pm$ 0.36 (b)
Placental weight				
Male	0.45 $\pm$ 0.05	0.43 $\pm$ 0.05	0.41 $\pm$ 0.05 (a)	0.37 $\pm$ 0.05 (b)
Female	0.43 $\pm$ 0.05	0.42 $\pm$ 0.05	0.41 $\pm$ 0.07	0.37 $\pm$ 0.05 (b)

(a) Significantly less than controls at  $p < 0.05$ .

(b) Significantly less than controls at  $p < 0.01$ .



Table 4. N-Hexane Rat Teratology: Mean Body Weights (g  $\pm$  std) for Virgins

Exposure Concentration	Exposure Day -14		Exposure Day 1		Exposure Day 8		Day of Sacrifice	
	N	Mean $\pm$ STD	Mean $\pm$ STD	Mean $\pm$ STD	Mean $\pm$ STD	Mean $\pm$ STD	Mean $\pm$ STD	Mean $\pm$ STD
0 ppm	10	260.0 $\pm$ 17.3	272.3 $\pm$ 18.0	283.0 $\pm$ 22.1	287.6 $\pm$ 23.2			
200 ppm	10	261.4 $\pm$ 22.2	273.0 $\pm$ 24.5	288.3 $\pm$ 27.8	290.9 $\pm$ 29.0			
1000 ppm	10	263.6 $\pm$ 26.3	269.1 $\pm$ 25.0	283.6 $\pm$ 28.7	282.4 $\pm$ 29.6			
5000 ppm	10	263.5 $\pm$ 24.4	268.3 $\pm$ 23.0	256.2 $\pm$ 27.0	252.7 $\pm$ 33.7	a		

a = Significantly different from control groups at  $p < 0.05$ .

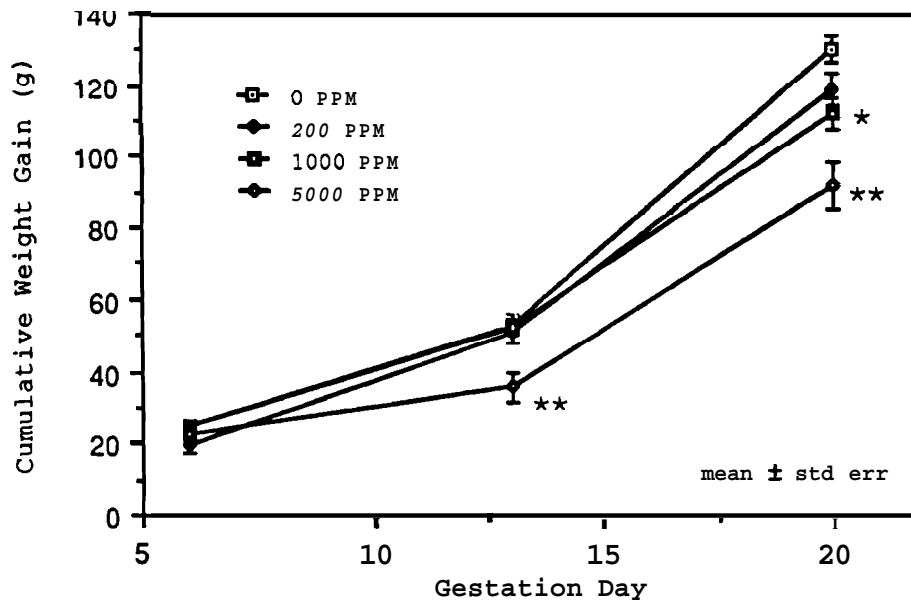
Table 5. N-Hexane Rat Teratology Study: Mean Body, Uterine, and Extra-gestational Weights (g  $\pm$  std) for Pregnant Dams.

Exposure Concentration	Body Weights					Weights	
	DG 0		DG 6	DG 13	DG 20	Extra-gestational Gain	
	N	Mean ±STD	Mean ±STD	Mean ±STD	Mean ±STD	Mean ±STD	Mean ±STD
0 ppm	23	278.0 ± 16.9	302.5 ± 18.0	331.2 ± 20.6	408.1 ± 29.2	79.2 ± 14.6	51.0 ± 13.4
200 ppm	24	275.8 ± 19.5	295.5 ± 24.6	326.4 ± 25.6	394.8 ± 34.8	78.2 ± 13.7	40.8 ± 20.8
1000 ppm	27	272.8 ± 21.0	297.2 ± 22.3	325.1 ± 24.1	385.2 ± 28.4	73.3 ± 16.5	39.2 ± 19.8
5000 ppm	28	274.6 ± 19.7	297.4 ± 23.9	310.2 ± 33.1	366.9 ± 45.0	69.5 ± 13.9	28.5 ± 17.5

a = Significantly different from control groups at  $p < 0.05$ .

b = Significantly different from control groups at  $p < 0.01$ .

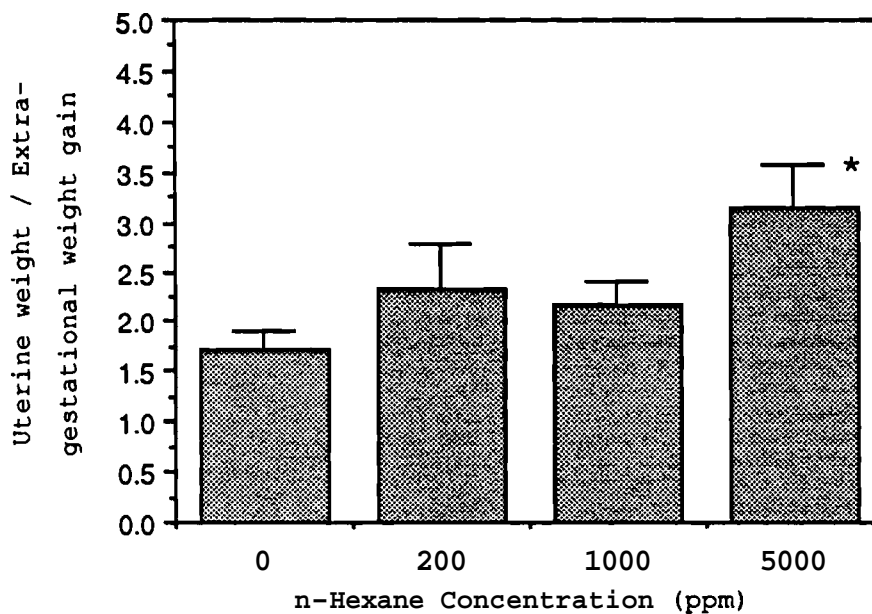
c = Uterine weight for animal 690 missed, n = 27.



• Significantly different from controls at  $p < 0.05$ .

\*\* Significantly different from controls at  $p < 0.01$ .

Figure 2. Cumulative weight gain for pregnant dams (dg 6 through dg 20) exposed to increasing concentrations of n-hexane during gestation.



\* Sig. different from control,  $p < 0.01$ .

Figure 3. The ratio of gravid uterine weight to maternal extra-gestational weight gain at 20 dg.

Fetal weights, means of litter means, male and female combined, were significantly reduced for the two highest exposure groups, 1000 and 5000 ppm, when compared to controls, Table 5. When mean fetal weights were examined on the basis of sex, male weights were found to be significantly reduced for the 1000 and 5000 ppm exposure groups as compared to controls. Mean female fetal weights were also reduced for both the 1000 and 5000 ppm groups when compared to controls; however, only the 5000 ppm group was significantly different from controls. Although there was a difference in the statistical significance of the treatment-related weight reduction between male and female fetuses, the percent reduction in mean fetal weights for male and female fetuses in the 5000 ppm group was equivalent,  $\approx 15\%$ .

An average of 373 fetuses per exposure group were examined for gross, visceral and skeletal defects, Table 6. No major malformations were found in any of the fetuses. Variations observed included dilated ureters, renal pelvic cavitation, rib anomalies, and reduced ossifications. Reduced ossifications in the pelvis, the skull, and the phalanges are presented as bone group totals in Table 6 although each bone in a group was evaluated individually, i.e. "pelvis" represents the ilium, the ischium, and the pubis.

There was an increase in the mean percent incidence per litter of reduced ossification in sternebrae 1-4<sup>1</sup>, Table 7. The increase was statistically significant for the 5000 ppm group, and the correlation to exposure concentration was highly significant ( $p < 0.001$ ).

## DISCUSSION

The only indication of developmental toxicity following exposure of pregnant rats to 200, 1000 or 5000 ppm n-hexane vapors on days 6-19 of gestation (consecutively) for 20 h/day was a small reduction in fetal body weight relative to controls. This fetal weight reduction was observed

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<sup>1</sup> The incidence of reduced ossification in sternebrae 5 and 6 are not reported here as they were ossified in only  $\approx 5\%$  of the control fetuses. These findings are consistent with our historical data.

Table 6. N-Hexane Rat Teratology Study: Variations Observed in Live Fetuses.

		Fetuses *				Litters			
n-Hexane (ppm)		0	200	1000	5000	0	200	1000	5000
Total fetuses examined (a)		339	350	392	408	23	24	27	28
Heads examined (b)		170	157	186	205	23	24	27	28
Skulls examined (c)		169	193	206	203	23	24	27	28
Dilated ureters	NO. (%)	25 (7.4)	24 (6.9)	20 (5.1)	12 (2.9)	9 (39.1)	13 (54.2)	11 (40.7)	7 (25.0)
Renal pelvic cavitation	NO. (%)	8 (2.4)	0 (0.0)	3 (0.8)	2 (0.5)	4 (17.4)	0 (0.0)	2 (7.4)	2 (7.1)
Supernumary ribs	NO. (%)	4 (1.2)	6 (1.7)	12 (3.1)	15 d (3.7)	3 (13.0)	4 (16.7)	2 (7.4)	6 (21.4)
Bent or knobby ribs	NO. (%)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.7)	0 (0.0)
Reduced Ossification:									
Sternebrae 1-4	NO. (%)	42 (12.4)	54 (15.4)	103 (26.3)	157 (38.5)	15 (65.2)	17 (70.8)	22 (81.5)	26 (92.9)
Vertebral centra	NO. (%)	28 (8.3)	16 (4.6)	19 (4.8)	36 (8.8)	12 (52.2)	8 (33.3)	11 (40.7)	14 (50.0)
Pelvis (d)	NO. (%)	11 (3.2)	7 (2.0)	21 (5.4)	21 (5.1)	4 (17.4)	6 (25.0)	9 (33.3)	7 (25.0)
Phalanges	NO. (%)	4 (1.2)	2 (0.6)	1 (0.3)	7 (1.7)	3 (13.0)	2 (8.3)	1 (3.7)	3 (10.7)
Skull (e)	NO. (%)	10 (5.9)	6 (3.1)	11 (5.3)	12 (5.9)	4 (17.4)	6 (25.0)	6 (22.2)	6 (21.4)

- A single fetus may be represented more than once in this table.
- a) 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.
- b) Heads removed from fetuses and fixed in **Bouin's** solution then examined for soft-tissue craniofacial malformations.
- c) Heads remained on the fetuses that were stained for skeletal examination; see **a)** above.
- d) The **ischium**, the **ilium** and the **pubis** were evaluated individually and then grouped. Approximately **90%** of reduced pelvic ossifications were in the pelvic bone.
- e) The **interparietal**, **parietal**, **supraoccipital**, **frontal** and **nasal** bones were evaluated individually and then grouped. Approximately **80%** of the reduced skull ossifications were in the **interparietal** or **parietal** bones.

Table 7. N-Hexane Rat Teratology Study: Observed variations -  
Mean percent per litter.

	n-Hexane Concentration (ppm)			
n-Hexane Concentration	0	200	1000	5000
Number of litters (a)	23	24	27	28
	% $\pm$ SID	% $\pm$ SID	% $\pm$ SID	% $\pm$ SID
Dilated ureter(s)	8.0 $\pm$ 14.5	6.8 $\pm$ 8.5	4.8 $\pm$ 7.0	3.0 $\pm$ 5.7
Renal pelvic cavitation	2.5 $\pm$ 6.0	0.0 $\pm$ 0.0	0.6 $\pm$ 2.4	0.4 $\pm$ 1.6
Supernumary ribs	1.2 $\pm$ 3.3	2.0 $\pm$ 5.5	3.3 $\pm$ 13.4	3.6 $\pm$ 9.7
Bent or knobby ribs	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.4 $\pm$ 2.1	0.0 $\pm$ 0.0
<b>Reduced Ossification:</b>				
Sternebrae 1-4 (b)	13.8 $\pm$ 21.6	16.3 $\pm$ 16.5	29.0 $\pm$ 28.6	38.7 $\pm$ 23.7 c
Vertebral centra	8.8 $\pm$ 16.4	5.8 $\pm$ 13.6	6.7 $\pm$ 12.4	8.5 $\pm$ 12.8
Pelvis	4.4 $\pm$ 16.3	2.2 $\pm$ 4.3	5.5 $\pm$ 10.9	5.4 $\pm$ 14.7
Phalanges	1.5 $\pm$ 4.8	0.6 $\pm$ 2.0	0.4 $\pm$ 2.1	2.3 $\pm$ 8.4
Skull	3.5 $\pm$ 10.4	1.8 $\pm$ 3.4	3.0 $\pm$ 6.4	3.0 $\pm$ 8.4

- a) A single fetus may be represented more than once in this table.  
b) The increase in the mean percent of the litter affected is directly correlated with exposure concentration ( $p < 0.01$ ).  
c) Significantly greater than control group ( $p < 0.05$ ).

for both sexes at the 1000 and 5000 ppm exposure levels (7% and 15%, respectively). There was no exposure-related increase in either the percent of resorbed fetuses or in the incidence of fetal malformations. The increased incidence of reduced ossification in sternebrae 1-4 and the reduction in fetal weight at the 5000 ppm level may have been inter-related and manifestations of a slight growth retardation.

The small amount of developmental toxicity to the conceptus was in contrast to the significant level of maternal toxicity observed following n-hexane exposures. A reduction in maternal extra-gestational weight gain was observed at all exposure levels although the reduction did not become statistically significant until the 5000 ppm level. Extra-gestational weight gain relative to control animals was reduced by 20, 23, and 45% for the 200, 1000, and 5000 ppm exposure groups, respectively.

The exposure-related decrease in fetal weight and the increase in the incidence of reduced ossification in sternebrae 1-4 in the offspring noted in this study have also been noted previously. Similar findings were reported by Bus et al. (1979) who exposed a relatively small number (<10) of Fisher 344 rats to 1000 ppm n-hexane vapor on 8-16 dg. Although they did not observe a statistically significant reduction in fetal body weight, they reported that ~25% of the fetuses in the exposed groups had reduced ossification of the 4<sup>th</sup> sternebra as compared to 0% in the control group, thus indicating some effect of treatment on the offspring. It was not possible to assess the level of maternal toxicity achieved in their study since no maternal data were reported. Bus et al. (1979) also pointed out that the lack of fetotoxicity or teratogenicity following gestational exposure to n-hexane vapors was not due to the inability of n-hexane or its major metabolites, methylbutylketone and 2,5-hexanedione, to reach the conceptus since the levels of parent compound and metabolites in the fetus closely approximated levels found in maternal blood.

Pregnancy did not appear to be a significant factor in n-hexane toxicity to adult females since virgin females, concurrently exposed to the same concentrations, demonstrated a similar reduction in weight gain. Like the pregnant females, virgins exposed to 5000 ppm n-hexane showed a significant reduction in body weight by the 8<sup>th</sup> day of exposure as compared to controls (The

8<sup>th</sup> day of exposure for virgins was equivalent to 13 dg in the pregnant group).

In summary, exposure to 200, 1000 or 5000 ppm n-hexane during gestation did not result in an increase in either the incidence of intrauterine death or in the incidence of fetal malformations. However, some fetal growth retardation as evidenced by an exposure-related reduction in mean fetal body weights and an exposure-related increase in the incidence of reduced ossification of sternebrae 1-4 in the fetuses was observed. An exposure-related reduction in maternal weight gain with respect to controls was also observed with the reduction becoming significant at the 5000 ppm level. The lowest n-hexane exposure concentration, 200 ppm, proved to be a no observable effect level for developmental toxicity.

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APPENDIX A

ANALYTICAL CHEMISTRY NARRATIVE AND  
DATA FOR N-HEXANE

APPENDIX B

ANALYTICAL CHEMISTRY LABORATORY AND  
FIELD AND W-10000

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-201) was received in two shipments. The first shipment arrived 4/2/86 and consisted of two 55-gallon drums containing 108 gallons of n-hexane (Identified as BNW Lot 51436-5). The second shipment arrived 4/17/86 and consisted of two 55-gallon drums containing 102 gallons of n-hexane (Identified as BNW Lot 51436-6).

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 11.5 kg of test material were required for each exposure day. The usage of n-hexane for the rat teratology study is summarized in Table 1.

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

<u>Exposure Period</u>	<u>RTI Lot#</u>	<u>BNW Lot#</u>	<u>Test Material Used</u>
5/13/86 - 5/21/86	H-201	51436-5 (Drum 2)	104.1 kg
5/22/86 - 5/30/86	H-201	51436-6 (Drum 1)	104.8 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 4 mm od x 6 ft glass column packed with 0.1% SP-1000 on 80/100 Carbowax B. Since RTI provided no reference material, portions of a previous shipment (BNW 50846-39-1) were placed in septum vials, identified as BNW 50846-145, stored in the freezer, then used as reference material. BNW Lot 51436-5 was analyzed for bulk purity and found to be 99.5% pure relative to the frozen reference material.

3. Vapor Concentration Monitoring

A Hewlett-Packard 5840 gas chromatographic system (employing a 1/8" od x 1.0 foot nickel column packed with 1% SP-1000 on 60/80 mesh Carbowax 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 distribution line, 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 od 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 4-6%. 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 994 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  $\pm 10\%$  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 0.02 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 0.19 min.; the retention time for n-hexane was 1.49 minutes. Thus, the partition ratio was about 6.8.

d. Precision, Linearity and Absolute Recovery Evaluation

Precision for the on-line GC was estimated from 5 measurements made on the 994 ppm on-line standard; a 0.4% coefficient of variation (CV) was observed (all values fell within  $\pm 1$  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 5/21/86. n-Hexane, **BNW** Lot 51436-5, 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 10.6 and 1.0 liter collection volumes for the 5000 ppm and 200 ppm chambers. Occupied chambers were sampled on 5/21/86 and samples were analyzed on 6/11/86. 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 1% breakthrough of total sample was observed for the 1.0 and 10.6 liter samples from the 203 ppm chamber. Breakthrough was found to be approximately 3% for the 1.0 liter sample and 35% for the 10.6 liter sample from the 5000 ppm chamber. These determinations were made by analysis of the secondary charcoal bed within the tubes. A peak observed at 3.5 minutes in the carbon disulfide blank was obscured by the n-hexane. Analysis of these samples showed no evidence of impurities or degradation products.

Gas Chromatography Degradation Analysis of n-Hexane  
Chamber Atmosphere with Charcoal Tube Sample Collection  
(occupied chambers)

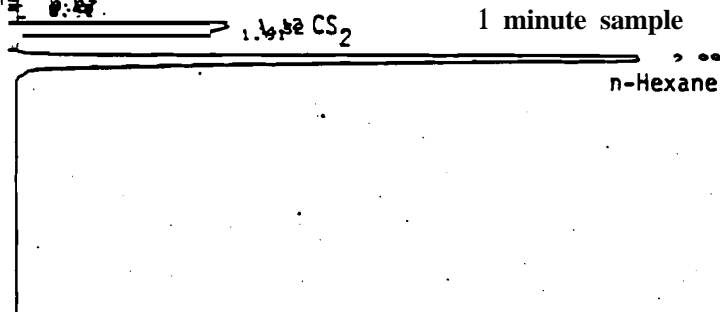
GC Parameters

Column: 2mm x 1.8m ID glass; packed  
with Porapak QS 100/120

TEMP1 400 200 200  
TIME1 15.88  
INJ TEMP 400 200 200  
FID TEMP 400 250 250  
CMT SPD 0.50  
ZERO 18.0  
ATTN 2+ 8  
FID SGNL 40  
SLP SENS 0.10  
AREA PEJ 1-  
FLOW A 0.8 38.7  
FLOW B 8.1 3.8

DELETE CHANGE RUN 2  
CHANGE RUN 0 2  
OPTN 3 2  
INJ/BTL STROKE 1 2 2  
CHANGE RUN 2 7 STOP  
START 0.83

200 ppm Front(next to glass wool)

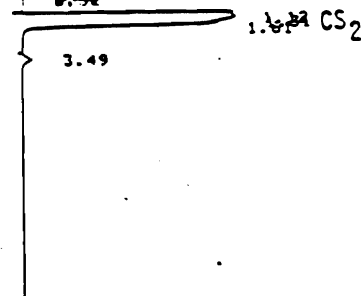


HP RUN 0 I JUN/11/86 TIME 17:21:01  
ID: 18786 BOTTLE 1

RT	AREA	AREA %
0.83	384	0.021
0.27	674	0.046
0.40	135	0.009
0.52	278	0.018
1.12	32478	2.283
1.32	289908	19.673
1.61	96848	6.572
2.98	1853888	71.458

DIL FACTOR: 1.0000 E+ 0

START 0.83 200 ppm Back(between foam plugs)  
0.42 1 minute sample



HP RUN 0 2 JUN/11/86 TIME 17:37:34  
IS: 18786 BOTTLE 3  
AREA %

RT	AREA	AREA %
0.83	261	0.068
0.27	786	0.182
0.40	143	0.033
0.52	298	0.069
1.12	27668	6.392
1.31	291288	67.297
1.61	181488	23.434
3.49	18968	2.533

n-Hexane Rat Teratology Study  
Appendix A - Chemistry

START 4 0:37 5000 ppm Front(next to glass wool)  
1.32 CS<sub>2</sub> 10 minute sample  
n-Hexane

HP RUN 13 JUN/11/86 TIME 20:38:49  
ID: 18706 BOTTLE 25  
AREA %

RT	AREA	AREA %
0.03	189	0.001
0.27	670	0.002
0.40	102	0.000
0.52	160	0.000
1.13	25330	0.074
1.30	384400	1.112
2.92	3393000	98.804

START 1 0:37 5000 ppm Back(between foam plugs)  
1.32 CS<sub>2</sub> 10 minute sample  
n-Hexane

HP RUN 14 JUN/11/86 TIME 20:55:17  
ID: 18706 BOTTLE 27  
AREA %

RT	AREA	AREA %
0.03	233	0.001
0.27	743	0.004
0.40	115	0.001
1.12	27750	0.146
1.32	383300	2.012
2.95	1964000	97.837

START 1 0:37 Blank-Front(next to glass wool)  
1.32 CS<sub>2</sub>  
3.50  
10.50

HP RUN 18 JUN/11/86 TIME 22:00:52  
ID: 18786 BOTTLE 35  
RRER %

RT	AREA	AREA %
0.03	210	0.051
0.27	822	0.200
0.52	235	0.057
1.12	24050	5.847
1.31	373700	90.850
3.50	12070	2.934
10.50	249	0.061

BULK CHEMICAL REANALYSIS

COMPOUND: n-HEXANE  
CAS# 110-54-3  
LOT# Phillips lot# H-116 (BNW#50846-39 both 1-20)  
APPEARANCE: Clear liquid  
RECEIPT DATE: 2/12/86  
ANALYSIS PERIOD: Initial  
STORAGE TEMPERATURE: Room Temperature  
SAMPLE SUBMITTAL DATE: 2/27/86  
SAMPLE ANALYSIS DATE: 316,7186  
ANALYSIS PROCEDURE: Method provided by MRL, dated December 17, 1984  
NOTEBOOK REFERENCE: BNW 5143610

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

ASSAY: Gas chromatography using a 6ft x 4mm glass column packed with 0.1% SP-1000 on 80/100 Caropak C.

Instrument: HP 5830A

Results: % Purity  
Date Bulk  
3186 RRF 0.5606 RSD  $\pm$  0.23%

Retention Time of n-Hexane -2.6 minutes.  
Retention Time of Internal Standard - 7.4 minutes.  
A minor impurity peak was detected at ~ 1.8 minutes

Test material sample was taken from bottle 1.

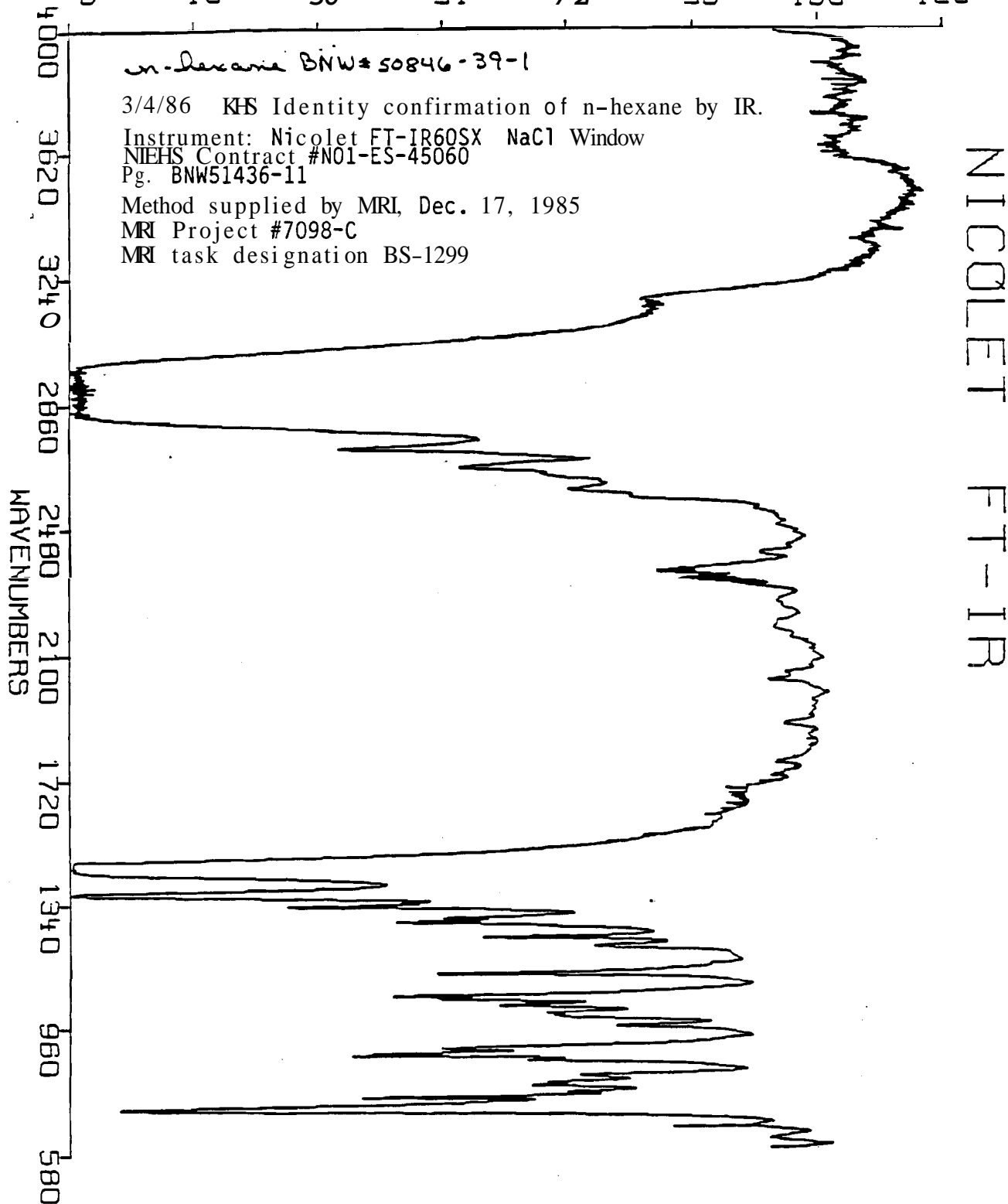
**CONCLUSIONS:** The basis of the analysis is quantitation of the major component of the bulk chemical by GC major peak comparison to a frozen reference material. No reference material was provided. 5 x 10 ml portions of n-hexane were placed in glass septum vials, sealed with teflon lined septa and stored frozen for use as reference materials in future analyses. Infrared spectra was obtained between 4000cm<sup>-1</sup> and 600cm<sup>-1</sup>. The spectra was similar to that provided by MRL.

Signature of Technician: Kathleen Stoney Date: 3-24-86

Signature of Chemist: Bill Koberg Date: 3/23/86



3-T-86 KHS Identity confirmation of n-hexane by IR  
Instrument: Nicolet FT-IR60SX NaCl windowed  
NIEHS Contract # N01-ES-45060  
Pg. BNW51436-11  
Method supplied by MRI, Dec. 17, 1985  
MRI Project #7098-C  
MRI task designation BS-1299



n-Hexane Rat Teratology Study  
Appendix A - Chemistry

3-6-82 cont  
7. re: are survey analysis - p. BWW 51436-60-11) (7)

BWW50846-39-1

U.C. 105830A 1807630

Column: 75:00 Carboxyl C/o.19. SP-1000 (1.9m x 4mm ID, 4000)

Time Control # NO1-53-43660

MEP-3099-C

MLT Tax exemption 88-199

Dec. 17, 1949

```

TEMP1      158      158
TEMP1      ta. 2
TEMP1      4.78
TEMP2      157
TEMP2      1.6
IMU TEMP    zaa      282
FID TEMP    258
OVER MAX    488

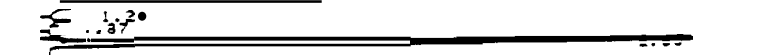
```

CHT SPD	8.58
ATTN 2T	12
FID SGHL	+8
SLP SENS	8.12
AREA REJ	1
FLOW A	2
FLOW B	62
CPTH	22

22  
XF1 1.8888 E- ■ ~~in-lane~~ BNWS0846-39-1

ATTN: \_\_\_\_\_ E-207 \_\_\_\_\_

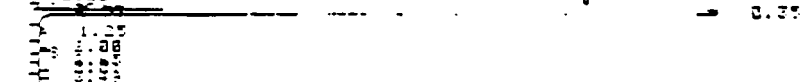
B.35



ST  
BOTTLE 33  
# 593BA  
NO METHOD

RT	AREA	AREA %
2.33	311888	8.872
2.35	48128888	93.137
1.24	121688	8.828
1.87	9528	8.882
2.65	18468888	2.428
7.44	18668888	4.712

Blank, viz. 1 - Toluene

[illegible][illegible]

RT	AREA	AREA %
0.26	688	0.000
0.33	294800	0.070
0.35	403400000	95.534
1.25	108700	0.026
2.00	2935	0.001
2.65	10100	0.002
3.01	784	0.000
3.49	214	0.000
7.47	19440000	4.367

N-hexane purity analysis - p. BNW51436-(10-11)

Bottle #BNW50846-39-1

GC-HP5830A N807630

Column: 80/100 Carbo-pack C/0.1% SP1000(1.8 m \* 4 mm id, glass)  
(BNW 50846 - 146)

( BNW 50846 - 146)

Method supplied by MRI: NIEHS Contract #N01-ES-45060

**MRI Project #7098-C**

**MRI Task Description BS-199**

Dec. 17, 1984.

# BULK CHEMICAL REANALYSIS

COMPOUND: n-HEXANE  
CAS# 110-54-3  
LOT# Phillips lot# H-201 (BNW 51436-5-1)  
APPEARANCE: Clear liquid  
RECEIPT DATE: 4/2/86  
ANALYSIS PERIOD: Initial  
STORAGE TEMPERATURE: Room Temperature  
SAMPLE SUBMITTAL DATE: 4/3/86  
SAMPLE ANALYSIS DATE: 4/3, 4/86 & 5/5/86  
ANALYSIS PROCEDURE: ØB-AC-3A15-ØØ  
NOTEBOOK REFERENCE: BNW 51436-33 & BNW 51436-45

IDENTITY: Infrared spectroscopy using a Nicolet FT-IR 60SX with 4mm NaCl windows and 0.1mm spacer. (Figures 1 and 2)

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

ASSAY: Gas chromatography using a 6ft x 4mm glass column packed with 0.1% SP-1000 on 80/100 Carbopak C.

Instrument: HP 5840A

RESULTS: Relative % Purity (Figures 3 and 4b)

Date Bulk

4/86 99.5

Retention time of n-Hexane -2.8 minutes.  
Retention time of internal standard -8.0 minutes.

ASSAY: Gas chromatography using a 6 ft x 2mm glass column packed with 0.1 % SP-1000 on 801100 Carbopack C.

Instrument: HP5840A

RESULTS: Impurity Profile

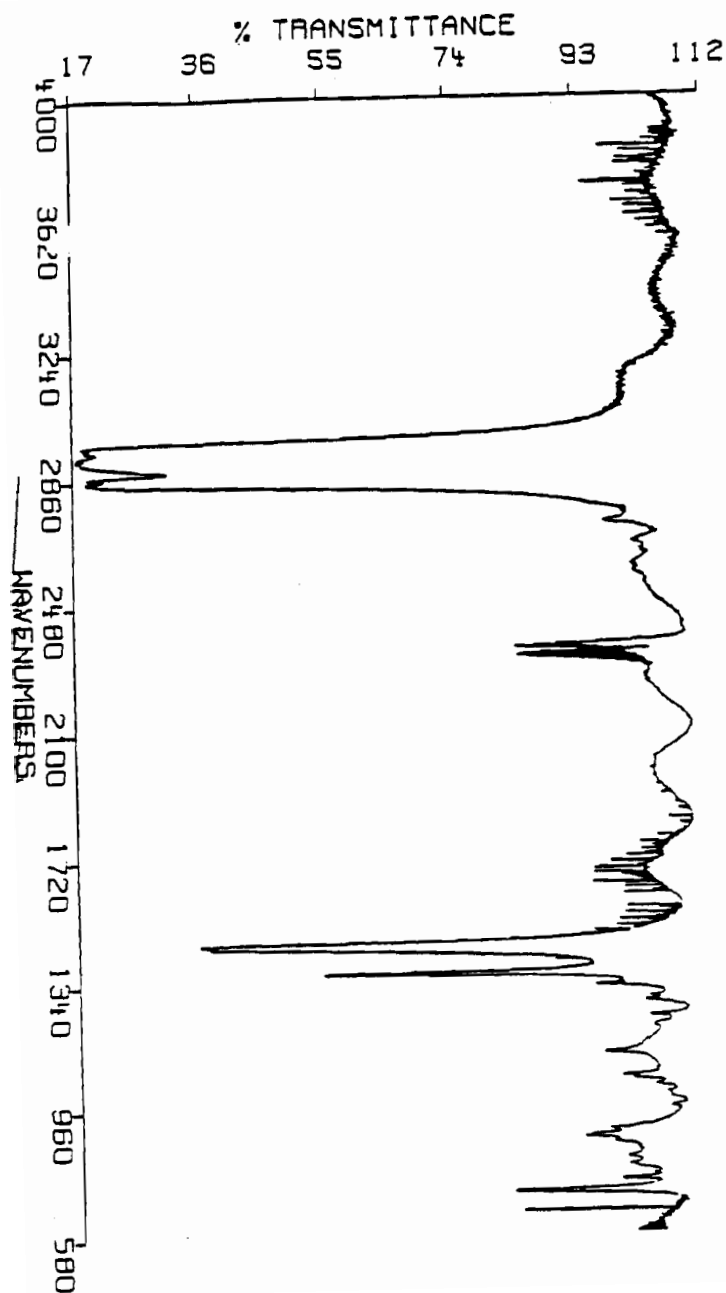
<u>Date</u>	<u>Area %</u>	Reference	Test
5/86	<u>-RT</u>	<u>Material</u>	<u>Material</u>
	9.62	0.113	0.182
	11.64	0.043	0.063
	11.98	0.003	
	16.92	0.001	
	24.90	0.003	0.004

At a retention time of -13.3 minutes a major peak of 99.84% area was observed for the reference material (Figure 5) and 99.75% area for the test material (Figure 6). The reference material showed 5 impurity peaks and the test material showed 3 impurity peaks all over 0.001%.

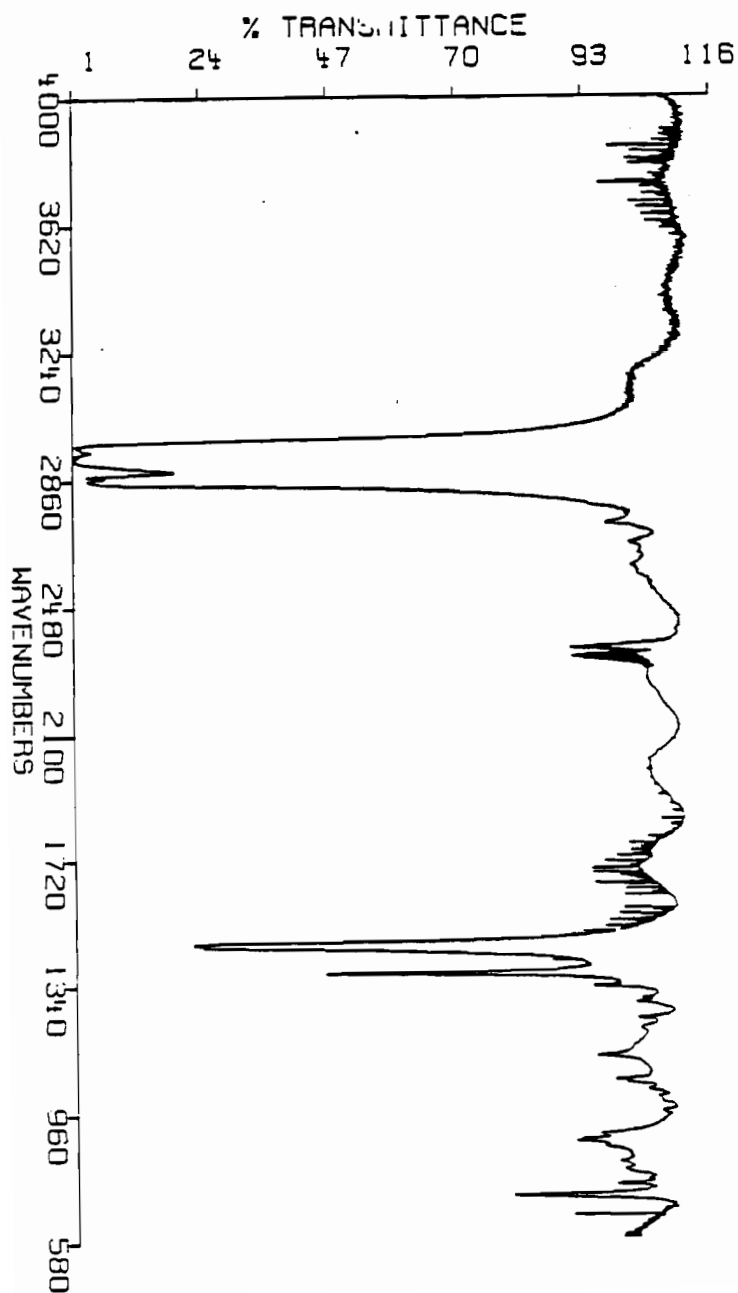
CONCLUSION: Gas chromatography shows this test material to be 99.5% pure by area ratio of an internal standard. The impurity profile showed three impurities greater than 0.001% for the test material. An infrared spectrum was obtained between 4000  $\text{cm}^{-1}$  and 600  $\text{cm}^{-1}$ . The spectrum was similar to previous BNW analysis.

Signature of Technician: K. L. Stoney Date: 5/15/86

Signature of Chemist: R. B. Wallace Date: 5/15/86



4-4-96 Kdl  
Reference n-Hexane #BUW50846-145-1  
Instrument: Nicolet FT-IR 60SX with 360711/14mm NaCl window  
~~Method # 2B-AC-3A15-065~~  
P. BUW51436-341  
Method # 2B-AC-3A15-065



4-4-86 Kld  
n-Hexane from drums BMU 51436-5-1  
~~sample provided by J.F. dated 6/22/86~~ wrong info rec'd -  
Instrument: Nicolet FT-IR 60SX w/836031 5-15-86 Kld  
1mm. NaCl windows, 0.1mm spacer  
P. BMU 51436-34  
Reflected 08-AC-3415-00

n-Hexane Rat Teratology Study  
Appendix A - Chemistry

4-3-86 KHL

Purity Analysis of n-hexane by H.C. major peak  
Method supplied by MFI: December 17, 1984 Comparison

~~Method supplied by MFI: December 17, 1984~~

~~Method supplied by MFI: December 17, 1984~~

~~Method supplied by MFI: December 17, 1984~~

wrong information  
S-15-56 KHL

ESCAPE Method # 08-AC-3A15-09

TEMP1 488 158 158

TIME1 15.88

INJ TEMP 400 200 208

FID TEMP 400 250 250

GC: HP5840A WA10706

Column: 1.8x4mm ID glass

80/100 Carboxack C/0.1% SP-1000

BNW50846-146

CHT SPD B.50

ZERO 18.8

HTTN 2+ 14

FID SGNL +8

SLP SENS 0.10

AREA REJ 1

FLOW A 8.8 71.5

FLOW B 8.0 3.7

3. BNW51436-33

DELETE CHANGE RUN 2

CHANGE RUN 0 2

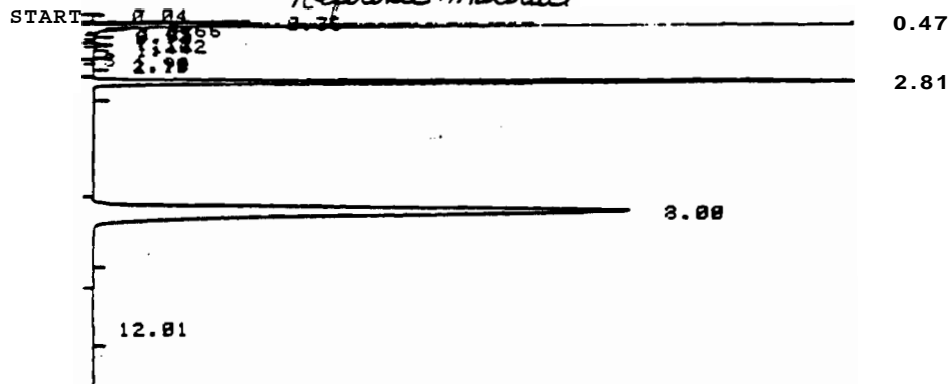
OPTN # 3 2

INJ/BTL STROKE: 1 2 2

CHANGE RUN 2 1 STOP

DIL FACTOR: 1.8000 E+ Ref # 1

Reference material BNW50846-145-1



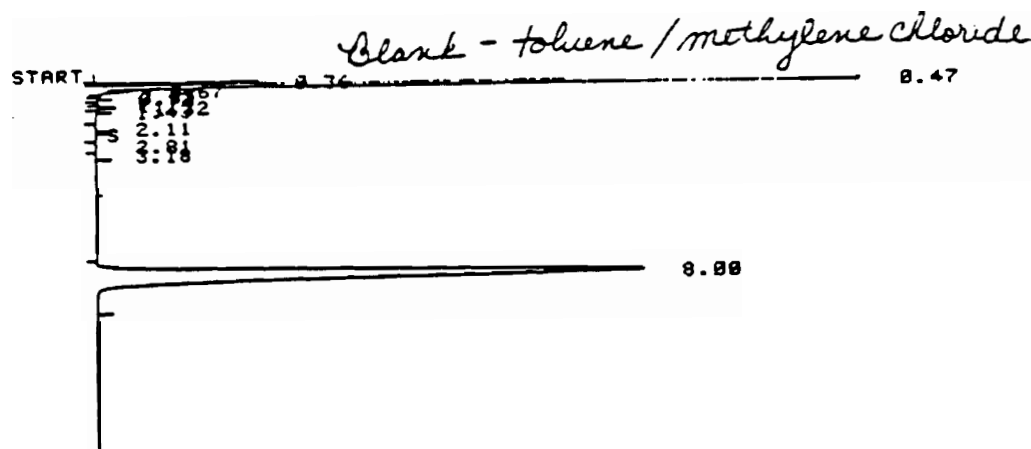
HP RUN # 2  
ID: 10786  
ARER %

APR/03/86  
BOTTLE 3

TIME 17:29:01

RT	HREA	AREA %
0.04	2	0.000
0.36	152500	0.113
0.47	121400000	90.104
0.66	29208	0.022
0.85	2692	0.002
0.93	568	0.001
1.18	4939	0.004
1.32	47000	0.035
1.44	7300	0.005
1.99	3156	0.002
2.10	1304	0.001
2.81	4016000	3.574
3.00	3260000	6.137
12.01	890	0.001

n-Hexane Rat Teratology Study  
Appendix A - Chemistry



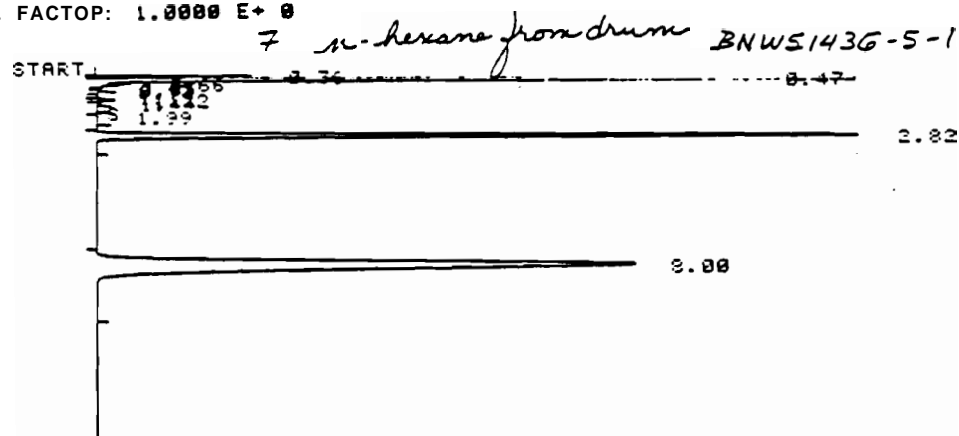
HP RUN # 19  
ID: 16786  
AREA %

APR/03/86  
BOTTLE 37

TIME 22:15:15

RT	AREA	AREA %
0.36	157500	0.121
0.47	121588800	93.398
0.67	30090	0.023
0.85	2670	0.002
0.93	855	0.001
1.19	4970	0.004
1.32	47370	0.036
1.43	498	0.000
2.11	1750	0.001
2.81	4993	0.004
3.18	487	0.000
8.00	9348000	6.417

DIL FACTOR: 1.0000 E+ 0



HP RUN # 14  
ID: 10706  
AREA %

APR/03/86  
BOTTLE 37

TIME 20:51:25

RT	AREA	AREA %
0.36	153300	0.114
0.47	121200000	90.033
0.66	29540	0.022
0.85	2584	0.002
0.93	723	0.001
1.19	4900	0.004
1.32	46950	0.035
1.44	11820	0.009
1.99	5383	0.004
2.82	4834000	3.591
8.00	8328000	6.196

DIL FACTOR: 1.0000 E+ 0



n-Hexane Rat Teratology Study  
Appendix A - Chemistry

HP RUN # 34  
ESCAPE  
ESCAPE  
TEMP1 400 50  
TIME1 5.00  
RATE 10.00  
TEMP2 488 225  
TIRE2 5.08  
INJ TEMP 400 200 199  
FID TEMP 400 250 250  
CHT SPD 0.50  
ZERO 10.0  
ATTN 21 18  
FID SCNL +8  
SLP SENS 0.10  
PRES REJ 0.8 31.6  
FLOW B 0.0 3.7  
TEMP1 400 50 49

MAY/05/86

TIME 10:45:00

5-5-86 KOB

Purity Analysis of n-Hexane by H.G.  
Completing Profile

Method DB-AC-3A15-00

C. HP5840P W10706

Column: 2mm x 1.8m ID

100 Carbowax C/O. 1% SP-1000

BNW51436-38-1

Samples: n-Hexane

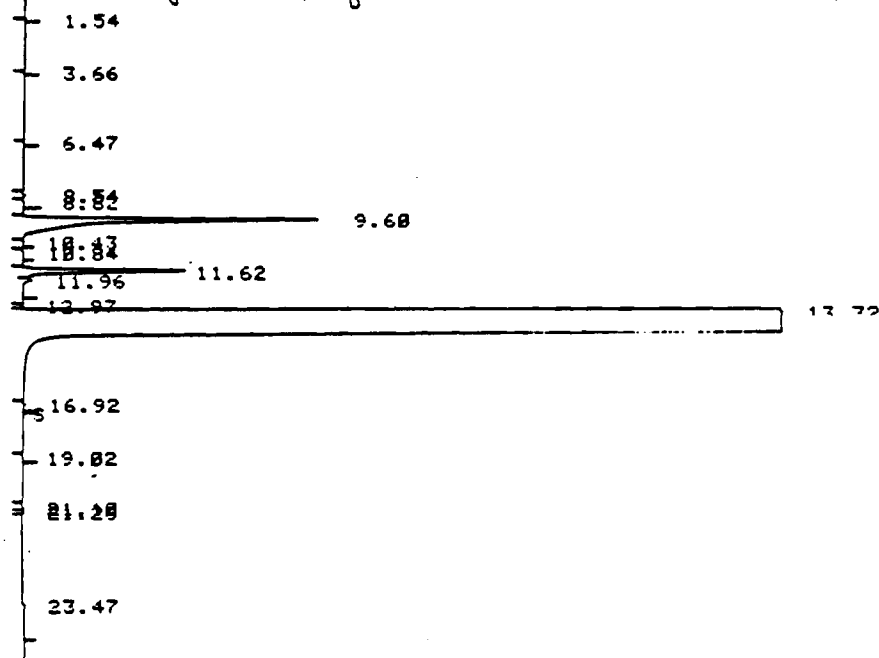
of BNW50846-145-1

Last day 3-29-86

drum BNW51436-5-1

3 BNW51436-45

? TEMP1 400 50 50  
? START Injection #2, Reference n-Hexane BNW51436-145-1, 1 µl



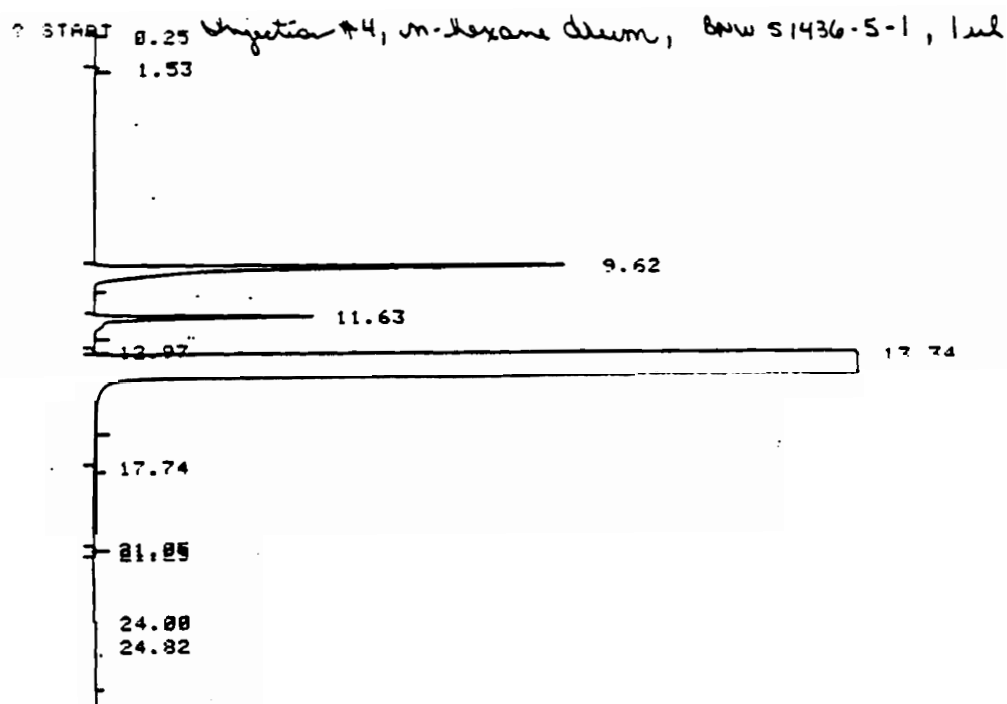
HP RUN # 36  
ID: 10706  
AREA %

MAY/05/86

TIME 11:34:26

RT	AREA	AREA %
1.54	234	0.000
3.66	133	0.000
6.47	225	0.000
8.54	2050	0.000
9.60	1388	0.000
10.43	590200	0.113
10.84	547	0.000
11.62	1393	0.000
11.96	229900	0.043
12.97	17910	0.003
13.72	23	0.000
16.92	528900000	99.336
19.02	3203	0.001
21.20	188	0.000
21.26	351	0.000
23.47	207	0.000
	14950	0.003

n-Hexane Rat Teratology Study  
Appendix A - Chemistry



HP RUN # 38 MAY/05/96 TIME 13:29:58  
ID:10706  
AREA %

RT	AREA	AREA %
0.25	6	0.000
1.53	2316	0.000
9.62	335600	0.182
11.63	335200	0.063
12.97	168	0.000
13.34	513600000	99.750
17.74	752	0.000
21.05	229	0.000
21.25	48	0.000
24.82	22130	0.004

DIL FACTOR: 1.0000 E+ 0

BULK CHEMICAL REANALYSIS

COMPOUND: n-HEXANE  
CAS# 110-54-3  
LOT# Phillips lot# H-116 (BNW 50846-39, sample removed from reservoir 3/29/86 • last day of study)  
APPEARANCE: Clear liquid  
RECEIPT DATE: 2/12/86  
ANALYSIS PERIOD: Last usage day  
STORAGE TEMPERATURE: Room Temperature  
SAMPLE SUBMITTAL DATE: 3/29/86  
SAMPLE ANALYSIS DATE: 4/3,4/86 & 5/5/86  
ANALYSIS PROCEDURE: ØB-AC-3A15-00  
NOTEBOOK REFERENCE: BNW 51436-33 & BNW 51436-45

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

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

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

Instrument: HP 5840A

RESULTS: Relative % Purity

Date Bulk

4/86 99.1

Retention time of n-Hexane -2.8 minutes.  
Retention time of internal standard -8.0 minutes.

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

Instrument HP5840A

RESULTS: Impurity Profile

Date Area %

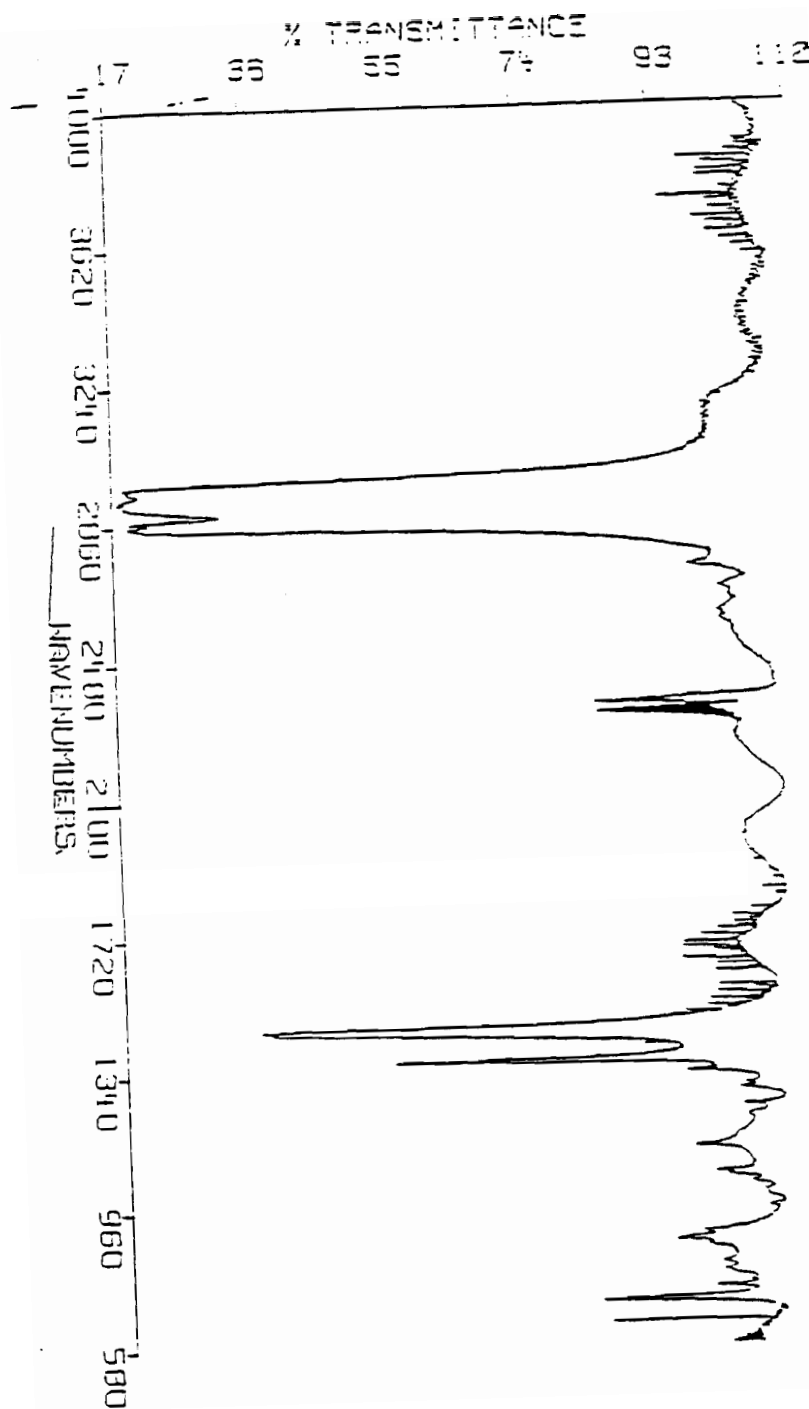
	<u>Area %</u>	<u>Reference Material</u>	<u>Test Material</u>
5/86	-RT		
	9.62	0.113	0.112
	11.64	0.043	0.044
	11.98	0.003	0.003
	16.92	0.001	
	24.90	0.003	0.005

A major peak of 99.84% area was observed at a retention time of -13.3 minutes for both the reference and test material. The reference material showed 5 impurity peaks and the test material showed 4 impurity peaks all  $\geq 0.001\%$ .

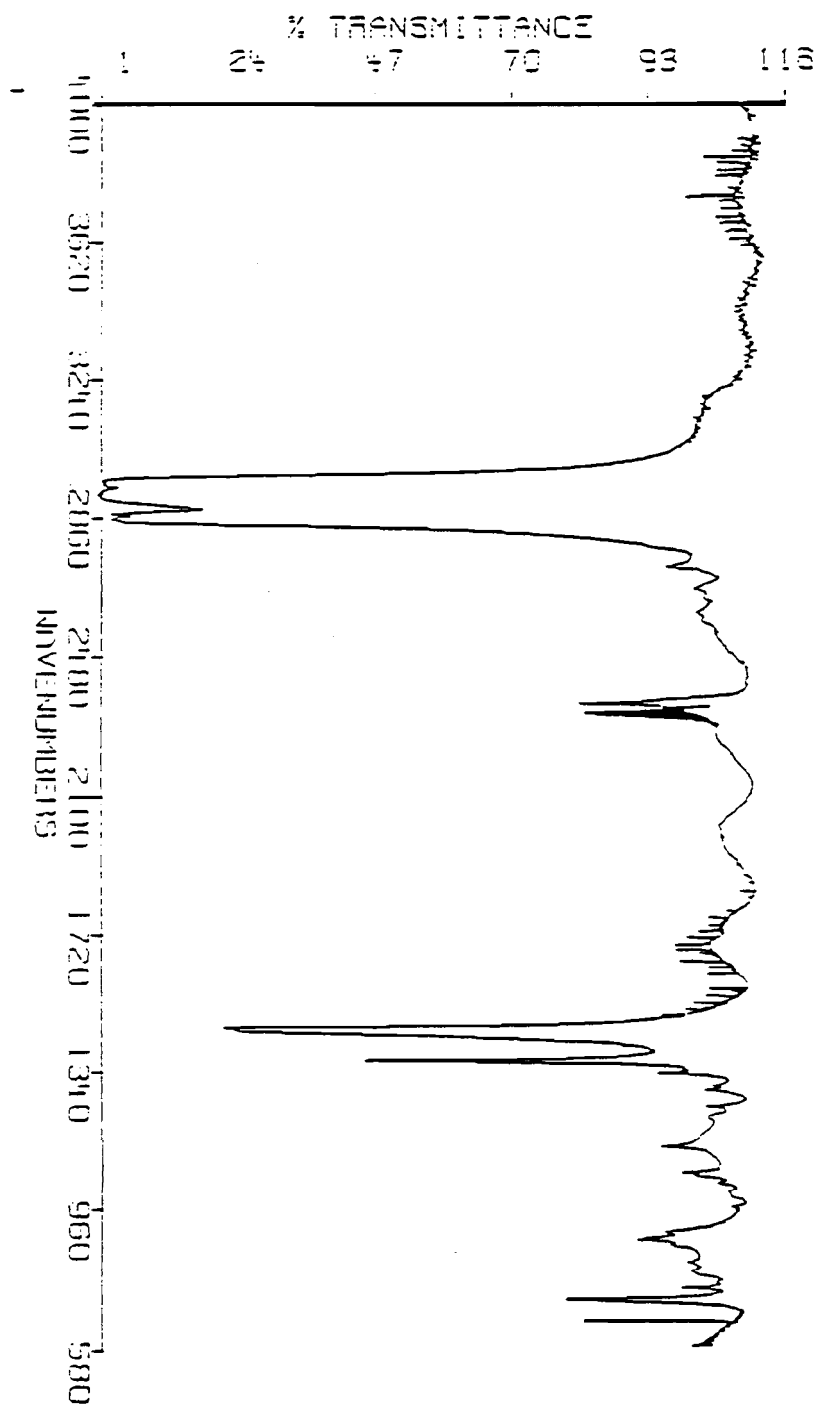
CONCLUSION: Gas chromatography shows this test material to be 99.1% pure by area ratio of an internal standard. The impurity profile showed four impurities greater than 0.001% for the test material. An infrared spectrum was obtained between 4000  $\text{cm}^{-1}$  and 600  $\text{cm}^{-1}$ . The spectrum was similar to previous BNW analysis.

Signature of Technician: KH Stoner Date: 5/8/86

Signature of Chemist: RR Weber Date: 5/8/86



11-17-86 Kdl  
Reference n-Hexane ABU50846-145-1  
Substance: NIST REF-1E 605X with 360711 / 11mm Mecl window / 6.1mm spec ex  
IR spectrum obtained by NIST, December 14, 1984. Source informed by  
NIST and AB-AC-3115-88  
P. 3300 31136-34

[illegible]

n-Hexane Rat Teratology Study  
Appendix A - Chemistry

1 400 50 65

STOP

HP RIJN # 34  
ESCAPE  
ESCAPE

MAY/05/86

TIME 10:45:08

5-5-96 KH

400 50 50

*Purity Analysis of n-Hexane by H.G.  
Simplicity Profile*

TIME1 5.00  
RHT 10.80  
TEMP2 400 225  
TIME2 5.00  
INJ TEMP 400 200 199  
FID TEMP 400 250 250

*Method # 08-AC-3A15-00*

*H.C. HP5840A W#10706*

*Column: 2mm x 1.8m ID glass*

*5% Carboxack C/o.1% SP-1000  
BNW51436-38-1*

CHT SPD 0.50  
ZERO 18.0  
ATTN 10  
FID 10  
SLP 10  
REF 10  
FLOW B 5.0 3.6 3.7

*Samples: n-Hexane*

*ref BNW50846-145-1*

*Last day 3-29-86*

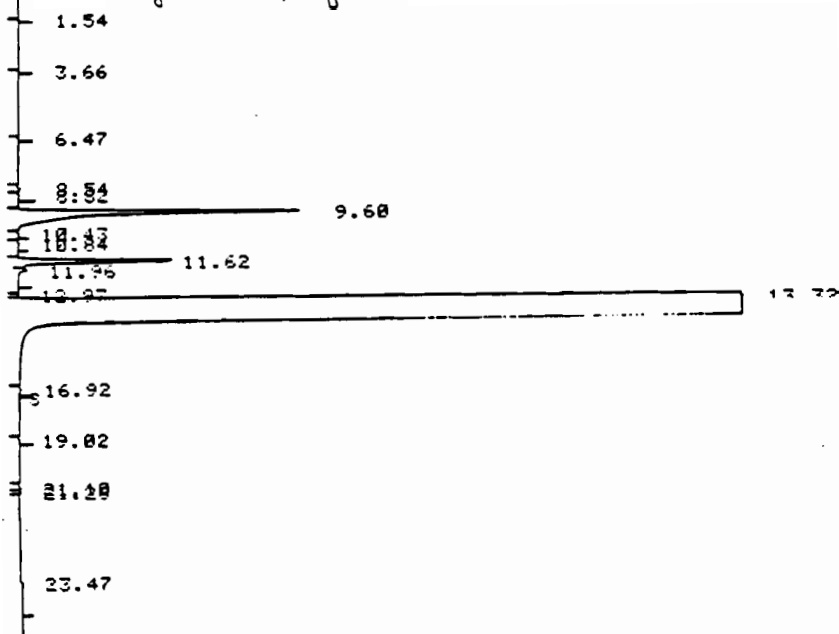
*drum BNW51436-5-1*

TEMP1 400 50 49  
TEMP1 400 50 49  
TEMP1 400 50 50

*P BNW51436-45*

3 TEMP1  
2 START

*Injection #2, Reference n-Hexane BNW51436-145-1, 1 µl*



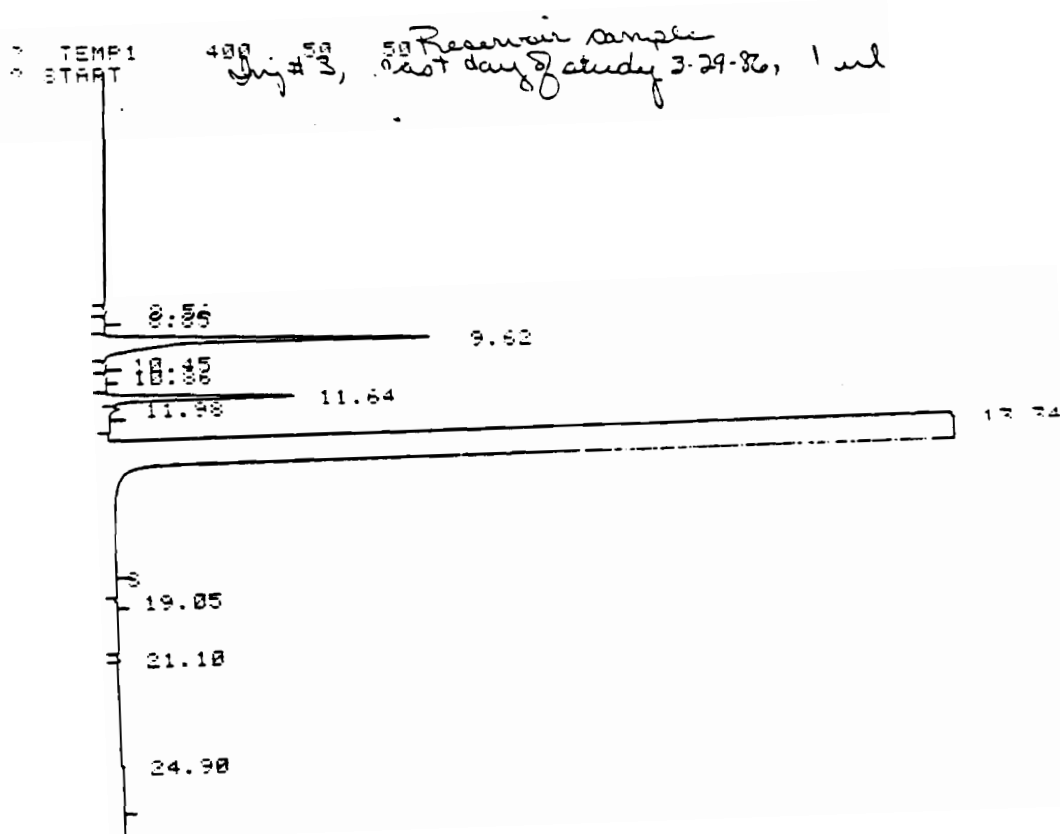
HP RIJN # 36  
ID: 10706  
AREA %

MAY/05/86

TIME 11:34:26

RT	AREA	HPEA %
1.54	234	0.000
3.66	133	0.000
6.47	225	0.000
8.54	2050	0.000
9.60	1388	0.000
10.84	599200	0.113
11.62	547	0.000
12.97	1393	0.000
13.32	229000	0.043
16.92	17910	0.003
19.02	28	0.000
21.20	528900000	99.836
23.47	2007	0.000

n-Hexane Rat Teratology Study  
Appendix A - Chemistry



NO RUN # 37 MAY/05/86 TIME 12:23:24  
13:10706  
AREA %

RT	AREA	AREA %
0.05	1417	0.000
9.62	435	0.000
10.05	5949000	0.112
10.88	143	0.000
11.64	725	0.000
11.98	233000	0.044
13.74	16420	0.003
19.05	528200000	9.935
21.10	155	0.000
24.90	474	0.000
24.90	16420	0.003

DIL FACTOR: 1.0000 E+ 0

TEMP1 400 50 50



4-3-86 KHL

Purity Analysis of n-hexane by H.C. major peak  
~~Method supplied by NRI: December 17, 1984 Comparison~~

~~NRI Contract no: NRI-ES-45060~~

~~NRI Project no: 7093-C~~

wrong information

~~NRI Task designation: 051299 5-15-86 KHL~~

ESCAPE

TEMP1 400 150 150  
TIME1 15.00  
INJ TEMP 400 200 200  
FID TEMP 400 250 250

CHT SPD 0.50  
ZERO 10.0  
ATTN 2+ 14  
FID SGNL +B  
SLP SENS 8.18  
AREA RES 1

FLOW A 0.0 71.5  
FLOW B 0.0 0.0

Method # 08B-AC-3A15-00

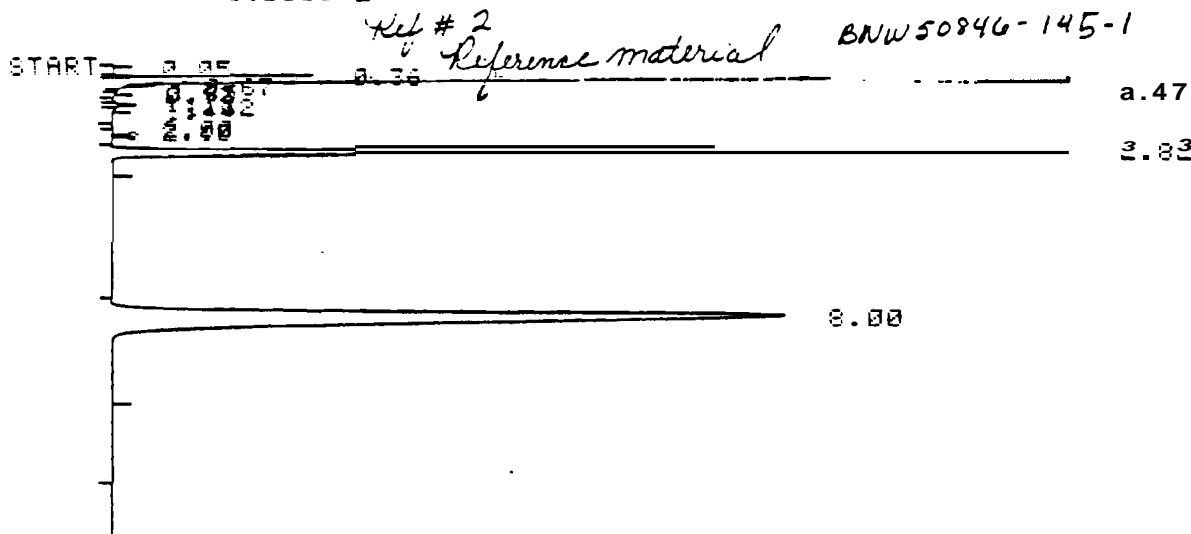
GC: HP5840A WA10706

Column: 1.8m x 4mm ID glass

8%100 Carbopack C/0.1% SP-1000  
BNW50846-146

P. BNW51436-33

DIL FACTOR: 1.0000 E+



HP RUN # 4  
ID:10706  
AREA %

APR/03/86  
BOTTLE 7

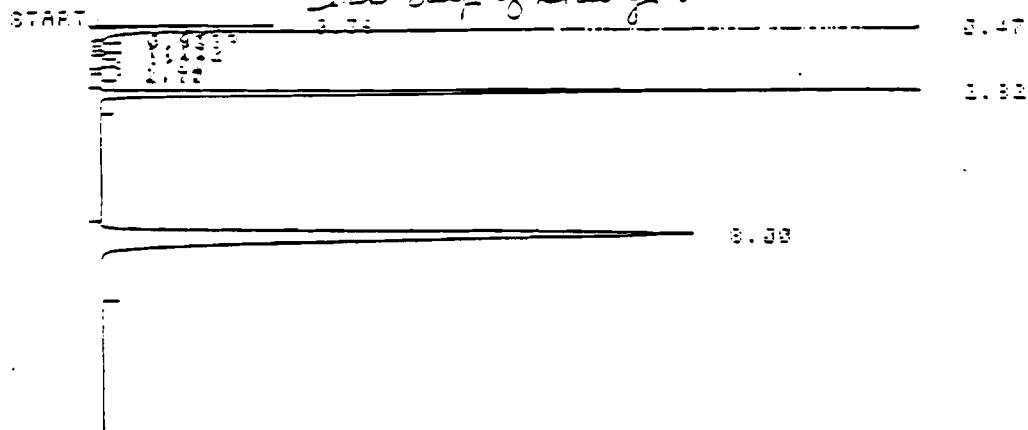
TIME 18:02:52

RT	AREA	AREA %
0.05	7	0.000
0.36	155100	0.115
0.47	121100000	90.098
0.67	29430	0.022
0.85	2671	0.002
0.93	0.000	0.001
1.10	4.000	0.004
1.20	4.000	0.005
1.44	7014	0.005
2.00	0.191	0.002
2.10	1040	0.001
2.00	4791000	3.565
0.00	9266000	6.150

n-Hexane Hat Teratology Study  
Appendix A - Chemistry

DIL FACTOR: 1.0000 E-0

#6 n-Hexane collected from receiver 3-29-86  
Last day of study



HS RUN = 11  
END 10786  
AREA 0

APR/03/86  
BOTTLE 21

TIME 20:31:00

RT	AREA	AREA %
0.36	156800	0.117
0.47	120600000	89.871
0.66	30420	0.023
0.85	2741	0.002
0.93	931	0.001
1.19	5012	0.004
1.32	47720	0.036
1.44	7492	0.006
1.99	3238	0.002
2.10	1296	0.001
2.82	4895000	3.648
8.00	8442000	6.291

JPW  
5/20/87

**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) is used for the inhalation exposures. The 2.3 m<sup>3</sup> (1.7 m<sup>3</sup> active mixing volume) stainless steel chamber contains three levels of caging, each level split into two offset tiers (Figure B1). The drawer-like stainless steel cage units comprise individual animal cages, feed troughs and automatic watering. Stainless steel catch pans for the collection of urine and feces are suspended below each cage unit.

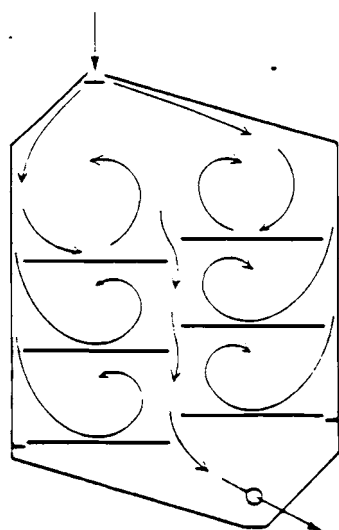
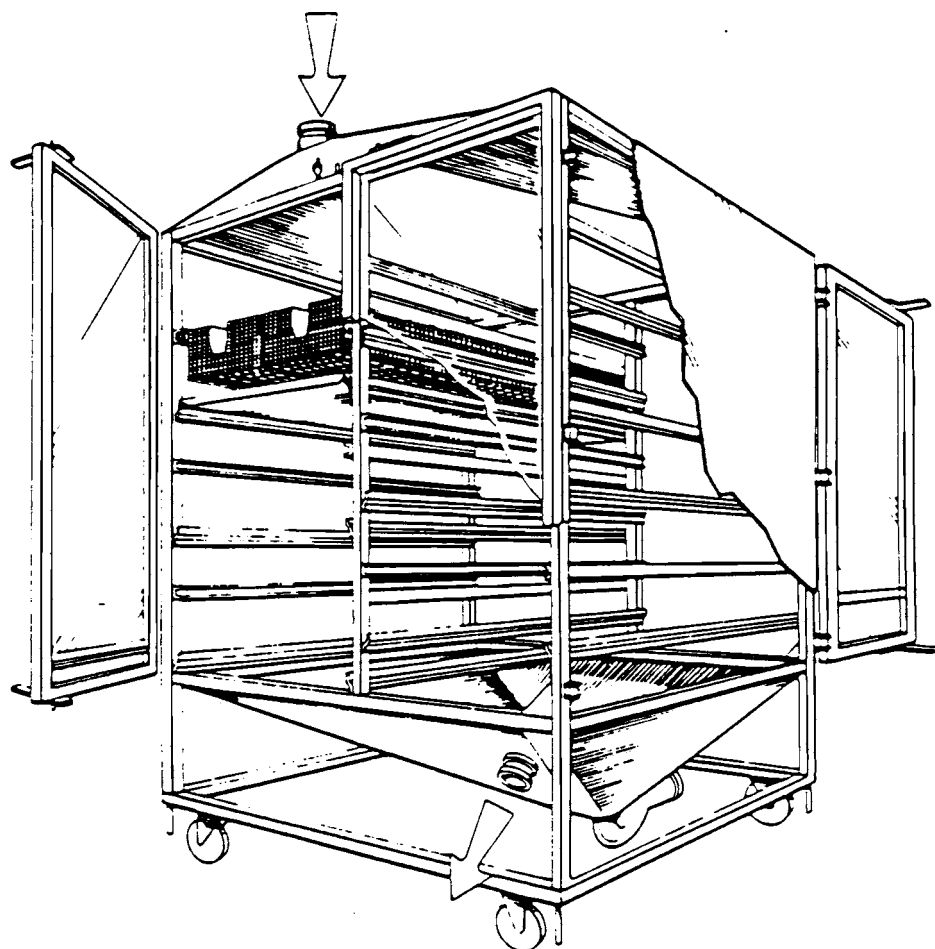
The catch pans, which remain in the chamber during exposure, were designed to aid in mixing to maintain uniform concentrations of aerosol, dust or vapors throughout the chamber. Incoming air is HEPA and charcoal filtered before addition of the test article. Incoming air containing a uniform mixture of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

### Exposure Suite System Description

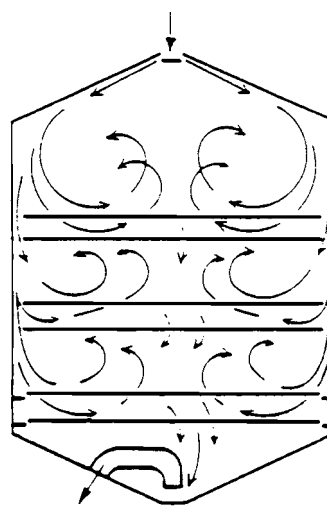
The hexane exposures were conducted using an automated data acquisition and control system in an exposure suite (Figures B2 and B3). This system monitors and controls the basic inhalation test system functions including chamber air flow, vacuum, temperature and relative humidity and test chemical concentration. The system computers, printers, magnetic data storage devices, interface equipment, and monitoring instruments are located in a central control room and interface with monitoring and control elements in three exposure rooms. All data acquisition and control originates from an executive computer which controls a multiplexing interface system. All experimental protocols related to data acquisition and control reside in this computer and are entered into software tables accessed by menus.

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

A dual point alarm system with user defined set points is available for each parameter measured. Action taken upon alarm depends 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 be a threat to the health of the animals alert a building power operator who is on duty 24 hours per day.



FRONT VIEW



SIDE VIEW

Figure B1. Inhalation Exposure Chamber.

n-Hexane Rat Teratology Study  
Appendix B - Exposure

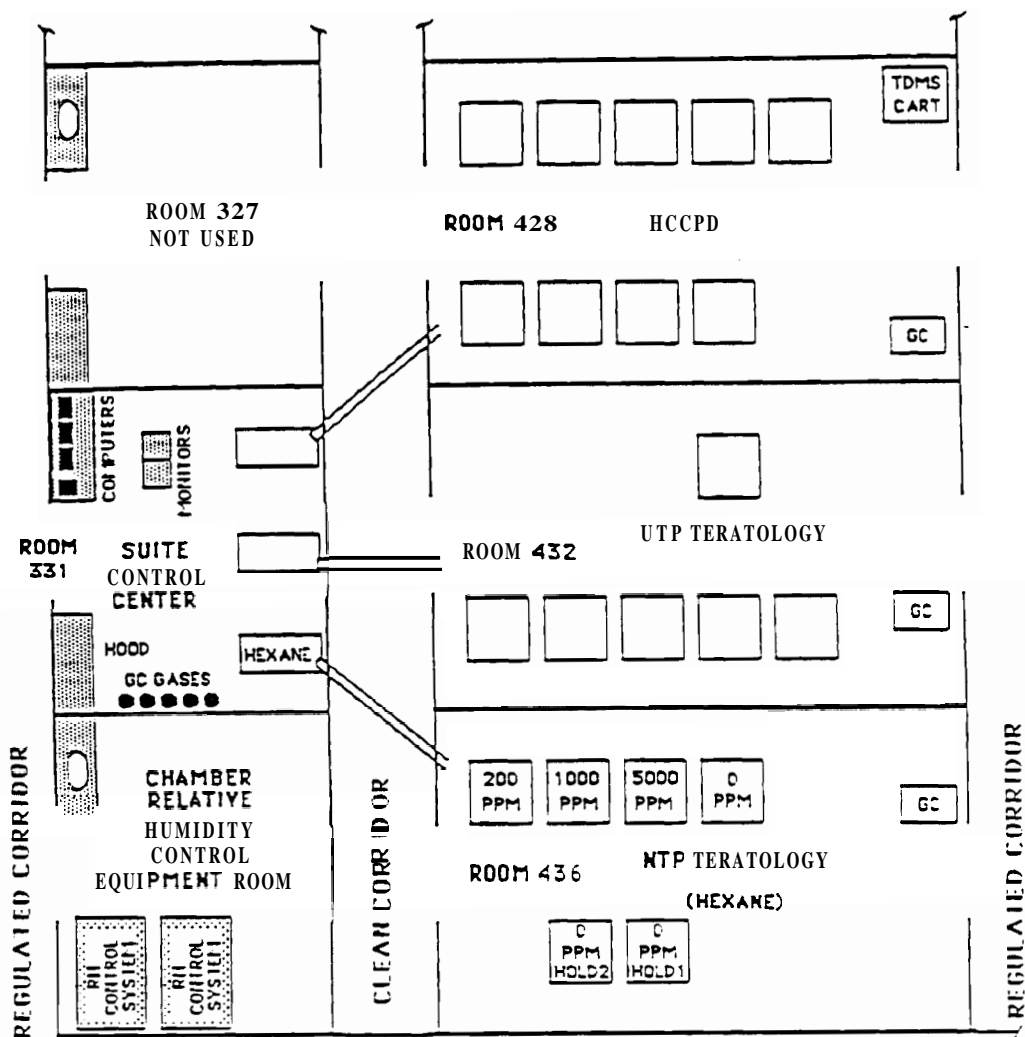


Figure B 2. Hexane Exposure Suite.

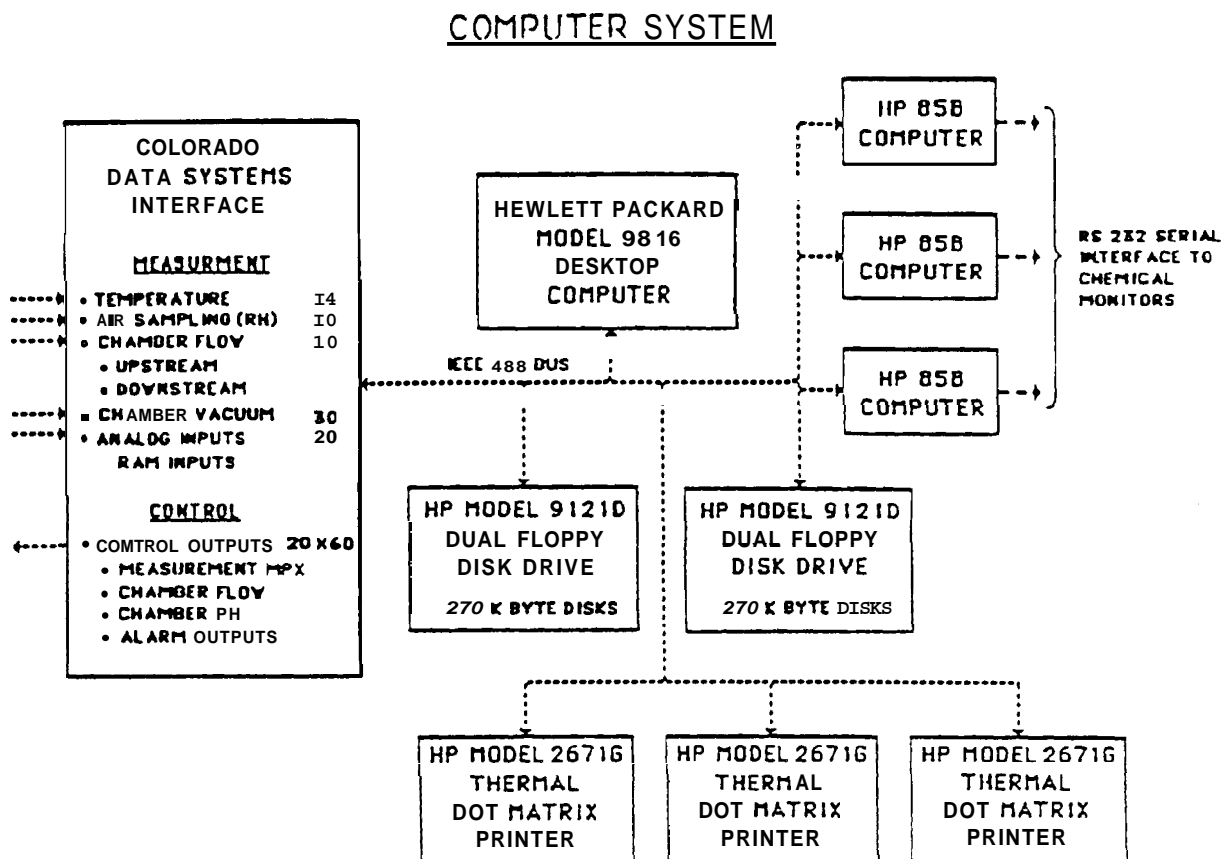


Figure E3. Data Acquisition System For n-Hexane Exposures.



Temperature is measured with an accuracy of approximately  $\pm 0.5^{\circ}\text{F}$  by Resistance Temperature Devices (RTD's) located at the measurement site. The RTD's are multiplexed to a digital thermometer which is interfaced to the computer. Chamber temperature is controlled primarily by controlling the temperature of the room housing the chambers.

Relative humidity (RH) is calculated with an accuracy of approximately  $\pm 6\%$  by pulling a sample from the measurement location through a Teflon® tube into a dewpoint hygrometer located in the control center. Measurements are made from different locations by a valving system which multiplexes the tubes to the hygrometer. Percent RH is calculated by the executive computer from temperature and dewpoint measurements. Chamber %RH is 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, determines the chamber %RH.

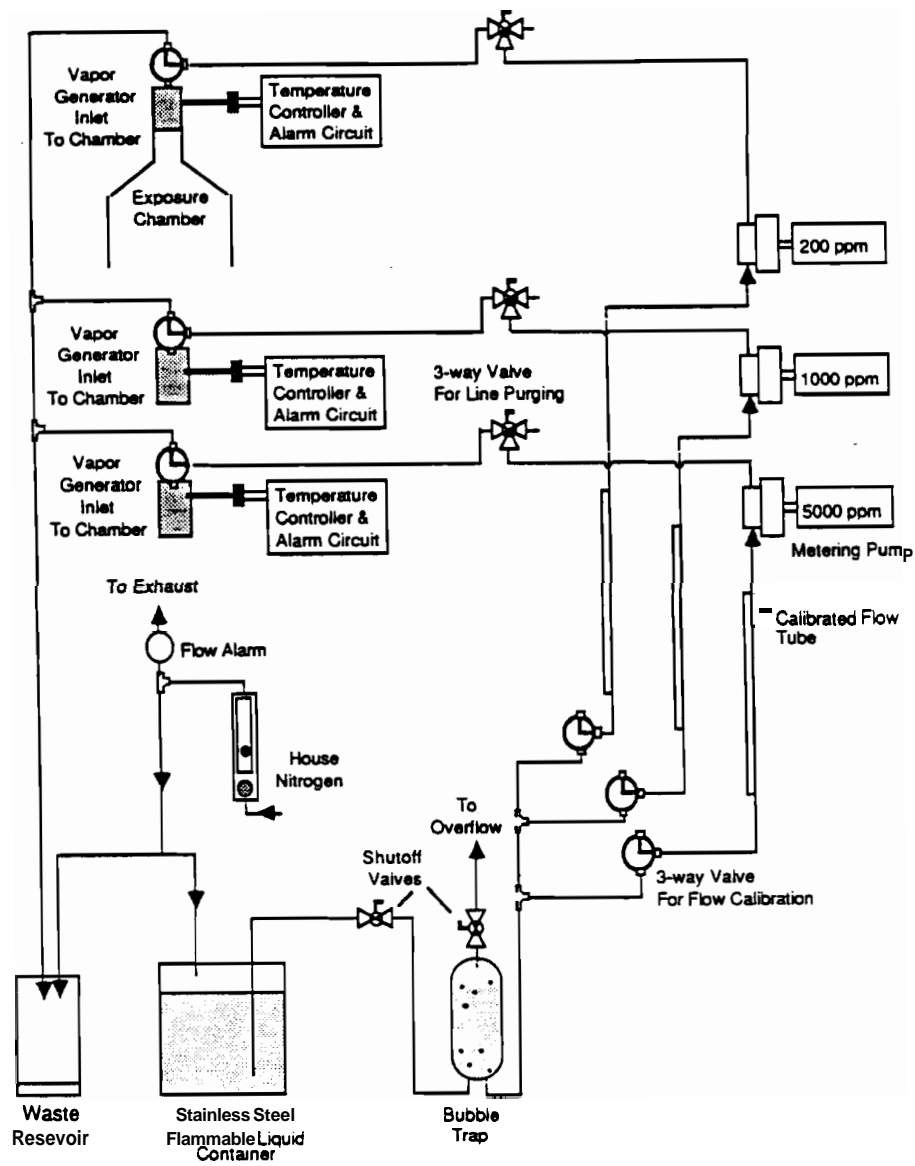
Chamber air flow is calculated with an accuracy of approximately  $\pm 15$  liters/min by measurement of the pressure drop across calibrated orifices located at the inlet and exhaust of each chamber. The desired flow orifice is attached by means of a multiplexed valve system to a calibrated pressure transducer located in the control center. Small leaks in the chambers can be detected by comparison of the measurement of inlet flow with that of the exhaust. Flow is maintained by a computer controlled pump in the exhaust line of each chamber.

Chamber vacuum, relative to the control center, is measured with an accuracy of approximately  $\pm 0.2$  cm H<sub>2</sub>O using the same pressure transducer system which measures chamber air flows. Chamber vacuum is maintained at approximately (-)1" H<sub>2</sub>O 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 64. Most of the generator is housed in a vented cabinet located in the Suite Control Center. The cabinet is vented to the building exhaust. The hexane to be vaporized is contained in a 19 liter stainless steel reservoir. This reservoir is filled daily from the original shipping container by the following method which is designed to prevent explosion during transfer. All oxygen in the reservoir is displaced with nitrogen through a purge port. The nitrogen pressure in the shipping container forces hexane through a filter and into the reservoir. The reservoir is on an electronic scale during filling so that the correct level is readily obtained. All metal containers are grounded. The filled reservoir is then transferred and installed into the generator cabinet.

During exposure the hexane is 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  $1 \times 10^{-5}$  to greater than 20 ml per minute are used.



Hexane Generation And Delivery System

Figure B 4. n-Hexane Generation and Delivery System.

The vaporizer (Figure B4) 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 residue buildup occurs. 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 is maintained below 50°C (the boiling point of hexane is about 70°C). The cylindrical vaporizer is 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 is attached downstream of the pump to facilitate measurement of the flow rate of the vapor generator. Measurement is accomplished by momentarily switching the three-way valve from the run position to the test position. A small bubble of air is 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) is timed with a stop watch. Flow rate is 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 air and is used as a check on chamber concentrations in addition to GC measurements.

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

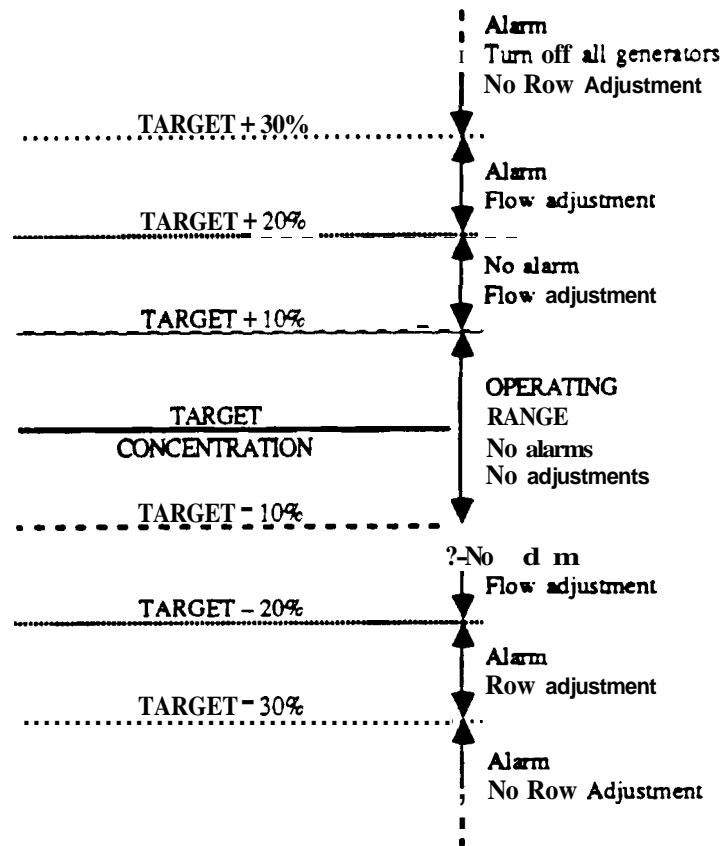
The exposure suite data acquisition and control computer automatically controls the concentration of hexane in the animal exposure chambers by adjusting the flow rate of dilution air through the chamber over a narrowly limited flow range. This is accomplished by adjusting the dilution air flow pump which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

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

The following conditions for alarms and concentration adjustments will apply:

- Concentration  $< \text{Target} + 10\%$  and  $> \text{Target} - 10\%$   
No action necessary—
- Concentration  $> \text{Target} + 10\%$  and  $\leq \text{Target} + 20\%$   
or  
 $< \text{Target} - 10\%$  and  $\geq \text{Target} - 20\%$   
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  $> \text{Target} + 20\%$  and  $\leq \text{Target} + 30\%$   
 $< \text{Target} - 20\%$  and  $\geq \text{Target} - 30\%$   
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  $> \text{Target} + 30\%$   
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  $< \text{Target} - 30\%$   
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 B5. The value of  $T_{90}$  was found to range from approximately 11 to 13 minutes. At a chamber air flow rate of 15 air changes per hour, the theoretical value for  $T_{90}$  is approximately 12.5 minutes. A  $T_{90}$  of 12 minutes was chosen for this study. The value of  $T_{10}$  ranged from 9 to 10 minutes.

n-Hexane Rat Teratology Study  
Appendix B - Exposure

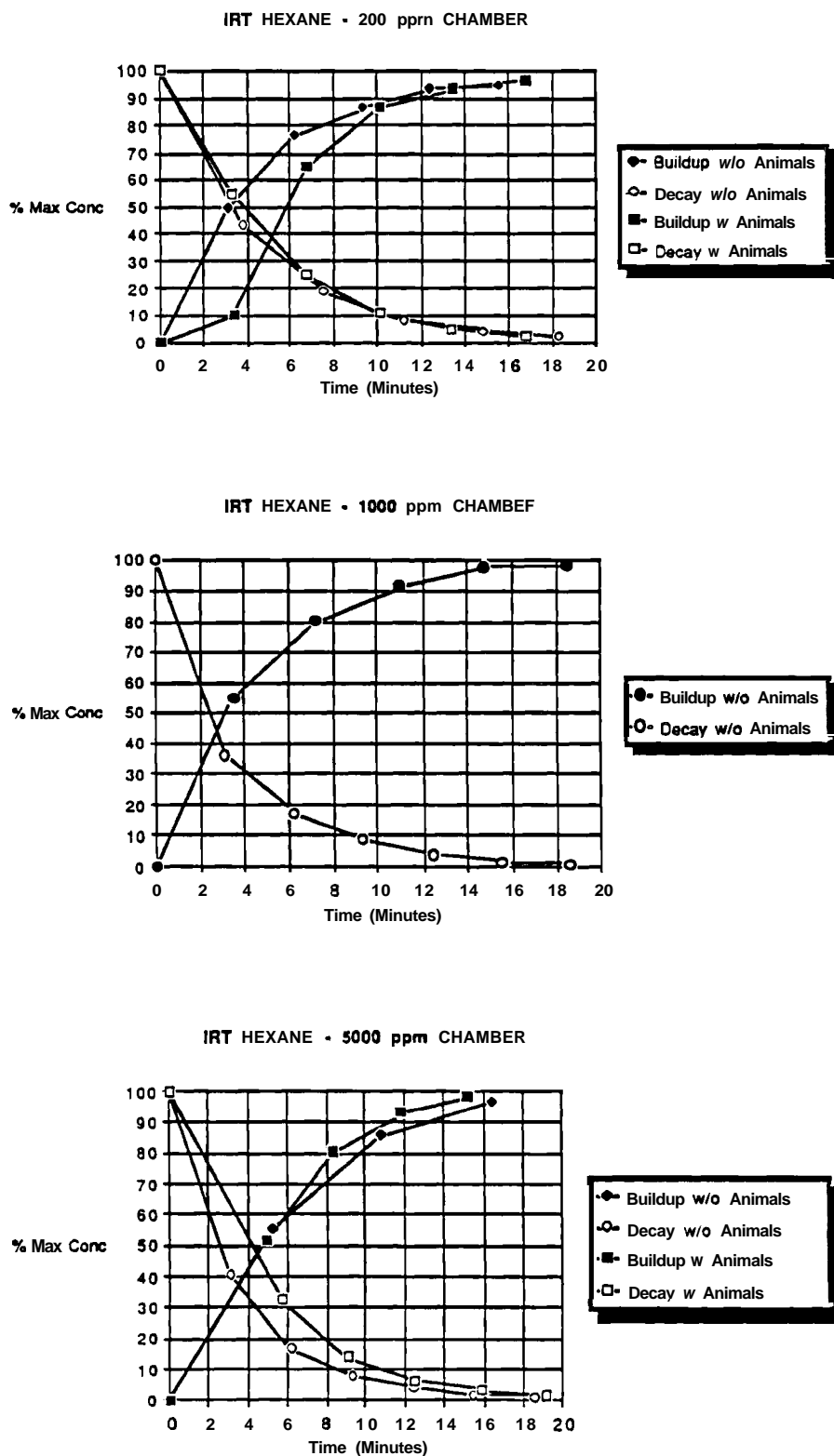


Figure B 5. Buildup and Decay of Vapor Concentrations With and Without Animals Present.

The buildup and decay of concentration with animals in the chambers were checked during the first week of the study (Figure B5). These tests were run on the 200 and 5000 ppm chambers. The values of  $T_{90}$  ranged from 11 to 11.5 minutes. The decay time,  $T_{10}$  with animals present ranged between 10 and 11 minutes.

#### 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 (F) and one in back (B), 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 B1. Uniformity in all chambers was found 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 Variability (TPV). Three factors contribute to the TPV. The first, the Between Port Variability (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 B1. Rat Teratology Study of Hexane in Rats - Summary of Chamber Uniformity Data Obtained before exposure (Prestart) and during exposure (Poststart).

Chamber	TPV (%RSD)		WPV (%RSD)		BPV (%RSD)	
	Prestart	Poststart	Prestart	Poststart	Prestart	Poststart
200 ppm	2.5	1.9	1.8	1.7	1.8	0.8
1000 ppm	1.2	0.6	0.2	0.3	1.2	0.4
5000 ppm	1.0	0.1	1.8	0.1	0	0.1

#### Chamber Uniformity Limits

WPV  $\leq$  5% RSD

BPV  $\leq$  5% RSD

TPV  $\leq$  7% RSD

### ENVIRONMENTAL DATA DURING EXPOSURE

Summations of chamber air flow, temperature and relative humidity data for the study are shown in Table B2. 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 74.2 and 76.8°F, all within the specified limits of 72 to 78°F. Temperature extremes ranged from 71.7 to 79.3°F. Mean daily temperatures in the 1000 ppm chamber exceeded the upper limit of 78°F on 3 days, resulting in 86% of samples falling in the operating range. The percent of temperature readings within the operating range for all other chamber were greater than 99%.

The mean values of relative humidity in all chambers for the study were between 52.5 and 57.7%, all within the specified limits of 40 to 70%. Relative humidity extremes (considering all chambers) ranged from 40 to 72% and at least 97% of all relative humidity readings were within specified limits throughout the study.

The mean values of chamber flow in all chambers for the study were between 14.3 and 15.3 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 10.9 to 16.9 CFM. The wide variations were due to the use of air flow to adjust concentrations during the nighttime hours.

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

### EXPOSURE DATA

Summaries of the concentration data for all chambers and the exposure room are included in Table B3. The daily mean concentrations for all chambers were within 8% of the target concentrations (the daily protocol required the daily means to be within  $\pm 10\%$  of the target concentrations). Standard deviations were outside the 10% protocol-defined limits on 3 days for the 200 ppm chamber and 1000 ppm chamber and 2 days for the 5000 ppm chamber. The percent of concentration readings within the operating range for the 1000 ppm chamber was 89%, the other chambers were greater than 98%.



**Table B2. Inhalation Toxicity Study of n-Hexane in Rats - Summation of Environmental Data for the Period when Animals were Housed in the Exposure Chamber. 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
1 0	74.2±1.0	99±1%	76.2	71.7	106	99
2 Hold 1	76.5±1.1	102±1%	77.7	74.3	16	100
2 Hold 2	74.9±1.7	100±2%	78.0	72.5	16	100
1200	76.1±1.0	102±1%	78.3	73.3	106	99
1 1000	76.8±1.2	102±2%	79.2	73.6	106	86
1 5000	75.1±0.8	100±1%	76.9	73.1	106	100

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
1 0	57.7±7.9	105±14%	72	40	106	97
2 Hold 1	52.5±3.3	95±6%	57	47	15	100
2 Hold 2	53.5±3.2	97±6%	59	48	15	100
1 200	53.5±4.6	97±9%	63	40	108	100
1 1000	55.0±5.3	100±10%	69	40	107	100
1 5000	55.7±4.2	101±7%	65	43	106	100

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
1 0	14.6±0.6	97±4%	16.3	13.9	108	100
2 Hold 1	15.3±0.1	102±1%	15.7	15.2	16	100
2 Hold 2	15.1±0.5	100±3%	16.2	14.7	16	100
1200	15.0±0.7	100±5%	16.1	11.9	111	99
1 1000	14.3±1.5	96±10%	16.9	10.9	111	98
1 5000	15.3±0.4	102±3%	15.9	13.2	109	100

Data Used for Analysis:

1 5/13/86- 5/29/86

2 5/13/86- 5/15/86

Table B3. Hexane Study in Rats - Summary of Concentration Data

		Concentration (PPM)					
		Acceptable Range = Target $\pm$ 10%					
Target		Percent			Number	Number	% Samples
Conc. (ppm)	Mean $\pm$ SD		Maximum	Minimum	Samples	In Range	In Range
Room	0.07 $\pm$ 0.5	_____	4	0	658	*643	*98
0	0.00 $\pm$ 0.00	_____	0	0	631	*631	*100
Hold 1 <b>1</b>	0.00 $\pm$ 0.01	_____	0.1	0	99	*99	*100
Hold 2 <b>1</b>	0.00 $\pm$ 0.00	_____	0	0	101	*101	*100
200	200 $\pm$ 15.9	100 $\pm$ 8%	276	0.7	618	604	98
1000	994 $\pm$ 89	99 $\pm$ 9%	1470	27	629	560	89
5000	4990 $\pm$ 312	100 $\pm$ 6%	5490	17	625	615	98
St. Gas	1010 $\pm$ 103	101 $\pm$ 10%	1100	7	639	631	99

\* Samples with concentration less than 4 ppm

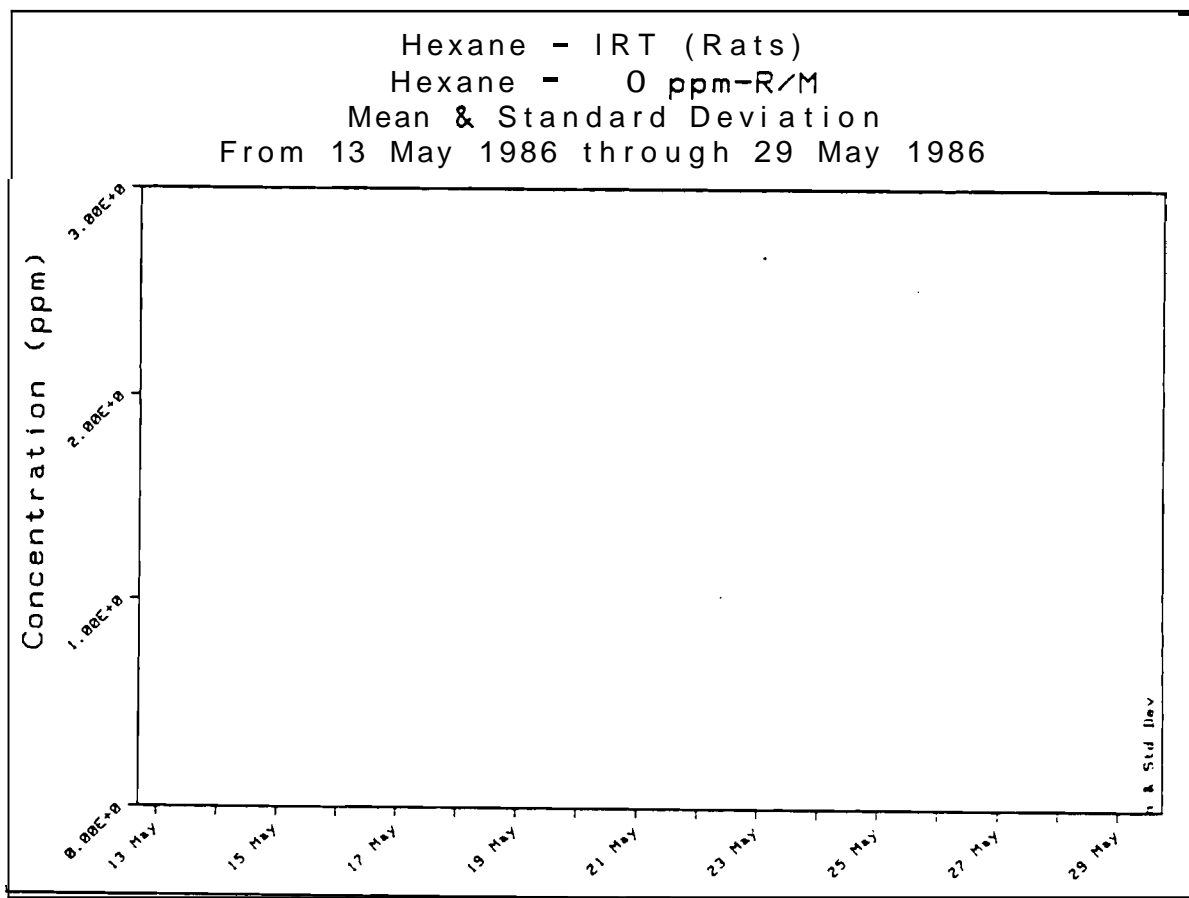
Dates Used for Analysis: 5/13/86 - 5/29/86 except **1** 5/13/86 - 5/15/86.

n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IPT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: hexane - 0 ppm-R/M/Concentration 0.00E+0 to 1.00E+0

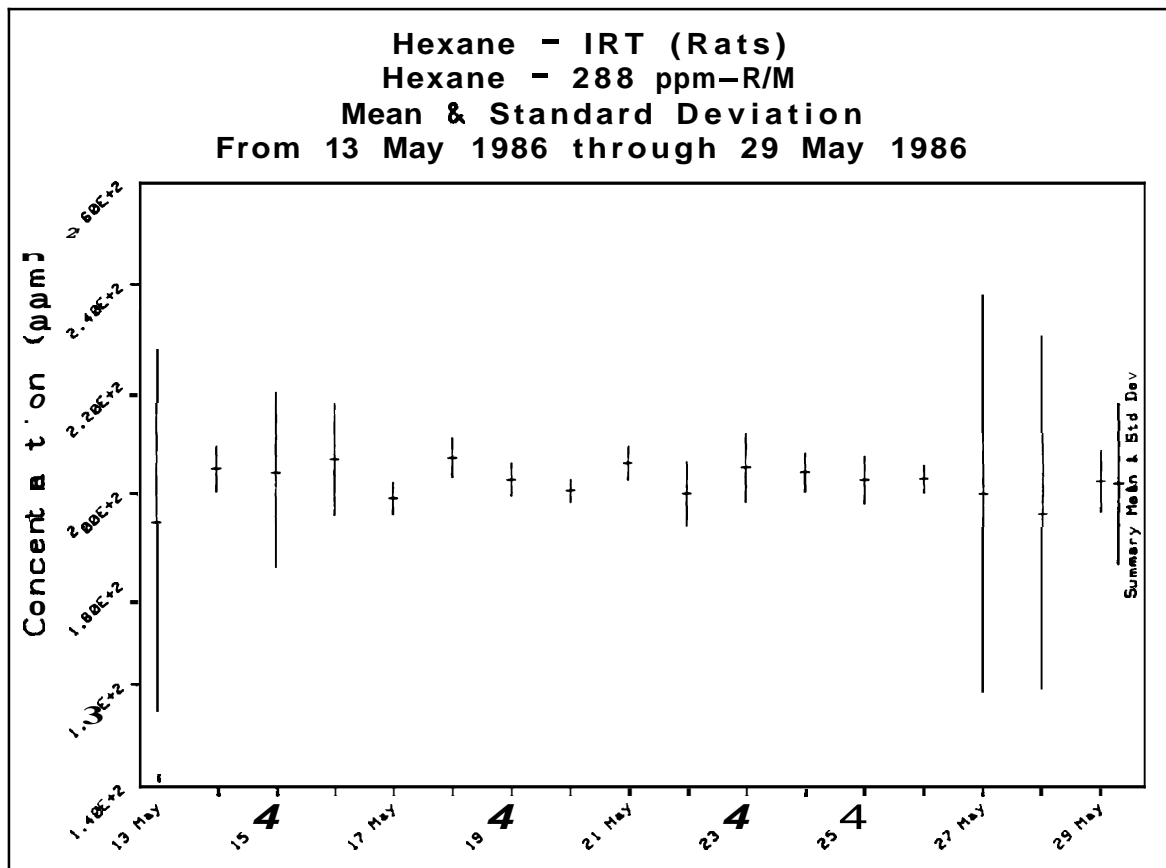
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	33.	33.	100%
14 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	35.	35.	100%
15 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	3.	3.	100%
16 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	34.	34.	100%
17 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	37.	37.	100%
18 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	38.	38.	100%
19 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	38.	38.	100%
20 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	4E.	46.	100%
21 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	42.	42.	100%
22 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
23 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	47.	47.	100%
24 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	43.	43.	100%
25 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	37.	37.	100%
26 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	44.	44.	100%
27 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	22.	22.	100%
28 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	41.	41.	100%
29 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	4E.	46.	100%
Summary	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	631.	631.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 200 ppm-R/M/Concentration								1.80E+2 to 2.20E+2	
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	1.91E+2	95%	3.616E+1	19%	2.05E+2	7.14E-1	30.	29.	97%
14 May 1986	2.02E+2	101%	4.629E+0	2%	2.08E+2	1.89E+2	32.	32.	100%
15 May 1986	2.01E+2	100%	1.756E+1	9%	2.76E+2	1.73E+2	35.	32.	91%
16 May 1986	2.03E+2	102%	1.117E+1	5%	2.34E+2	1.73E+2	31.	27.	87%
17 May 1986	1.96E+2	98%	3.200E+0	2%	2.02E+2	1.88E+2	33.	33.	100%
18 May 1986	2.04E+2	102%	3.897E+0	2%	2.09E+2	1.95E+2	37.	37.	100%
19 May 1986	1.99E+2	100%	3.271E+0	2%	2.11E+2	1.95E+2	38.	38.	100%
20 May 1986	1.97E+2	99%	2.344E+0	1%	2.02E+2	1.91E+2	41.	41.	100%
21 May 1986	2.05E+2	102%	3.464E+0	2%	2.20E+2	1.99E+2	38.	37.	97%
22 May 1986	1.98E+2	99%	6.438E+0	3%	2.12E+2	1.86E+2	42.	42.	100%
23 May 1986	2.04E+2	102%	6.839E+0	3%	2.32E+2	1.94E+2	43.	42.	98%
24 May 1986	2.03E+2	101%	3.892E+0	2%	2.12E+2	1.96E+2	37.	37.	100%
25 May 1986	2.01E+2	101%	4.747E+0	2%	2.11E+2	1.88E+2	34.	34.	100%
26 May 1986	2.01E+2	101%	2.717E+0	1%	2.08E+2	1.96E+2	37.	37.	100%
27 May 1986	1.98E+2	99%	3.967E+1	20%	2.18E+2	1.61E+1	24.	22.	92%
28 May 1986	1.94E+2	97%	3.513E+1	18%	2.09E+2	5.14E+0	42.	40.	95%
29 May 1986	2.00E+2	100%	6.171E+0	3%	2.16E+2	1.88E+2	44.	44.	100%
Summary	2.00E+2	100%	1.590E+1	8%	2.76E+2	7.14E-1	618.	604.	98%

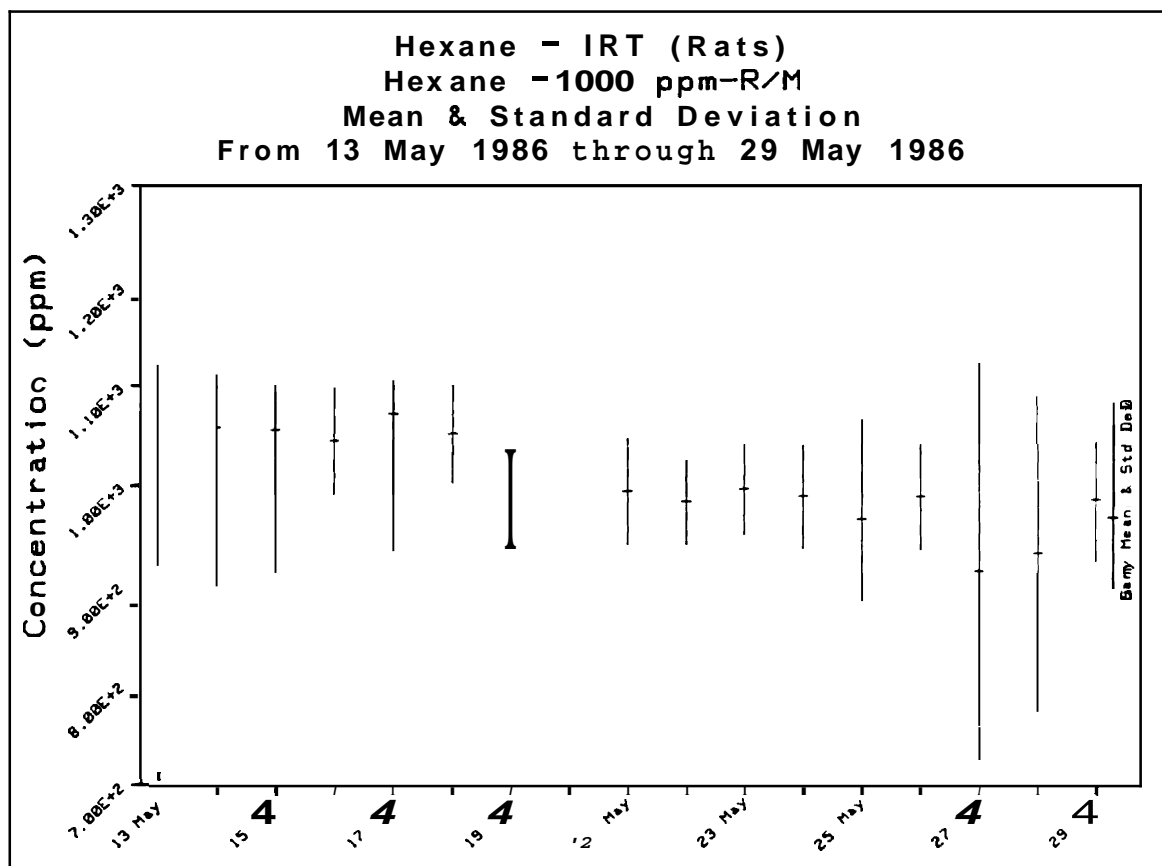


n-Hexane Rat Teratology Study  
Appendix B - Exposure

**Daily Sumnation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986**

**Summary Data for: Hexane -1000 ppm-R/M/Concentration** 9.00E+2 to 1.10E+3

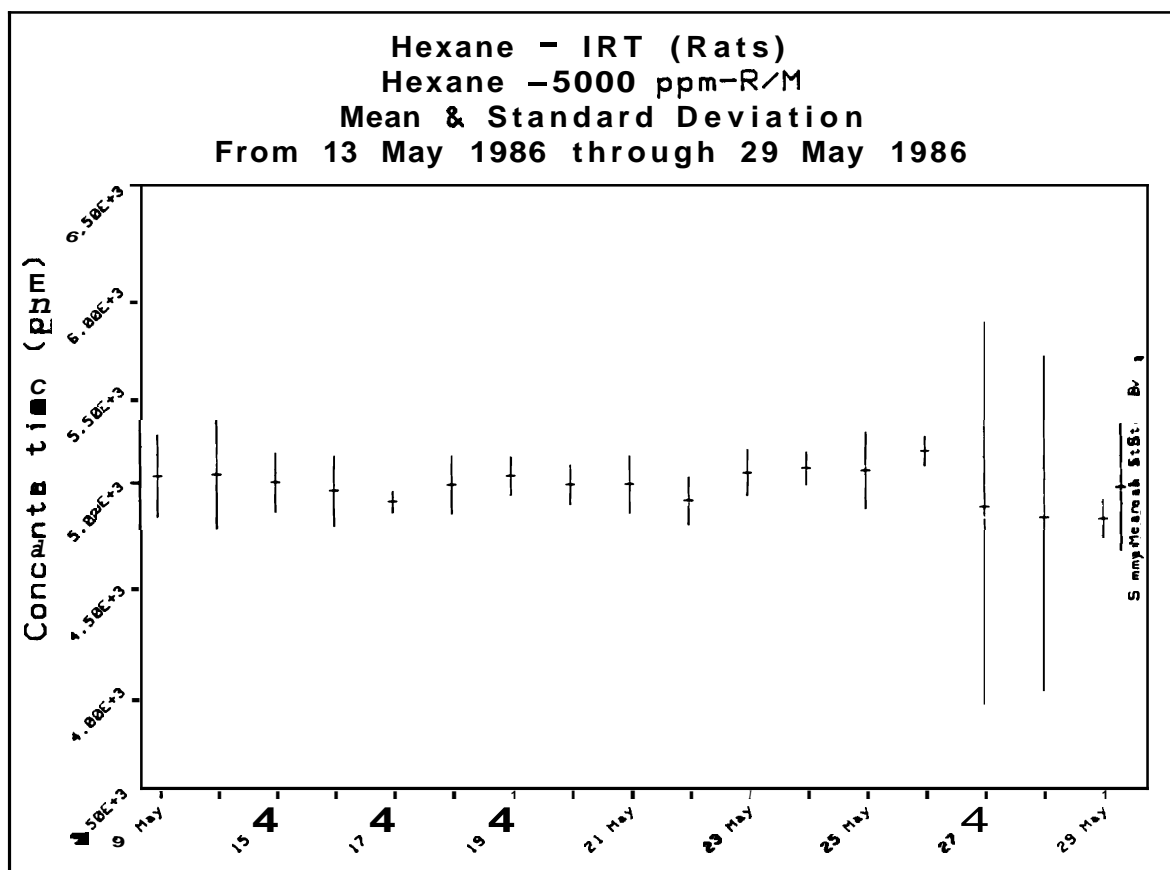
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	1.02E+3	102%	1.000E+2	10%	1.29E+3	8.14E+2	31.	23.	74%
14 May 1986	1.01E+3	101%	1.059E+2	11%	1.31E+3	8.80E+2	34.	28.	82%
15 May 1986	1.00E+3	100%	9.054E+1	9%	1.24E+3	8.68E+2	35.	27.	77%
16 May 1986	9.93E+2	99%	5.325E+1	5%	1.09E+3	9.02E+2	31.	31.	100%
17 May 1986	1.02E+3	102%	8.513E+1	8%	1.32E+3	9.13E+2	34.	31.	91%
18 May 1986	1.00E+3	100%	4.852E+1	5%	1.17E+3	8.98E+2	37.	35.	95%
19 May 1986	9.96E+2	100%	5.735E+1	6%	1.24E+3	9.16E+2	39.	37.	95%
20 May 1986	9.88E+2	99%	5.131E+1	5%	1.17E+3	9.18E+2	41.	39.	95%
21 May 1986	1.01E+3	101%	5.280E+1	5%	1.15E+3	8.97E+2	38.	34.	89%
22 May 1986	9.98E+2	100%	4.187E+1	4%	1.10E+3	8.98E+2	42.	41.	98%
23 May 1986	1.01E+3	101%	4.517E+1	4%	1.11E+3	9.06E+2	44.	43.	98%
24 May 1986	9.99E+2	100%	5.163E+1	5%	1.12E+3	8.78E+2	38.	35.	92%
25 May 1986	9.76E+2	98%	9.113E+1	9%	1.13E+3	6.03E+2	35.	31.	89%
26 May 1986	9.99E+2	100%	5.247E+1	5%	1.14E+3	8.73E+2	38.	35.	92%
27 May 1986	9.25E+2	92%	1.982E+2	21%	1.47E+3	4.68E+2	26.	16.	62%
28 May 1986	9.42E+2	94%	1.689E+2	18%	1.11E+3	2.70E+1	42.	36.	86%
29 May 1986	1.01E+3	101%	5.787E+1	6%	1.16E+3	8.18E+2	44.	38.	86%
Summary	9.94E+2	99%	8.891E+1	9%	1.47E+3	2.70E+1	629.	560.	89%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane -5000 ppm-R/M/Concentration								4.50E+3 to 5.50E+3	
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	5.03E+3	101%	2.040E+2	4%	5.49E+3	4.67E+3	31.	31.	100%
14 May 1986	5.04E+3	101%	2.698E+2	5%	5.34E+3	4.17E+3	34.	32.	94%
15 May 1986	5.00E+3	100%	1.481E+2	3%	5.26E+3	4.72E+3	35.	35.	100%
16 May 1986	4.96E+3	99%	1.759E+2	4%	5.47E+3	4.67E+3	31.	31.	100%
17 May 1986	4.90E+3	98%	5.465E+1	1%	4.99E+3	4.74E+3	34.	34.	100%
18 May 1986	4.98E+3	100%	1.442E+2	3%	5.24E+3	4.60E+3	38.	38.	100%
19 May 1986	5.03E+3	101%	9.618E+1	2%	5.27E+3	4.74E+3	39.	39.	100%
20 May 1986	4.98E+3	100%	9.988E+1	2%	5.12E+3	4.77E+3	42.	42.	100%
21 May 1986	4.98E+3	100%	1.434E+2	3%	5.23E+3	4.70E+3	39.	39.	100%
22 May 1986	4.90E+3	98%	1.187E+2	2%	5.30E+3	4.75E+3	42.	42.	100%
23 May 1986	5.04E+3	101%	1.149E+2	2%	5.28E+3	4.71E+3	44.	44.	100%
24 May 1986	5.06E+3	101%	8.195E+1	2%	5.21E+3	4.87E+3	38.	38.	100%
25 May 1986	5.05E+3	101%	1.890E+2	4%	5.26E+3	4.48E+3	35.	33.	94%
26 May 1986	5.14E+3	103%	7.300E+1	1%	5.26E+3	4.97E+3	38.	38.	100%
27 May 1986	4.87E+3	97%	9.537E+2	20%	5.38E+3	7.35E+2	24.	21.	88%
28 May 1986	4.81E+3	96%	8.346E+2	17%	5.22E+3	1.66E+1	37.	34.	92%
29 May 1986	4.96E+3	99%	9.480E+1	2%	5.13E+3	4.75E+3	44.	44.	100%
Summary	4.99E+3	100%	3.117E+2	6%	5.49E+3	1.66E+1	625.	615.	98%

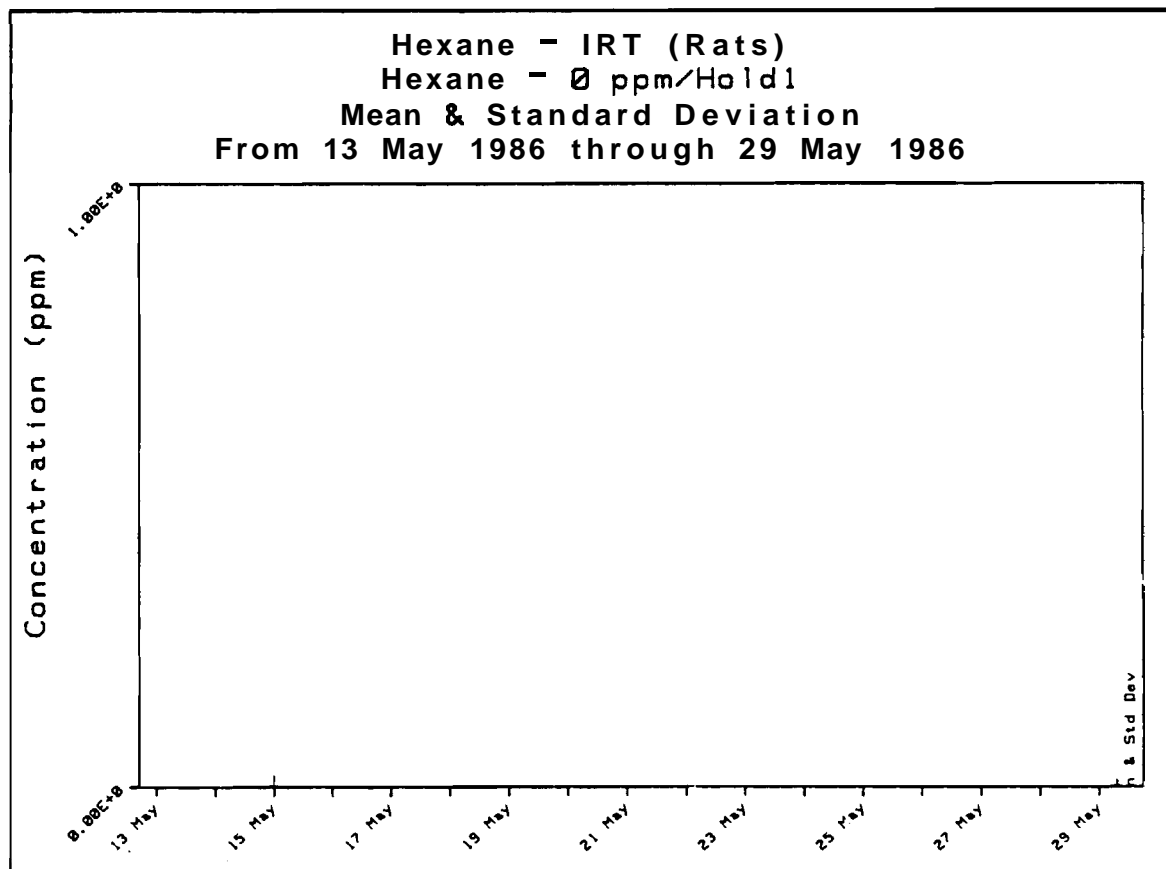


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

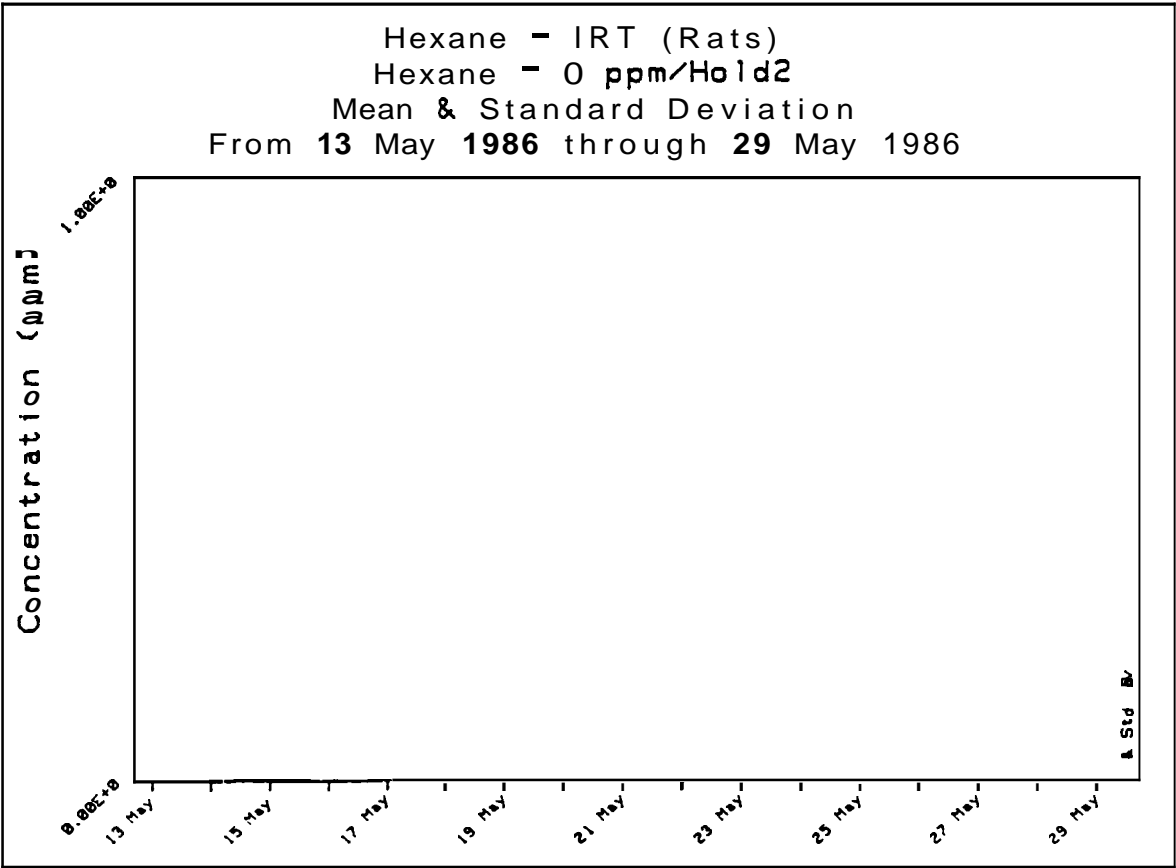
Summary Data for: Hexane - 0 ppm/hold/Concentration

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	0.00E+0	OK	0.000E+0	0%	0.00E+0	0.00E+0	31.	31.	100%
14 May 1986	0.00E+0	OK	0.000E+0	OK	0.00E+0	0.00E+0	33.	33.	100%
15 May 1986	2.80E-3	0%	1.654E-2	592%	9.79E-2	0.00E+0	35.	35.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	9.89E-4	0%	9.836E-3	995%	9.79E-2	0.00E+0	99.	99.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986									
Summary Data for: Hexane - 0 ppm/Hold2/Concentration								0.00E+0 to 1.00E+0	
Date	Mean	X Taraet	Std Oev	X RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	31.	31.	100%
14 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	34.	34.	100%
15 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	36.	36.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	101.	101.	100%

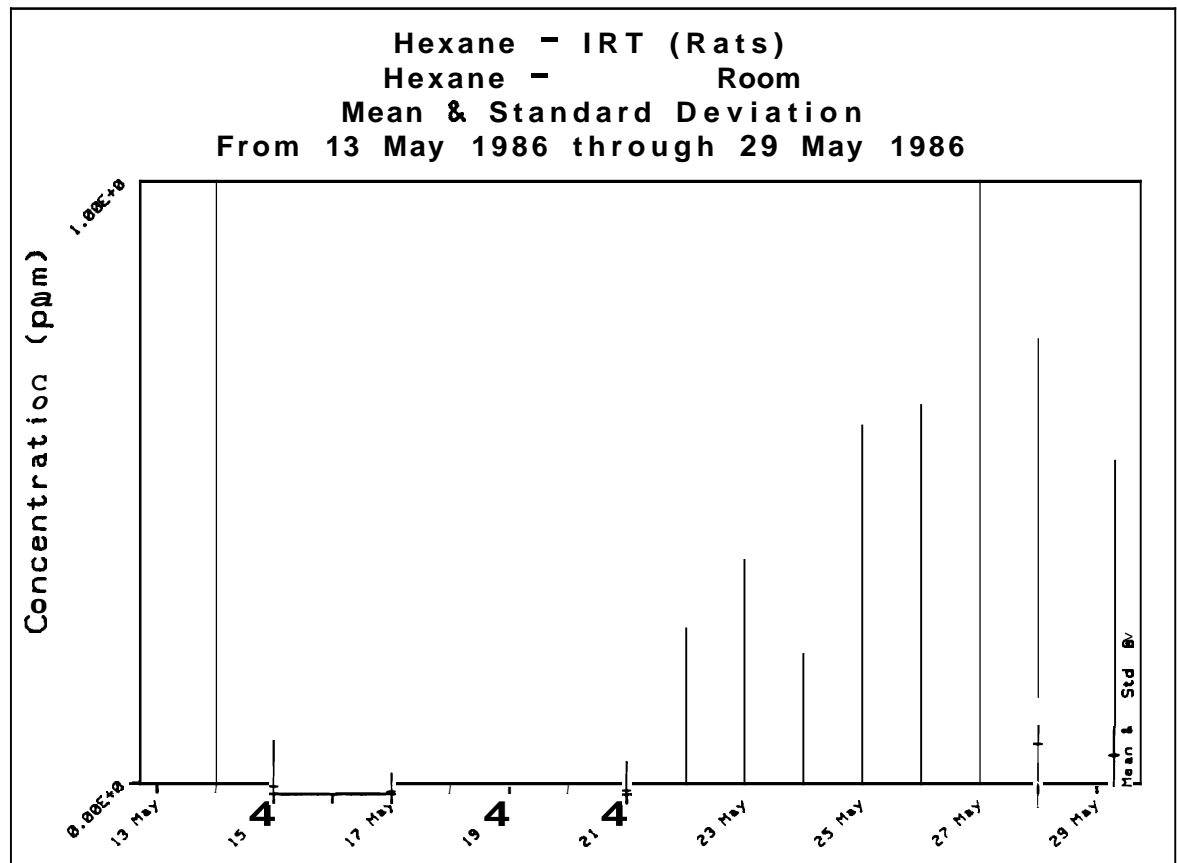




n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

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
13 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	31.	31.	100%
14 May 1986	4.81E-1	0%	1.338E+0	278%	4.18E+0	0.00E+0	34.	30.	88%
15 May 1986	1.27E-2	0%	7.428E-2	583%	4.33E-1	0.00E+0	34.	34.	100%
16 May 1986	0.00E+0	0%	0.000E+0	OK	0.00E+0	0.00E+0	34.	34.	100%
17 May 1986	4.84E-3	0%	2.944E-2	608%	1.79E-1	0.00E+0	37.	37.	100%
18 May 1986	0.00E+0	0%	0.000E+0	OK	0.00E+0	0.00E+0	38.	38.	100%
19 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	38.	38.	100%
20 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	45.	45.	100%
21 May 1986	7.38E-3	0%	4.783E-2	648%	3.10E-1	0.00E+0	42.	42.	100%
22 May 1986	3.35E-2	OK	2.247E-1	671%	1.51E+0	0.00E+0	45.	44.	98%
23 May 1986	6.31E-2	0%	3.065E-1	486%	2.01E+0	0.00E+0	47.	46.	98%
24 May 1986	3.14E-2	0%	1.822E-1	581%	1.19E+0	0.00E+0	43.	42.	98%
25 May 1986	8.64E-2	0%	5.110E-1	592%	3.02E+0	0.00E+0	35.	34.	97%
26 May 1986	9.10E-2	0%	5.415E-1	595%	3.58E+0	0.00E+0	44.	43.	98%
27 May 1986	5.63E-1	0%	1.058E+0	188%	3.35E+0	0.00E+0	22.	17.	77%
28 May 1986	1.07E-1	0%	6.344E-1	594%	4.15E+0	0.00E+0	43.	42.	98%
29 May 1986	0.00E+0	0%	0.000E+0		0.00E+0	0.00E+0	46.	46.	100%
Summary	7.16E-2	0%	4.650E-1	649%	4.18E+0	0.00E+0	658.	643.	98%

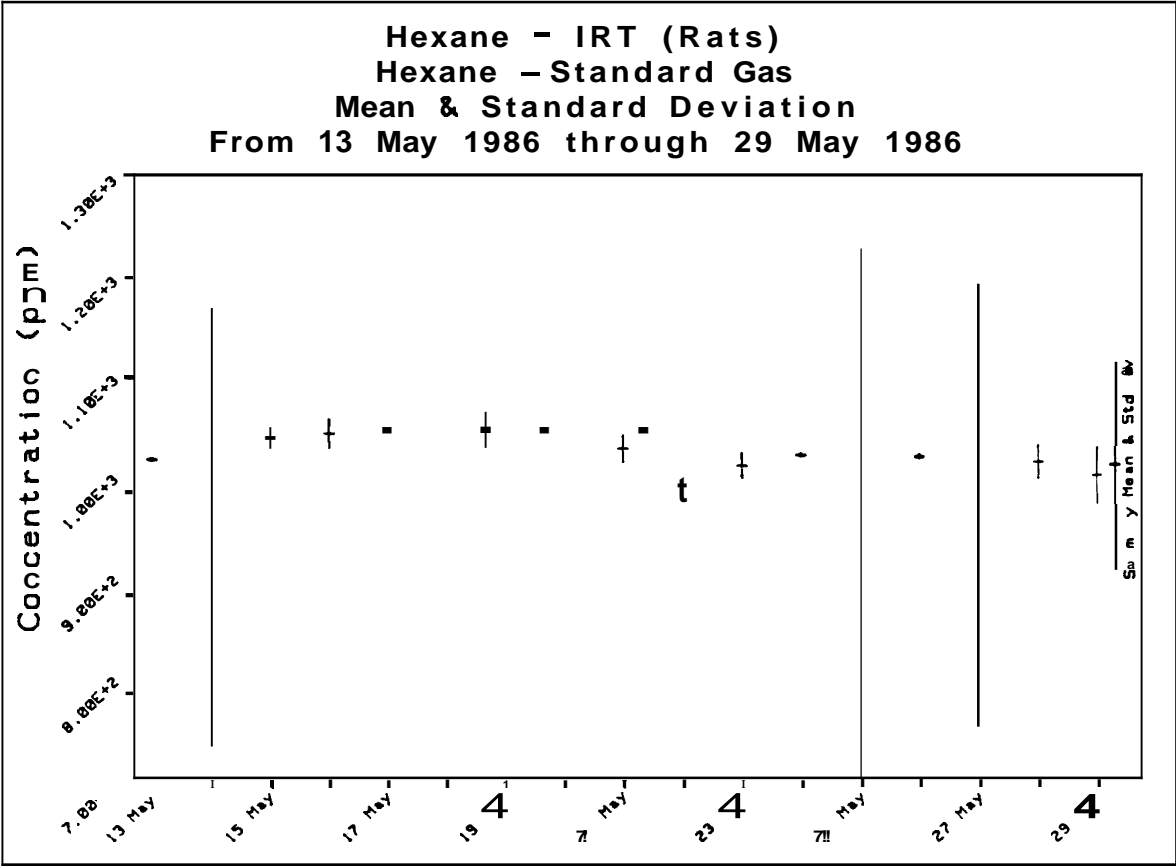


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

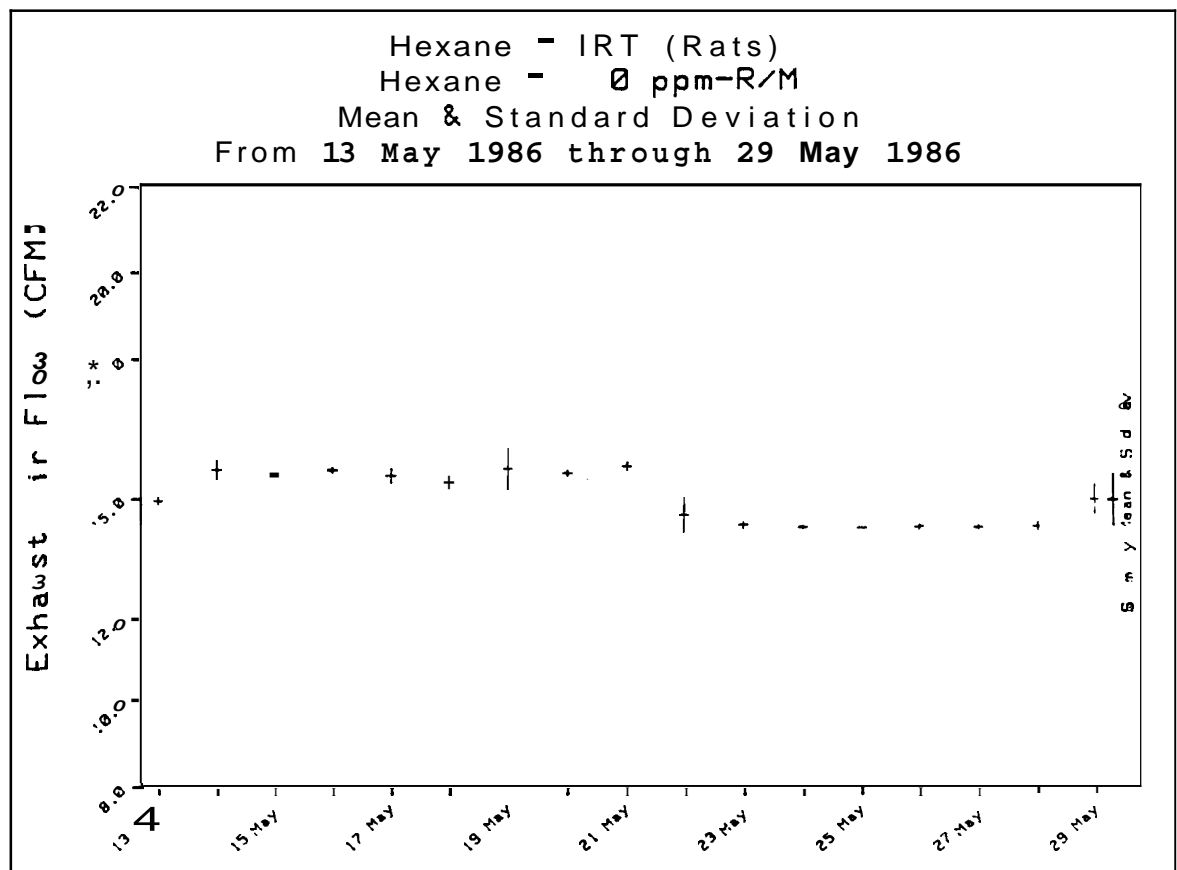
Summary Data for: Hexane -Standard Gas/Concentration 9.00E+2 to 1.10E+3

Date	Mean	X Target	Std Dev	% RSD	Maximum	Minimum	N	N in	X N in
13 May 1986	1.02E+3	102%	1.586E+0	0%	1.02E+3	1.01E+3	32.	32.	100%
14 May 1986	9.51E+2	95%	2.185E+2	23%	1.02E+3	6.96E+0	31.	28.	90%
15 May 1986	1.04E+3	104%	6.828E+0	1%	1.04E+3	1.01E+3	36.	36.	100%
16 May 1986	1.05E+3	105%	1.426E+1	1%	1.10E+3	1.03E+3	31.	31.	100%
17 May 1986	1.02E+3	102%	1.157E+0	0%	1.03E+3	1.02E+3	35.	35.	100%
18 May 1986	1.03E+3	103%	1.626E+1	2%	1.05E+3	1.00E+3	39.	39.	100%
19 May 1986	1.03E+3	103%	9.719E-1	0%	1.03E+3	1.03E+3	39.	39.	100%
20 May 1986	1.03E+3	103%	8.985E-1	0%	1.03E+3	1.03E+3	43.	43.	100%
21 May 1986	1.03E+3	103%	1.328E+1	1%	1.03E+3	9.92E+2	39.	39.	100%
22 May 1986	9.85E+2	98%	1.247E+1	1%	1.02E+3	9.58E+2	43.	43.	100%
23 May 1986	1.01E+3	101%	1.252E+1	1%	1.02E+3	9.88E+2	44.	44.	100%
24 May 1986	1.02E+3	102%	1.716E+0	0%	1.02E+3	1.01E+3	39.	39.	100%
25 May 1986	9.02E+2	90%	3.243E+2	36%	1.02E+3	8.87E+0	35.	31.	89%
26 May 1986	1.02E+3	102%	1.826E+0	0%	1.03E+3	1.01E+3	39.	39.	100%
27 May 1986	9.70E+2	97%	2.204E+2	23%	1.05E+3	1.57E+1	21.	20.	95%
28 May 1986	1.01E+3	101%	1.637E+1	2%	1.03E+3	9.95E+2	49.	49.	100%
29 May 1986	9.97E+2	100%	2.761E+1	3%	1.05E+3	9.63E+2	44.	44.	100%
Summary	1.01E+3	101%	1.031E+2	10%	1.10E+3	6.96E+0	639.	631.	99%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

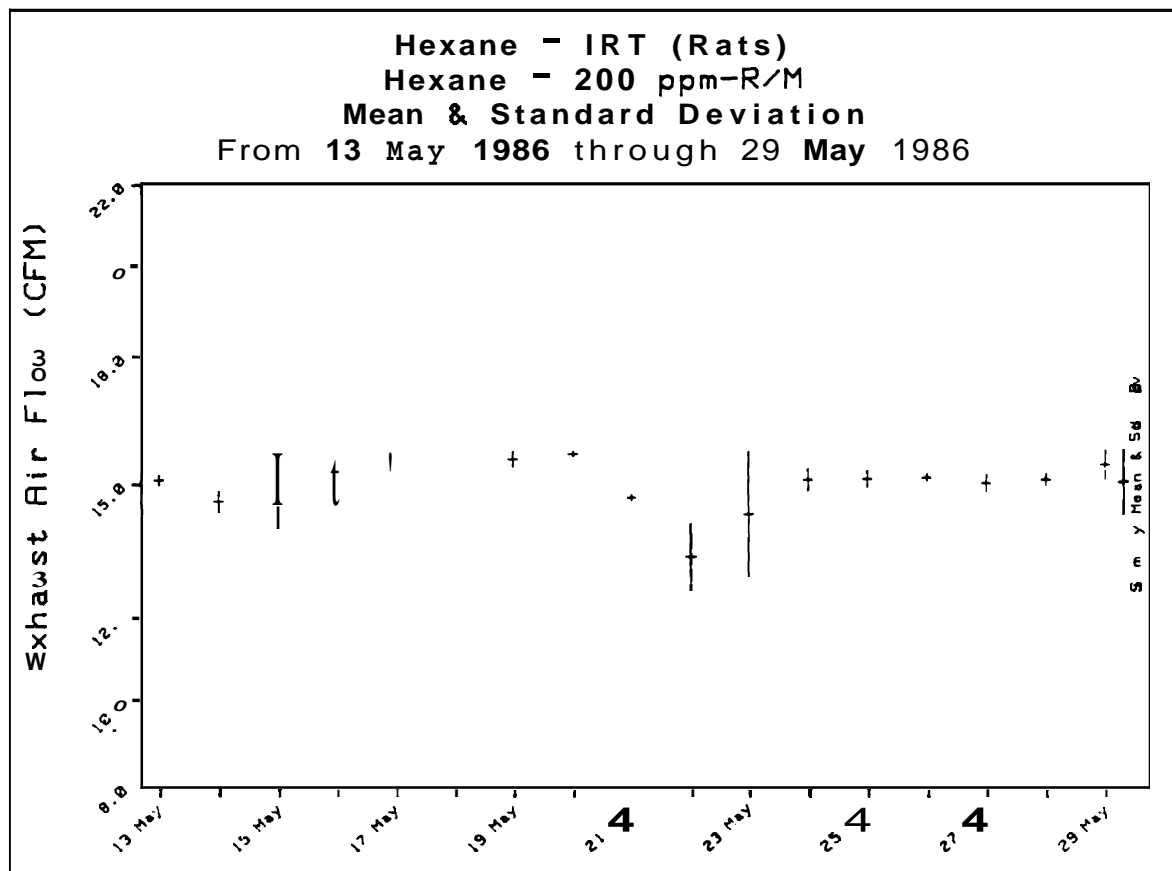
Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986									
Summary Data for: Hexane - 0 ppm-R/M/Exhaust Air Flow 12.0 to 18.0									
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	15.0	100%	.09	1%	15.1	14.9	5.	5.	100%
14 May 1986	15.2	101%	.21	1%	15.4	14.9	5.	5.	100%
15 May 1986	15.2	101%	.04	0%	15.3	15.2	6.	6.	100%
16 May 1986	15.1	101%	.05	0%	15.2	15.1	6.	6.	100%
17 May 1986	15.0	100%	.16	1%	15.2	14.8	5.	5.	100%
18 May 1986	14.8	99%	.10	1%	15.0	14.7	6.	6.	100%
19 May 1986	15.3	102%	.46	3%	16.3	14.9	7.	7.	100%
20 May 1986	15.2	101%	.08	0%	15.3	15.1	7.	7.	100%
21 May 1986	15.3	102%	.10	1%	15.5	15.2	6.	6.	100%
22 May 1986	14.3	95%	.40	3%	15.2	14.1	7.	7.	100%
23 May 1986	14.1	94%	.08	1%	14.2	14.0	7.	7.	100%
24 May 1986	14.0	93%	.04	0%	14.1	14.0	6.	6.	100%
25 May 1986	14.0	93%	0.00	0%	14.0	14.0	7.	7.	100%
26 May 1986	13.9	93%	.05	0%	14.0	13.9	7.	7.	100%
27 May 1986	13.9	93%	.05	0%	14.0	13.9	7.	7.	100%
28 May 1986	13.9	93%	.08	1%	14.1	13.9	7.	7.	100%
29 May 1986	14.6	98%	.34	2%	14.9	13.9	7.	7.	100%
Summary	14.6	97%	.58	4%	16.3	13.9	108.	108.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

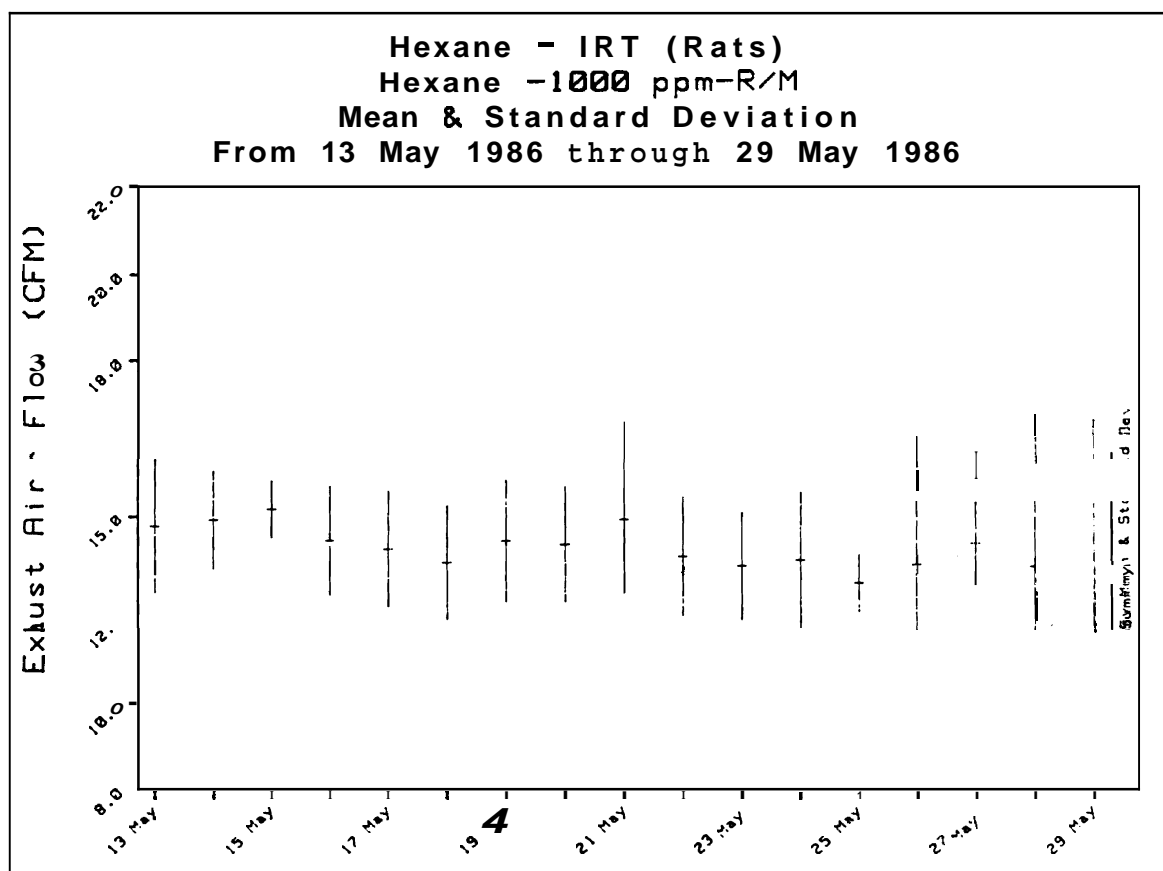
Oilv Sumnation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 200 ppm-R/M/Exhaust Air Flow									
Date	Mean	% Target	Std Dev	X RSD	Maximum	Minimum	N	N in	X N in
13 May 1986	15.1	101%	.12	1%	15.3	15.0	5.	5.	100%
14 May 1986	14.6	97%	.25	2%	15.0	14.3	5.	5.	100%
15 May 1986	14.9	99%	.86	6%	16.1	14.1	6.	6.	100%
16 May 1986	15.1	101%	.59	4%	15.7	14.6	6.	6.	100%
17 May 1986	15.6	104%	.10	1%	15.7	15.5	6.	6.	100%
18 May 1986	15.2	101%	.07	OK	15.3	15.1	7.	7.	100%
19 Hay 1986	15.6	104%	.18	1%	15.7	15.2	7.	7.	100%
20 May 1986	15.7	105%	.07	0%	15.8	15.6	7.	7.	100%
21 May 1986	14.7	98%	.08	1%	14.8	14.6	7.	7.	100%
22 May 1986	13.3	89%	.76	6%	14.8	12.6	7.	7.	100%
23 May 1986	14.3	95%	1.45	10%	15.3	11.9	7.	6.	86%
24 May 1986	15.1	101%	.24	2%	15.2	14.6	6.	6.	100%
25 May 1986	15.1	101%	.18	1%	15.2	14.7	7.	7.	100%
26 May 1986	15.1	101%	.09	1%	15.2	15.0	7.	7.	100%
27 May 1986	15.0	100%	.19	1%	15.2	14.6	7.	7.	100%
28 May 1986	15.1	100%	.13	1%	15.3	15.0	7.	7.	100%
29 May 1986	15.4	103%	.33	2%	15.8	15.1	7.	7.	100%
Summary	15.0	100%	.73	5%	16.1	11.9	111.	110.	99%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986									
Summary Data for: Hexane -1000 ppm-R/M/Exhaust Air Flow								12.0 to 18.0	
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	14.8	99%	1.56	11%	16.6	12.5	5.	5.	100%
14 May 1986	14.9	99%	1.14	8%	16.8	13.8	5.	5.	100%
15 May 1986	15.2	101%	.66	4%	15.8	14.0	6.	6.	100%
16 May 1986	14.4	96%	1.26	9%	15.8	12.8	6.	6.	100%
17 May 1986	14.2	95%	1.35	9%	15.8	12.7	6.	6.	100%
18 May 1986	13.9	93%	1.32	10%	15.7	12.5	7.	7.	100%
19 May 1986	14.4	96%	1.42	10%	16.5	13.0	7.	7.	100%
20 May 1986	14.3	96%	1.34	9%	16.1	12.5	7.	7.	100%
21 May 1986	14.9	99%	1.71	11%	16.7	13.0	7.	7.	100%
22 May 1986	14.0	94%	1.38	10%	16.2	12.9	7.	7.	100%
23 May 1986	13.8	92%	1.25	9%	15.7	12.7	7.	7.	100%
24 May 1986	14.0	93%	1.58	11%	16.2	12.6	6.	6.	100%
25 May 1986	13.4	89%	.67	5%	14.7	12.6	7.	7.	100%
26 May 1986	14.4	96%	1.83	13%	16.3	12.4	7.	7.	100%
27 May 1986	14.9	99%	.96	6%	15.5	12.7	7.	7.	100%
28 May 1986	14.3	95%	2.42	17%	16.9	10.9	7.	5.	71%
29 May 1986	14.1	94%	2.51	18%	16.9	12.0	7.	7.	100%
Summary	14.3	96%	1.48	10%	16.9	10.9	111.	109.	98%

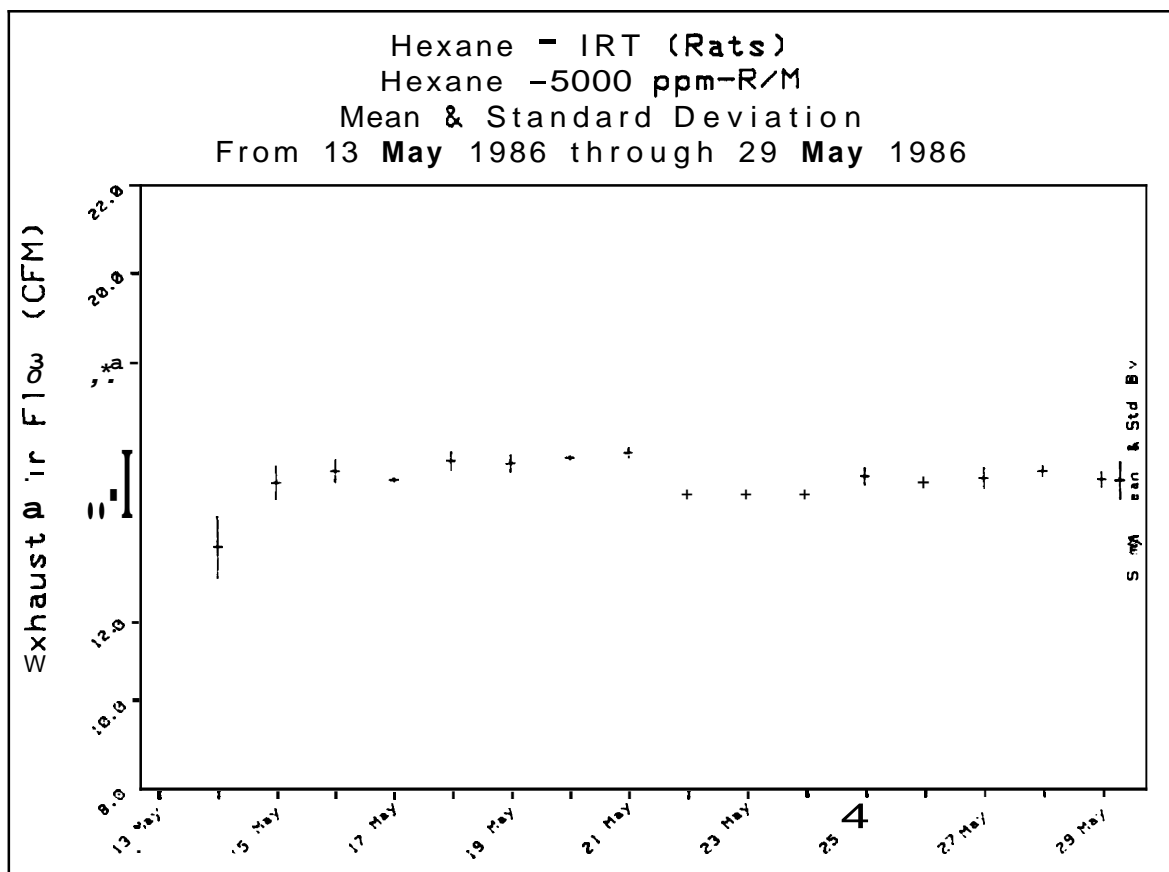


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Oilv Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

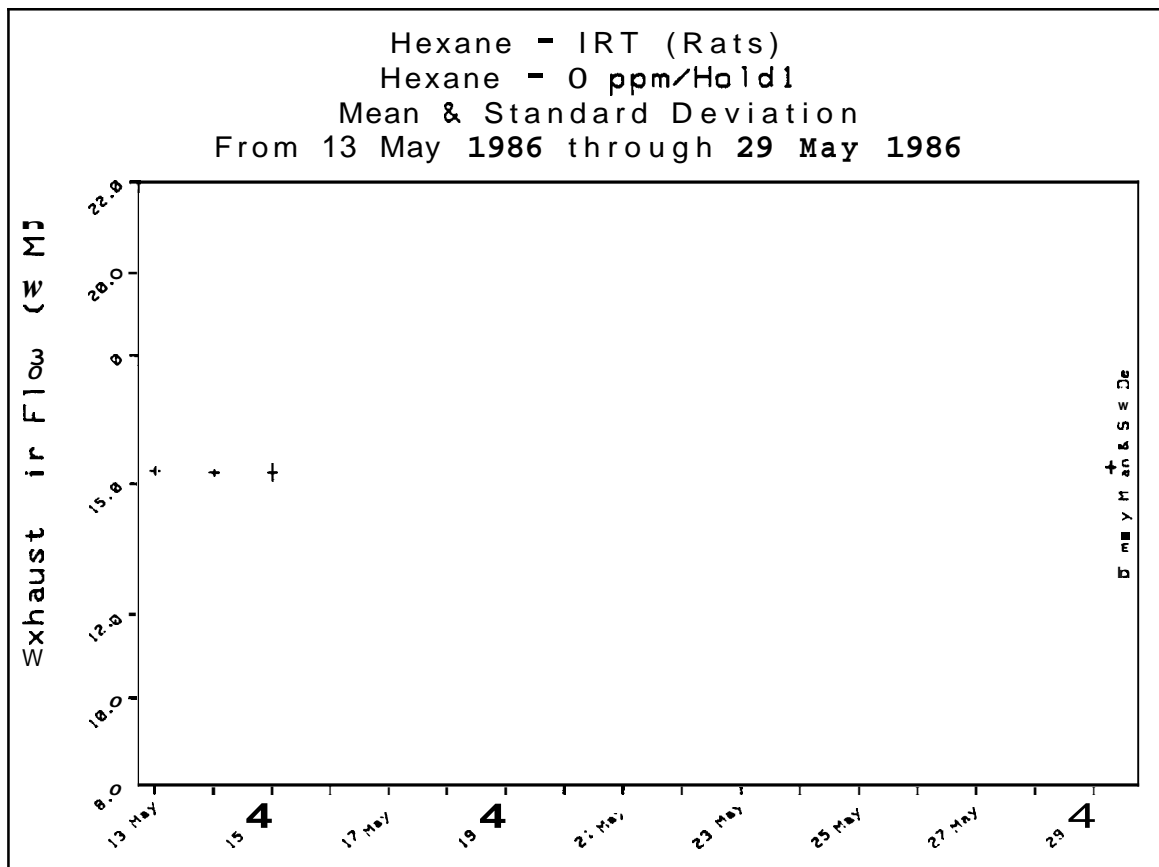
Summary Data for: Hexane -5000 ppm-R/M/Exhaust Air Flow

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	14.6	97%	.77	5%	15.3	13.3	5.	5.	100%
14 May 1986	14.4	96%	.71	5%	14.9	13.2	5.	5.	100%
15 May 1986	15.1	101%	.37	2%	15.4	14.4	6.	6.	100%
16 May 1986	15.4	102%	.27	2%	15.7	15.1	6.	6.	100%
17 May 1986	15.1	101%	.05	0%	15.2	15.1	6.	6.	100%
18 May 1986	15.6	104%	.21	1%	15.8	15.2	6.	6.	100%
19 May 1986	15.5	104%	.20	1%	15.7	15.1	7.	7.	100%
20 May 1986	15.7	104%	.05	0%	15.7	15.6	7.	7.	100%
21 May 1986	15.8	105%	.12	1%	15.9	15.6	6.	6.	100%
22 May 1986	15.4	102%	.27	2%	15.6	14.8	7.	7.	100%
23 May 1986	15.2	102%	.30	2%	15.5	14.7	7.	7.	100%
24 May 1986	15.3	102%	.08	1%	15.4	15.2	6.	6.	100%
25 May 1986	15.2	101%	.19	1%	15.5	15.0	7.	7.	100%
26 May 1986	15.0	100%	.09	1%	15.1	14.9	7.	7.	100%
27 May 1986	15.4	102%	.24	2%	15.5	15.0	7.	7.	100%
28 May 1986	15.5	104%	.13	1%	15.7	15.4	7.	7.	100%
29 May 1986	15.3	102%	.19	1%	15.6	15.1	7.	7.	100%
Summary	15.3	102%	.42	3%	15.9	13.2	109.	109.	100%



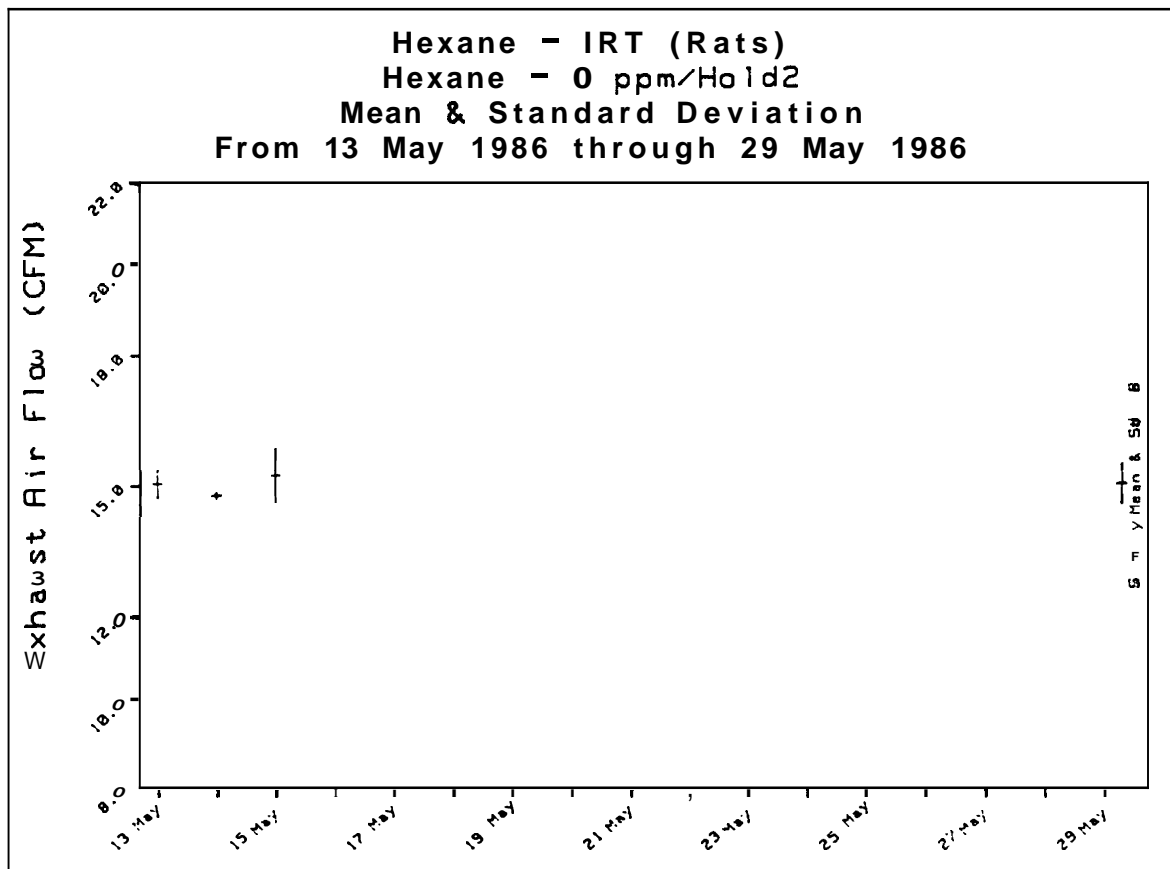
n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986									
Summary Data for: Hexane - 0 ppm/Hold1/Exhaust Air Flow								12.0 to 18.0	
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	15.3	102%	.09	1%	15.5	15.3	5.	5.	100%
14 May 1986	15.3	102%	.07	0%	15.4	15.2	5.	5.	100%
15 May 1986	15.3	102%	.20	1%	15.7	15.2	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	15.3	102%	.13	1%	15.7	15.2	16.	16.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986									
Summary Data for: Hexane - 0 ppm/Hold2/Exhaust Air Flow									
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	15.1	100%	.33	2%	15.4	14.7	5.	5.	100%
14 May 1986	14.8	99%	.07	0%	14.9	14.7	5.	5.	100%
15 May 1986	15.3	102%	.63	4%	16.2	14.8	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	15.1	100%	.46	3%	16.2	14.7	16.	16.	100%



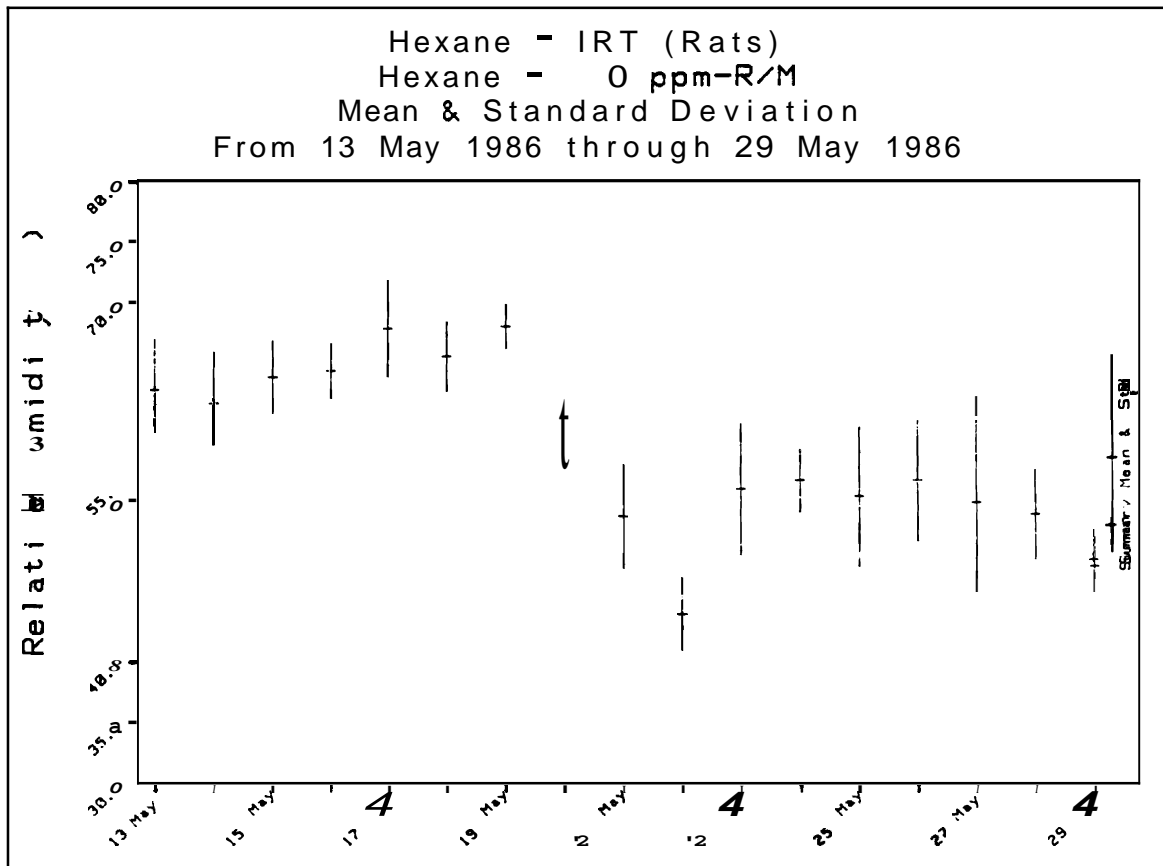


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 0 ppm-R/M/Relative Humidity 40.0 to 70.0

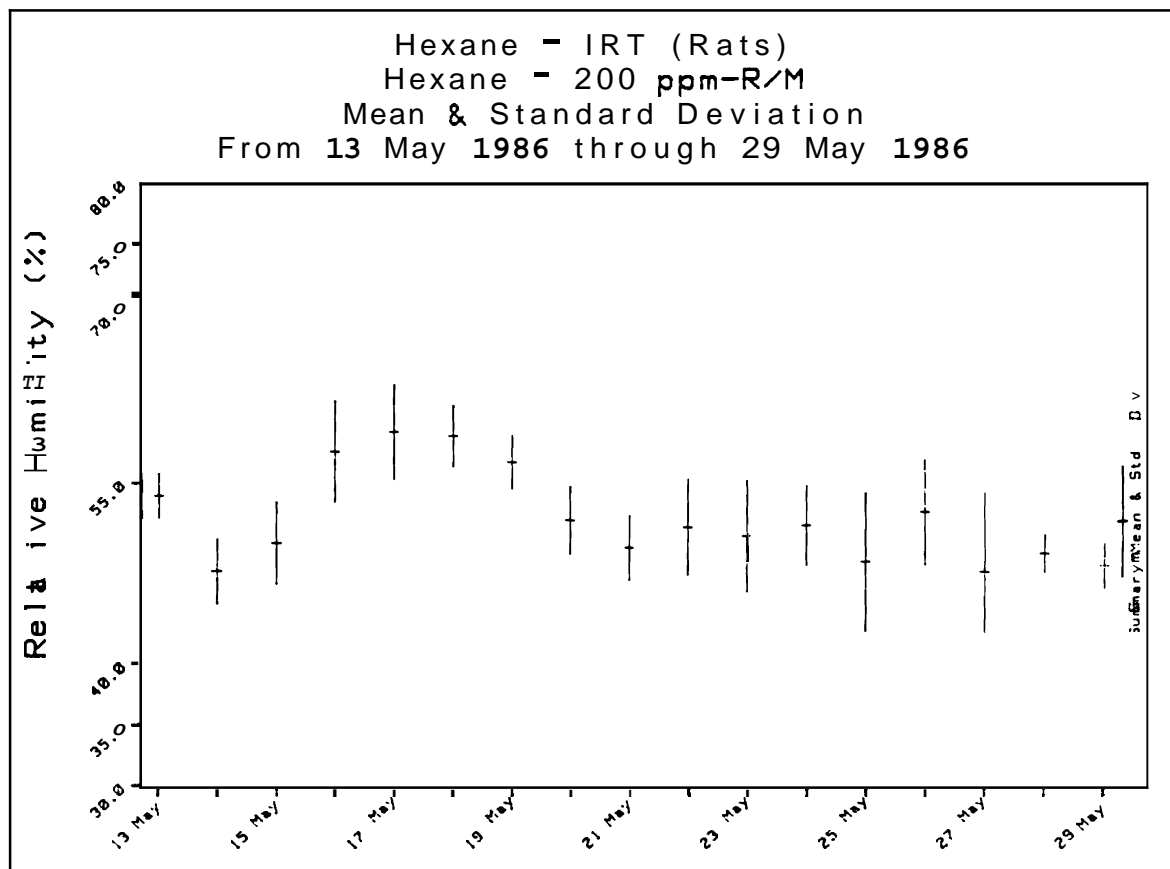
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	63.5	115%	4.12	6%	69.0	59.0	4.	4.	100%
14 May 1986	62.4	113%	4.16	7%	68.0	58.0	5.	5.	100%
15 May 1986	64.5	117%	2.95	5%	68.0	60.0	6.	6.	100%
16 May 1986	65.0	118%	2.24	3%	68.0	62.0	5.	5.	100%
17 May 1986	67.8	123%	3.92	6%	72.0	62.0	6.	5.	83%
18 May 1986	65.6	119%	2.82	4%	71.0	63.0	7.	6.	86%
19 May 1986	68.0	124%	1.79	3%	71.0	66.0	6.	5.	83%
20 May 1986	59.3	108%	3.04	5%	63.0	54.0	7.	7.	100%
21 May 1986	52.9	96%	4.30	8%	58.0	45.0	7.	7.	100%
22 May 1986	44.0	80%	3.00	7%	48.0	40.0	7.	7.	100%
23 May 1986	55.1	100%	5.46	10%	60.0	46.0	7.	7.	100%
24 May 1986	55.8	102%	2.64	5%	59.0	52.0	6.	6.	100%
25 May 1986	54.5	99%	5.82	11%	60.0	47.0	6.	6.	100%
26 May 1986	55.9	102%	5.05	9%	62.0	50.0	7.	7.	100%
27 May 1986	54.0	98%	8.25	15%	61.0	43.0	6.	6.	100%
28 May 1986	53.0	96%	3.70	7%	57.0	47.0	7.	7.	100%
29 May 1986	48.7	89%	2.43	5%	51.0	44.0	7.	7.	100%
Summary	57.7	105%	7.85	14%	72.0	40.0	106.	103.	97%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daaly Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

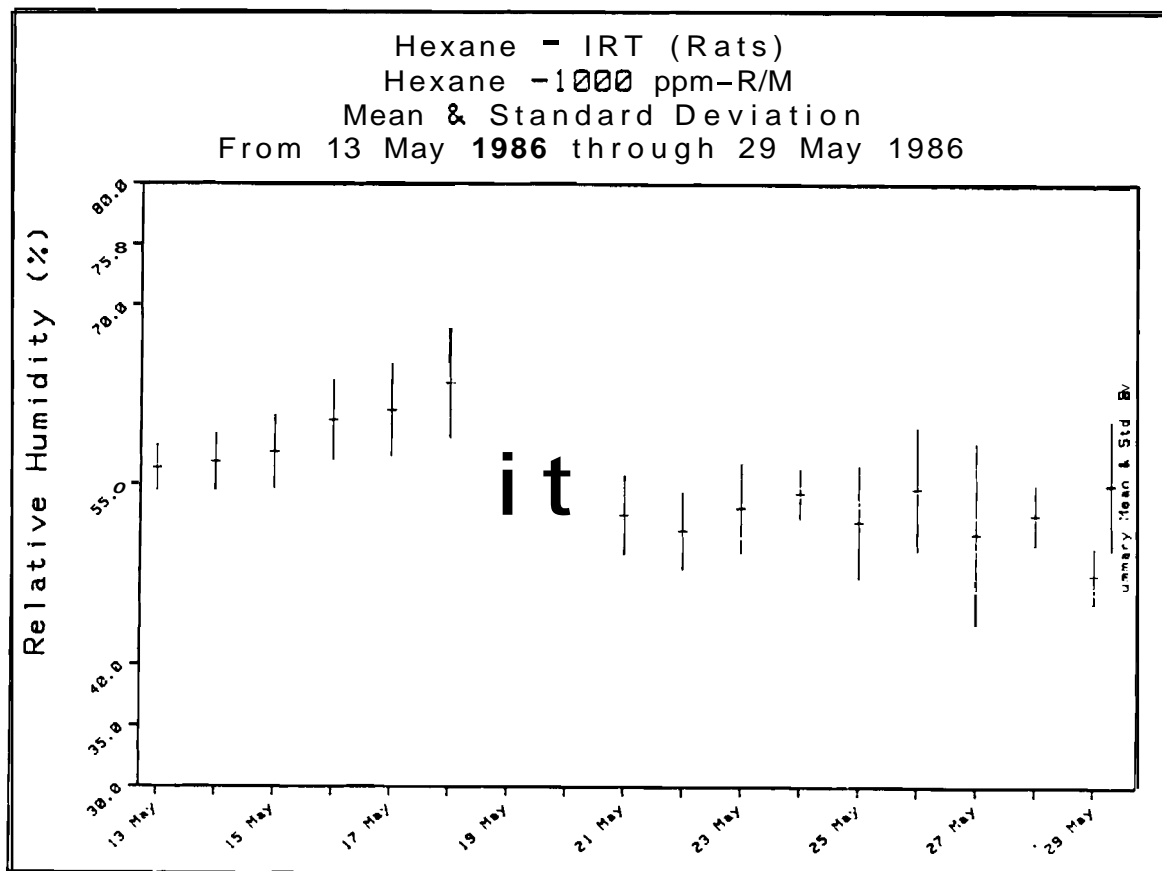
Summary Data for: Hexane - 200 ppm-R/M/Relative Humidity 40.0 to 70.0									
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	54.0	98%	1.83	3%	56.0	52.0	4.	4.	100%
14 May 1986	51.4	93%	2.70	5%	54.0	48.0	5.	5.	100%
15 May 1986	53.8	98%	3.43	6%	59.0	49.0	6.	6.	100%
16 May 1986	51.7	105%	4.23	7%	62.0	52.0	7.	7.	100%
17 May 1986	59.3	108%	3.98	7%	63.0	53.0	6.	6.	100%
18 May 1986	59.0	107%	2.58	4%	62.0	55.0	7.	7.	100%
19 May 1986	56.8	103%	2.23	4%	59.0	54.0	6.	6.	100%
20 May 1986	53.6	97%	2.82	5%	58.0	50.0	7.	7.	100%
21 May 1986	51.3	93%	2.69	5%	55.0	47.0	7.	7.	100%
22 May 1986	53.0	96%	4.00	8%	57.0	48.0	7.	7.	100%
23 May 1986	52.3	95%	4.61	9%	57.0	46.0	7.	7.	100%
24 May 1986	53.2	97%	3.31	6%	57.0	48.0	6.	6.	100%
25 May 1986	50.2	91%	5.71	11%	56.0	43.0	6.	6.	100%
26 May 1986	54.3	99%	4.39	8%	61.0	47.0	7.	7.	100%
27 May 1986	49.3	90%	6.56	13%	55.0	40.0	6.	6.	100%
28 May 1986	50.9	92%	1.57	3%	53.0	48.0	7.	7.	100%
29 May 1986	49.9	91%	1.86	4%	53.0	47.0	7.	7.	100%
Summary	53.5	97%	4.58	9%	63.0	40.0	108.	108.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

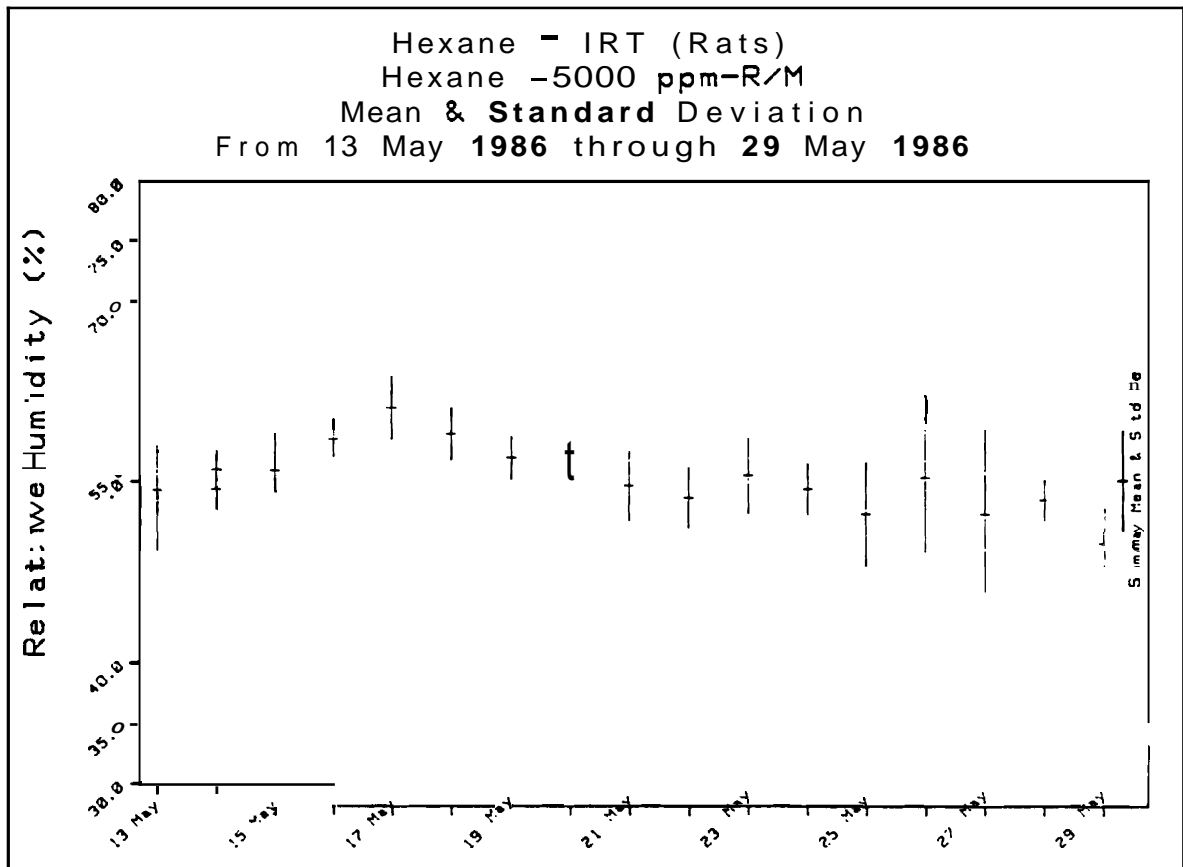
Summary Data for: Hexane -1000 ppm-R/M/Relative Humidity								
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	% N in
13 May 1986	56.5	103%	1.91	3%	59.0	55.0	4.	100%
14 May 1986	57.0	104%	2.35	4%	59.0	53.0	5.	100%
15 May 1986	57.8	105%	3.06	5%	61.0	52.0	6.	100%
16 May 1986	60.5	<b>110%</b>	3.33	6%	65.0	57.0	6.	100%
17 May 1986	61.3	112%	3.83	6%	65.0	56.0	6.	100%
18 May 1986	63.6	116%	4.54	7%	69.0	59.0	7.	100%
19 May 1986	56.2	102%	2.56	5%	59.0	53.0	6.	100%
20 May 1986	55.7	<b>101%</b>	2.36	4%	59.0	52.0	7.	100%
21 May 1986	52.6	96%	3.26	6%	56.0	46.0	7.	100%
22 May 1986	51.3	93%	3.20	6%	54.0	46.0	7.	100%
23 May 1986	53.1	97%	3.72	7%	57.0	47.0	7.	100%
24 May 1986	54.3	99%	2.07	4%	56.0	51.0	6.	100%
25 May 1986	52.0	95%	4.69	9%	58.0	44.0	6.	100%
26 May 1986	54.7	99%	5.09	9%	62.0	48.0	7.	100%
27 May 1986	51.0	93%	7.54	15%	58.0	40.0	<b>6.</b>	100%
28 May 1986	52.6	96%	2.51	5%	56.0	49.0	7.	100%
29 May 1986	47.6	86%	2.30	5%	52.0	45.0	7.	100%
Summary	55.0	<b>100%</b>	5.33	10%	69.0	40.0	107.	107.



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Sumnation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane -5000 ppm-R/M/Relative Humidity								40.0 to 70.0	
Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum	N	N in	X N in
13 May 1986	53.2	97%	4.99	9%	60.0	49.0	4.	4.	100%
14 May 1986	54.6	99%	2.97	5%	58.0	51.0	5.	5.	100%
15 May 1986	56.2	102%	3.13	6%	60.0	52.0	6.	6.	100%
16 May 1986	58.8	107%	1.48	3%	61.0	57.0	5.	5.	100%
17 May 1986	61.2	111%	2.64	4%	64.0	57.0	6.	6.	100%
18 May 1986	59.0	107%	2.16	4%	63.0	56.0	7.	7.	100%
19 May 1986	57.0	104%	1.79	3%	59.0	54.0	6.	6.	100%
20 May 1986	59.6	108%	1.72	3%	62.0	57.0	7.	7.	100%
21 May 1986	55.3	101%	2.87	5%	60.0	51.0	7.	7.	100%
22 May 1986	54.3	99%	2.50	5%	58.0	51.0	7.	7.	100%
23 May 1986	56.1	102%	3.13	6%	59.0	51.0	7.	7.	100%
24 May 1986	55.0	100%	2.10	4%	57.0	51.0	6.	6.	100%
25 May 1986	53.0	96%	4.29	8%	58.0	47.0	6.	6.	100%
26 May 1986	56.0	102%	6.11	11%	65.0	47.0	7.	7.	100%
27 May 1986	53.0	96%	7.07	13%	59.0	43.0	6.	6.	100%
28 May 1986	54.1	98%	1.68	3%	56.0	52.0	7.	7.	100%
29 May 1986	50.7	92%	2.75	5%	53.0	45.0	7.	7.	100%
Summary	55.7	101%	4.15	7%	65.0	43.0	106.	106.	100%

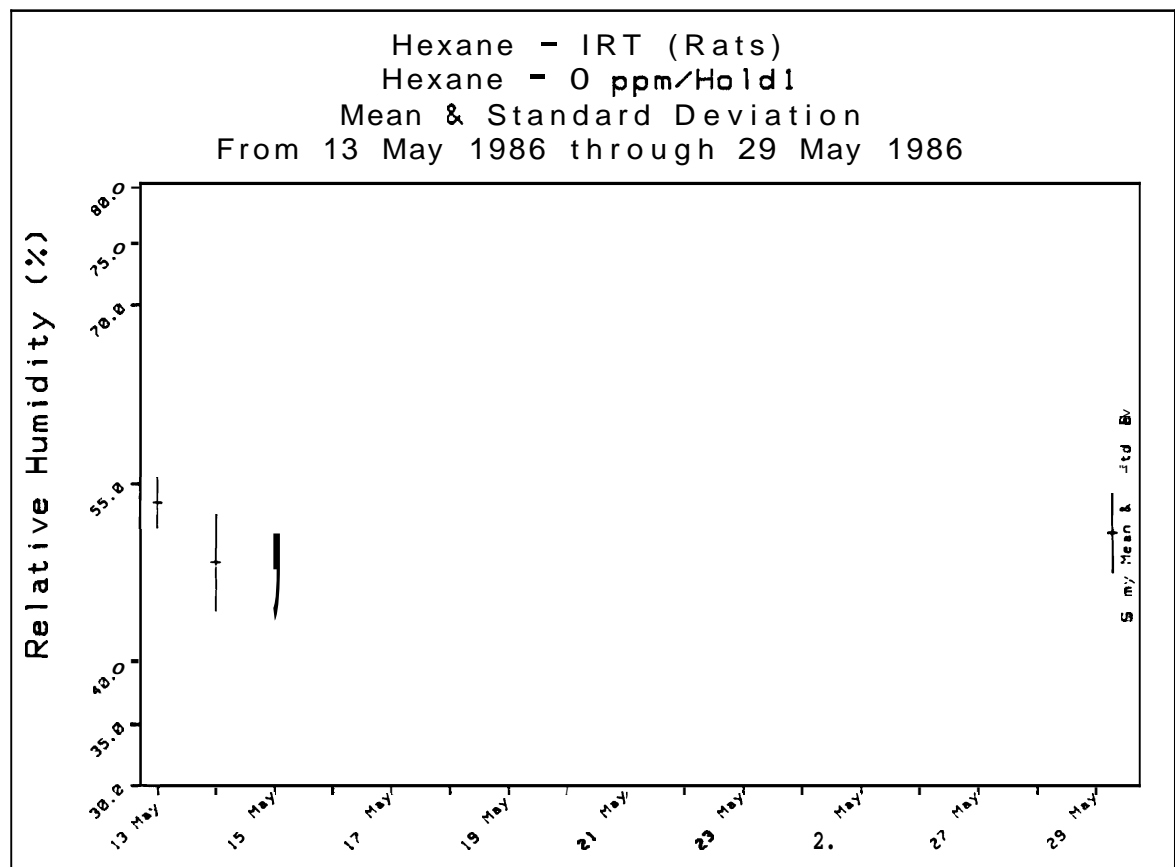


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 0 ppm/hold1/Relative Humidity

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	53.5	97%	2.08	4%	56.0	51.0	4.	4.	100%
14 May 1986	53.0	96%	4.06	8%	57.0	47.0	5.	5.	100%
15 May 1986	51.3	93%	3.44	7%	56.0	48.0	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	52.5	95%	3.29	6%	57.0	47.0	15.	15.	100%

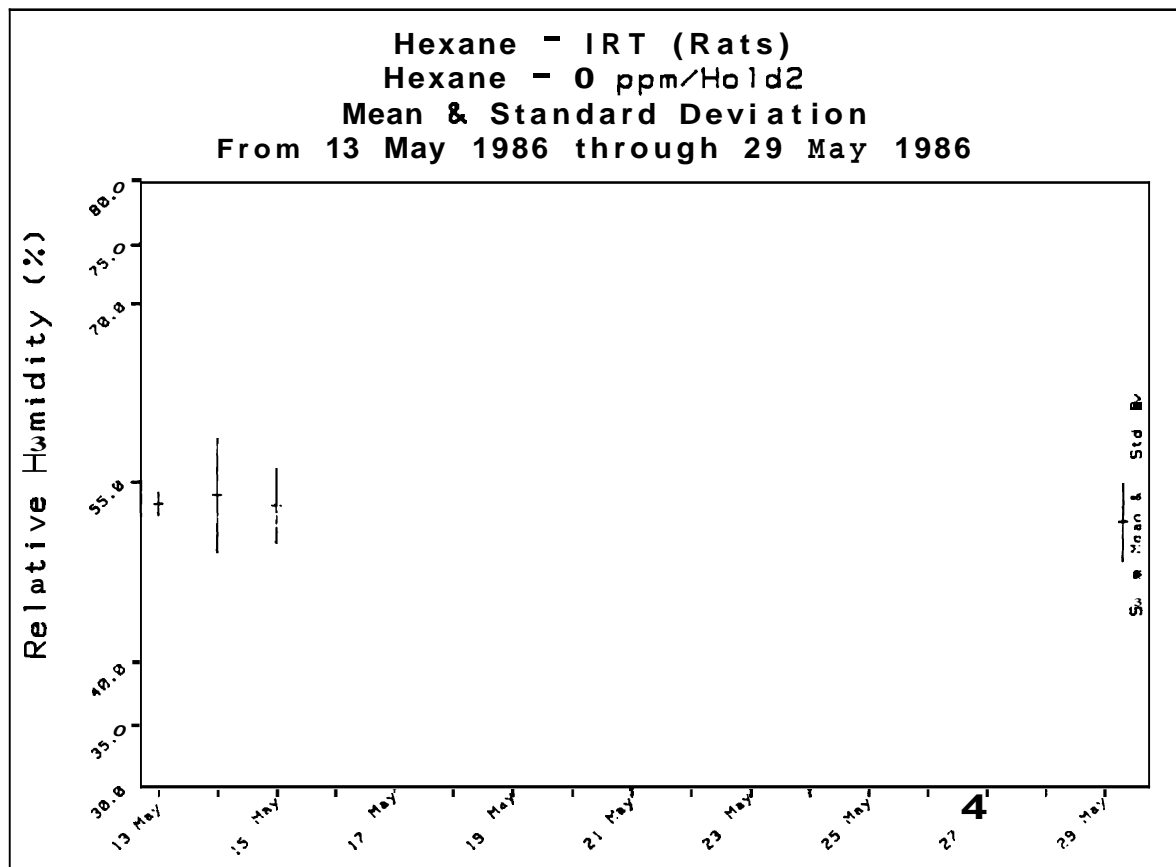


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 0 ppm/Hold2/Relative Humidity

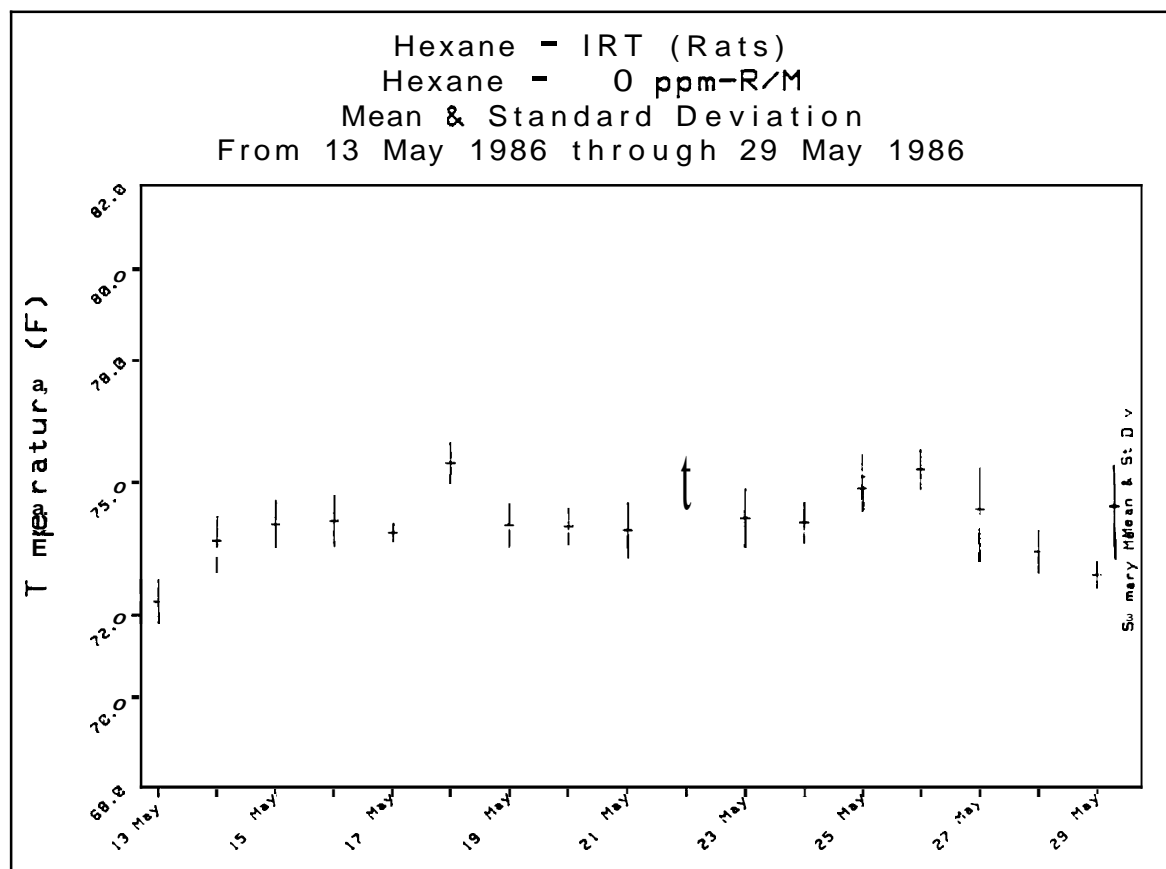
Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum	N	40.0 to 70.0 N in	X N in
13 May 1986	53.2	97%	.96	2%	54.0	52.0	4.	4.	100%
14 May 1986	54.0	98%	4.74	9%	59.0	48.0	5.	5.	100%
15 May 1986	53.2	97%	3.13	6%	57.0	50.0	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	53.5	97%	3.20	6%	59.0	48.0	15.	15.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Sumnation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

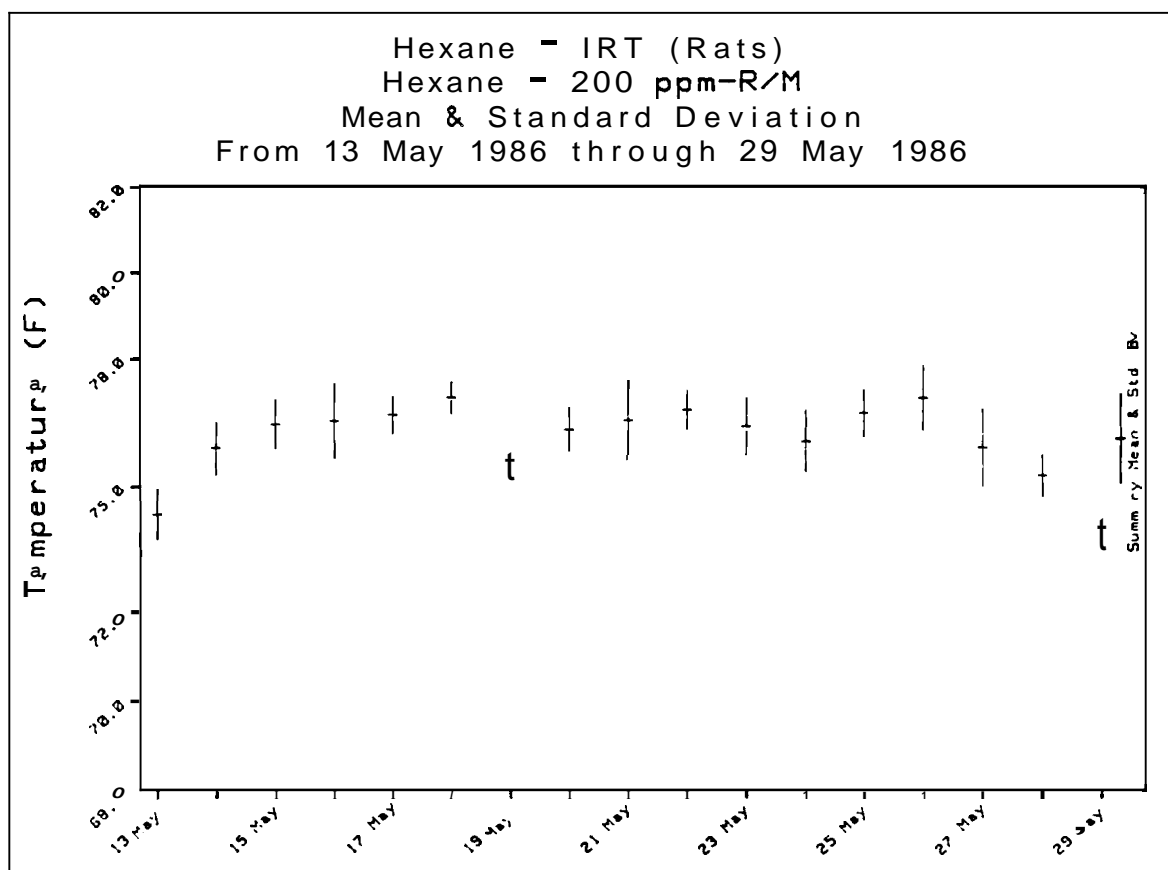
Summary Data for: Hexane - 0 ppm-R/M/Temperature 72.0 to 78.0									
Date	Mean	% Target	Std Dev	% RSO	Maximum	Minimum	N	N in	% N in
13 May 1986	72.3	96%	.51	1%	73.1	71.7	5.	4.	80%
14 May 1986	73.6	98%	.55	1%	74.2	73.0	5.	5.	100%
15 May 1986	74.8	100%	.55	1%	75.4	73.9	6.	6.	100%
16 May 1986	74.8	100%	.59	1%	75.6	74.0	5.	5.	100%
17 May 1986	74.5	99%	.22	0%	74.8	74.3	6.	6.	100%
18 May 1986	75.6	101%	.47	1%	76.2	74.9	7.	7.	100%
19 May 1986	74.0	99%	.51	1%	74.7	73.3	6.	6.	100%
20 May 1986	74.0	99%	.42	1%	74.4	73.3	6.	6.	100%
21 May 1986	73.9	98%	.64	1%	74.6	72.7	7.	7.	100%
22 May 1986	75.2	100%	.63	1%	75.8	74.0	6.	6.	100%
23 May 1986	74.3	99%	.68	1%	75.2	73.1	7.	7.	100%
24 May 1986	74.2	99%	.47	1%	74.6	73.6	7.	7.	100%
25 May 1986	75.0	100%	.51	1%	75.5	74.2	6.	6.	100%
26 May 1986	75.1	100%	.46	1%	76.1	74.8	7.	7.	100%
27 May 1986	74.2	99%	.96	1%	74.9	72.1	7.	7.	100%
28 May 1986	73.5	98%	.49	1%	73.9	72.5	7.	7.	100%
29 May 1986	72.9	97%	.31	0%	73.4	72.5	6.	6.	100%
Summary	74.2	99%	.95	1%	76.2	71.7	106.	105.	99%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 200 ppm-R/M/Temperature								
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in
13 May 1986	74.4	99%	.58	1%	75.3	73.7	5.	5.
14 May 1986	75.9	101%	.62	1%	76.6	75.2	5.	5.
15 May 1986	76.5	102%	.57	1%	77.0	75.4	6.	6.
16 May 1986	76.5	102%	.88	1%	77.4	75.5	5.	5.
17 May 1986	76.7	102%	.43	1%	77.1	75.9	6.	6.
18 May 1986	77.1	103%	.37	0%	77.4	76.5	7.	7.
19 May 1986	75.5	101%	.34	0%	76.1	75.1	6.	6.
20 May 1986	76.4	102%	.50	1%	77.0	75.6	6.	6.
21 May 1986	76.6	102%	.93	1%	77.4	74.7	7.	7.
22 May 1986	76.8	102%	.45	1%	77.4	76.1	6.	6.
23 May 1986	76.4	102%	.67	1%	77.2	75.6	7.	7.
24 May 1986	76.1	101%	.72	1%	77.1	75.0	7.	7.
25 May 1986	76.7	102%	.54	1%	77.2	75.8	6.	6.
26 May 1986	77.1	103%	.75	1%	78.3	76.1	7.	6.
27 May 1986	75.9	101%	.89	1%	76.7	74.0	7.	7.
28 May 1986	75.3	100%	.48	1%	75.9	74.5	7.	7.
29 May 1986	73.9	99%	.40	1%	74.5	73.3	6.	6.
Summary	76.1	102%	1.03	1%	78.3	73.3	106.	105.

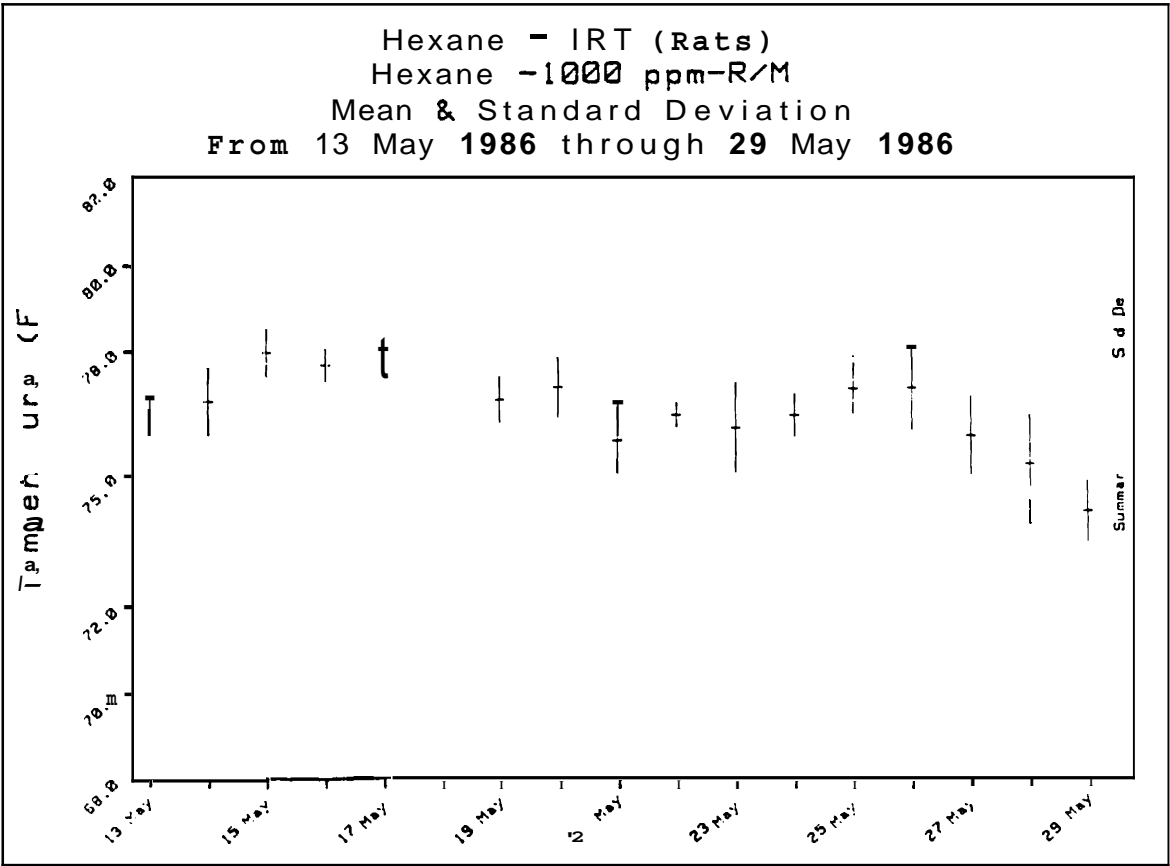




n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats)      From 13 May 1986 through 29 May 1986  
 Summary Data for: Hexane -1000 ppm-R/M/Temperature      72.0 to 78.0

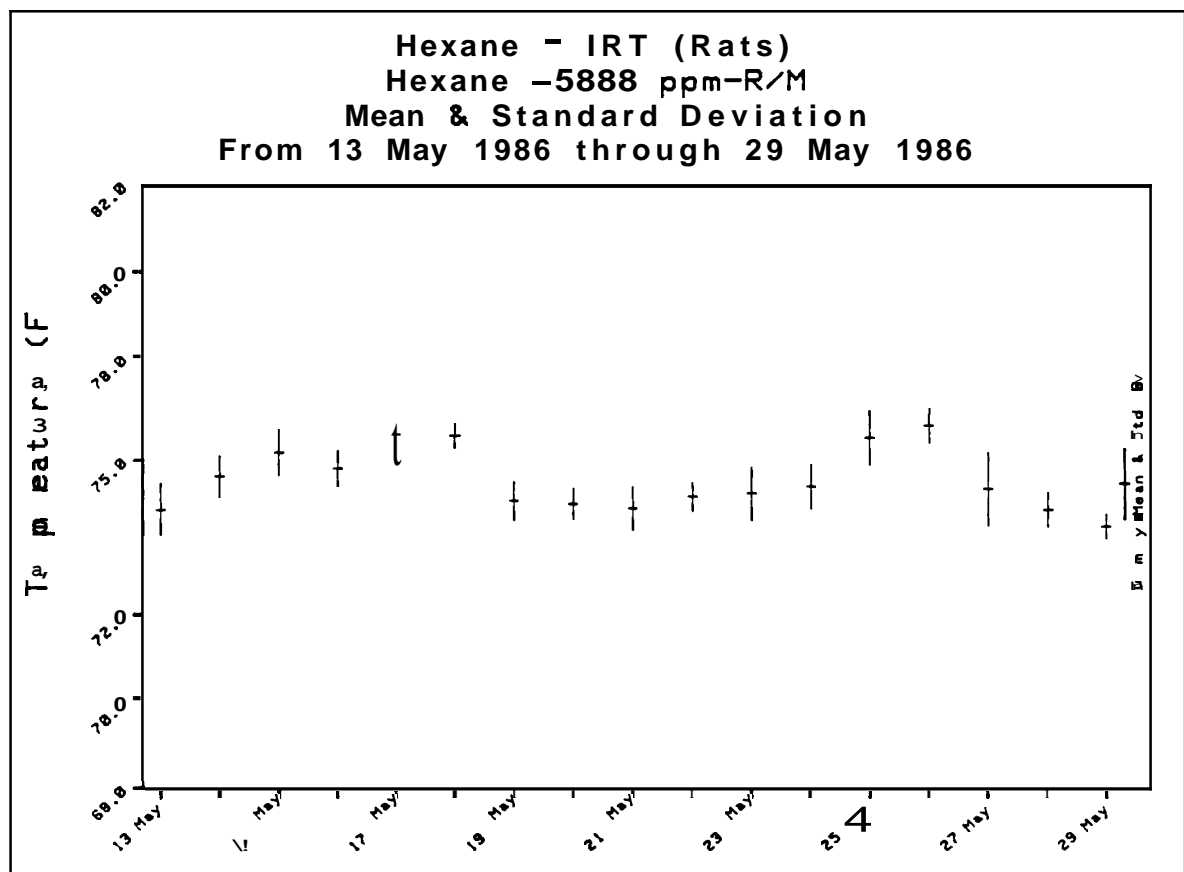
Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	75.6	101%	.81	1%	76.6	74.5	5.	5.	100%
14 May 1986	76.8	102%	.77	1%	77.9	76.1	5.	5.	100%
15 May 1986	78.1	104%	.54	1%	78.7	77.2	6.	2.	33%
16 May 1986	77.8	104%	.36	0%	78.4	77.5	5.	4.	80%
17 May 1986	78.2	104%	.49	1%	78.7	77.5	6.	2.	33%
18 May 1986	78.5	105%	.61	1%	79.2	77.8	7.	3.	43%
19 May 1986	77.0	103%	.52	1%	77.6	76.1	6.	6.	100%
20 May 1986	77.3	103%	.69	1%	78.0	76.5	6.	6.	100%
21 May 1986	76.1	101%	.77	1%	77.2	74.9	7.	7.	100%
22 May 1986	76.6	102%	.28	0%	76.9	76.3	6.	6.	100%
23 May 1986	76.3	102%	1.03	1%	77.5	74.5	7.	7.	100%
24 May 1986	76.6	102%	.48	1%	77.2	76.1	7.	7.	100%
25 May 1986	77.2	103%	.57	1%	78.1	76.4	6.	5.	83%
26 May 1986	77.2	103%	.95	1%	78.9	76.2	7.	6.	86%
27 May 1986	76.1	102%	.90	1%	77.4	74.4	7.	7.	100%
28 May 1986	75.5	101%	1.12	1%	77.1	73.8	7.	7.	100%
29 May 1986	74.6	100%	.71	1%	75.5	73.6	6.	6.	100%
Summary	76.8	102%	1.21	2%	79.2	73.6	106.	91.	86%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Overall Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

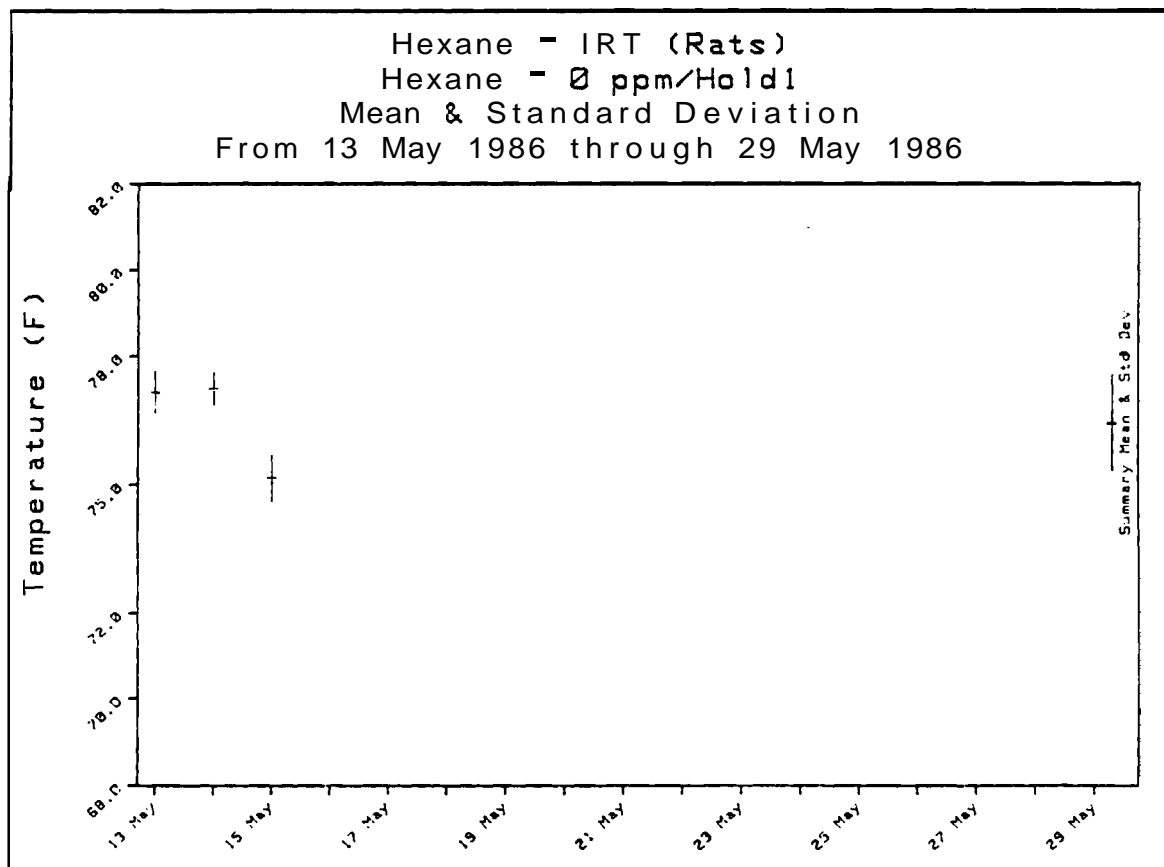
Summary Data for: Hexane -5000 ppm-R/M/Temperature 72.0 to 78.0									
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	73.9	99%	.59	1%	74.7	73.3	5.	5.	100%
14 May 1986	74.3	99%	.47	1%	74.9	73.6	5.	5.	100%
15 May 1986	75.8	101%	.53	1%	76.4	75.1	6.	6.	100%
16 May 1986	75.4	101%	.40	1%	75.8	74.9	5.	5.	100%
17 May 1986	76.0	101%	.49	1%	76.9	75.6	6.	6.	100%
18 May 1986	76.2	102%	.28	0%	76.6	75.8	7.	7.	100%
19 May 1986	74.9	100%	.45	1%	75.2	74.2	6.	6.	100%
20 May 1986	74.8	100%	.35	0%	75.2	74.2	6.	6.	100%
21 May 1986	74.7	100%	.49	1%	75.3	73.8	7.	7.	100%
22 May 1986	75.0	100%	.32	0%	75.5	74.7	6.	6.	100%
23 May 1986	75.0	100%	.61	1%	75.8	74.2	7.	7.	100%
24 May 1986	75.2	100%	.50	1%	76.1	74.5	7.	7.	100%
25 May 1986	75.9	101%	.62	1%	76.8	75.1	6.	6.	100%
26 May 1986	76.1	102%	.40	1%	76.9	75.7	7.	7.	100%
27 May 1986	74.9	100%	.83	1%	75.6	73.1	7.	7.	100%
28 May 1986	74.5	99%	.38	1%	75.0	73.8	7.	7.	100%
29 May 1986	74.1	99%	.28	0%	74.4	73.8	6.	6.	100%
Summary	75.1	100%	.81	1%	76.9	73.1	106.	106.	100%



n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 0 ppm/Hold1/Temperature									
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	77.2	103%	.48	1%	77.7	76.5	5.	5.	100%
14 May 1986	77.3	103%	.38	0%	77.7	76.9	5.	5.	100%
15 May 1986	75.2	100%	.55	1%	75.9	74.3	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	76.5	102%	1.12	1%	77.7	74.3	16.	16.	100%

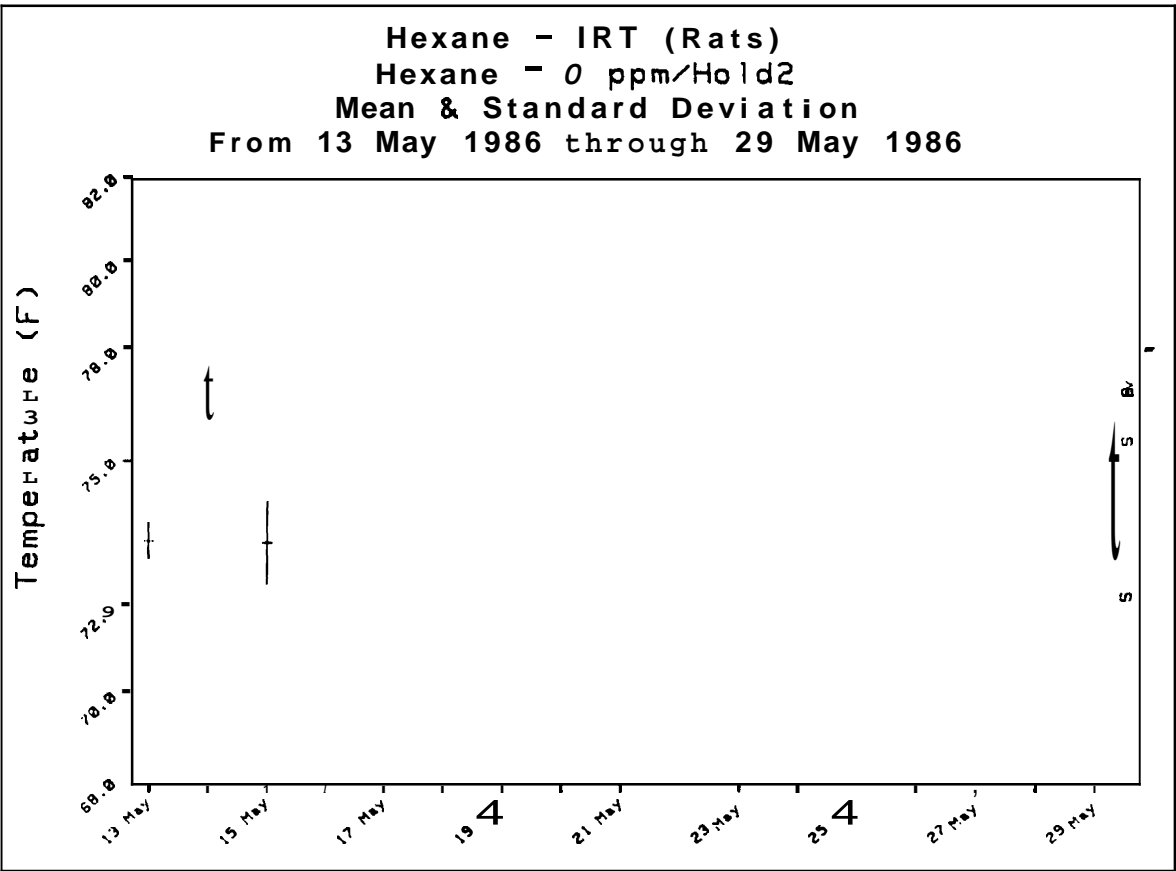


n-Hexane Rat Teratology Study  
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Summary Data for: Hexane - 0 ppm/Hold2/Temperature 72.0 to 78.0

Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	73.9	99%	.42	1%	74.6	73.5	5.	5.	100%
14 May 1986	77.0	103%	.63	1%	78.0	76.4	5.	5.	100%
15 May 1986	73.9	99%	.95	1%	75.1	72.5	6.	6.	100%
16 May 1986									
17 May 1986									
18 May 1986									
19 May 1986									
20 May 1986									
21 May 1986									
22 May 1986									
23 May 1986									
24 May 1986									
25 May 1986									
26 May 1986									
27 May 1986									
28 May 1986									
29 May 1986									
Summary	74.9	100%	1.65	2%	78.0	72.5	16.	16.	100%



### 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: INHALATION REPRODUCTIVE TOXICOLOGY - n-HEXANE RAT TERATOLOGY

REPORTING PERIOD: May 12 - 31, 1986

NOTE: 24 Hour Data Collection Period extends from ~8:00 a.m. to ~8:00 a.m.

COMPILED BY:

*Mark S. Chell*

DATE:

*7/1/86*

#### CHAMBER CONCENTRATION

DATE  
5/13/86

##### DISCUSSION OR EXPLANATION

During the exposure period, concentration in the 200 ppm chamber (1 reading = 0.7 ppm) exceeded the lower critical operating limit (800 ppm). There was no indication of any problem and the next sample cycle showed the expected concentration level. Although the daily mean was within operating limits (mean = 191 ppm), the standard deviation (36.2 ppm) exceeded the  $\pm 10\%$  requirement. No action was taken.

Also during the exposure period, the 1000 ppm chamber (3 readings = 1234, 1216, and 1288 ppm) exceeded the upper critical operating limits (1200 ppm). Necessary adjustments were made to chamber dilution air flow to bring concentrations within specs. The daily mean and standard deviation were within operating limits (mean =  $1020 \pm 100$  ppm).

The executive computer hung up at 01:18 and failed to trigger the security alert, consequently no one was contacted to correct the condition until staff arrived later in the morning. No environmental or concentration data was collected until 06:46 when the problem was detected and corrected. Also, because of the hangup, no control of chamber conditions was possible. The first GC readings of concentration following correction of the computer problem were:

200 ppm 1st reading = 201.9 ppm

1000 ppm 1st reading = 1075 ppm

5000 ppm 1st reading = 5313 ppm

Since these readings are within 3% of the final GC readings taken before the computer hung up, it is reasonable to assume that the system ran stable for the intervening 5 1/2 hour period. The stability of the system operation can be confirmed by mass balance measurements i.e. by subtracting the mass of material consumed during monitoring periods from that consumed during the entire exposure period.

5/14/86

During the exposure period, the 1000 ppm chamber (3 readings = 1307, 1293, and 1204 ppm) exceeded the upper critical operating limits (1200 ppm). Necessary adjustments were made to chamber dilution air flow or chemical pump rate to bring concentrations within specs.

At 22:51 the executive computer hung up entering data from the CDS box. Communication was restored at 00:13. No data collection or environmental control was possible during the intervening 1 1/4 hours. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 203.8 ppm

1000 ppm 1st reading = 903.8 ppm

5000 ppm 1st reading = 5135 ppm

At 3:48 the executive computer alerted the specialist that the chamber concentrations in all chambers were exceeding the lower critical operating limits. The specialist on call checked chemical pump rates and chamber airflows and found that chamber concentrations were within specs via mass balance

n-Hexane Rat Teratology Study  
Appendix B - Exposure

- determinations.** Repeated mass balance **determinations** indicated that **concentrations** were close to specs. At **7:28** it was discovered that the sample flow **rate** to the GC was **too** low for correct readings. GC data for this period has been excluded from the daily summation and results of mass balance **determinations** were added.
- 5/15/86 During the exposure period, concentration in the 200 ppm chamber (1 reading = 275.7 ppm) and the 1000 ppm chamber (1 reading = 1244 ppm) exceeded the upper critical operating **limits** (240 and 1200 ppm, respectively). **Necessary adjustments** were **made** to chamber dilution air flow or chemical pump rate to bring concentrations within **specs**. Daily **means** were unaffected.  
At 02:19 the executive computer hung up **entering** data from the CDS box. Communication was restored at 03:49. No data collection or environmental **control** was possible during the intervening 1 1/2 hours. **All** indications are that the exposure was stable during this period. **The first GC readings** following resumption of data collection were:  
200 ppm 1st reading = 212.7 ppm  
1000 ppm 1st reading = 1030 ppm  
5000 ppm 1st reading = 4962 ppm  
At 05:53 the executive computer again hung up entering data from the CDS box. Communication was **restored** at 07:28. No data collection or environmental control was possible during the **intervening** 1 1/2 hours. **All** indications are that the exposure was stable during this **period**. The first GC readings following resumption of data collection were:  
200 ppm 1st reading = 192.7 ppm  
1000 ppm 1st reading = 1008 ppm  
5000 ppm 1st reading = 4717 ppm
- 5/16/86 The executive **computer** hung up at 02:30 and **failed** to **trigger** the security **alert**, consequently no one **was** contacted to correct the condition until **staff arrived later** in the morning. No environmental or **concentration data** was **collected** until 06:32 when the problem was **detected** and corrected. Also, because of the **hangup**, no **control** of chamber conditions was possible. The **first GC readings** of **concentration** following **correction** of the **computer** problem were:  
200 ppm 1st reading = 192.8 ppm  
1000 ppm 1st reading = 975.1 ppm  
5000 ppm 1st reading = 4753 ppm  
Since these readings are within 2% of the final GC readings before the computer hung up, it is reasonable to assume that the system ran stable for the **intervening** 4 hour period.
- 5/17/86 During the exposure **period**, **concentration** in the 1000 ppm chamber (2 readings, 1251 and 1318 ppm) **exceeded** the upper critical operating **limit** (1200 ppm). **Adjustments** were made to the chamber dilution air flow and chemical pump rate to bring the concentration within specs. Daily mean and standard deviation were unaffected by the excursion.  
At 19:37 the executive computer hung up entering data from the CDS box. Communication was **restored** at 21:01. No data collection or environmental control was possible during the intervening 1 1/2 hours. **All** indications are that the exposure was stable during **this** period. Other communication failures occurred at 22:42 (restored at 00:15) and 3:36 (restored at 5:04). From the **first GC readings** following restoration of communication, the system appears to have run stable during the **intervening periods**.
- 5/18/86 At 19:20 the executive computer hung up entering data from the CDS box. Communication was restored at 20:14. No data collection or environmental control was possible **during** the intervening 1 hour. **All** indications are that the exposure was stable during this period. The **first GC readings** following resumption of data collection were:  
200 ppm 1st reading = 207.8 ppm  
1000 ppm 1st reading = 977.1 ppm  
5000 ppm 1st reading = 5110 ppm  
At 06:02 the executive computer again hung up. Data collection and exposure control was resumed at 06:51.
- 5/19/86 The exposure was started 1 hour 13 minutes late due to the failure to properly seal a chamber

n-Hexane Rat Teratology Study  
Appendix B - Exposure

following animal care tasks.

At 05:15 the executive computer hung up while entering data from the CDS box. The condition was not corrected until 06:50. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 199.0 ppm  
1000 ppm 1st reading = 987.6 ppm  
5000 ppm 1st reading = 4970 ppm

During the exposure period, 1 reading for the 1000 ppm chamber (1244 ppm) exceeded the upper critical operating limit (1200 ppm). The computer adjusted chamber air flow to increase dilution and bring the concentration within bounds.

5/20/86

At 05:46 the executive computer hung up while entering data from the CDS box. The condition was not corrected until 06:23. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 199.8 ppm  
1000 ppm 1st reading = 967.8 ppm  
5000 ppm 1st reading = 5011 ppm

5/21/86

At 01:54 the executive computer hung up entering data from the CDS box. Communication was restored at 03:12. No data collection or environmental control was possible during the intervening 1-1/4 hour. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 207.8 ppm  
1000 ppm 1st reading = 977.1 ppm  
5000 ppm 1st reading = 5110 ppm

5/22/86

The exposure was started 1 hour 17 minutes late due to the failure to properly seal a chamber following animal work tasks. The computer will not allow exposures to begin until all chambers pass a leak test

5/24/86

At 00:36 the executive computer hung up while entering data from the CDS box. The condition was not corrected until 02:00. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 203.2 ppm  
1000 ppm 1st reading = 1014 ppm  
5000 ppm 1st reading = 4947 ppm

At 06:00 the executive computer again hung up while entering data from the CDS box. The condition was not corrected until 07:20. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 203.7 ppm  
1000 ppm 1st reading = 996.9 ppm  
5000 ppm 1st reading = 4974 ppm

5/25/86

The start of exposures was delayed - 3 hours because of the evacuation of the building necessitated by a fire alarm

During the exposure period, an air bubble napped in the inlet line to the 1000 ppm chemical pump resulted in a drop in chamber concentration (1 reading = 603.2 ppm) which exceeded the lower critical operating limit (800 ppm). The exposure specialist removed the air bubble and concentration returned to spec by the next sample rotation.

Hexane to 3 ppm was detected in the exposure room. Further investigation revealed that sample flow through the sample lines had dropped below the set flowrate. This resulted in the reversal of flow direction, sample being drawn from a location other than the room.

At 05:24 the executive computer again hung up while entering data from the CDS box. The condition was not corrected until 07:17. All indications are that the exposure was stable during this period. The first GC readings following resumption of data collection were:

200 ppm 1st reading = 201.6 ppm  
1000 ppm 1st reading = 944.0 ppm

n-Hexane Rat Teratology Study  
Appendix B - Exposure

5/27/86	<p style="text-align: center;"><b>5000 ppm 1st reading = 5105 ppm</b></p> <p>Twenty-five minutes after expiration of the <b>T90</b>, the exposure system shut off for <b>unknown</b> reasons. Generation resumed 11 minutes later, however chamber concentrations recorded during this period exceeded the lower critical operating limits. Reported values were: <b>1000 ppm</b> chamber, 1 reading = 540 ppm; and <b>5000 ppm</b> chamber, 1 reading = 735 ppm During the next sample cycle, concentration in the <b>1000 ppm</b> chamber (1 reading = 1467 ppm) <b>exceeded</b> the upper critical operating limit (1200 ppm). The system was again shut off, resulting in low chamber readings the following sample cycle, <b>e.g.</b> 200 ppm chamber, 1 reading = 16.1 ppm; 1000 ppm chamber, 1 reading = 468 ppm; and 5000 ppm chamber, 1 reading = 3616 ppm Generation was again resumed. At <b>21:58</b> the GC <b>stream</b> select valve <b>stuck</b> and failed to cycle. Mass balance measurements were used to predict chamber concentration throughout the remainder of the exposure <b>period</b>. These measurements indicated that the <b>1000 ppm</b> chamber ran below the lower critical operating limit. No adjustments <b>were attempted</b>. Daily mean concentrations were within specs but standard deviations exceeded the <b>±10%</b> operating limit. Reported data are:</p> <p style="margin-left: 40px;">200 ppm mean = 198 ± 40 ppm 1000 ppm mean = 925 ± 198 ppm 5000 ppm mean = 4870 ± 954 ppm</p>
5/28/86	<p>The stream select valve to the GC was incorrectly connected and prevented the proper <b>determination</b> of chamber concentration for the <b>5000 ppm</b> chamber. Mass balance (<b>i.e.</b> chemical pump delivery rate and chamber dilution air flow rate) was used to determine chamber concentration <b>after</b> startup. The problem was remedied about 2 hours 20 minutes into the exposure. GC readings of the 5000 ppm chamber after correction of the problem indicated that concentration was within specs. At ~02:00 the alarm loop tripped for unknown reasons and shut off the exposure system The exposure system was turned back on manually at <b>~02:55</b> and chamber concentrations were reestablished by <b>03:11</b>. Low <b>concentrations</b> exceeding the lower critical operating limits were reported as follows:</p> <p style="margin-left: 40px;">200 ppm 2 readings: 5.1 and 85.0 ppm 1000 ppm 3 readings: <b>27.0, 570</b>, and 783 ppm 5000 ppm 1 reading: 16.6 ppm</p> <p>Though daily mean concentrations were within specs, standard deviations exceeded the operating limit of <b>±10%</b> because of the system shutdown.</p>

#### TEMPERATURE & RELATIVE HUMIDITY

<u>DATE</u>	<u>DISCUSSION OR EXPLANATION</u>
5/12/86	Several chambers exceeded the lower operating limit for mean temperature ( <b>72°F</b> ). This was the <b>first day</b> of holding in the exposure chambers and the effect of animal loading was unknown so the room temperature had <b>been</b> lowered <b>2-3°F</b> in anticipation of greater heat removal capability. Those chambers exceeding the lower limit were <b>0 ppm</b> , mean = 69.8 ± 1.9°F; 200 ppm, mean = 71.5 ± 1.7°F; and <b>5000 ppm</b> , mean = 71.8 ± 1.9°F.
5/15/86	Mean temperature for the <b>1000 ppm</b> chamber ( <b>78.1°F</b> , maximum = <b>78.7°F</b> ) exceeded the operating limit ( <b>78°F</b> ). Room temperature was reduced 1°F.
5/17/86	Mean temperature for the 1000 ppm chamber ( <b>78.2°F</b> , maximum = <b>78.7°F</b> ) exceeded the operating limit (78°F). No action taken at this time. Room temperature was reduced 1°F on 5/19/86.
5/18/86	Mean temperature for the 1000 ppm chamber ( <b>78.5°F</b> , maximum = <b>79.2°F</b> ) exceeded the <b>operating</b> limit ( <b>78°F</b> ). No action taken at this time. Room temperature was reduced 1°F on 5/19/86.

#### CHAMBER FLOW & VACUUM

<u>DATE</u>	<u>DISCUSSION OR EXPLANATION</u>
5/15/86	Low vacuum was detected in the <b>0 ppm</b> Hold 2 chamber (1 reading = 0.2" H <sub>2</sub> O). Water <b>was</b> placed in the trap at the bottom of the chamber and vacuum returned to specs.



**APPENDIX C**

**DEVELOPMENTAL TOXICOLOGY DATA**

APPENDIX C

DEVELOPMENTAL TECHNOLOGY DATA

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

1

0 ppm n-Hexane

MATNO	Pre-study Wt	Exposure Day 1	Exposure Day 8	Sacrifice Wt
498	246.60	263.40	269.40	278.60
661	270.00	276.00	289.80	299.70
595	268.20	285.00	284.20	279.90
609	260.80	264.00	279.20	283.70
610	243.40	246.20	255.00	262.10
680	256.60	266.00	277.20	282.90
708	283.40	302.20	322.80	330.00
771	286.60	298.80	318.20	323.10
878	253.00	263.80	267.20	272.80
883	232.80	257.80	266.60	283.60

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MATNO	Pro-study Wt	Exposure Day 1	Exposure Day 8	Sacrifice Wt
496	249.80	266.80	263.20	270.90
600	270.80	279.60	296.80	296.60
664	240.80	260.60	270.00	267.90
669	266.80	280.00	296.60	297.70
575	249.80	273.80	291.20	297.90
618	305.80	311.80	327.20	327.30
712	228.00	232.40	239.40	242.40
724	284.80	278.40	301.20	308.30
888	282.00	308.00	327.60	335.80
923	259.00	281.80	272.00	288.40

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

Females

3

-----1000 ppm n-Hexane-----				
MATNO	Pre-study Wt	Exposure Day 1	Exposure Day 8	Sacrifice Wt
622	268.60	268.00	270.60	261.20
629	323.80	314.80	346.20	333.10
686	261.60	263.60	276.60	286.70
642	260.00	271.00	280.00	276.10
764	246.60	263.40	280.80	286.80
876	285.40	299.80	314.20	321.80
895	232.60	227.40	240.60	233.00
902	256.60	263.40	275.20	275.70
973	240.60	247.80	264.00	257.00
975	271.60	281.60	288.40	294.10

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

Females

-----5000 ppm n-Hexane-----

MATNO	Pre-study Wt	Exposure Day 1	Exposure Day 8	Sacrifice Wt
459	242.40	245.00	234.40	240.50
480	246.80	246.80	242.80	250.70
491	232.40	252.40	204.00	233.10
543	266.20	257.60	263.40	244.80
660	250.80	257.00	257.60	248.60
754	262.00	276.20	244.20	182.50
773	276.60	276.40	283.20	272.90
803	282.40	292.80	268.20	286.90
824	257.40	260.60	263.40	258.90
906	317.80	318.00	301.40	307.80

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

1

-----0 ppm n-Hexane-----												
MATNO	Prestudy Wt	0 dg Wt	8 dg Wt	13 dg Wt	20 dg Wt	Uter Wt	Pregnant	IMPLANT	LIVE	EARLY	LATE	DEAD
450	283.60	281.00	297.40	319.40	313.60	0.80	0	.	.	.	.	.
507	249.40	256.00	283.00	308.40	375.00	72.60	1	14	13	1	0	0
512	260.80	272.20	302.60	316.80	308.90	0.60	0	.	.	.	.	.
514	263.20	269.80	293.00	336.40	409.70	82.10	1	18	17	1	0	0
548	281.00	291.00	315.80	353.20	422.40	85.80	1	17	16	0	1	0
550	265.00	265.40	307.80	333.60	393.20	89.30	1	18	17	1	0	0
553	255.20	259.60	287.40	326.60	392.60	65.40	1	14	12	1	1	0
566	272.20	284.80	300.20	312.40	402.70	57.90	1	12	10	2	0	0
567	257.80	258.40	282.00	282.60	276.00	0.50	0	.	.	.	.	.
568	277.00	282.40	317.00	358.80	458.30	95.40	1	17	17	0	0	0
579	276.20	290.60	320.20	339.80	439.50	94.70	1	19	18	1	0	0
604	272.60	287.80	318.60	352.40	435.90	86.30	1	17	17	0	0	0
612	295.80	302.80	328.00	373.60	445.10	90.50	1	18	16	2	0	0
620	244.00	246.00	282.20	299.80	272.20	1.20	0	.	.	.	.	.
632	310.60	315.20	343.80	358.00	454.90	84.10	1	18	16	2	0	0
646	246.00	265.80	296.20	307.80	408.30	86.70	1	15	15	0	0	0
647	240.40	250.20	269.40	287.40	346.00	69.10	1	13	13	0	0	0
676	247.60	266.60	284.00	333.40	401.40	74.70	1	15	14	0	1	0
681	274.00	287.80	307.20	339.40	414.00	84.40	1	16	15	0	1	0
695	229.00	239.00	241.60	247.00	256.40	0.90	0	.	.	.	.	.
746	259.80	272.40	303.40	322.00	424.30	92.00	1	17	16	1	0	0
785	259.80	269.60	294.40	303.60	393.30	77.60	1	17	16	1	0	0
805	273.20	293.60	303.00	322.00	407.70	62.40	1	13	11	2	0	0
882	230.00	238.40	258.60	275.60	249.10	0.60	0	.	.	.	.	.
926	256.40	255.60	282.80	322.20	375.20	61.10	1	14	12	2	0	0
936	279.60	300.20	328.00	338.60	429.90	90.60	1	18	18	0	0	0
963	270.20	277.60	294.80	344.00	414.50	102.40	1	19	19	0	0	0
969	257.20	262.20	284.20	313.20	357.40	41.10	1	11	9	2	0	0
976	257.60	266.60	295.80	329.60	385.40	74.70	1	14	12	2	0	0

C-5

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

2

TMT=200 ppm n-Hexane

MATNO	Prestudy Wt	0 dg Wt	8 dg Wt	13 dg Wt	20 dg Wt	Uter Wt	Pregnant	IMPLANT	LIVE	EARLY	LATE	DEAD
445	266.2w	291.6w	325.8w	357.0w	415.3w	51.10	1	10	10	0	0	0
448	298.6w	296.4w	313.2w	342.8w	435.4w	99.60	1	18	18	0	0	0
453	271.8w	274.8w	287.4w	309.2w	361.1w	65.00	1	15	12	3	0	0
499	274.2w	284.4w	299.6w	320.0w	297.6w	0.60	0	.	.	.	.	.
516	269.0w	282.4w	303.6w	338.2w	436.5w	105.20	1	17	17	0	0	0
534	250.2w	258.2w	281.6w	294.8w	275.7w	0.70	0	.	.	.	.	.
561	245.8w	263.2w	275.0w	309.8w	378.0w	75.90	1	13	13	0	0	0
562	314.8w	324.4w	356.6w	392.2w	465.5w	61.80	1	14	13	1	0	0
570	302.4w	287.8w	308.6w	350.2w	418.4w	54.60	1	9	9	0	0	0
590	245.8w	259.0w	284.0w	310.4w	363.1w	69.30	1	15	13	0	2	0
601	237.2w	251.8w	273.0w	306.8w	361.5w	75.50	1	15	15	0	0	0
613	275.6w	286.0w	304.2w	335.2w	399.8w	75.40	1	15	13	2	0	0
614	284.2w	289.4w	323.8w	345.6w	409.5w	88.80	1	19	17	2	0	0
629	262.8w	264.0w	293.4w	333.6w	402.8w	84.10	1	16	16	0	0	0
640	246.4w	263.6w	274.8w	315.0w	375.5w	77.50	1	17	17	0	0	0
652	251.2w	256.4w	284.2w	305.2w	375.7w	76.20	1	16	15	1	0	0
662	239.8w	252.0w	261.8w	290.8w	366.4w	81.60	1	16	15	1	0	0
671	264.4w	273.6w	307.6w	333.4w	423.0w	95.90	1	17	17	0	0	0
688	269.2w	279.0w	306.0w	342.2w	416.4w	80.20	1	13	13	0	0	0
696	242.0w	277.6w	261.4w	284.4w	351.8w	79.40	1	15	15	0	0	0
716	247.8w	253.2w	283.6w	298.6w	251.1w	0.50	0	.	.	.	.	.
763	286.0w	302.8w	317.0w	327.8w	404.1w	93.30	1	17	17	0	0	0
770	269.8w	275.6w	301.4w	331.6w	398.6w	74.20	1	15	15	0	0	0
777	239.6w	261.6w	277.2w	312.8w	376.3w	67.00	1	13	13	0	0	0
823	256.2w	262.8w	285.0w	294.2w	277.7w	0.60	0	.	.	.	.	.
843	261.2w	276.4w	300.8w	334.8w	412.5w	84.00	1	18	15	3	0	0
896	233.0w	242.4w	255.0w	266.8w	261.0w	1.00	0	.	.	.	.	.
931	284.0w	294.6w	307.4w	348.4w	423.7w	94.60	1	18	18	0	0	0
933	265.8w	267.0w	294.0w	307.4w	287.7w	0.70	0	.	.	.	.	.
942	229.8w	234.0w	244.8w	276.8w	303.2w	65.40	1	16	14	2	0	0

C-6



n-Hexane Rat Teratology Study: End Weights (g) for Sperm-positive Females

3

100 ppm n-Hexane

MATNO	Prestudy Wt	0 dg Wt	6 dg Wt	13 dg Wt	20 dg Wt	Uter Wt	Pregnant	IMPLANT	LIVE	EARLY	LATE	DEAD
460	252.00	254.00	278.60	309.20	361.60	71.90	1	16	15	1	0	0
470	231.60	229.40	249.80	278.40	332.70	74.80	1	15	15	0	0	0
476	248.00	254.80	266.60	284.80	338.30	62.20	1	15	14	1	0	0
481	260.00	261.00	278.60	309.80	378.10	66.90	1	15	13	1	1	0
510	274.40	280.40	311.80	345.20	423.40	78.50	1	16	16	0	0	0
520	286.40	290.60	319.40	340.40	358.80	12.40	1	4	2	1	1	0
544	272.60	281.00	306.00	315.00	373.30	76.60	1	17	16	0	1	0
549	265.60	288.60	310.20	333.00	397.10	78.30	1	17	15	2	0	0
555	253.80	260.80	288.20	317.40	387.00	86.90	1	18	17	1	0	0
580	273.60	283.00	292.60	337.40	408.30	78.40	1	17	16	1	0	0
591	242.00	260.00	281.60	310.20	379.30	68.60	1	14	14	0	0	0
635	260.00	263.00	285.00	317.80	380.20	80.10	1	16	16	0	0	0
649	250.00	265.00	295.60	338.20	397.90	61.50	1	15	15	0	0	0
653	249.80	271.20	291.20	326.40	410.90	85.60	1	18	16	1	1	0
664	237.80	248.00	270.60	295.40	350.30	69.50	1	14	13	1	0	0
689	262.60	277.00	302.40	325.60	366.60	48.10	1	14	9	5	0	0
691	287.40	284.40	315.20	333.20	317.40	0.70	0	.	.	.	.	.
697	240.40	254.60	279.00	297.60	375.90	76.40	1	14	13	1	0	0
768	286.40	300.80	319.00	344.40	376.80	66.30	1	17	16	1	0	0
807	260.00	268.00	295.60	338.80	375.60	51.10	1	11	9	1	1	0
836	270.40	286.80	298.60	311.80	286.00	0.70	0	.	.	.	.	.
855	321.60	336.60	353.40	387.00	456.70	87.80	1	21	18	3	0	0
905	241.80	266.20	303.60	336.00	400.50	81.60	1	16	15	1	0	0
911	265.00	277.00	307.80	326.00	430.70	83.20	1	17	17	0	0	0
918	273.80	275.60	309.80	324.60	420.70	97.20	1	18	18	0	0	0
921	253.80	255.20	278.00	296.40	362.00	81.70	1	15	15	0	0	0
925	277.60	291.80	303.80	329.40	307.50	0.60	0	.	.	.	.	.
944	267.80	274.80	296.40	327.60	388.30	85.40	1	17	17	0	0	0
965	276.40	306.20	340.60	369.00	369.10	85.50	1	16	16	0	0	0
972	276.60	283.20	313.00	346.80	400.80	81.20	1	16	16	0	0	0

C-7

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

4

-----5000 ppm n-Hexane-----

MATNO	Prestudy Wt	0 dg Wt	6 dg Wt	13 dg Wt	20 dg Wt	Uter Wt	Pregnant	IMPLANT	LIVE	EARLY	LATE	DEAD
451	260.80	284.00	286.80	305.80	366.00	67.10	1	16	14	2	0	0
457	292.80	297.20	319.00	317.00	413.90	67.90	1	17	16	0	1	0
458	244.60	281.40	270.80	268.80	269.60	0.60	0	.	.	.	.	0
472	252.20	264.40	276.80	304.60	376.70	80.60	1	17	17	0	0	0
488	248.20	252.00	281.80	284.00	320.00	60.80	1	15	15	0	0	0
505	246.60	251.60	279.80	303.20	278.70	0.80	0	.	.	.	.	0
536	275.00	282.80	304.20	328.00	379.90	61.20	1	14	14	0	0	0
538	278.80	288.20	294.80	327.20	406.70	89.50	1	18	18	0	0	0
542	270.40	290.00	310.00	333.80	402.00	79.50	1	15	15	0	0	0
574	245.60	244.40	256.60	297.80	339.10	29.90	1	6	6	0	0	0
586	302.20	317.40	353.80	361.80	415.90	69.70	1	16	15	1	0	0
608	267.00	270.40	306.60	251.20	345.90	63.40	1	15	15	0	0	0
622	248.60	258.40	277.20	297.20	336.20	69.80	1	16	16	0	0	0
623	266.20	275.80	311.20	337.00	394.00	76.70	1	16	15	1	0	0
636	280.40	291.80	307.80	326.80	360.60	68.40	1	18	15	3	0	0
641	231.60	238.60	269.60	251.60	327.40	69.20	1	15	15	0	0	0
658	241.80	252.40	275.60	305.40	352.50	64.40	1	15	14	1	0	0
690	264.20	262.80	303.40	244.40	202.10	.(a)	1	14	12	2	0	0
762	242.60	263.40	286.40	303.80	361.60	61.70	1	17	14	2	1	0
800	264.20	279.40	297.40	302.20	378.20	83.10	1	18	17	0	1	0
806	229.00	242.40	246.00	269.00	342.00	83.90	1	18	18	0	0	0
814	279.60	284.00	313.00	348.20	372.10	41.00	1	10	8	2	0	0
863	275.60	301.40	332.00	341.20	392.20	70.00	1	14	14	0	0	0
866	267.60	263.80	283.00	243.80	307.20	49.50	1	11	10	1	0	0
880	278.40	311.00	328.40	340.60	419.50	91.30	1	19	19	0	0	0
922	265.00	277.60	295.20	320.40	371.70	66.90	1	14	14	0	0	0
938	257.60	274.60	300.60	335.20	386.00	72.90	1	15	15	0	0	0
948	274.20	279.60	302.80	334.20	404.30	86.20	1	17	16	1	0	0
951	276.20	278.80	317.80	345.00	424.80	78.70	1	17	16	0	1	0
964	259.60	281.60	308.20	328.20	374.40	72.40	1	17	15	2	0	0

a) Uterus inadvertently not weighed.

C-8

n-Hexane Rat Teratology Study: Raw Fetal Data 1

-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
507	1	1	2	3.10	0.41					
507	2	1	2	3.00	0.36					
507	3	1	1	3.64	0.43	DIUR				
507	4	1	1	3.60	0.40					
507	5	1	1	3.46	0.43					
507	6	1	2	3.21	0.43					
507	7	1	1	3.28	0.49					
507	8	1	1	3.60	0.62					
507	9	1	1	3.36	0.46					
507	10	1	1	3.70	0.46					
507	11	1	1	3.92	0.61					
507	12	1	2	3.62	0.46					
507	13	2	.	.	.					
507	14	1	1	4.02	0.54	DIUR				
514	1	1	2	3.19	0.49	DIUR	ROST			
514	2	1	2	3.10	0.40					
514	3	1	2	2.83	0.34	ROST				
514	4	1	2	3.24	0.45					
514	5	1	2	3.17	0.50	DIUR	ROSK			
514	6	1	1	3.19	0.38	ROST				
514	7	1	2	3.00	0.31					
514	8	1	1	3.35	0.47					
514	9	1	1	2.98	0.29	ROST				
514	10	1	1	3.31	0.42	DIUR				
514	11	1	2	2.98	0.36	ROST	ROVE			
514	12	1	1	3.40	0.46					
514	13	1	2	3.14	0.44					
514	14	2	.	.	.					
514	15	1	2	2.78	0.41	ROST				
514	16	1	2	3.24	0.47					
514	17	1	1	3.26	0.39					
514	18	1	2	2.95	0.46					
548	1	1	1	3.51	0.47					
548	2	1	2	3.45	0.39	ROVE				
548	3	1	1	3.79	0.40	ROST				
548	4	1	2	3.53	0.38					
548	5	1	2	3.60	0.38	ROPH				
548	6	1	1	3.84	0.43					
548	7	4	.	.	.					
548	8	1	2	3.49	0.36					
548	9	1	2	3.49	0.41					
548	10	1	1	3.86	0.33	ROST				
548	11	1	1	3.42	0.38					
548	12	1	2	3.60	0.48					
548	13	1	1	3.65	0.34					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data 2

Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
648	14	1	1	3.64	0.37					
648	16	1	2	3.66	0.43					
648	16	1	2	3.39	0.36					
648	17	1	1	3.43	0.60	ROST				
660	1	1	1	3.39	0.43					
660	2	1	1	3.76	0.46	ROVE				
660	3	1	2	3.49	0.42					
660	4	2	.	.	.					
550	6	1	2	3.43	0.43	DIUR				
550	6	1	1	3.63	0.40					
660	7	1	2	3.46	0.42	DIUR	ROST			
660	8	1	2	3.71	0.41					
660	9	1	1	3.96	0.48	DIUR	RPCA			
660	10	1	2	3.71	0.39					
660	11	1	2	3.46	0.37					
660	12	1	2	3.26	0.34					
660	13	1	2	3.66	0.38					
550	14	1	1	3.40	0.42	DIUR	RPCA	ROPB		
660	16	1	1	3.33	0.37	DIUR	ROPB	ROST		
660	16	1	1	3.49	0.36					
660	17	1	1	3.92	0.38	DIUR	RPCA			
550	18	1	2	3.80	0.46					
663	1	1	2	3.06	0.44					
663	2	1	1	3.46	0.60					
663	3	1	1	3.80	0.47					
663	4	1	1	3.71	0.48					
663	6	1	1	3.66	0.63					
663	6	2	.	.	.					
553	7	1	2	3.50	0.41					
663	8	1	2	3.01	0.43					
553	9	1	1	3.40	0.55					
663	10	1	1	3.71	0.49					
663	11	1	1	3.30	0.44					
663	12	1	1	3.70	0.62					
663	13	1	1	3.46	0.39					
663	14	4	.	.	.					
666	1	1	2	2.69	0.68	DIUR	ROST			
666	2	1	1	4.43	0.64	DIUR				
666	3	1	2	3.93	0.69	ROST				
666	4	1	2	3.82	0.62	DIUR				
666	6	1	1	4.32	0.68	ROVE				
666	6	1	1	3.89	0.48	DIUR	RPCA			
666	7	1	2	3.94	0.64					
666	8	1	2	3.10	0.61	DIUR	RPCA	ROST		
666	9	1	2	3.90	0.66					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data 3

0 ppm n-Hexane										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN6
568	10	2	.	.	.					
568	11	2	.	.	.					
568	12	1	2	4.00	0.43	DIUR				
568	1	1	1	3.77	0.55					
568	2	1	1	3.63	0.57	ROVE				
568	3	1	2	3.69	0.52					
568	4	1	1	3.77	0.43					
568	5	1	2	3.39	0.34					
568	6	1	2	3.65	0.44	ROVE				
568	7	1	1	3.03	0.42	ROST	ROVE	ROPB		
568	8	1	2	3.69	0.53					
568	9	1	1	3.96	0.43	ROVE				
568	10	1	1	3.92	0.58					
568	11	1	1	3.93	0.44	ROVE				
568	12	1	2	3.69	0.41					
568	13	1	2	3.61	0.48					
568	14	1	1	3.58	0.39					
568	15	1	2	3.59	0.39					
568	16	1	1	3.59	0.39					
568	17	1	2	3.59	0.38					
579	1	1	1	3.67	0.51					
579	2	1	2	3.39	0.56					
579	3	1	2	3.48	0.17					
579	4	1	1	3.88	0.55					
579	5	2	.	.	.					
579	6	1	1	3.64	0.51					
579	7	1	1	3.71	0.51					
579	8	1	2	3.17	0.44	ROST				
579	9	1	1	3.56	0.47					
579	10	1	2	1.93	0.34	ROSK	ROST	ROVE	ROPB	ROPH
579	11	1	1	3.55	0.43					
579	12	1	1	3.87	0.49					
579	13	1	1	3.44	0.51					
579	14	1	1	3.73	0.43					
579	15	1	2	3.63	0.41					
579	16	1	2	3.86	0.42					
579	17	1	2	3.72	0.36					
579	18	1	1	3.17	0.54					
579	19	1	1	3.91	0.48					
604	1	1	2	2.51	0.38					
604	2	1	1	3.47	0.38	ROST				
604	3	1	1	3.39	0.40					
604	4	1	2	3.26	0.41					
604	5	1	1	3.59	0.40					
604	6	1	2	3.37	0.37					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data 4

-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
604	7	1	1	3.30	0.36	DIUR				
604	8	1	1	3.10	0.43					
604	9	1	2	2.96	0.40					
604	10	1	1	3.39	0.40					
604	11	1	2	3.21	0.36					
604	12	1	2	3.03	0.36					
604	13	1	2	2.92	0.37					
604	14	1	1	3.28	0.31					
604	15	1	1	3.36	0.40					
604	16	1	1	3.48	0.42					
604	17	1	1	3.64	0.42					
612	1	1	1	3.16	0.50	ROST				
612	2	1	2	3.59	0.38					
612	3	2	.	.	.					
612	4	1	2	3.46	0.47	ROST				
612	5	1	1	3.88	0.42					
612	6	1	1	3.80	0.40	ROST				
612	7	1	1	3.32	0.41					
612	8	1	1	3.97	0.46					
612	9	1	1	3.78	0.41					
612	10	1	2	3.24	0.43					
612	11	1	2	3.64	0.36					
612	12	1	2	3.48	0.40					
612	13	2	.	.	.					
612	14	1	1	3.94	0.47					
612	15	1	1	3.97	0.51	ROST	SRRR			
612	16	1	2	3.58	0.42					
612	17	1	1	4.29	0.41	SRRR				
612	18	1	1	4.17	0.50					
632	1	1	1	3.63	0.36	DIUR				
632	2	1	2	3.53	0.36					
632	3	1	2	3.25	0.33					
632	4	1	2	3.80	0.36					
632	5	2	.	.	.					
632	6	1	2	3.30	0.34					
632	7	1	2	3.52	0.39					
632	8	1	1	3.69	0.36					
632	9	1	1	4.04	0.39	DIUR	RPCA			
632	10	2	.	.	.					
632	11	1	2	3.27	0.33	ROST				
632	12	1	2	3.79	0.32					
632	13	1	2	3.64	0.33					
632	14	1	2	3.84	0.36					
632	15	1	2	3.79	0.44	ROST	SRRR			
632	16	1	2	3.98	0.40					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

6

-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN6
632	17	1	2	3.53	0.36					
632	18	1	1	.	.					
646	1	1	1	3.42	0.38	DIUR	RPCA			
646	2	1	2	3.74	0.46					
646	3	1	1	3.83	0.56	DIUR	RPCA			
646	4	1	1	3.86	0.48					
646	5	1	1	3.42	0.41					
646	6	1	1	3.68	0.40					
646	7	1	1	4.14	0.41					
646	8	1	2	3.90	0.41					
646	9	1	2	3.86	0.42					
646	10	1	1	4.09	0.38					
646	11	1	1	4.18	0.47					
646	12	1	2	3.79	0.49					
646	13	1	2	3.67	0.39					
646	14	1	1	3.87	0.51					
646	15	1	1	4.23	0.43					
647	1	1	2	3.59	0.45					
647	2	1	2	3.65	0.40					
647	3	1	1	4.18	0.45					
647	4	1	1	3.98	0.45					
647	5	1	2	3.04	0.53					
647	6	1	1	3.94	0.44					
647	7	1	2	3.49	0.49					
647	8	1	1	3.73	0.41					
647	9	1	2	3.73	0.39					
647	10	1	1	3.06	0.62	ROST				
647	11	1	1	3.51	0.45					
647	12	1	2	3.73	0.50					
647	13	1	1	3.75	0.51					
676	1	1	1	3.55	0.43					
676	2	1	1	3.33	0.44					
676	3	1	2	3.29	0.38					
676	4	1	2	3.23	0.39					
676	5	1	2	3.34	0.43					
676	6	1	2	3.25	0.36					
676	7	1	2	3.45	0.40					
676	8	1	1	3.44	0.44					
676	9	1	2	3.41	0.42					
676	10	1	2	3.22	0.37					
676	11	4	.	.	.					
676	12	1	2	3.19	0.40					
676	13	1	1	3.51	0.40					
676	14	1	1	3.83	0.41	DIUR				
676	15	1	2	3.13	0.43					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

6

-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
681	1	1	1	3.54	0.46					
681	2	1	1	2.58	0.42	ROVE				
681	3	1	2	3.32	0.39	ROVE				
681	4	1	1	3.58	0.46					
681	5	1	1	3.79	0.42					
681	6	1	1	3.82	0.46					
681	7	4	.	.	.					
681	8	1	2	3.33	0.37	ROST				
681	9	1	2	3.71	0.39					
681	10	1	1	3.88	0.46					
681	11	1	2	3.64	0.42					
681	12	1	1	3.73	0.41					
681	13	1	1	3.77	0.49					
681	14	1	2	3.70	0.33					
681	15	1	2	3.55	0.36					
681	16	1	2	3.51	0.38					
746	1	1	2	3.20	0.45					
746	2	1	2	3.69	0.48					
746	3	1	1	4.15	0.61					
746	4	1	1	4.09	0.44					
746	5	1	2	3.75	0.43					
746	6	1	2	3.74	0.48					
746	7	1	1	3.94	0.67	ROVE				
746	8	1	1	4.05	0.60					
746	9	1	1	3.53	0.41					
746	10	1	2	.	0.47					
746	11	1	1	3.99	0.66					
746	12	1	1	3.94	0.46					
746	13	1	2	3.93	0.42					
746	14	1	2	3.91	0.49					
746	15	2	.	.	.					
746	16	1	1	4.00	0.51					
746	17	1	2	3.65	0.61					
785	1	1	2	3.01	0.36					
785	2	2	.	.	.					
785	3	1	1	3.26	0.44					
785	4	1	2	3.02	0.37					
785	5	1	2	2.91	0.38	ROSK				
785	6	1	2	2.98	0.34					
785	7	1	2	3.03	0.39	ROSK				
785	8	1	2	3.06	0.31					
785	9	1	1	3.18	0.40					
785	10	1	2	2.62	0.39					
785	11	1	1	3.01	0.39	ROSK				
785	12	1	1	3.26	0.40					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

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n-Hexane Rat Teratology Study: Raw Fetal Data

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0 ppm n-Hexane											
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5	
785	13	1	2	3.14	0.48						
785	14	1	1	2.92	0.41						
785	15	1	2	2.54	0.37						
785	16	1	1	2.81	0.36	ROVE					
785	17	1	1	3.02	0.27	ROSK	ROVE				
805	1	1	1	4.02	0.63						
805	2	2	.	.	.						
805	3	1	2	3.39	0.41						
805	4	1	1	3.51	0.48						
805	5	1	1	3.92	0.39						
805	6	1	1	3.82	0.42						
805	7	1	1	3.87	0.62						
805	8	1	2	2.61	0.63	ROST					
805	9	2	.	.	.						
805	10	1	2	3.48	0.58						
805	11	1	1	3.73	0.42						
805	12	1	2	3.30	0.40						
805	13	1	1	4.06	0.47						
926	1	1	2	2.88	0.62						
926	2	2	.	.	.						
926	3	1	1	3.36	0.48						
926	4	1	1	3.15	0.66						
926	5	1	1	3.32	0.46	ROST					
926	6	1	1	3.10	0.39	ROST					
926	7	1	2	3.04	0.42						
926	8	1	1	3.42	0.43						
926	9	1	2	3.29	0.46						
926	10	1	2	3.30	0.46						
926	11	1	2	3.09	0.47						
926	12	1	2	3.24	0.60						
926	13	2	.	.	.						
926	14	1	2	3.12	0.38						
936	1	1	2	3.48	0.73	ROVE					
936	2	1	2	3.49	0.39						
936	3	1	1	3.49	0.48						
936	4	1	2	3.85	0.63						
936	5	1	1	3.59	0.48						
936	6	1	1	2.88	0.36						
936	7	1	2	2.93	0.44						
936	8	1	2	3.28	0.46	ROVE					
936	9	1	2	2.85	0.43						
936	10	1	2	3.15	0.43						
936	11	1	2	2.92	0.41						
936	12	1	1	3.20	0.43						
936	13	1	1	3.61	0.37						

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
938	14	1	2	3.48	0.43					
938	15	1	1	3.57	0.61					
938	16	1	1	3.54	0.49					
938	17	1	2	2.91	0.34					
938	18	1	2	3.28	0.47					
963	1	1	1	3.40	0.46					
963	2	1	1	3.38	0.43					
963	3	1	2	3.32	0.48					
963	4	1	1	3.63	0.48					
963	5	1	1	3.73	0.38					
963	6	1	1	4.03	0.39					
963	7	1	2	3.36	0.40					
963	8	1	1	3.76	0.47					
963	9	1	1	4.01	0.43					
963	10	1	2	3.80	0.34					
963	11	1	1	2.73	0.37					
963	12	1	2	3.34	0.44					
963	13	1	2	3.33	0.43	ROST				
963	14	1	1	3.46	0.48					
963	15	1	1	3.74	0.26	ROST				
963	16	1	2	3.40	0.36					
963	17	1	2	3.54	0.44	ROST				
963	18	1	1	3.85	0.46					
963	19	1	1	3.82	0.37					
969	1	1	2	1.90	0.69	ROSK	ROST	ROPB	ROPH	
969	2	2	.	.	.					
969	3	1	1	2.33	0.54	ROST	ROPB			
969	4	1	2	1.95	0.44	ROSK	ROST	ROVE	ROPB	ROPH
969	5	1	1	2.47	0.44	ROST	ROPB			
969	6	1	1	2.44	0.41	ROSK	ROST			
969	7	1	1	2.07	0.66	ROST	ROPB			
969	8	2	.	.	.					
969	9	1	2	2.23	0.42	ROST	ROVE	ROPB		
969	10	1	1	2.24	0.67	ROST	ROPB			
969	11	1	1	2.40	0.46	ROSK	ROST			
978	1	1	2	2.75	0.64					
978	2	1	1	4.06	0.68	SRRR	ROVE			
978	3	1	1	4.33	0.68	ROVE				
976	4	2	.	.	.					
976	6	1	2	3.93	0.46					
978	6	1	1	4.79	0.62	ROVE				
976	7	1	2	3.66	0.47	ROVE				
976	8	1	2	3.94	0.49	ROVE				
976	9	2	.	.	.					
976	10	1	1	3.78	0.53	ROVE				

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----0 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
978	11	1	1	4.33	0.58					
978	12	1	1	4.28	0.46	ROVE				
978	13	1	1	4.41	0.51	DIUR	ROVE			
978	14	1	1	4.22	0.50	DIUR	ROVE			

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
445	1	1	1	3.23	0.41					
445	2	1	2	3.14	0.47					
445	3	1	1	3.34	0.40					
445	4	1	1	3.31	0.61	ROST	ROVE			
445	6	1	1	3.16	0.43	ROVE				
445	6	1	2	3.17	0.44	ROVE				
445	7	1	2	3.04	0.41	ROVE				
445	8	1	2	3.18	0.42	ROST	ROVE			
445	9	1	1	3.19	0.46	DIUR	ROVE			
445	10	1	2	3.10	0.46					
448	1	1	2	3.67	0.60					
448	2	1	2	3.87	0.46					
448	3	1	2	3.69	0.41					
448	4	1	2	3.45	0.39					
448	5	1	2	3.59	0.44					
448	6	1	1	3.66	0.40					
448	7	1	1	3.91	0.46					
448	8	1	2	3.67	0.47					
448	9	1	2	3.82	0.60					
448	10	1	1	3.63	0.43					
448	11	1	2	3.42	0.43	ROST				
448	12	1	1	3.81	0.39					
448	13	1	2	4.03	0.46					
448	14	1	2	3.61	0.37	ROST				
448	15	1	1	3.75	0.44					
448	16	1	2	4.01	0.40					
448	17	1	2	3.97	0.61					
448	18	1	1	3.90	0.42					
453	1	1	1	3.51	0.40	SRRR				
453	2	1	1	3.44	0.40	ROST				
453	3	1	2	3.39	0.43	ROST	SRRR			
453	4	2	.	.	.					
453	5	2	.	.	.					
453	6	1	1	3.50	0.36	ROST	SRRR			
453	7	1	2	3.45	0.40					
453	8	1	1	3.54	0.43					
453	9	1	1	3.83	0.36					
453	10	1	2	3.22	0.39					
453	11	1	2	3.41	0.38					
453	12	1	1	3.49	0.48					
453	13	1	2	3.49	0.38					
453	14	1	1	3.70	0.34					
453	15	2	.	.	.					
516	1	1	2	4.17	0.35					
516	2	1	2	4.07	0.39					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
518	3	1	2	4.32	0.41					
518	4	1	2	4.31	0.39					
518	5	1	2	4.33	0.39					
518	6	1	2	4.86	0.40					
518	7	1	2	4.12	0.33					
518	8	1	2	4.39	0.36	DIUR				
518	9	1	1	4.83	0.40					
518	10	1	2	4.86	0.38					
518	11	1	1	4.89	0.36					
518	12	1	2	4.67	0.36					
518	13	1	1	4.48	0.36					
518	14	1	2	4.88	0.39					
518	15	1	1	6.07	0.40					
518	16	1	2	4.91	0.36					
518	17	1	1	4.93	0.44					
581	1	1	2	3.80	0.50	ROVE				
581	2	1	1	3.90	0.66					
581	3	1	1	3.83	0.60					
581	4	1	2	3.78	0.60					
581	5	1	1	4.16	0.66					
581	6	1	1	3.79	0.47					
581	7	1	2	3.86	0.66					
581	8	1	2	3.61	0.63	DIUR				
581	9	1	1	3.86	0.63					
581	10	1	2	3.66	0.48	DIUR				
581	11	1	2	3.69	0.49					
581	12	1	1	3.98	0.61					
581	13	1	1	4.13	0.66					
582	1	1	2	2.80	0.44					
582	2	1	1	3.08	0.46	ROST				
582	3	1	2	2.88	0.36					
582	4	1	1	3.27	0.32	SRRR				
582	5	1	1	3.09	0.32	ROST	ROPB			
582	6	2	.	.	.					
582	7	1	2	2.71	0.31	ROST	ROPB			
582	8	1	1	3.12	0.38					
582	9	1	1	2.83	0.39					
582	10	1	1	3.32	0.31					
582	11	1	2	2.88	0.32					
582	12	1	1	3.48	0.36					
582	13	1	1	3.48	0.34					
582	14	1	1	3.47	0.41					
570	1	1	2	3.12	0.60	ROST				
570	2	1	2	3.24	0.46	ROVE				
570	3	1	1	3.81	0.66					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
670	4	1	1	3.63	0.67	ROSK	ROST	ROVE	ROPB	
670	6	1	2	3.30	0.69					
<del>570</del>	6	1	1	3.89	0.62					
670	7	1	2	3.66	8.60					
670	8	1	1	3.93	0.62					
670	9	1	1	3.99	0.61	ROVE				
690	1	1	2	2.81	8.36	ROST	ROPB			
690	2	4	.	.	.					
<del>590</del>	3	1	2	3.58	0.40					
690	4	1	2	3.28	0.40	ROST				
<del>590</del>	6	1	2	2.30	0.31	ROST				
690	6	4	.	.	.					
<del>590</del>	7	1	1	3.18	0.43	ROST				
690	8	1	2	3.13	0.31	ROST				
690	9	1	2	2.36	0.39	ROSK	ROST	ROPH	ROVE	
690	<del>10</del>	1	2	3.32	0.41					
690	11	1	1	3.67	0.39	ROST				
690	12	1	1	3.66	0.40					
690	13	1	1	3.40	0.43	ROST				
<del>690</del>	14	1	1	3.49	0.49					
690	16	1	2	3.29	0.62					
601	1	1	2	3.18	0.40					
601	2	1	2	3.29	0.44					
601	3	1	2	3.40	0.40					
601	4	1	1	3.62	0.36	DIUR				
601	6	1	2	3.66	8.43	ROST				
601	6	1	2	3.36	0.36	ROST				
601	7	1	1	3.40	0.41					
601	8	1	2	3.32	0.37					
601	9	1	2	3.28	0.40					
601	<del>10</del>	1	1	3.47	0.40					
601	11	1	1	3.31	0.39	DIUR				
601	12	1	1	3.16	0.33	ROVE				
601	13	1	2	3.36	0.36					
601	14	1	1	3.62	0.40					
601	16	1	2	3.32	0.34					
613	1	1	2	3.38	0.43					
813	2	2								
613	3	1	1	4.00	0.46					
613	4	1	1	3.87	0.47	DIUR	ROST			
613	6	1	2	3.98	0.62	ROST				
813	6	1	2	3.80	0.46					
613	7	1	2	3.81	0.47					
613	8	1	2	3.84	0.47	SRRR				
613	9	1	1	4.16	0.60	DIUR				

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----200 ppm n-Hexane-----

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
613	10	1	1	3.59	0.42					
613	11	1	2	3.78	0.60	ROST				
613	12	1	1	4.10	0.61					
613	13	2	.	.	.					
613	14	1	1	4.20	0.46					
613	15	1	2	3.49	0.36	DIUR				
614	1	1	1	2.73	0.38	DIUR				
614	2	2	.	.	.					
614	3	1	2	3.28	0.52					
614	4	1	2	3.39	0.37					
614	5	1	1	3.47	0.43	ROST				
614	6	1	1	3.60	0.38					
614	7	1	2	3.19	0.39					
614	8	1	2	3.11	0.36					
614	9	1	1	3.72	0.47					
614	10	2	.	.	.					
614	11	1	2	3.42	0.43					
614	12	1	1	3.59	0.40					
614	13	1	2	3.53	0.43					
614	14	1	1	3.38	0.25					
614	15	1	2	3.55	0.34	ROST				
614	16	1	1	3.73	0.38	DIUR				
614	17	1	2	3.52	0.45					
614	18	1	1	3.49	0.36					
614	19	1	2	3.71	0.41					
629	1	1	1	3.19	0.57					
629	2	1	1	3.80	0.37	DIUR				
629	3	1	1	3.86	0.35	DIUR				
629	4	1	2	3.82	0.37					
629	5	1	2	3.34	0.39					
629	6	1	1	3.47	0.41					
629	7	1	2	3.36	0.36	ROST				
629	8	1	1	3.33	0.34	DIUR				
629	9	1	2	3.31	0.39					
629	10	1	2	3.27	0.41					
629	11	1	1	3.49	0.37	ROST				
629	12	1	2	3.20	0.32					
629	13	1	1	3.57	0.37	DIUR				
629	14	1	2	2.69	0.32					
629	15	1	2	1.96	0.27	ROSK	ROST	ROVE	ROPB	ROPH
629	16	1	1	3.34	0.44					
640	1	1	1	2.81	0.35					
640	2	1	2	2.86	0.46	ROST				
640	3	1	1	2.91	0.43	ROVE				
640	4	1	2	3.16	0.47					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----200 ppm n-Hexane-----										
Mat No	Sit.	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
640	5	1	1	2.93	0.49	ROVE				
640	6	1	1	3.04	0.40					
640	7	1	1	2.93	0.38					
640	8	1	1	2.78	0.31					
640	9	1	1	2.86	0.38					
640	10	1	2	2.84	0.36					
640	11	1	1	2.86	0.36					
640	12	1	2	2.88	0.37	ROST				
640	13	1	1	3.08	0.37					
640	14	1	2	2.83	0.33	ROST				
640	15	1	2	2.60	0.44	ROST				
640	16	1	1	3.17	0.43	ROST				
640	17	1	2	2.79	0.44					
652	1	1	1	3.66	0.46	ROSK				
652	2	1	1	3.71	0.48					
652	3	1	1	3.39	0.43	DIUR				
652	4	1	2	3.53	0.38					
652	5	1	2	3.19	0.36	ROPB				
652	6	1	2	3.45	0.40					
652	7	1	2	3.30	0.42					
652	8	1	2	3.52	0.60					
652	9	1	2	3.00	0.43					
652	10	1	2	3.23	0.37					
652	11	1	2	3.25	0.37					
652	12	2	.	.	.					
652	13	1	1	3.70	0.45					
652	14	1	2	3.41	0.37					
652	15	1	2	3.33	0.37					
652	16	1	2	3.09	0.38					
662	1	1	1	4.24	0.43					
662	2	2	.	.	.					
662	3	1	2	3.50	0.38	ROVE				
662	4	1	1	3.80	0.37					
662	5	1	2	3.68	0.40					
662	6	1	2	3.45	0.46					
662	7	1	2	3.52	0.41					
662	8	1	2	3.78	0.36					
662	9	1	2	3.80	0.41					
662	10	1	1	4.24	0.46					
662	11	1	1	3.68	0.47	ROST				
662	12	1	1	3.73	0.36					
662	13	1	2	3.40	0.36					
662	14	1	1	4.03	0.47					
662	15	1	1	2.17	0.28	ROSK	ROST	ROPB		
662	16	1	1	4.13	0.36					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]



## n-Hexane Rat Teratology Study: Raw Fetal Data

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-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
671	1	1	1	3.01	0.50					
671	2	1	1	3.72	0.43					
671	3	1	2	3.28	0.37					
671	4	1	1	4.11	0.45					
671	5	1	1	3.98	0.50					
671	6	1	1	4.20	0.43					
671	7	1	2	3.73	0.41					
671	8	1	1	4.08	0.44					
671	9	1	1	4.11	0.40					
671	10	1	2	3.61	0.35					
671	11	1	1	4.10	0.46					
671	12	1	2	3.47	0.38					
671	13	1	1	4.00	0.40					
671	14	1	2	3.91	0.37					
671	15	1	2	4.10	0.49					
671	16	1	1	4.29	0.47					
671	17	1	2	3.89	0.40	DIUR				
688	1	1	1	4.36	0.42	SRRR				
688	2	1	1	4.01	0.51					
688	3	1	2	4.12	0.59					
688	4	1	2	4.24	0.54					
688	5	1	2	3.72	0.45					
688	6	1	2	2.95	0.65	ROST				
688	7	1	1	4.37	0.52					
688	8	1	1	3.88	0.60					
688	9	1	2	3.87	0.45					
688	10	1	1	4.45	0.51					
688	11	1	1	4.42	0.57					
688	12	1	2	4.17	0.48					
688	13	1	2	4.20	0.49	DIUR				
696	1	1	1	3.69	0.52					
696	2	1	2	3.34	0.46					
696	3	1	2	3.34	0.41	ROST				
696	4	1	2	3.70	0.38					
696	5	1	2	3.42	0.43					
696	6	1	2	3.38	0.38					
696	7	1	2	3.38	0.39					
696	8	1	1	3.66	0.34					
696	9	1	1	3.82	0.37					
696	10	1	1	3.57	0.43					
696	11	1	1	3.94	0.48					
696	12	1	1	3.31	0.34	ROST				
696	13	1	1	3.83	0.39					
696	14	1	2	3.39	0.24					
696	15	1	1	3.64	0.38					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
763	1	1	2	3.93	0.47					
763	2	1	1	3.76	0.39					
763	3	1	1	3.81	0.47					
763	4	1	2	3.64	0.36					
763	6	1	1	3.66	0.43					
763	6	1	2	3.72	0.39					
763	7	1	1	4.07	0.46					
763	8	1	1	3.79	0.43					
763	9	1	2	4.14	0.46					
763	10	1	1	4.00	0.41					
763	11	1	1	4.02	0.43	ROSK				
763	12	1	2	3.72	0.43					
763	13	1	2	3.92	0.40					
763	14	1	1	3.93	0.46					
763	16	1	2	3.76	0.41					
763	16	1	2	3.70	0.40					
763	17	1	1	3.72	0.40					
770	1	1	1	3.44	0.60					
770	2	1	1	3.42	0.61					
770	3	1	1	3.62	0.40					
770	4	1	2	3.27	0.47					
770	6	1	2	3.07	0.37					
770	6	1	2	3.31	0.60					
770	7	1	1	3.36	0.64					
770	8	1	2	3.13	0.38	ROST				
770	9	1	1	3.11	0.38					
770	10	1	2	3.02	0.39					
770	11	1	1	3.19	0.39					
770	12	1	2	2.86	0.29	ROST				
770	13	1	1	3.70	0.43					
770	14	1	1	3.40	0.36					
770	16	1	2	3.12	0.40					
777	1	1	1	3.48	0.37					
777	2	1	2	3.46	0.42					
777	3	1	2	3.37	0.34					
777	4	1	1	3.68	0.44					
777	6	1	2	3.69	0.36					
777	6	1	1	3.38	0.43					
777	7	1	2	3.07	0.47					
777	8	1	1	3.89	0.41					
777	9	1	2	3.48	0.41					
777	10	1	2	3.60	0.36					
777	11	1	2	3.36	0.42					
777	12	1	2	3.18	0.41					
777	13	1	1	3.18	0.34					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
843	1	2	.	.	.					
843	2	1	1	3.94	0.45	DIUR				
843	3	1	1	3.49	0.40	ROST				
843	4	1	1	3.97	0.41	DIUR	ROST			
843	5	2	.	.	.					
843	6	1	2	3.78	0.45	DIUR				
843	7	1	2	3.33	0.42					
843	8	2	.	.	.					
843	9	1	2	3.54	0.42					
843	10	1	1	3.75	0.41	ROST				
843	11	1	2	3.68	0.51					
843	12	1	2	3.86	0.48	ROST				
843	13	1	1	4.41	0.54	DIUR				
843	14	1	1	3.78	0.36					
843	15	1	1	3.96	0.40					
843	16	1	2	3.68	0.45					
843	17	1	2	3.64	0.43					
843	18	1	2	3.18	0.43					
931	1	1	2	3.53	0.34					
931	2	1	2	3.87	0.37					
931	3	1	2	3.38	0.39					
931	4	1	1	3.98	0.45					
931	5	1	2	3.82	0.48					
931	6	1	2	3.68	0.35					
931	7	1	2	3.62	0.41	DIUR				
931	8	1	1	3.78	0.39					
931	9	1	2	3.28	0.41					
931	10	1	1	2.69	0.47					
931	11	1	1	3.68	0.29					
931	12	1	2	3.52	0.46					
931	13	1	1	4.22	0.46					
931	14	1	2	3.65	0.38					
931	15	1	1	4.01	0.54					
931	16	1	1	3.50	0.35					
931	17	1	2	3.68	0.41					
931	18	1	2	3.68	0.34					
942	1	1	1	2.58	0.44					
942	2	1	1	3.20	0.45	ROST				
942	3	1	1	3.44	0.44	ROST				
942	4	1	2	3.11	0.41	ROST				
942	5	1	1	3.08	0.43	ROST				
942	6	1	1	3.11	0.51	ROST				
942	7	1	2	3.06	0.44	ROST				
942	8	1	2	2.78	0.35	DIUR				
942	9	2	.	.	.					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Row Fetal Data

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-----200 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN6
942	10	1	2	3.06	0.40					
942	11	1	2	2.80	0.44					
942	12	1	1	3.29	0.44					
942	13	1	1	3.22	0.50					
942	14	1	1	3.41	0.46	ROST				
942	15	1	1	2.39	0.42	ROST				
942	16	2	.	.	.					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
460	1	1	2	2.35	0.37	ROST				
460	2	1	2	2.82	0.35					
460	3	1	1	2.76	0.58					
460	4	1	1	2.88	0.44					
460	5	1	1	3.03	0.39					
460	6	1	1	3.19	0.49					
460	7	1	1	3.11	0.48					
460	8	1	1	2.84	0.44					
460	9	1	1	3.03	0.40					
460	10	1	2	2.60	0.39	ROST				
460	11	1	2	2.74	0.44					
460	12	1	1	3.17	0.48					
460	13	1	2	3.04	0.52					
460	14	1	1	3.18	0.35					
460	15	1	1	2.78	0.47					
460	16	2	.	.	.					
470	1	1	1	3.27	0.29	ROST				
470	2	1	2	3.07	0.40	ROST				
470	3	1	2	3.04	0.41	ROST				
470	4	1	1	3.37	0.40	ROST				
470	5	1	2	3.54	0.45					
470	6	1	2	3.24	0.42	ROST				
470	7	1	1	3.34	0.42					
470	8	1	1	3.06	0.39	ROST				
470	9	1	1	2.66	0.43	ROST	ROPB			
470	10	1	2	2.83	0.33	ROST				
470	11	1	1	3.26	0.44	ROST				
470	12	1	1	3.65	0.39	ROST				
470	13	1	1	3.09	0.39	ROST				
470	14	1	2	3.24	0.39	ROST				
470	15	1	1	3.36	0.38	ROST				
476	1	1	2	2.61	0.32	ROST				
476	2	1	2	2.88	0.32	ROST				
476	3	1	1	2.92	0.33	ROST				
476	4	1	2	2.90	0.30					
476	5	1	2	2.82	0.34	ROST				
476	6	1	2	3.00	0.33	ROSK				
476	7	1	2	3.08	0.33	ROST				
476	8	1	2	2.87	0.43	ROST				
476	9	1	1	3.21	0.35	ROVE				
476	10	1	1	2.88	0.39	ROSK	ROST			
476	11	1	2	2.90	0.38	ROST				
476	12	1	2	2.82	0.32					
476	13	2	.	.	.					
476	14	1	1	3.21	0.40					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
476	16	1	1	3.04	0.36					
481	1	4	.	.	.					
481	2	1	1	3.10	0.39	ROST				
481	3	1	2	3.66	0.36	ROST				
481	4	1	2	3.26	0.34	ROST				
481	5	1	2	3.11	0.32	ROST	ROVE			
481	6	1	1	3.46	0.44					
481	7	1	2	3.46	0.39					
481	8	2	.	.	.					
481	9	1	1	3.62	0.40	ROST				
481	10	1	2	3.13	0.36	ROVE				
481	11	1	1	3.64	0.43	ROST				
481	12	1	1	3.49	0.41	ROST				
481	13	1	2	3.66	0.40	ROST				
481	14	1	1	3.33	0.38	ROST	ROVE			
481	16	1	1	3.19	0.46					
610	1	1	1	2.98	0.39	ROSK	ROVE			
610	2	1	2	2.89	0.37	ROST				
610	3	1	2	2.66	0.39	ROSK	ROPB			
610	4	1	1	3.34	0.46					
610	6	1	2	3.71	0.42					
610	6	1	1	2.81	0.40	ROST				
610	7	1	1	3.32	0.46					
610	8	1	1	3.66	0.60					
610	9	1	2	2.73	0.39	DIUR				
610	10	1	2	2.94	0.40					
610	11	1	2	2.46	0.41	ROSK	ROST	ROPB		
610	12	1	1	3.19	0.39					
610	13	1	1	3.36	0.43					
610	14	1	2	3.62	0.47					
610	16	1	2	3.02	0.38					
610	16	1	2	3.43	0.43					
620	1	1	1	3.33	0.68	ROST	ROVE			
620	2	4	.	.	.					
520	3	2	.	.	.					
520	4	1	2	3.27	0.71	ROST				
544	1	4	.	.	.					
544	2	1	2	3.07	0.39	ROST				
544	3	1	2	3.17	0.33	DIUR				
544	4	1	1	3.30	0.41	ROST				
544	5	1	1	3.51	0.37					
544	6	1	2	3.28	0.39	ROST				
544	7	1	2	3.38	0.36	ROST				
544	8	1	2	3.33	0.23	ROST				
544	9	1	1	3.32	0.33	ROST				

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
 Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
644	10	1	2	2.98	0.36	ROST				
644	11	1	1	3.10	0.42	ROST				
644	12	1	2	3.21	0.32	ROST				
644	13	1	2	3.17	0.30	ROST				
644	14	1	2	3.31	8.37	ROST				
644	16	1	2	3.20	0.34					
644	16	1	1	3.37	0.40					
644	17	1	2	3.36	0.38	ROST				
649	1	1	1	3.47	0.34					
649	2	1	1	3.60	0.39					
649	3	1	1	3.48	0.36					
649	4	1	2	2.98	0.36					
649	6	1	2	3.32	8.32					
649	6	2	.	.	.					
649	7	1	2	3.41	0.43					
649	8	1	1	3.78	0.43					
649	9	1	2	3.48	0.41					
649	10	1	2	3.39	0.37					
649	11	2	.	.	.					
649	12	1	1	3.48	0.42					
649	13	1	2	3.30	0.38					
649	14	1	1	3.82	0.41					
649	16	1	1	3.84	0.43					
649	16	1	1	3.73	0.42					
649	17	1	1	3.85	0.39					
666	1	1	1	3.13	0.42					
666	2	1	2	3.10	0.38					
666	3	1	1	3.88	0.45					
666	4	1	1	3.22	0.42	ROST				
666	6	1	2	3.51	0.44					
555	6	1	1	3.27	0.38	ROST				
555	7	1	1	3.24	0.48	DIUR	ROST			
555	8	1	2	3.17	0.34					
555	9	1	1	3.03	0.39	DIUR				
555	10	1	1	3.34	0.39	DIUR	ROST			
555	11	1	1	3.23	0.50	ROST				
555	12	1	2	3.19	0.37					
555	13	1	2	3.05	0.40					
555	14	2	.	.	.					
555	15	1	2	3.44	0.43	DIUR				
555	16	1	2	2.98	0.38	ROST				
555	17	1	2	3.29	0.34					
555	18	1	1	3.89	0.41					
580	1	1	1	3.42	0.38					
580	2	1	1	3.50	0.35					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----1000 ppm n-Hexane-----										
Mat No	Sit.	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN6
580	3	1	2	3.18	0.36					
580	4	1	1	2.97	0.31	ROST				
580	5	1	1	3.32	0.33					
580	6	1	1	3.38	0.32	ROST				
580	7	1	2	3.22	0.34					
580	8	1	2	3.44	0.38					
580	9	1	1	3.47	0.34					
580	10	1	2	3.08	0.33					
580	11	2	.	.	.					
580	12	1	1	3.66	0.33					
580	13	1	1	3.39	0.36					
580	14	1	1	3.46	0.36					
580	15	1	1	3.42	0.33	ROST				
580	16	1	2	3.13	0.33	ROST				
580	17	1	1	3.04	0.27					
591	1	1	1	3.03	0.63					
591	2	1	2	3.02	0.36	ROST				
591	3	1	2	3.64	0.40					
591	4	1	2	2.98	0.44					
591	5	1	2	3.61	0.49					
591	6	1	1	3.40	0.40					
591	7	1	2	3.21	0.49					
591	8	1	2	3.40	0.42					
591	9	1	2	2.61	0.33	ROSK				
591	10	1	2	3.20	0.48	ROST				
591	11	1	2	3.09	0.44					
591	12	1	1	3.61	0.41					
591	13	1	2	3.02	0.40					
591	14	1	2	3.28	0.48					
635	1	1	2	3.31	0.39					
635	2	1	2	3.62	0.36					
635	3	1	2	3.26	0.43					
635	4	1	2	3.37	0.36					
635	5	1	2	2.86	0.40					
635	6	1	1	3.41	0.38					
635	7	1	2	2.67	0.39	ROST				
635	8	1	2	3.26	0.46	ROST	ROVE			
635	9	1	1	3.06	0.44					
635	10	1	2	3.60	0.27					
635	11	1	1	3.41	0.36	ROST				
635	12	1	2	3.08	0.42	ROST				
635	13	1	2	3.37	0.40	ROST				
635	14	1	1	3.41	0.41					
635	15	1	2	3.46	0.38					
635	16	1	2	3.16	0.46					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]



n-Hexane Rat Teratology Study: Raw Fetal Data

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1000 ppm n-Hexane

Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
649	1	1	2	2.60	0.37	ROST	SRRR			
649	2	1	1	2.99	0.47	ROST	SRRR			
649	3	1	1	2.61	0.36	ROPB	ROST			
649	4	1	1	2.28	0.36					
649	5	1	2	2.66	0.36	SRRR				
649	6	1	2	2.48	0.34	ROST				
649	7	1	1	2.08	0.31	SRRR				
649	8	1	1	2.47	0.35	ROSK	SRRR			
649	9	1	1	2.20	0.37	ROST				
649	10	1	1	1.89	0.36	ROSK	ROST	ROPB		
649	11	1	2	2.44	0.36	SRRR				
649	12	1	2	2.43	0.30	SRRR				
649	13	1	2	2.84	0.44	SRRR				
649	14	1	1	2.73	0.36	SRRR				
649	15	1	1	2.61	0.36	ROST	SRRR	ROPB		
653	1	1	1	3.38	0.39					
653	2	1	2	2.80	0.46					
653	3	1	2	3.26	0.41					
653	4	1	1	3.70	0.45	ROPB				
653	5	1	2	3.63	0.48					
653	6	1	2	3.67	0.43					
653	7	1	2	3.60	0.60					
653	8	1	2	3.28	0.48	ROPB				
653	9	1	2	3.29	0.41					
653	10	4	.	.	.					
653	11	1	1	3.41	0.51	ROST				
653	12	1	2	3.13	0.39					
653	13	1	2	3.22	0.39					
653	14	1	2	3.08	0.34					
653	15	1	2	3.59	0.48					
653	16	1	1	3.57	0.49					
653	17	2	.	.	.					
653	18	1	2	3.57	0.48					
664	1	1	2	3.19	0.35	ROST				
664	2	1	1	3.40	0.37					
664	3	1	2	3.58	0.40	ROST				
664	4	1	2	3.37	0.37	ROST				
664	5	1	2	3.50	0.45	ROST				
664	6	1	1	3.53	0.35	ROST				
664	7	1	1	3.55	0.42					
664	8	1	1	3.72	0.48	ROST				
664	9	2	.	.	.					
664	10	1	2	3.38	0.37					
664	11	1	2	3.92	0.40	DIUR	ROST			
664	12	1	1	3.71	0.40					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
664	13	1	2	3.78	0.39					
664	14	1	2	3.69	0.39					
689	1	1	2	3.17	0.42					
689	2	1	2	3.30	0.47					
689	3	2		.	.					
689	4	1	1	3.50	0.57	ROVE				
689	6	2	.	.	.					
689	6	1	2	3.24	0.50	ROST				
689	7	2	.	.	.					
689	8	1	2	3.38	0.45	ROST	ROVE			
689	9	2	.	.	.					
689	10	1	1	3.48	0.53					
689	11	1	2	2.57	0.47	ROST	ROVE			
689	12	1	2	3.65	0.45					
689	13	2	.	.	.					
689	14	1	2	3.51	0.49					
697	1	1	1	3.88	0.49					
697	2	2	.	.	.					
697	3	1	1	4.25	0.48					
697	4	1	1	3.85	0.38	DIUR				
697	6	1	2	3.85	0.47					
697	6	1	2	4.01	0.44					
697	7	1	1	3.73	0.40					
697	8	1	1	3.83	0.44					
697	9	1	1	4.09	0.47					
697	10	1	1	3.75	0.40					
697	11	1	2	3.63	0.61	ROST	ROPB			
697	12	1	2	3.60	0.44					
697	13	1	2	3.98	0.37					
697	14	1	2	3.87	0.48					
768	1	1	2	2.40	0.37					
768	2	1	1	2.85	0.38	ROST				
768	3	1	2	2.68	0.57					
768	4	1	1	2.53	0.38	ROPB				
768	6	1	2	2.73	0.44					
768	6	1	1	2.44	0.40	ROPB				
768	7	1	2	2.24	0.33	ROPB				
768	8	2	.	.	.					
768	9	1	2	2.42	0.28	ROST				
768	10	1	2	2.31	0.40	ROST				
768	11	1	2	2.19	0.29	ROST	ROPB			
768	12	1	1	2.67	0.41	ROPB				
768	13	1	2	2.37	0.34					
768	14	1	2	2.27	0.32	ROST	ROPB			
768	16	1	2	2.64	0.38					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

## n-Hexane Rat Teratology Study: Raw Fetal Data

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-----1000 ppm n-Hexane-----

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
788	I6	I	I	2.26	0.35	ROST	ROPB			
788	17	I	I	2.65	0.38					
807	I	I	I	3.32	0.37	ROSK	ANON	ROPH	ROPB	
807	2	I	I	3.47	0.54	SRRR	ROPB			
807	3	I	2	3.09	0.49	ROSK	SRRR			
807	4	I	2	3.84	0.45					
807	6	I	I	3.65	0.66					
807	6	I	2	3.51	0.47					
807	7	2								
807	8	4								
807	9	I	I	3.31	0.37	ROPB				
807	10	I	I	3.49	0.44	DIUR				
807	11	I	I	3.60	0.48					
866	I	1	I	2.98	0.42					
855	2	I	2	2.63	0.28	DIUR	RPCA			
866	3	1	I	3.20	0.37					
866	4	1	2	2.85	0.37	ROST	ROVE			
866	6	I	I	2.92	0.42					
855	8	I	I	2.79	0.41	DIUR				
866	7	2								
866	8	I	I	3.04	0.49					
866	9	I	1	3.37	0.39	DIUR	RPCA			
866	10	I	I	2.39	0.37	ROST				
855	11	I	I	3.47	0.44	DIUR				
866	12	I	I	3.39	0.52					
866	13	I	I	2.83	0.36					
866	14	I	2	3.03	0.43					
866	15	I	2	2.88	0.41	ROVE				
866	16	I	2	3.10	0.45					
866	17	I	2	3.02	0.42					
866	18	I	I	2.85	0.38					
866	19	I	I	2.82	0.39	ROPB				
866	20	2								
866	21	2								
906	I	I	I	3.18	0.44					
906	2	I	I	3.57	0.47					
906	3	I	I	3.40	0.60					
906	4	I	I	3.77	0.48					
906	6	I	I	3.70	0.47					
906	6	I	2	3.46	0.48					
906	7	I	2	3.31	0.42					
906	8	I	2	3.47	0.43					
906	9	2								
906	10	I	2	3.64	0.47					
906	11	I	I	3.52	0.47	DIUR				

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

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-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
906	12	1	1	3.66	0.67					
906	13	1	1	3.66	0.48					
906	14	1	1	3.61	0.63					
906	16	1	1	3.63	0.61	DIUR	ROST			
906	16	1	1	3.62	0.43					
911	1	1	2	3.07	0.32					
911	2	1	2	2.49	0.33					
911	3	1	2	2.97	0.38					
911	4	1	1	3.46	0.38					
911	6	1	1	3.69	0.39					
911	6	1	2	3.41	0.46					
911	7	1	2	3.11	0.39					
911	8	1	1	3.42	0.39					
911	9	1	1	3.36	0.42					
911	10	1	2	3.46	0.38					
911	11	1	1	3.40	0.39					
911	12	1	2	3.17	0.40					
911	13	1	2	3.28	0.37					
911	14	1	2	3.16	0.33					
911	16	1	2	3.40	0.42					
911	16	1	2	3.36	0.38					
911	17	1	2	3.78	0.46					
918	1	1	1	3.48	0.42	ROST				
918	2	1	1	3.68	0.63					
918	3	1	2	3.24	0.48					
918	4	1	2	3.66	0.60					
918	6	1	2	3.62	0.48	DIUR	RPCA			
918	6	1	2	3.34	0.44					
918	7	1	2	3.66	0.39					
918	8	1	1	3.67	0.46					
918	9	1	1	2.29	0.24	ROSK	ROST	ROPB		
918	10	1	1	3.27	0.46	ROST				
918	11	1	2	3.32	0.42	ROST				
918	12	1	2	3.69	0.37	ROVE				
918	13	1	2	3.70	0.44					
918	14	1	2	3.68	0.40	ROST				
918	16	1	2	3.69	0.62					
918	16	1	2	3.40	0.44					
918	17	1	1	3.23	0.41					
918	18	1	1	3.64	0.47	ROST				
921	1	1	1	3.67	0.40	DIUR				
921	2	1	1	3.78	0.46					
921	3	1	1	4.04	0.41					
921	4	1	1	3.67	0.46	ROST	ROVE			
921	6	1	2	3.86	0.40					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----1000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
921	6	1	1	4.19	0.44	ROVE				
921	7	1	2	2.84	0.31	DIUR	ROST	ROVE		
921	8	1	1	4.03	0.46					
921	9	1	2	3.62	0.38					
921	10	1	2	3.88	0.40					
921	11	1	2	3.90	0.39					
921	12	1	2	4.04	0.42					
921	13	1	2	3.86	0.41	ROVE				
921	14	1	1	3.63	0.43					
921	15	1	2	4.06	0.40					
944	1	1	1	3.32	0.41	ROVE				
944	2	1	2	3.17	0.30					
944	3	1	2	3.37	0.46					
944	4	1	1	3.29	0.37					
944	5	1	2	3.18	0.39					
944	6	1	1	3.32	0.33					
944	7	1	2	3.18	0.32					
944	8	1	1	3.65	0.38					
944	9	1	1	3.24	0.42					
944	10	1	1	3.08	0.32					
944	11	1	2	3.30	0.36					
944	12	1	2	3.22	0.37					
944	13	1	1	3.18	0.32					
944	14	1	2	3.14	0.36					
944	15	1	2	3.41	0.40					
944	16	1	1	3.63	0.34					
944	17	1	2	3.25	0.39					
965	1	1	2	3.10	0.34					
965	2	1	1	3.67	0.43					
965	3	1	2	3.69	0.41					
965	4	1	2	3.19	0.47					
965	5	1	1	3.17	0.44					
965	6	1	2	3.47	0.44					
965	7	1	2	3.17	0.36					
965	8	1	1	3.60	0.39					
965	9	1	2	3.54	0.43					
965	10	1	2	3.30	0.40					
965	11	1	1	3.62	0.43					
965	12	1	2	3.42	0.39					
965	13	1	1	3.44	0.39					
965	14	1	1	3.66	0.40					
965	15	1	1	3.93	0.40					
965	16	1	2	3.70	0.21					
972	1	1	2	3.33	0.36					
972	2	1	1	3.44	0.41					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----1000 ppm n-Hexane-----										
Mat No	Sit.	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
972	3	1	1	3.48	0.38	DIUR				
972	4	1	2	3.46	0.40					
972	6	1	1	3.24	0.28	DIUR	ROVE			
972	6	1	1	2.94	0.29					
972	7	1	2	2.97	0.38	ROST				
972	8	1	2	3.36	0.37					
972	9	1	1	3.41	0.37					
972	10	1	1	3.70	0.40					
972	11	1	2	3.14	0.41					
972	12	1	1	3.32	0.34					
972	13	1	2	3.27	0.37					
972	14	1	1	3.48	0.40					
972	16	1	2	3.72	0.48					
972	16	1	1	3.61	0.32					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
451	1	1	1	3.20	0.42	DIUR				
451	2	1	1	3.21	0.37	ROST				
451	3	1	2	3.23	0.44					
451	4	1	1	2.87	0.44	ROST				
451	5	1	1	3.03	0.36					
451	6	1	2	3.10	0.39					
451	7	1	1	3.23	0.44					
451	8	2	.	.	.					
451	9	1	2	1.92	0.39	ROST	ROPH			
451	10	2	.	.	.					
451	11	1	1	3.34	0.42	DIUR				
451	12	1	1	3.42	0.38					
451	13	1	2	3.14	0.35					
451	14	1	2	3.17	0.43					
451	15	1	1	3.57	0.39					
451	16	1	2	3.47	0.49					
457	1	1	2	2.54	0.39					
457	2	1	1	2.51	0.31	ROPB				
457	3	1	2	2.62	0.37	ROST				
457	4	1	1	2.83	0.38	ROST				
457	5	1	1	2.81	0.38					
457	6	1	2	2.76	0.41	ROST				
457	7	1	2	2.57	0.34	ROST				
457	8	1	1	2.60	0.32	ROST				
457	9	1	2	2.67	0.34	ROST				
457	10	1	2	2.46	0.38	ROST				
457	11	4	.	.	.					
457	12	1	2	2.41	0.30	ROST	ROPB			
457	13	1	2	2.48	0.25	ROST	ROVE			
457	14	1	2	2.51	0.36	DIUR	ROST			
457	15	1	1	2.86	0.34	ROST				
457	16	1	1	2.82	0.39	DIUR	RPCA			
457	17	1	1	2.73	0.35	ROST	ROVE			
472	1	1	2	3.00	0.36	ROST				
472	2	1	1	3.25	0.34	ROST				
472	3	1	2	2.93	0.37	ROST				
472	4	1	2	2.61	0.33	ROST	ROVE			
472	5	1	1	3.05	0.41	ROST				
472	6	1	1	3.16	0.48	ROST				
472	7	1	2	3.06	0.37					
472	8	1	1	3.19	0.32					
472	9	1	1	3.02	0.33					
472	10	1	2	2.95	0.49					
472	11	1	1	2.99	0.36	ROST				
472	12	1	1	2.95	0.36					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN6
472	13	1	2	3.03	0.35					
472	14	1	1	3.08	0.32	ROST	ROVE			
472	15	1	1	3.01	0.28					
472	16	1	2	3.29	0.29	ROST				
472	17	1	1	3.31	0.40					
488	1	1	1	2.69	0.30	ROST				
488	2	1	2	2.52	0.29	ROST	ROVE			
488	3	1	1	2.78	0.32	ROST				
488	4	1	1	2.78	0.35					
488	5	1	2	2.48	0.27					
488	6	1	1	2.69	0.27					
488	7	1	2	2.30	0.25	ROST				
488	8	1	1	2.22	0.29	ROST	ROPB			
488	9	1	2	2.48	0.28					
488	10	1	2	2.27	0.28					
488	11	1	1	2.78	0.31					
488	12	1	1	2.58	0.33	ROST				
488	13	1	1	2.58	0.25	ROST				
488	14	1	1	2.57	0.33	ROST	ROPB			
488	15	1	1	2.58	0.29					
538	1	1	1	3.08	0.31					
538	2	1	2	2.77	0.38					
538	3	1	2	2.84	0.31	ROST				
538	4	1	2	2.79	0.38	ROST				
538	5	1	2	2.65	0.40					
538	6	1	2	2.63	0.28	ROST	ROPB	ROVE		
538	7	1	2	2.86	0.30	ROST				
538	8	1	1	3.00	0.28					
538	9	1	1	2.77	0.28	ROST				
538	10	1	1	2.31	0.31	ROST				
538	11	1	2	2.86	0.31					
538	12	1	2	2.95	0.33	ROST				
538	13	1	2	3.03	0.35					
538	14	1	2	2.95	0.31	ROST				
538	1	1	2	2.85	0.38	ROVE				
538	2	1	1	3.21	0.39	ROVE				
538	3	1	2	3.03	0.38					
538	4	1	1	2.98	0.42	ROST				
538	5	1	2	3.28	0.52					
538	6	1	2	3.29	0.42	DIUR				
538	7	1	1	3.16	0.43	ROVE				
538	8	1	2	3.24	0.37					
538	9	1	2	2.91	0.38	DIUR	ROST	ROVE		
538	10	1	2	3.09	0.43	ROST	ROVE			
538	11	1	2	2.69	0.47	DIUR	RPCA	ROVE		

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]



n-Hexane Rat Teratology Study: Raw Fetal Data

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-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
638	12	1	1	3.33	0.44	ROST	ROVE			
638	13	1	1	3.29	0.43	ROVE				
638	14	1	1	3.61	0.46					
638	16	1	1	3.33	0.62					
638	16	1	1	3.60	0.37	ROVE				
638	17	1	1	3.46	0.42	ROVE				
638	18	1	1	3.22	0.40					
642	1	1	1	3.68	0.41					
642	2	1	1	3.46	0.43	ROVE				
642	3	1	2	3.62	0.40					
642	4	1	2	3.63	0.48					
642	6	1	1	3.80	0.44					
642	6	1	2	3.79	0.36	ROST				
542	7	1	2	3.54	0.48					
542	8	1	1	3.59	0.41					
542	9	1	2	3.42	0.44					
542	10	1	1	3.59	0.39					
542	11	1	2	3.35	0.42					
542	12	1	2	3.68	0.37	SRRR				
542	13	1	1	3.21	0.44					
542	14	1	1	3.47	0.42	ROVE				
542	15	1	2	3.46	0.44					
574	1	1	1	2.96	0.48					
574	2	1	1	2.68	0.57	DIUR				
574	3	1	1	2.68	0.38	ROST				
574	4	1	1	3.26	0.51	ROST				
574	5	1	2	2.88	0.45	ROST	ROPH			
574	6	1	2	2.63	0.42					
586	1	1	1	2.70	0.29	ROST				
586	2	1	1	2.42	0.31	ROST				
586	3	1	1	2.99	0.38	ROST				
586	4	1	2	2.59	0.34	ROST				
586	5	1	2	2.70	0.30	ROST				
586	6	1	2	2.96	0.35	ROST				
586	7	1	2	3.21	0.39					
586	8	1	1	3.56	0.36					
586	9	1	1	3.22	0.32					
586	10	1	2	3.00	0.37	ROST				
586	11	1	2	3.17	0.36	ROVE				
586	12	1	2	3.15	0.34	ROST				
586	13	1	1	3.29	0.38					
586	14	1	2	3.06	0.41					
586	15	2	.	.	.					
586	16	1	2	2.74	0.30					
608	1	1	1	2.16	0.39	ROST	ROPB			

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
608	2	1	2	2.51	0.39					
608	3	1	1	2.44	0.32					
608	4	1	1	2.41	0.43	DIUR				
608	5	1	2	2.40	0.39					
608	6	1	2	2.35	0.32					
608	7	1	1	2.51	0.36					
608	8	1	2	2.60	0.34					
608	9	1	2	2.43	0.38					
608	10	1	1	2.27	0.30					
608	11	1	1	2.31	0.38					
608	12	1	1	2.47	0.39					
608	13	1	1	2.53	0.35	ROPB				
608	14	1	2	2.62	0.38					
608	15	1	2	2.15	0.36	ROST				
622	1	1	2	2.72	0.33					
622	2	1	2	2.80	0.30					
622	3	1	2	2.79	0.33					
622	4	1	1	2.89	0.29	ROST				
622	5	1	2	2.85	0.30	ROST				
622	6	1	1	2.82	0.31	ROST				
622	7	1	1	3.19	0.32	ROST				
622	8	1	1	3.23	0.34	ROST	ROVE			
622	9	1	2	2.81	0.29	ROST				
622	10	1	2	2.64	0.29	ROST				
622	11	1	1	2.94	0.29	ROST				
622	12	1	1	2.98	0.30	ROST	ROSK			
622	13	1	2	2.82	0.29	ROST				
622	14	1	1	2.98	0.30	ROST				
622	15	1	1	3.19	0.30					
622	16	1	1	3.04	0.31					
623	1	1	1	2.99	0.39	ROST				
623	2	1	2	2.92	0.44					
623	3	1	1	3.37	0.42	ROST				
623	4	1	2	3.04	0.43					
623	5	1	1	3.35	0.48	ROST				
623	6	1	1	3.36	0.43					
623	7	1	2	3.92	0.44	ROVE				
623	8	1	2	3.15	0.36	ROVE				
623	9	2	.	.	.					
623	10	1	2	2.97	0.42					
623	11	1	1	3.35	0.42					
623	12	1	1	3.19	0.39					
623	13	1	1	3.32	0.38	ROSK				
623	14	1	2	2.78	0.36	ROST				
623	15	1	1	3.55	0.43					

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

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-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
623	16	1	1	3.37	0.33					
636	1	1	2	2.93	0.37					
636	2	2	.	.	.					
636	3	1	2	2.94	0.40					
636	4	1	1	3.04	0.31					
636	5	1	2	3.12	0.34					
636	6	1	2	3.00	0.32					
636	7	2	.	.	.					
636	8	1	1	2.56	0.31					
636	9	1	2	2.61	0.40	ROST				
636	10	1	1	2.97	0.34	ROST				
636	11	1	2	2.79	0.33					
636	12	2	.	.	.					
636	13	1	2	3.16	0.33					
636	14	1	2	2.99	0.37					
636	15	1	1	2.99	0.33					
636	16	1	2	2.80	0.34					
636	17	1	1	2.88	0.31					
636	18	1	2	3.12	0.37					
641	1	1	1	2.46	0.39					
641	2	1	2	3.16	0.36					
641	3	1	2	3.00	0.46					
641	4	1	1	3.30	0.39					
641	5	1	2	2.81	0.38					
641	6	1	2	3.06	0.36					
641	7	1	2	2.96	0.40					
641	8	1	2	2.90	0.33					
641	9	1	2	2.96	0.38					
641	10	1	2	3.06	0.38					
641	11	1	1	2.93	0.38					
641	12	1	1	3.21	0.43					
641	13	1	1	2.98	0.39					
641	14	1	1	2.96	0.37					
641	15	1	1	3.03	0.36					
658	1	1	1	2.90	0.31	ROSK	ROST			
658	2	1	1	2.73	0.32	ROST				
658	3	1	1	3.03	0.22	ROSK	ROST			
658	4	1	2	2.97	0.36					
658	5	1	1	3.26	0.36	ROST				
658	6	1	2	2.91	0.40	ROST				
658	7	1	1	3.01	0.32	ROST				
658	8	1	2	2.96	0.23	ROST				
658	9	1	2	3.03	0.36					
658	10	1	2	2.87	0.38					
658	11	1	2	2.90	0.36	ROST				

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

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
668	12	1	1	3.07	0.47					
658	13	2	.	.	.					
658	14	1	2	3.00	0.31					
658	15	1	2	2.89	0.35					
690	1	1	2	1.79	0.37	ROST				
690	2	1	2	1.82	0.32	ROST	SRRR			
690	3	1	2	1.39	0.27	ROSK	ROST	ROPE	ROPH	
690	4	1	1	1.54	0.28	ROST	ROPE			
690	5	1	1	1.53	0.30	ROSK	ROST	ROPE		
690	6	1	2	1.48	0.27	ROST	ROPE			
690	7	1	2	1.19	0.27	ROSK	ROST	ROVE	ROPE	ROPH
690	8	1	2	1.40	0.28	ROST	ROVE	ROPE	ROPH	
690	9	2	.	.	.					
690	10	1	1	1.81	0.32	ROSK	ROST	ROPE		
690	11	2	.	.	.					
690	12	1	1	1.26	0.34	ROST	ROVE	ROPH		
690	13	1	1	1.33	0.28	ROSK	ROPE	ROVE	ROPH	
690	14	1	1	1.84	0.30	ROST	ROPB			
762	1	4	.	.	.					
762	2	2	.	.	.					
762	3	1	1	2.63	0.39	DIUR				
762	4	1	1	2.79	0.49	ROST				
762	5	2	.	.	.					
762	6	1	2	2.45	0.30					
762	7	1	2	2.75	0.34	ROST				
762	8	1	1	2.67	0.41					
762	9	1	2	2.67	0.32	ROST				
762	10	1	2	2.51	0.34					
762	11	1	1	2.86	0.36	ROST				
762	12	1	2	2.60	0.34					
762	13	1	1	2.67	0.36					
762	14	1	1	2.89	0.38	SRRR				
762	15	1	1	2.95	8.46					
762	16	1	2	2.76	8.36	ROST				
762	17	1	2	2.90	8.36	ROST				
800	1	1	1	3.10	0.38					
800	2	1	1	3.31	0.36					
800	3	4	.	.	.					
800	4	1	2	3.00	0.43					
800	5	1	2	3.25	0.43					
800	6	1	1	3.44	0.43					
800	7	1	2	3.50	0.33	ROST				
800	8	1	2	2.89	0.38	ROST				
800	9	1	1	3.37	0.46					
800	10	1	1	3.37	0.38					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
 Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
800	11	1	1	3.43	0.36	ROVE				
800	12	1	1	3.60	0.37	ROVE				
800	13	1	1	3.29	0.46					
800	14	1	1	2.63	0.39	ROST				
800	15	1	1	3.09	0.41					
800	16	1	1	3.15	0.37					
800	17	1	1	3.33	0.39	ROST				
800	18	1	1	3.21	0.42	ROST				
806	1	1	1	2.41	0.44	ROST	ROPB			
806	2	1	1	3.12	0.39					
806	3	1	1	3.10	0.38					
806	4	1	1	3.14	0.46	ROSK				
806	5	1	1	3.31	0.70	ROST				
806	6	1	1	3.49	0.37	ROST				
806	7	1	1	3.14	0.47	ROST				
806	8	1	1	3.22	0.32					
806	9	1	1	2.46	0.29	ROST	IOPB			
806	10	1	1	3.01	0.31	ROST				
806	11	1	1	3.02	0.30					
806	12	1	1	3.03	0.30	ROST				
806	13	1	1	2.93	0.39					
806	14	1	1	2.64	0.27	ROST				
806	15	1	1	3.51	0.40	ROST				
806	16	1	1	2.69	0.35	ROST				
806	17	1	1	3.10	0.34	ROST				
806	18	1	1	2.96	0.36		IOPB			
814	1	1	1	3.32	0.39					
814	2	1	1	3.35	0.37					
814	3	1	1	3.36	0.45					
814	4	1	1	3.32	0.39					
814	5	2	2	.	.					
814	6	2	1	3.59	0.44	ROST				
814	7	1	1	3.31	0.40					
814	8	1	1	2.85	0.36	ROST				
814	9	1	1	2.85	0.36	ROVE				
814	10	1	1	2.49	0.44	ROVE				
863	1	1	1	3.01	0.33					
863	2	1	1	3.11	0.39					
863	3	1	1	2.46	0.37					
863	4	1	1	2.97	0.41					
863	5	1	1	3.31	0.26					
863	6	1	1	3.35	0.39					
863	7	1	1	3.68	0.41					
863	8	1	1	3.12	0.42					
863	9	1	1	3.22	0.39					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat **Teratology** Study: Raw Fetal Data

36

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
863	10	1	2	3.01	0.39					
863	11	1	1	3.36	0.38					
863	12	1	2	3.17	0.40					
863	13	1	1	3.49	0.41					
863	14	1	2	2.79	0.39					
868	1	1	2	2.21	0.50					
868	2	1	2	3.66	0.45	ROST				
868	3	1	2	2.94	0.54					
868	4	1	1	3.52	0.43	SRRR				
868	5	1	2	3.59	0.45	ROST	SRRR			
868	6	1	2	2.36	0.61	ROST				
868	7	1	2	3.58	0.40	SRRR				
868	8	1	2	3.63	0.39					
868	9	1	2	2.35	0.48	ROST				
868	10	1	1	3.28	0.40					
868	11	2	.	.	.					
880	1	1	1	2.97	0.34	ROST				
880	2	1	2	3.17	0.31					
880	3	1	2	3.02	0.34					
880	4	1	1	3.50	0.37					
880	5	1	2	3.19	0.33	SRRR				
880	6	1	1	3.60	0.35	SRRR				
880	7	1	2	3.22	0.33	ROSK	SRRR			
880	8	1	2	3.23	0.41	DIUR	ROVE	SRRR		
880	9	1	1	2.93	0.32	ROSK	ROST	ROVE		
880	10	1	1	3.16	0.30	ROVE				
880	11	1	1	3.27	0.31	ROVE				
880	12	1	1	3.27	0.33	SRRR				
880	13	1	1	3.37	0.44	SRRR				
880	14	1	2	2.84	0.33	ROST				
880	15	1	2	3.32	0.33					
880	16	1	1	3.26	0.38	ROST	SRRR			
880	17	1	2	2.98	0.30	SRRR				
880	18	1	1	3.31	0.32	DIUR	ROST			
880	19	1	1	3.55	0.32					
922	1	1	1	3.08	0.35					
922	2	1	1	2.99	0.37	ROVE				
922	3	1	1	3.05	0.38					
922	4	1	2	2.82	0.33	ROST	ROVE			
922	5	1	2	3.04	0.49	ROST				
922	6	1	1	2.93	0.50	ROST				
922	7	1	1	3.24	0.38	ROST				
922	8	1	2	2.85	0.47					
922	9	1	1	3.17	0.49					
922	10	1	2	2.99	0.38					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

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n-Hexane Rat Teratology Study: Raw Fetal Data

37

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN6
922	11	1	1	2.88	0.40					
922	12	1	2	3.17	0.48	ROST				
922	13	1	1	3.17	0.34	ROST				
922	14	1	2	2.79	0.24	ROST				
938	1	1	2	3.06	0.34					
938	2	1	2	2.96	0.27					
938	3	1	1	3.49	0.32					
938	4	1	1	3.41	0.36					
938	5	1	2	3.16	0.26	ROST				
938	6	1	2	2.89	0.32					
938	7	1	1	3.44	0.37					
938	8	1	1	3.39	0.35	ROST				
938	9	1	1	2.90	0.29					
938	10	1	2	3.07	0.29					
938	11	1	2	2.93	0.27	ROST				
938	12	1	1	3.46	0.35	ROST				
938	13	1	1	3.42	0.34					
938	14	1	2	3.45	0.34					
938	15	1	2	2.42	0.40					
948	1	1	1	3.20	0.50					
948	2	1	1	3.57	0.47	ROST				
948	3	1	1	3.68	0.48	ROST				
948	4	1	1	3.33	0.39	ROST				
948	5	1	2	3.37	0.50	ROST				
948	6	1	1	3.93	0.44					
948	7	1	1	3.70	0.44	ROST				
948	8	1	1	3.20	0.43					
948	9	1	1	3.83	0.43	ROST				
948	10	1	1	3.49	0.41	ROST				
948	11	1	1	3.71	0.44	ROST				
948	12	2	.	.	.					
948	13	1	2	3.40	0.45					
948	14	1	1	3.87	0.51					
948	15	1	2	2.93	0.44	ROST				
948	16	1	1	3.76	0.50	SRRR				
948	17	1	1	3.80	0.49	ROST				
951	1	1	1	2.99	0.36					
951	2	1	1	2.55	0.33	ROST	ROPB			
951	3	1	2	2.68	0.43	ROPB				
951	4	1	1	3.39	0.45					
951	5	1	1	3.31	0.43					
951	6	1	1	2.78	0.39					
951	7	1	2	2.62	0.42	ROST				
951	8	1	1	3.30	0.43	ROST				
951	9	1	2	2.76	0.38	ROST				

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]

n-Hexane Rat Teratology Study: Raw Fetal Data

38

-----5000 ppm n-Hexane-----										
Mat No	Site	Status	Sex	Fetal Wt (g)	Placenta Wt (g)	ABN1	ABN2	ABN3	ABN4	ABN5
951	10	1	2	2.92	0.34					
951	11	4	.	.	.					
951	12	1	1	3.23	0.46					
951	13	1	1	3.22	0.38					
951	14	1	2	3.20	0.43					
951	15	1	1	3.15	0.41					
951	16	1	1	3.19	0.40					
951	17	1	1	3.04	0.40					
964	1	2	.	.	.					
964	2	1	2	2.85	0.33	ROST				
964	3	1	2	2.85	0.38					
964	4	1	1	3.58	0.38	ROST				
964	5	1	1	3.43	0.40	ROST				
964	6	1	1	3.41	0.37					
964	7	1	1	3.10	0.33	ROST				
964	8	1	1	2.70	0.38	ROST				
964	9	1	1	3.22	0.38	ROST				
964	10	1	1	2.98	0.32					
964	11	1	2	3.43	0.38					
964	12	1	1	3.32	0.37					
964	13	1	1	3.45	0.43					
964	14	1	2	2.76	0.34	ROST				
964	15	1	1	3.40	0.37	ROST				
964	16	1	1	3.04	0.38	ROST				
964	17	2	.	.	.					

Status: 1 = Live; 2 = Early Resorption; 4 = Late Resorption  
Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities [ABNn]



## Code Sheet for Identification of Fetal Abnormalities

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ANOR	Bent or knobby rib.
DIUR	Dilated ureter.
ROPB	Reduced ossification - pelvis.
ROPH	Reduced ossification - phalanges.
ROSK	Reduced ossification - skull.
ROST	Reduced ossification - sternabrae 1-4.
ROVE	Reduced ossification - vertebrae.
RPCA	Renal pelvic cavitation.
SRRR	Supernumerary rib.

CALENDAR OF EVENTS: RAT TERATOLOGY STUDY OF n-HEXANE

Receipt of animals:	4/1/86 (ARS #860047; birthdate 2/6/86)
Initial health screen:	4/21/86
Detection of copulation (0 dg):	(A) 5/07/86 (B) 5/08/86 (C) 5/09/86 (D) 5/10/86
Exposure (20 hours/day; 6-19 dg):	(A) 5/13-26/86 (B) 5/14-27/86 (C) 5/15-28/86 (D) 5/16-29/86 (VIRGINS) 5/15-28/86
Sacrifice (20 dg):	(A) 5/27/86 (B) 5/28/86 (C) 5/29/86 (D) 5/30/86 (VIRGINS) 5/29/86
Completion of fetal exams	5/1/87

n-Hexane Rat Teratology Study: Animal Disposition Summary

Males:	Received		146
	Health Screen	5	
	Used for breeding	140	
	Excessed (bad teeth)	1	
		---	---
	Total	146	146
Females:	Received		536
	Health Screen	5	
	Teratology Study	119	
	Teratology Study-removed	1	
	Virgins	40	
	Sperm-negative-excessed	233	
	Sperm-positive-excessed	18	
	Behavior Pilot Study <sup>a</sup>	120	
		---	---
		536	536

The following animals had ulcers in the cardiac region of the stomach at the time of sacrifice:

608	pregnant
690	pregnant
716	non-pregnant
754	virgin

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a) This study has been reported elsewhere.



APPENDIX D

ANIMAL HEALTH SCREEN

APPENDIX C

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ANIMAL HEALTH SCREEN

ARC DIAGNOSTIC LABORATORY REPORT

INVESTIGATOR <u>Hickitt/Mast</u>	LAB NO. <u>C71</u>
EXPERIMENT <u>Hexane - Rat Teratolgy</u>	DATE <u>4/21/86</u>
COST CODE <u>—</u>	ANIMAL OR SHIP'NT NO. <u>860047</u>
BUILDING <u>LSL II</u>	SOURCE <u>Ch. received R24</u> REC'D <u>4-1-86</u>
PEN, ROOM <u>429</u>	SPECIES & STRAIN <u>RAT (1)</u>
	SEX <u>5M/5F</u> AGE <u>B.D. 2-6-86</u>

SPECIMEN SUBMITTED AND CLINICAL HISTORY:

Received 10 rats (5 male #1-5, 5 female #6-10) for  
pre-exposure health screening including gross  
macroscopic, serology and histopathology

LABORATORY RESULTS

Gross necropsy: No significant findings REF 5/14/86

Summary: A number of incidental lesions were seen in  
the histopathology but none which considered a significant  
indication of infectious disease. CEL 5/14/86

Referred for study on 4/29/86 - See p. 108. Ser 2/23/86

RESULTS  
ARC DIAGNOSTIC LABORATORY ELISA REPORT

LAB NO. 671  
PAGE 2 OF 2

TEST: Sindai  
Positive Control: - Lot: 07575  
Negative Control: - Exp.: 12/86  
Animal # 1 Result -  
2 -  
3 -  
4 -  
5 -  
6 -  
7 -  
8 -  
9 -  
10 -

TEST: Kilham/H1  
Positive Control: + Lot: 07557  
Negative Control: - Exp.: 11/86  
Animal # 1 Result -  
2 -  
3 -  
4 -  
5 -  
6 -  
7 -  
8 -  
9 -  
10 -

TEST: PVM  
Positive Control: - Lot: 08625  
Negative Control: - Exp.: 7/86  
Animal # 1 Result -  
2 -  
3 -  
4 -  
5 -  
6 -  
7 -  
8 -  
9 -  
10 -

TEST: RCV/SDA  
Positive Control: + Lot: 07175  
Negative Control: - Exp.: 10/86  
Animal # 1 Result -  
2 -  
3 -  
4 -  
5 -  
6 -  
7 -  
8 -  
9 -  
10 -

TEST: MAM  
Positive Control: + Lot: 07787  
Negative Control: - Exp.: 12/86  
Animal # 1 Result -  
2 -  
3 -  
4 -  
5 -  
6 -  
7 -  
8 -  
9 -  
10 -

Initial: AEJ

Date: not performed  
4/22/86

SG  
5/14/86



n-Hexane Rat Teratology Study  
Appendix D - Health Screen

## HEALTH EVALUATION

## HISTOPATHOLOGY

ARC Lab. # 071

Histo Lab. # 286-1106

[illegible]



**APPENDIX E**

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**QUALITY ASSURANCE STATEMENT**

APPENDIX E

QUALITY ASSURANCE STATEMENT

n-HEXANE RAT TERATOLOGY STUDY  
(Final Report)

Quality Assurance Statement

Listed below **are** the phases **and/or** procedures included in the study described in this report which were reviewed by the Quality Assurance Unit during the period, **3/1/86 - 6/30/86**, specifically for this study and the dates the reviews **were** performed and findings reported to management. (**All** findings were reported to the study **director** or his designee at the time of the review.)

Phase/Procedure Reviewed	Review Date	Date Findings Submitted in Writing to Study Director/Management
Dosing	3/27/86	3/28/86
<b>Animal</b> Receipt	4/01/86*	4/07/86
Randomization	4/07/86*	4/07/86
Health Screen	4/21/86*	4/28/86
Animal Identification	5/01/86*	5/02/86
Data	5/01/86*	5/02/86
Mating	5/08/86*	5/09/86
Body Weights	5/09/86*	5/09/86
Dosing	5/21/86*	5/23/86
<b>Necropsy</b>	5/28/86*	6/02/86
Data	8/21&9/6,7/87*	10/01/87
Draft Report	9/3,6,7,28-30/87	10/01/87
Final Report	1/08/88	1/08/88

\* Reviewed specifically for **this** study.

Patricia S. Ruemler  
Quality Assurance Specialist

11/8/88  
Date

R. L. Gelman  
Quality Assurance Specialist

11/8/88  
Date



APPENDIX F

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PROTOCOL AND CAGE MAPS

APPENDIX I

PROTOCOL AND CASE MASS



## INHALATION REPRODUCTIVE TOXICOLOGY STUDY PROTOCOL **n-HEXANE**

I. **TITLE:** Teratology Study of n-Hexane in Rats

### 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, 1980). In summary, polyneuropathies have been reported following exposure of workers to n-hexane contained in adhesives or when 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 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 (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. (1982), using  $^{14}\text{C}$ -labeled n-hexane in 6-hour exposures, found that the distribution of radioactivity was dose-dependent.

In studies designed to address the possibility that exposure to hexane may affect prenatal development Bus et al. (1979) also determined the distribution and half-lives of n-hexane ( $t_{1/2} = 1.2 \text{ hr}$ ) and 2,5-hexanedione ( $t_{1/2} = 3.9 \text{ hr}$ ) 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 during the first 3 postnatal weeks in the group exposed from 8-16 dg, but the possibility of maternally-mediated effects or postnatal exposure via milk was not examined.

Other developmental studies include those of Marks et al. (1981) who found that oral administration of n-hexane (2.2 g/kg) daily from 6 through 15 dg in rats 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 anesthetized offspring were found in one 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 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 during gestation.

Since it **appears** that toxicity is a function of concentration vs. time factors, an adequate assessment of the **teratologic** potential requires **evaluations** after prolonged exposures to high concentrations in several species. To accomplish this, the study in rats **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 (ie., 6 through 20 dg), with detailed teratologic evaluations performed at 20 dg. A similar study will be performed with mice to obtain comparative data in another species. To examine the potential for **neurotoxicity**, 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, development, and sensory-motor functions.

Reported effects on lipid metabolism suggest the possibility that the ovaries and/or ovulation may be **affected** by inhalation exposure. Although the limited **data** of Howell and Cooper (1981) regarding preconception and **preimplantation** exposure indicate 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 female rats.

### **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. Bryan Hardin  
Dr. Bernard Schwetz

### **IV. TESTING LABORATORY**

#### **A. Facility**

Pacific Northwest Laboratories (PNL)  
P.O. Box 999; Richland, Washington 99352

B. Study Co-Directors:

Dr. Melvin R. Sikov

Dr. Patricia L. Hackett

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: 4/30/86

B. **Animals** arrive: week of 3/31/86

C. Quarantine, health evaluation and identification of females: 3/31/86 - 4/28/86

D. Initiation of breeding procedures and randomization of animals into treatment groups:  
4/28/86

E. Initiation of exposure: 5/5/86

F. Initiation of **necropsies**: 5/19/86

G. Evaluation of fetal specimens and data: 5/19/86 - 7/15/86

H. Completion of draft report: 8/15/86

I. Completion of **final** report: 10/15/86

VI. TEST SYSTEM

A. Species: Rat

B. Strain: **Outbred** derivative of Sprague Dawley [Cr1:CD(SD)BR]

C. Number of Animals and Supplier: 260 female **and** 60 **male** animals will be purchased from Charles River Breeding Laboratories, Raleigh, NC

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

E. Experimental Animals (Females): 40 rats (to be exposed as virgins) will be randomly selected and assigned to four dose groups (10/group) from the total **female** pool (ØB-DT-3BØB). ~~The~~ remaining female **rats** 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 determination of sperm in the vagina) will be designated as 0 dg.

F. Number of Animals in Study: A minimum of 30 sperm-positive females (to obtain 20 pregnant females) and 10 virgins will comprise each of the four treatment groups. The minimum number of sperm-positive females to be exposed will be 120.

G. Test System Justification: The use of rats as a test system was specified by the sponsor. Since differences in sensitivity to induced neuropathies following exposure to the hexane metabolite, 2,5-hexanedione, have been reported for rats and mice. Data from this study will be compared with the results from a concurrent **teratology** study in mice which will be

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-11** Building.
2. Temperatures in **all rooms** will be maintained at  $73 \pm 3$  °F and relative humidities at  $50 \pm 15\%$  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, **5** rats per cage, in wire-mesh cages.
4. During the breeding period the animals will be housed (**2 females:1** male) in the quarantine room.
5. Sperm-positive females **will** be acclimated **from** 0 to 3 dg in individual compartments of wire-mesh cages within exposure chambers (with chamber doors open). **On** 3 dg the animals will be moved to the exposure room and put into chambers. Chambers doors will be closed and baseline environmental data recorded **until** the beginning of exposure to the chemical. Virgin **females will** be acclimated under the same conditions.

B. **Feed:** NIH-07 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 **daily**.

C. **Randomization:** Virgin females **will** be randomly chosen and assigned to dose groups on the day of **ear tagging** and **first** weighing. Weights **will** be **ranked** from lightest to heaviest and then each animal **will** be 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 sperm detection (0 dg), the mated rats will be weighed and assigned to dose groups as defined above.

### **D. Identification:**

1. All female **rats** will be individually identified by metal ear tags prior to mating (**ØB-DT-3BØ1**).
2. Exposure groups will be designated by distinctive toe clipping and by placement within the individual compartments of the chamber cage units (**ØB-DT-3BØ1**).
3. 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 1.

- E. 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:  $\text{CH}_3(\text{CH}_2)_4\text{CH}_3$
- 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  
PNL 1<sup>st</sup> Shipment: BNW 50846-39
- H. Date of Receipt: 1<sup>st</sup> Shipment **2/12/86**
- I. Test Article Preparation and Storage **Areas**: 2-day reserve in **Rms** 311 or 315 **LSL-II**; the remainder in the Research Technology Laboratory (RTL) chemical storage facility.
- J. The vehicle control will be **filtered** air.
- K. Analytical Chemistry:
  - 1. Upon receipt, identity and gross purity analyses of the **bulk** chemical will be performed by infrared spectroscopy. Gas chromatography (GC) will be used to determine purity by major **peak** comparison and also to generate an impurity profile (**ØB-AC-3A15**). Upon completion of the animal exposures GC will be used to determine test material purity and generate an impurity profile.
  - 2. n-Hexane concentrations within the exposure chambers will be monitored (**ØB-AC-3B1P**) using an HP-5840 gas chromatograph **calibrated** by the method detailed in **ØB-AC-3CØW** (see Attachment 1).

## 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 1 of this protocol.

## **X. EXPERIMENTAL DESIGN AND DOSE LEVELS**

- A. **Experimental Design**: Four groups of animals, consisting of at least 30 **sperm-positive** rats in each group, will be exposed to the test chemical on 14 consecutive days (6 dg through 19 dg). The animals will be necropsied on 20 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 for quantitative follicle counts. These animals **will** be exposed for 14 consecutive **days** concurrently with the **sperm-positive** animals and sacrificed the day following cessation of exposure.
- B. **Exposure Regimen**: Target chamber concentrations of **n-hexane** will be 0 (filtered air), 200, 1000 and 5000 ppm. Sperm-positive rats and the virgin females will be exposed for 20 hrs/day for 14 consecutive days. Control rats (0 ppm) will be housed in an exposure chamber in the same room, and will be handled in the same manner as the rats 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  $75 \pm 3$  °F and relative humidities at  $55 \pm 15\%$ . Air flow **will** be maintained at  $15 \pm 3$  cfm and the chamber pressure at approximately 2.5 cm (1 inch) 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 and duration were approved by the Co-Project Officers.

## **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** rats **will** be weighed during the week prior to mating. Virgin females (10/group) will be **randomly** selected at this time (see Randomization, pg. 5). After breeding sperm-positive females will be weighed on 0, 6, 13, and 20 dg (ØB-DT-3BØC). Virgin females **will** be weighed on the 1<sup>st</sup> and 7<sup>th</sup> day of exposure and on the day of necropsy. The body weight on 0 dg will be used for randomization of sperm-positive animals (ØB-DT-3BØB) into four exposure groups.

C. Scheduled Necropsy: The rats are scheduled to be euthanized with CO<sub>2</sub> on 20 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~~ fetuses live ~~at~~ maternal sacrifice; 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-3B1J). Collected ovaries ~~will~~ be **fixed** in Bouin's Fluid for 24 hr then transferred to 70% ethanol and sent Dr. Mattison at National Center for Toxicological Research, Pine Bluff, AK for sectioning and quantitative follicle counts.

D. Indices of Effects: The following parameters, expressed as mean  $\pm$  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 0, 6, 13, and 20 dg
- Weight of gravid uterus
- **Extragestational** weight and weight gain



- Number of implantation **sites/litter**
- Number of litters with live fetuses
- Number and percent of live **fetuses/litter**
- Body weight of live **fetuses/litter**
- Body weight of live **male** and female **fetuses/litter**
- Placental weights from live **fetuses/litter**
- Sex ratio of **fetuses/litter**
- Number and percent of **early** and late **resorptions/litter**  
Number and percent of **non-live/litter** (early and late **resorptions** and dead fetuses)
- Listing of malformations and variations observed in **fetuses/litters**  
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 L

## **XIII. STORAGE OF STUDY MATERIALS**

All raw data and study records will be retained in the Project Office (room 1519); all tissues and fetal specimens will be temporarily stored in the Teratology Laboratory (**room** 1428). Both of these rooms are located in Life Science Laboratory II, **Battelle**, Pacific Northwest Laboratories. 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. **One** copy of the microfiche **and** the microfiche index will be sent to Dr. **Hardin** (NIOSH). The Quality Assurance Unit at **PNL** will retain the following materials:

- 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**.)
- Bound **PNL** laboratory notebooks.

TABLE 1. PROPOSED STATISTICAL METHODS

INDICES	ARCSIN TRANS- FORMATION	ANOVA	CHI- SQUARE	FISHER'S EXACT	TREND TESTS ARMITAGE ORTHOGONAL
MATERNAL:					
Number/percent dead			•		•
Body weight		•			•
Weight of gravid uterus		•			•
Extragestational weight		•			•
REPRODUCTIVE:					
Number/percent pregnant					
Number of implantation sites/litter		•			•
Number/percent resorp- tions/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 mal- formed fetuses/litter					

Analysis of variance (Steel and Torrie, 1980)  
Chi-square test (Siegel, 1956)  
Fisher's exact test (Siegel, 1956)  
Armitage's trend test (1955)  
Orthogonal contrast trend test (Winer, 1971)

#### **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 or 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 the initiation of the study and approved by the PNL Study **Director(s)**, the PNL QAU Officer and the NTP Project **Officer(s)**.
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. Schedule for cleaning, calibrating, inspecting and maintaining equipment
2. Documentation of routine cleaning, inspection, calibration, and **maintenance of equipment**.
3. 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 material to the NTP repository.

E. Delivery System for Test Material:

1. Detailed descriptions of systems for 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 airflow data.

F. Animal Records:

1. Animal receiving records including supplier, species, strain, birth week, sex, number of animals of each sex, receiving date and condition upon receipt
2. Health evaluation records of **findings**, written release **from quarantine/acclimation** or reasons for rejection for **use in** the study 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 **death/euthanasia** of animals occurring prior to scheduled **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 2.

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 resolve 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 **room 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 of ten pages and Appendix II of two pages.

**XVII. APPROVAL BY PNL**

PL Hackett  
Co-Study Director

Date: 4/4/86

\_\_\_\_\_  
Co-Study Director

Date: 4/4/86

Edn Crow  
Quality Assurance Auditor

Date: 4-8-86

**XVIII. APPROVAL BY NTP**

BA Schwetz  
Co-Study Officer

Date: 20 May 86

Bryan D. Harris  
Co-Study Officer

Date: 20 May 1986

**XIX. REFERENCES**

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ATTACHMENT I

DESCRIPTION OF THE EXPOSURE SYSTEM FOR  
INHALATION REPRODUCTIVE TOXICOLOGY STUDIES

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## 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<sup>3</sup>, the chamber has an active mixing volume of 1.7 m<sup>3</sup>, 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# 03-BE-3D06.

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<sup>2</sup> and of a rat cage 270 cm<sup>2</sup> (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 0B-BE-5E01. Maintenance of the system is detailed in SOP #0B-BE-3D0E. Routine operation of the computer system is detailed in SOP #0B-BE-3G04. Routine daily operation of the system hardware is detailed in SOP #0B-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 located 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  $1 \times 10^{-3}$  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~~<sup>®</sup> 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 DB-BE-3B2Y and QB-BE-3DQM.

## 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 polytetrafluoroethylene.

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  $\geq$  non-critical low limit and  $\leq$  non-critical high limit:

No action

- . Concentration  $<$  non-critical low limit but  $\geq$  critical low limit:

Increase concentration by decreasing chamber air flow.

- Concentration < critical low limit:

Increase concentration by increasing 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 #0B-AC-3C0W).

Daily operating procedures for the concentration monitoring system are contained in SOP #0B-AC-3B1P. Routine maintenance of the gas chromatograph is covered in SOP #0B-AC-3D02.

The uniformity of the distribution of test chemicals in the chamber will be checked before the start of the study following SOP #0B-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 #0B-BE-3C0U) and #0B-BE-3C0B). An alarm condition will automatically shut off the flow of test compound to all chambers.

## D. ENVIRONMENTAL MONITORING

### 1. Temperature Measurements

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 ~~measures at 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 ~~#0B-BE-3C0D~~ and ~~0B-BE-3C0L~~). 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:

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

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 (~~0B-BE-3C0J~~ and ~~0B-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 RE 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 Control

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 rate, 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 #08-BE-3D02.

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 #08-BE-3D02.

#### 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 RE control system. Typically, a chamber full of animals will require the addition of dry air to maintain the proper RE. 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 21716). 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 0B-BE-5E03, 0B-BE-3E0A, and 0B-BE-3E0B.

#### 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 equipment 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 #2
- 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 operate 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 survival of the animals are **alarmed**. If a system malfunctions, an **alarm** is tripped in the power operator's office. A power operator is on duty 24-hours/day, 7 days/week. If the power-operator is not authorized to correct the problem that caused the **alarm**, he immediately calls the appropriate personnel, including the Task Leader(s) or the Principal Investigator(s) of the program(s) affected.

#### References

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

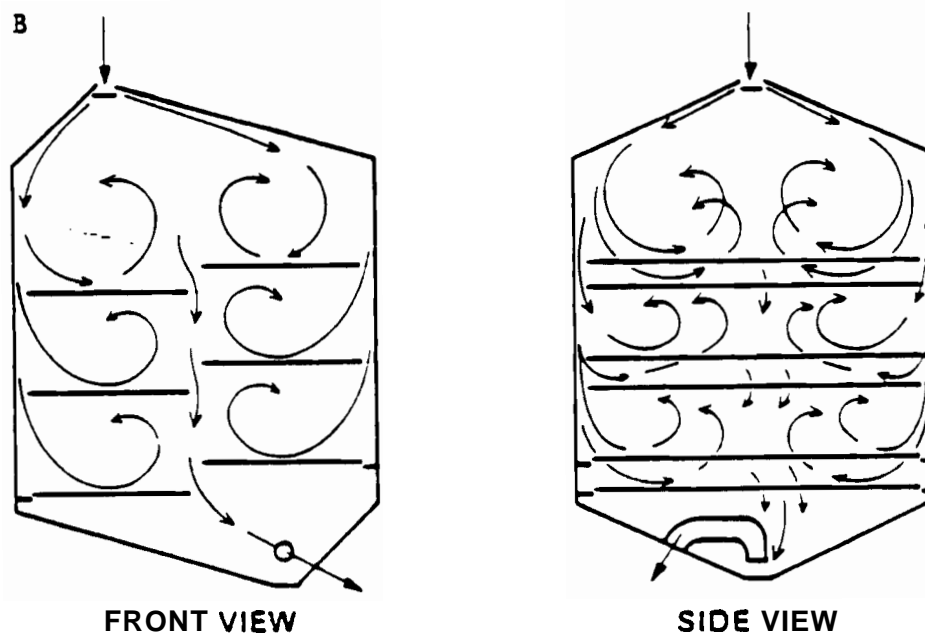
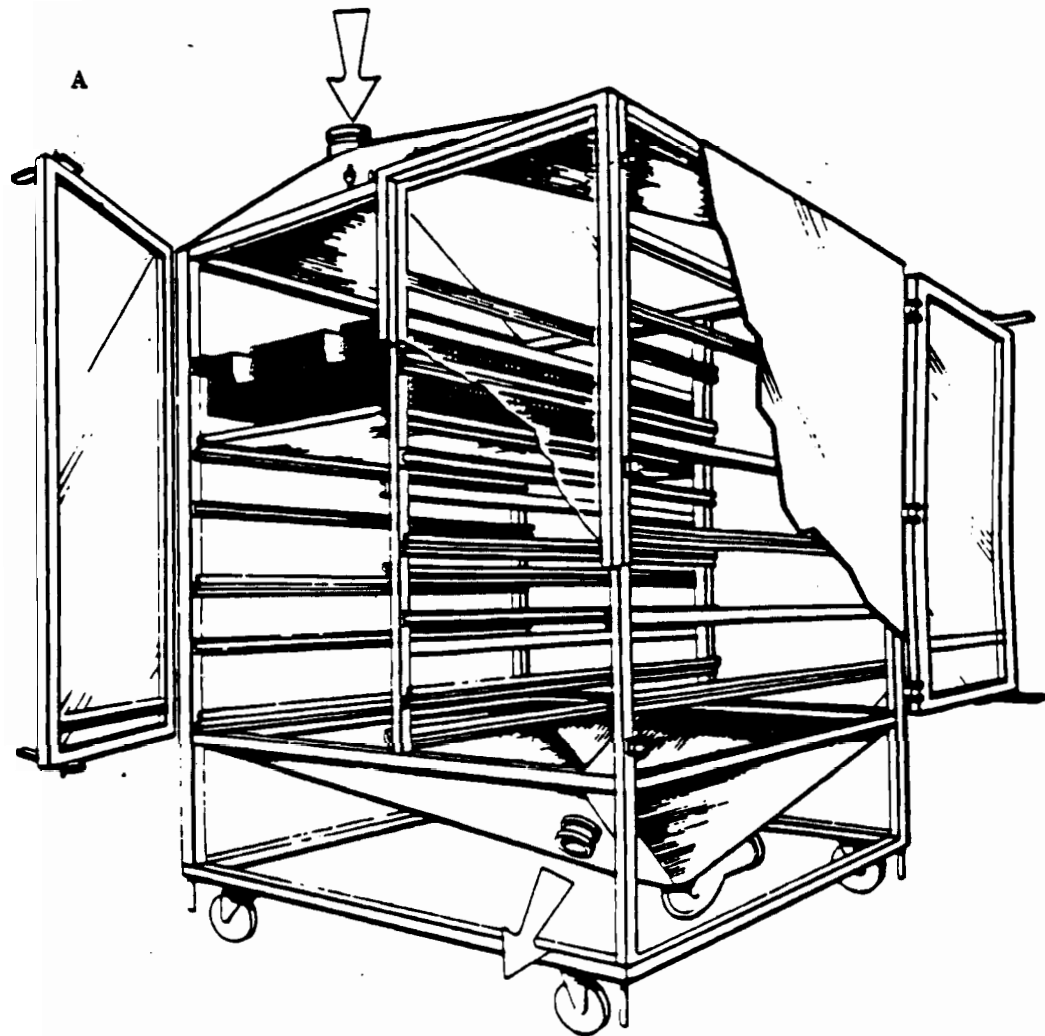


FIGURE 1. Inhalation Exposure Chamber Designed at BNW  
(A. Oblique cutaway view of the chamber;  
B. Airflow patterns)

# EXPOSURE SUITE #1

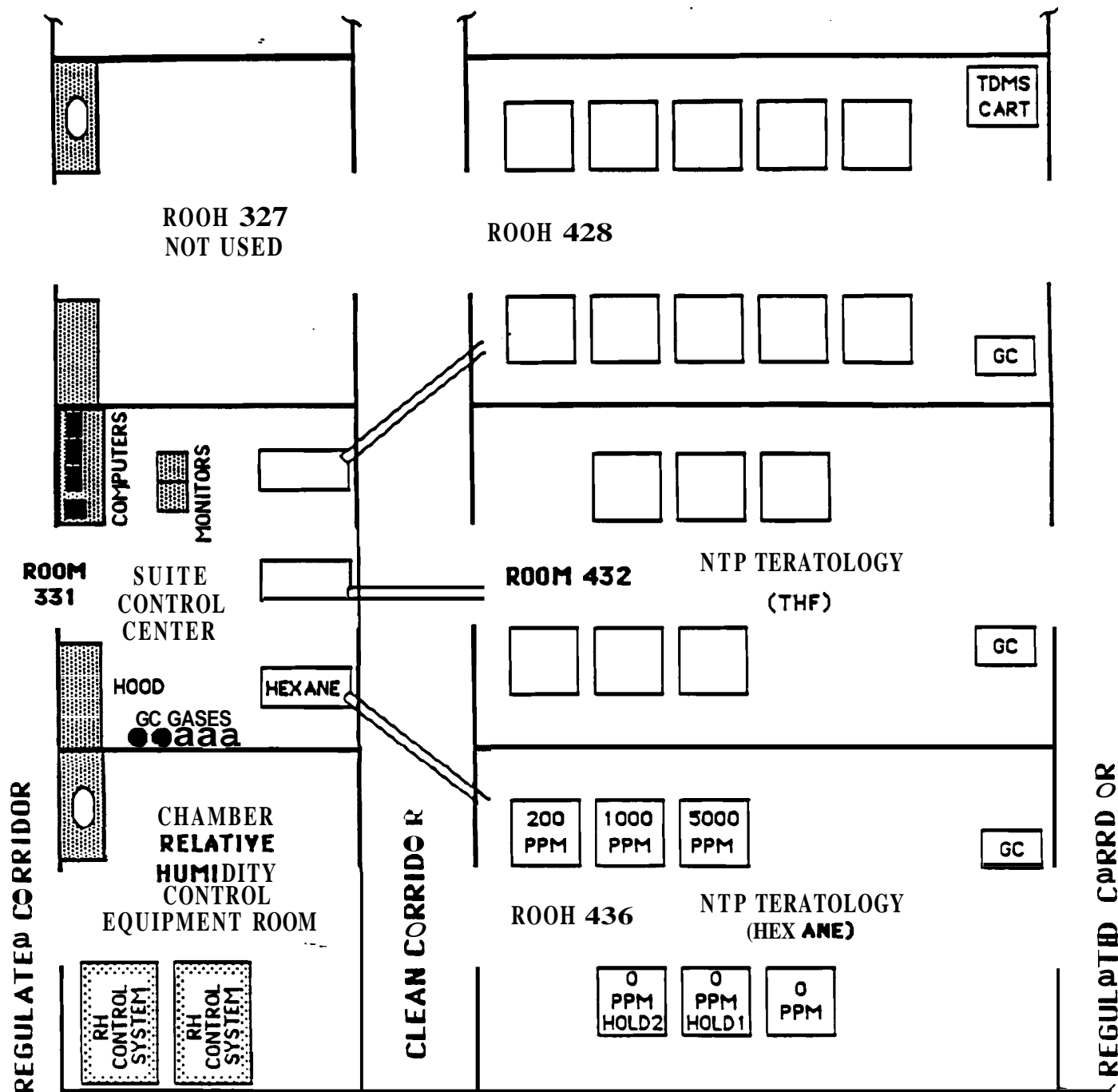


FIGURE 2. Schematic Diagram of the Three Exposure Rooms in the Automated Inhalation Exposure Suite.

# COMPUTER SYSTEM

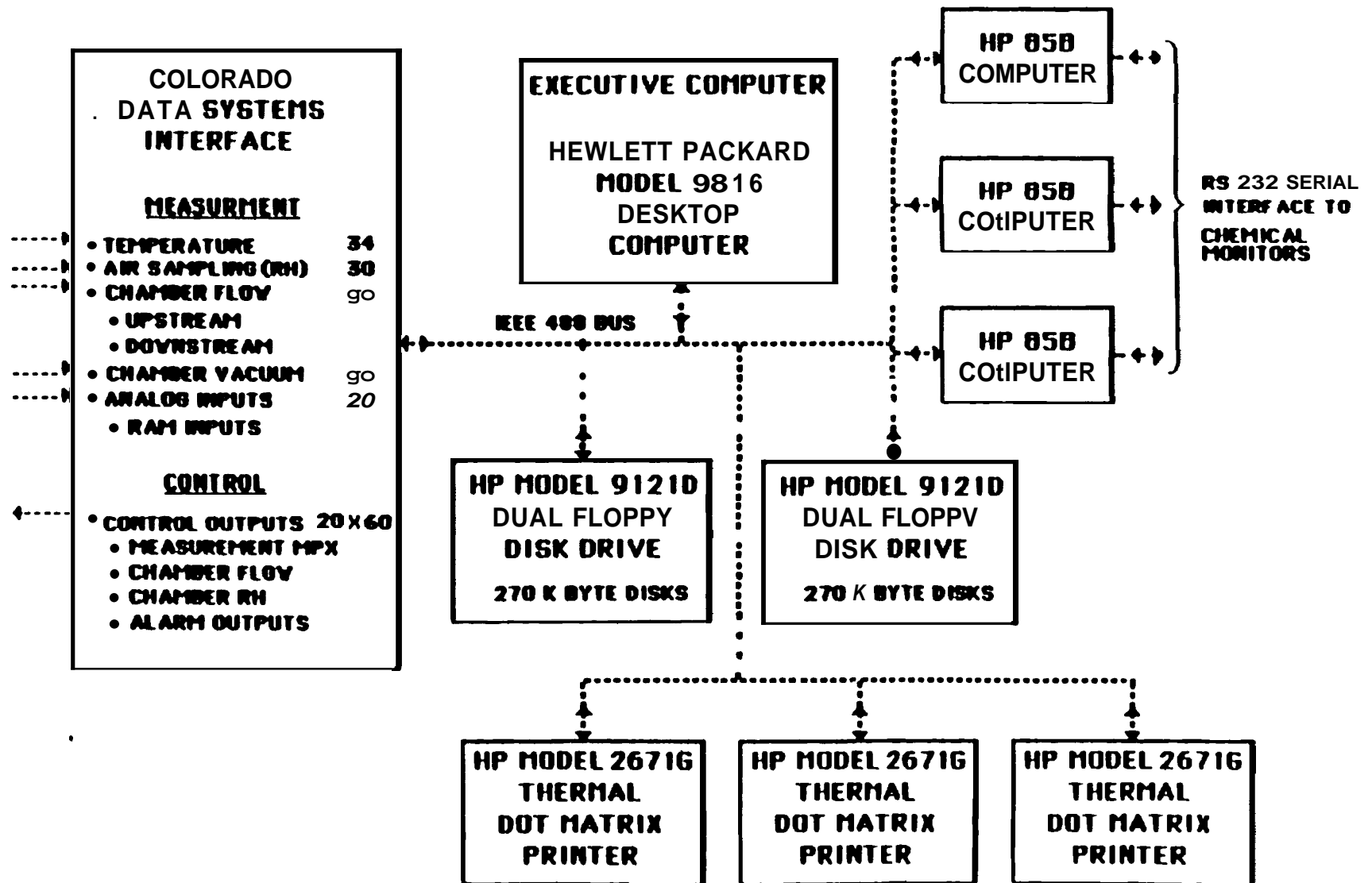


FIGURE 3. Block Diagram of Data Acquisition and Control Computers and Interface Instrumentation

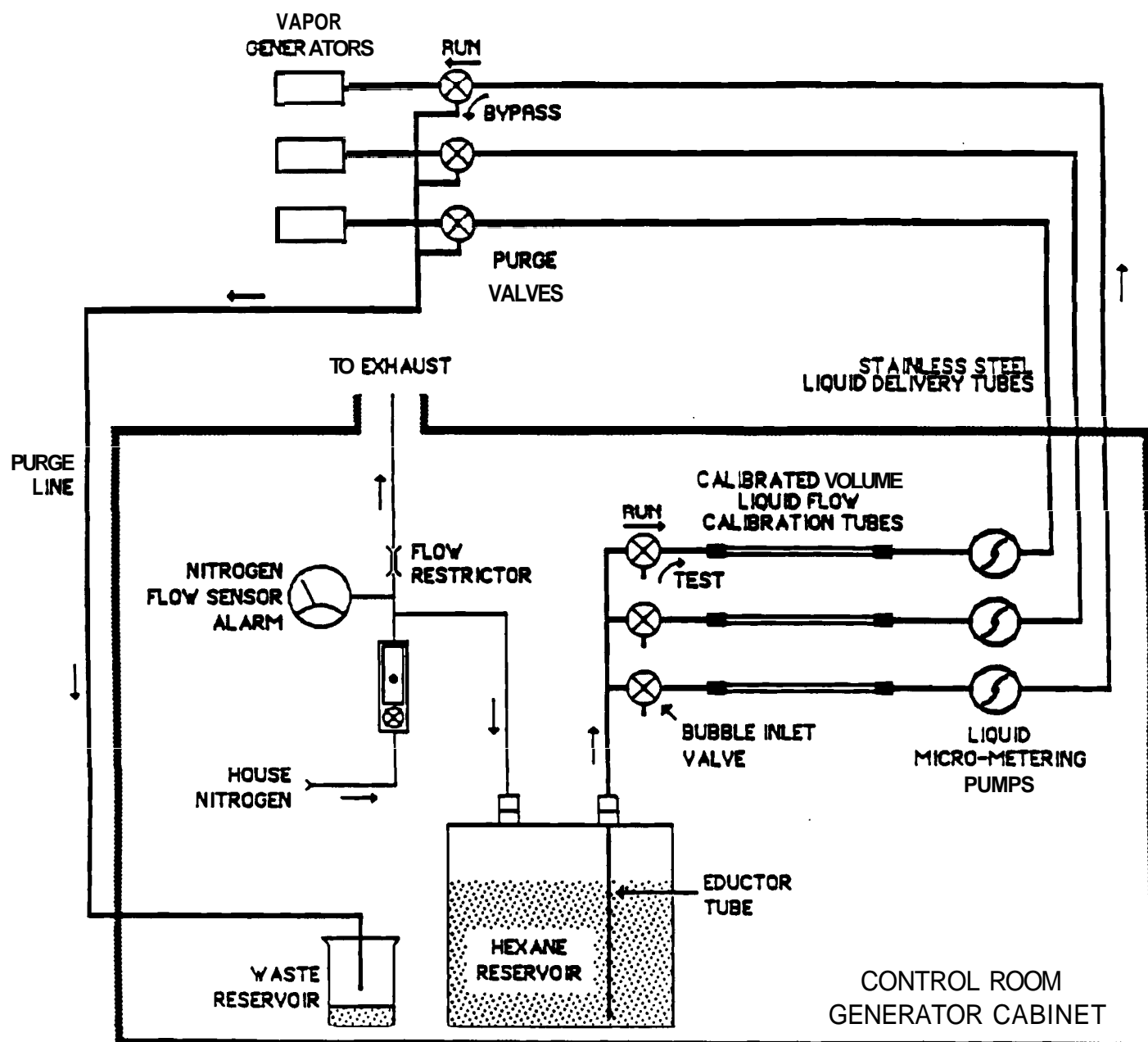


FIGURE 4. Schematic Diagram of the Hexane Vapor Generation System.



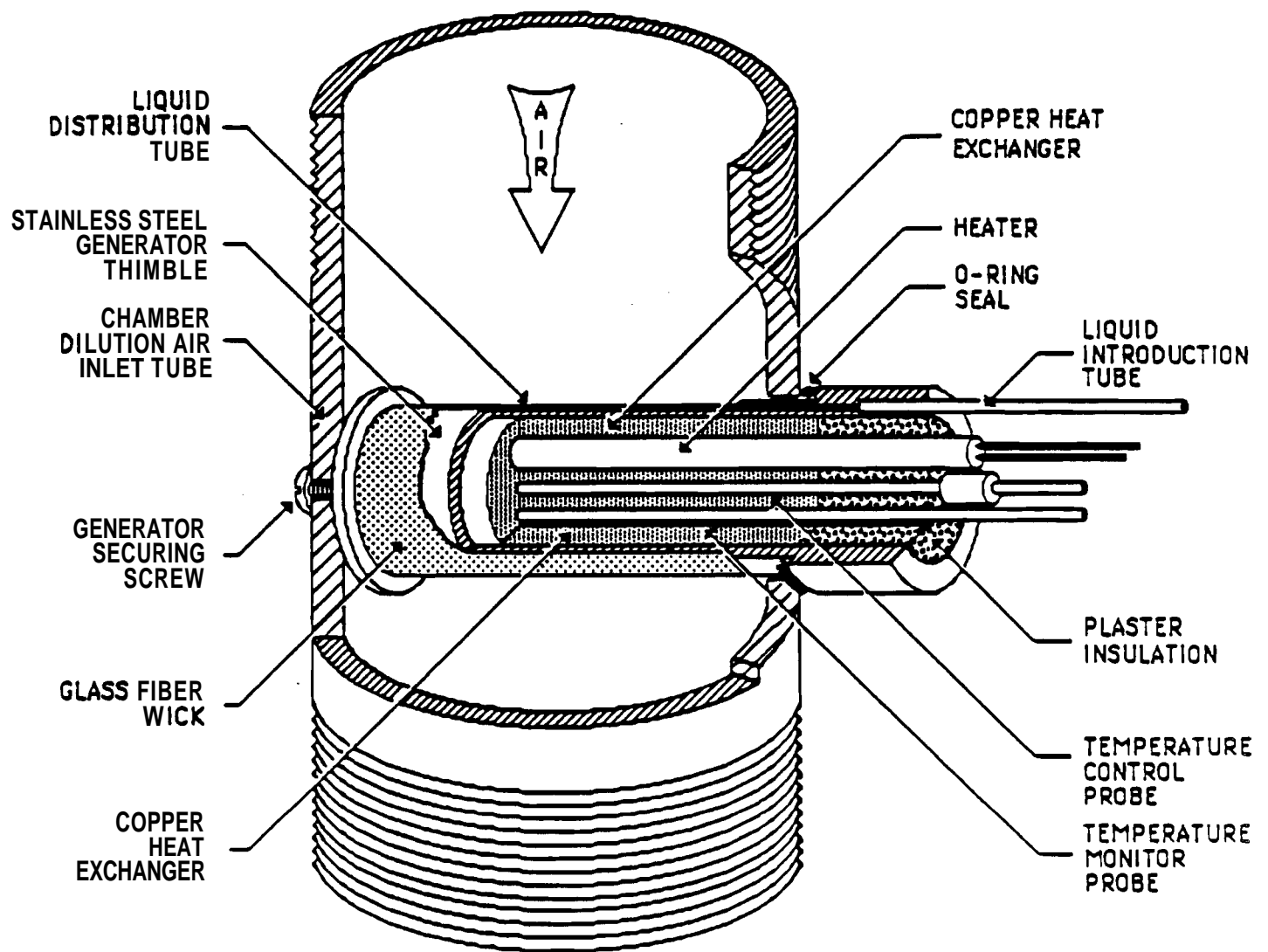


FIGURE 5. Cutaway Drawing of the Hexane Vapor Generator Located in the Fresh-Air Inlet Tube of the Exposure Chamber.

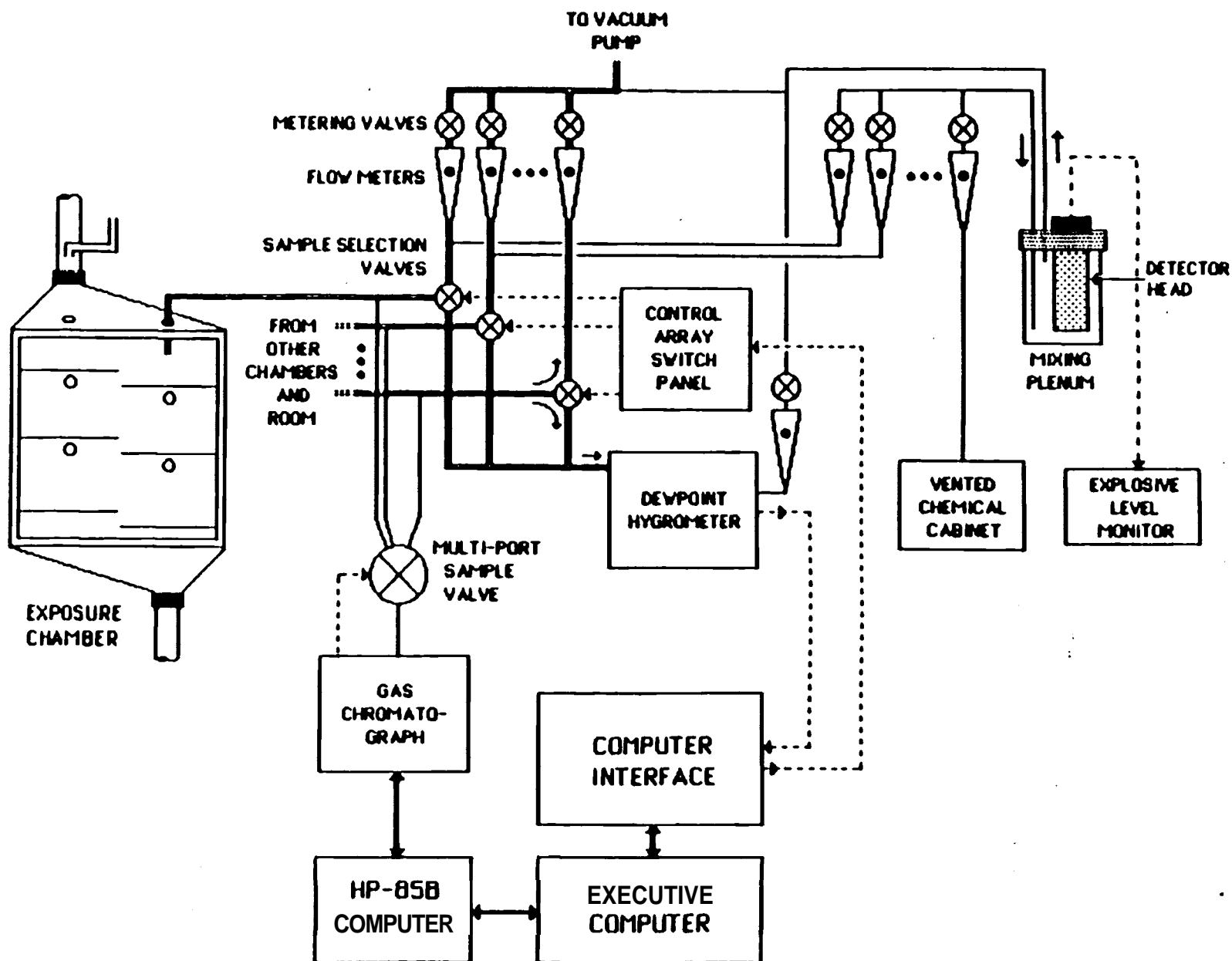


FIGURE 6. Schematic Diagram of the Dewpoint, Chemical Concentration, and Explosive Level Monitoring Systems

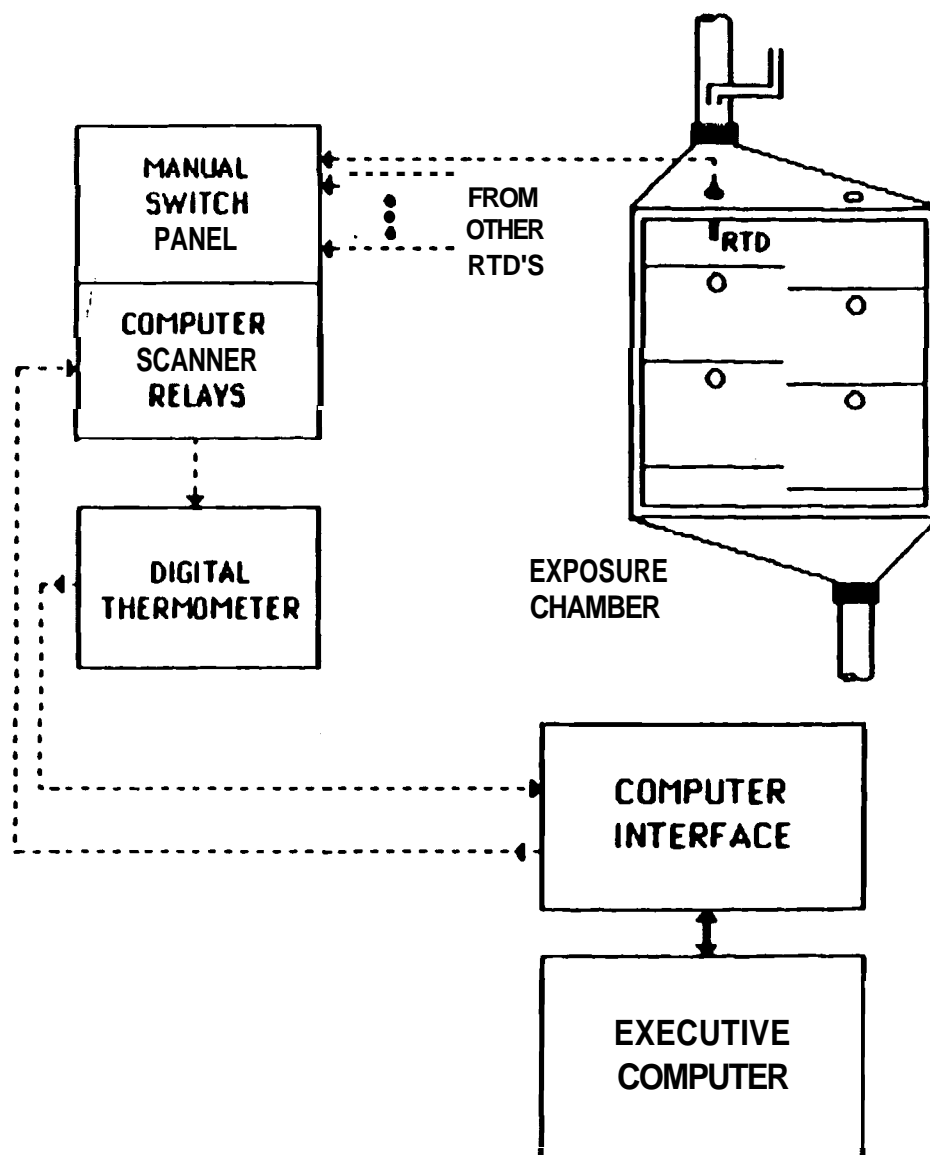


FIGURE 7. Schematic Diagram of Temperature Monitoring System

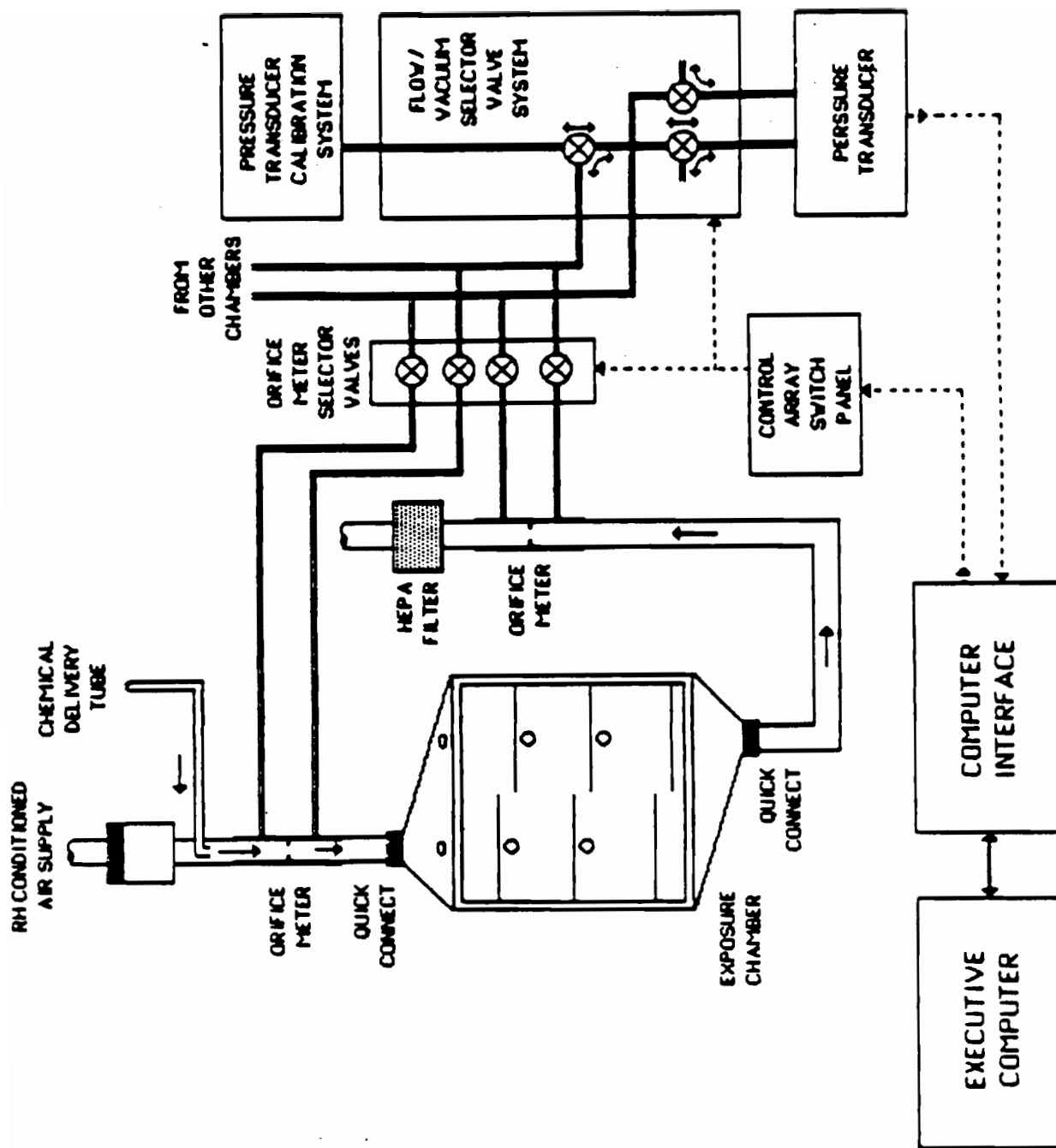


FIGURE 8. Schematic Diagram of the Chamber Flow and Vacuum Monitoring System

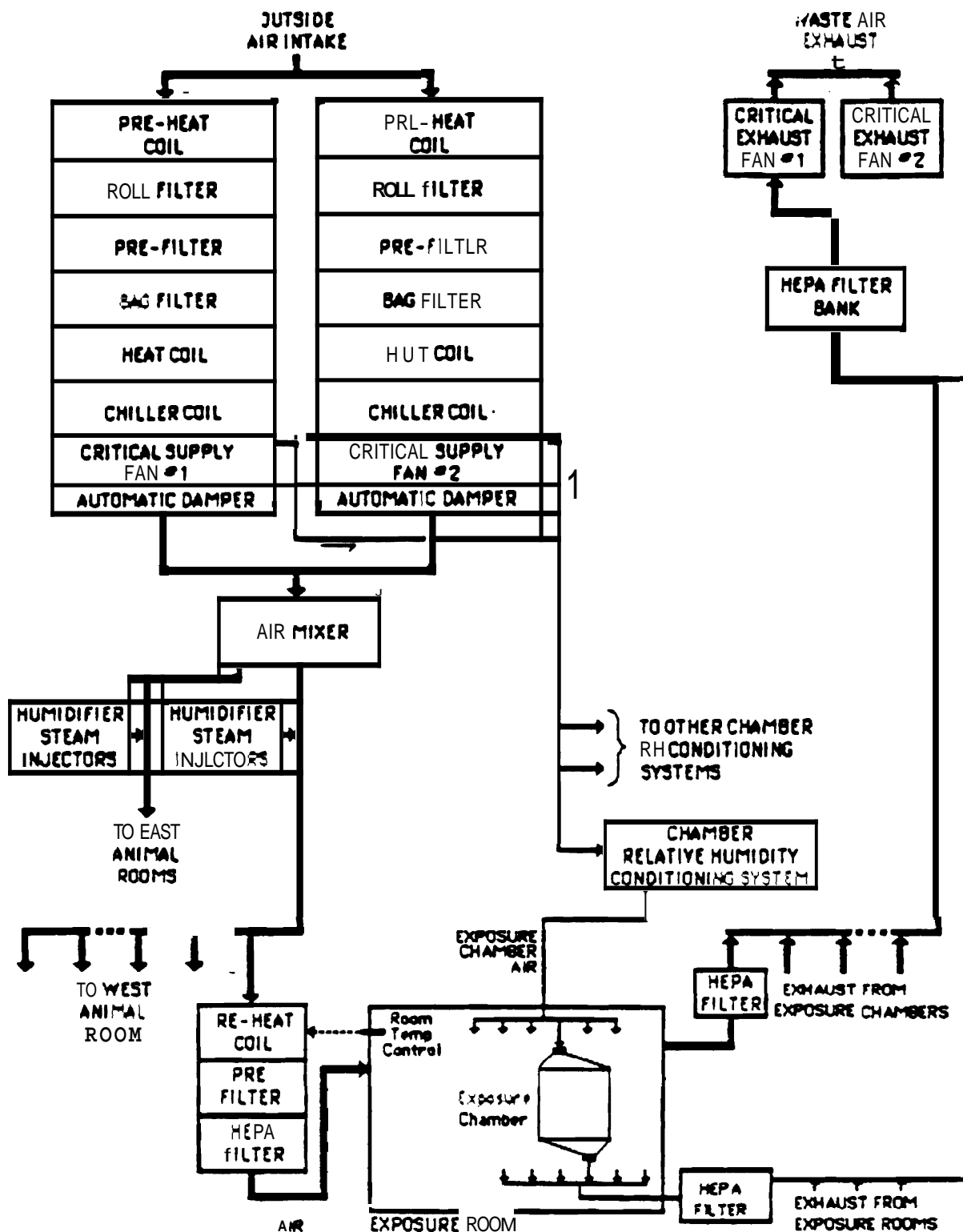


FIGURE 9. Air Handling System for Animal Rooms  
of Life Sciences II Building

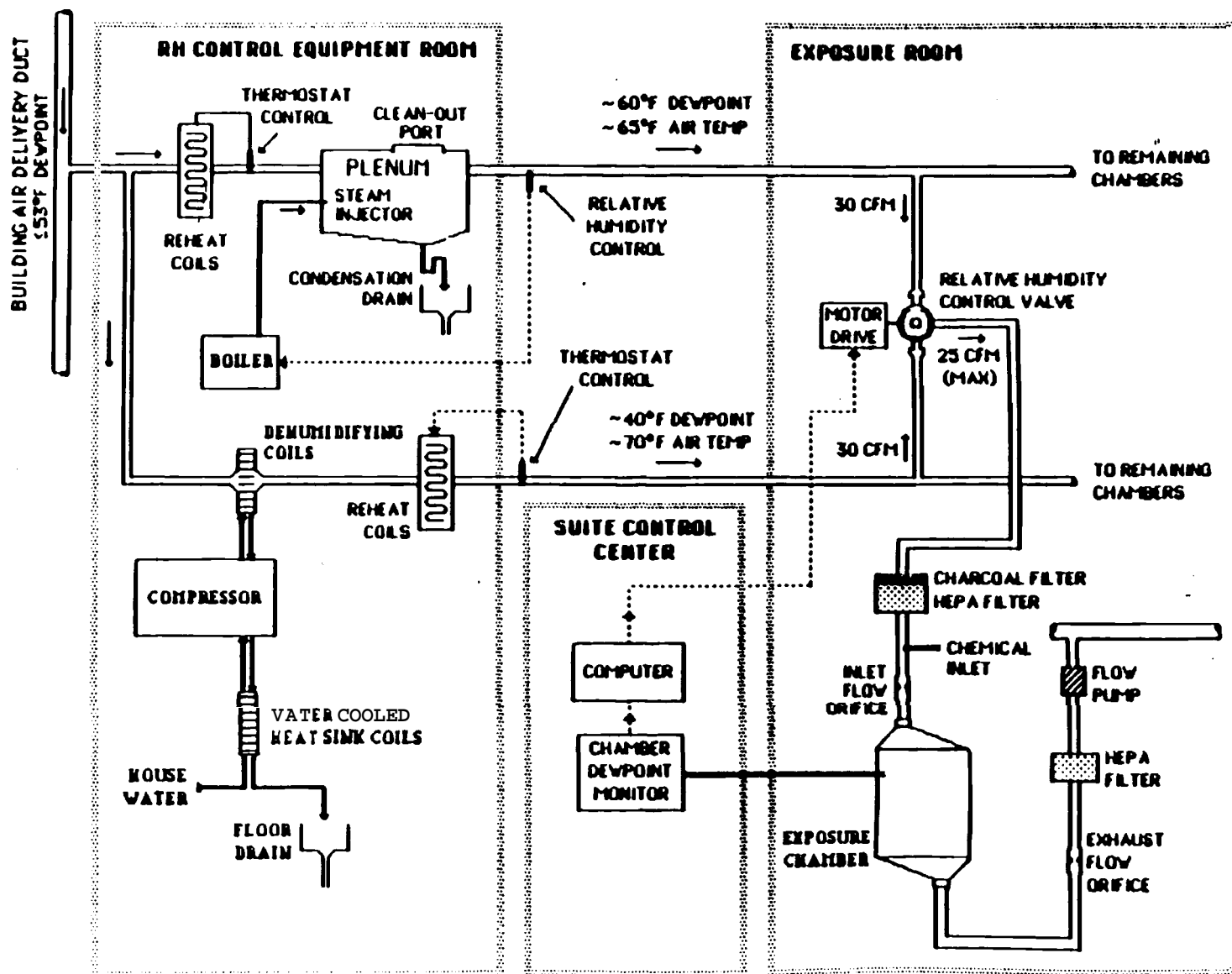


FIGURE 10. Schematic Diagram of Chamber Relative Humidity Control System

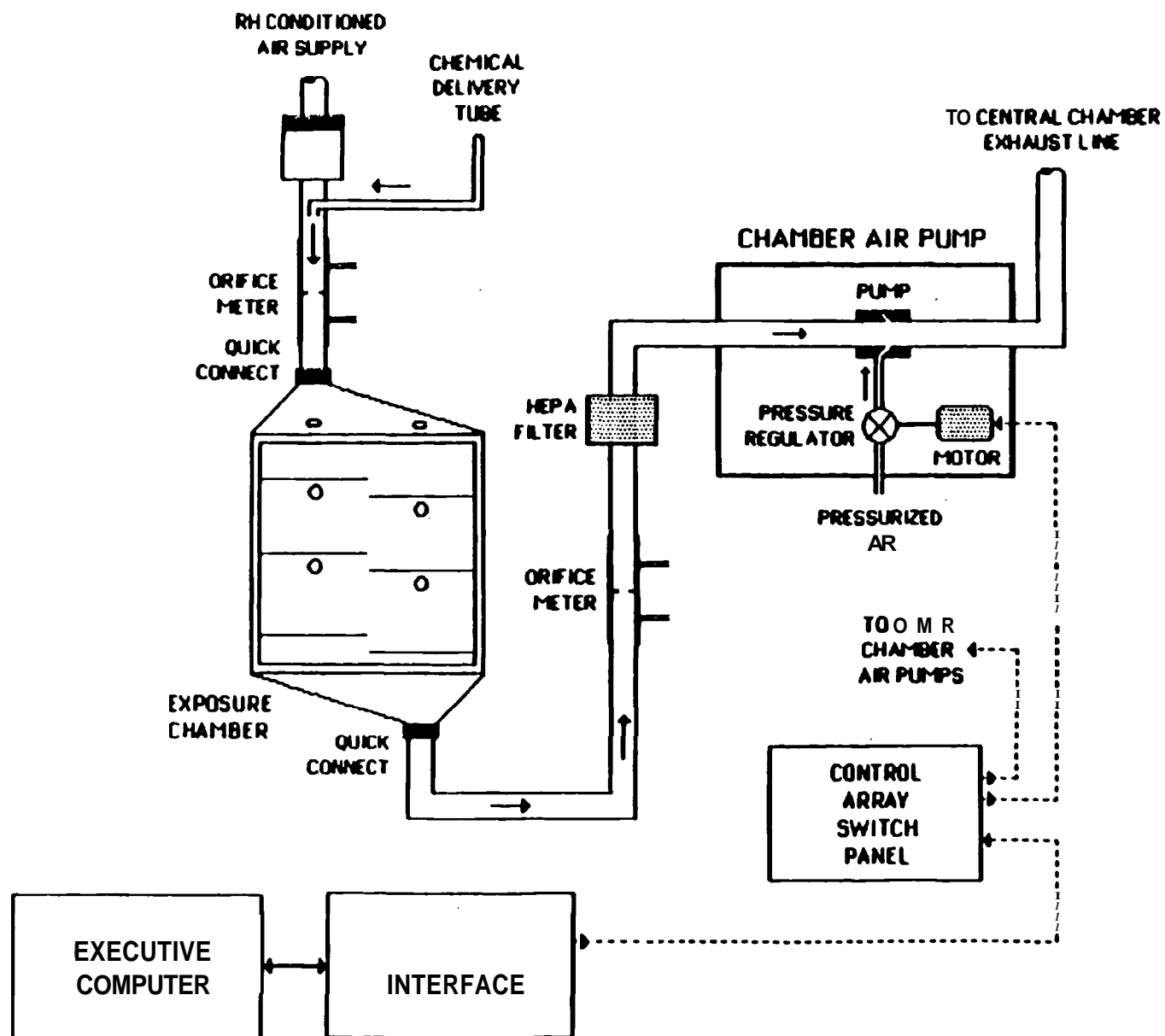


FIGURE 11. Schematic Diagram of the Chamber Air Flow Pump and Air Flow Control System

Era #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	Relative 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	HQH
21:08	Ch #1	-- Room 324	Vacuum	<BSI	.8	HQH
21:10	Ch #2	-- Room 324	Relative 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	2.5	HQH
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	KE	4	HQH
21:21	Ch #1	-- Room 324	Vacuum	<BSI	.8	HQH
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	HQH
21:27	LJF This is a demonstration of the comment routine. 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	HQH
21:48	Ch #1	-- Room 324	Vacuum	<BSI	.8	HQH
21:50	Ch #2	-- Room 324	Relative Humidity	<OKI	35.	%
21:53	Ch #3	-- Room 324	Concentration	OKI	5.000E+1	PPM
21:56	Ch #2	-- Room 436	Relative Humidity	(BSE	65.	%
21:56	Ch #2	-- Room 436	Vacuum	OKE	1.5	HQH

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: D0D0.  
000.D  
00.00  
D.000  
.0000  
0.000ESZ

**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.

Summation for the File: 23 July 1985

Exposure: Demonstration

Temperature	Mean	X Targ	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	2	76.3	72.7	15	72.0
Ch #03	73.20	101	.134	3	75.3	70.7	15	72.0
Ch #04	3.20	95	.131	2	75.6	65.7	15	72.0
Ch #05	73.31	101	.131	2	76.3	68.7	15	72.0
Ch #06	73.4	102	.139	2	75.3	72.7	15	72.0
Ch #07	69.40	95	.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	% Tam	Std Dev	% RSD	Maximum	Minimum	N	Target
Ch #01	14.10	94	.300	3	17.0	12.0	8	15.0
Ch #02	17.90	110	.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	13.30	92	.300	2	15.0	12.0	16	15.0
Ch #05	10.80	72	.200	3	12.0	8.0	18	15.0
Ch #06	14.80	99	.400	3	17.0	12.0	15	15.0
Ch #07	16.30	112	.300	4	18.0	14.0	14	15.0
Ch #08	14.60	91	.400	3	17.0	12.0	15	15.0
Relative Humidity	Mean	% Tam	Std Dev	% RSD	Maximum	Minimum	N	Target
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.

n-Hexane Rat Teratology Study  
Appendix F - Study Protocol

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	69.2	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	69.1	70.0	72.0	74.0
23 Jul			16:49	69.3	70.0	72.0	74.0
23 Jul		Ch #03	16:40	69.0	70.0	72.0	74.0
23 Jul		Ch #04	16:59	75.1	70.0	72.0	74.0
23 Jul			17:09	74.9	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	67.1	70.0	72.0	74.0
23 Jul			16:20	69.1	70.0	72.0	74.0
23 Jul		Room	16:23	69.0	70.0	72.0	74.0
23 Jul			16:41	69.9	70.0	72.0	74.0
23 Jul	Flow	Ch #01	12:45	11.2	12.0	15.0	17.0
23 Jul			15:23	18.1	12.0	15.0	17.0
23 Jul		Ch #05	15:33	9.1	12.0	15.0	17.0
23 Jul			10:23	20.1	12.0	15.0	17.0
23 Jul		Ch #08	16:41	20.2	12.0	15.0	17.0
23 Jul	Concentration	Ch #03	10:45	4.560E+00	5.000E+00	7.500E+00	1.000E+01
23 Jul			10:50	4.350E+00	5.000E+00	7.500E+00	1.000E+01
23 Jul			11:01	4.200E+00	5.000E+00	7.500E+00	1.000E+01
23 Jul			11:14	4.130E+00	5.000E+00	7.500E+00	1.000E+01
23 Jul			11:29	4.520E+00	5.000E+00	7.500E+00	1.000E+01
23 Jul		Ch #06	9:06	1.143E+11	5.000E+00	7.500E+00	1.000E+01
23 Jul			9:21	1.194E+11	5.000E+00	7.500E+00	1.000E+01
23 Jul			9:46	1.053E+11	5.000E+00	7.500E+00	1.000E+01
23 Jul		Ch #08	11:46	1.001E+11	5.000E+00	7.500E+00	1.000E+01
23 Jul			12:07	1.003E+11	5.000E+00	7.500E+00	1.000E+01

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.

## **ATTACHMENT 2**

### **STANDARD OPERATING PROCEDURES FOR INHALATION REPRODUCTIVE TOXICOLOGY STUDIES**

## STANDARD OPERATING PROCEDURES FOR INHALATION REPRODUCTIVE TOXICOLOGY STUDIES

### EXPOSURE SYSTEM

CDS DMM Card Calibration	ØB-BE-3CØT
Bubbler Sample Collection via the Critical Orifice Sample System	ØB-BE-3CØQ
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
Digital Anemometer Calibration	ØB-BE-3CØS
Dwyer Manometer Calibration Check	ØB-BE-3CØX
Validyne Pressure Transducer Calibration	ØB-BE-3CØW
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 Computer Program Documentation	ØB-BE-5EØ1
Exposure Suite Data Analysis Program Documentation	ØB-BE-5EØ3
Exposure Suite Data Analysis Program Operation	ØB-BE-3EØB
Exposure Suite Routine Computer Operation	ØB-BE-3GØ4
Exposure Suite Routine Data Disk Operation	ØB-BE-3EØA
Software Change Protocol	ØB-BE-5EØ2
Study Protocol Entry into Exposure Suite Computers	ØB-BE-3EØ9
Exposure Suite Emergency Evacuation Procedure	ØB-BE-3SØ1
Exposure Suite QC, Maintenance and Calibration	ØB-BE-3DØE
Selection of RTD's and Digital Thermometer Calibration	ØB-BE-3CØD
Omega RTD Thermometer Calibration	ØB-BE-3CØL
ERDCO FGD Maintenance & Calibration	ØB-BE-3CØU
Flammable Gas Detector (ERDCO) Checkout Procedures	ØB-BE-3CØB
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
Use of Mettler H51 Analytical Balance	ØB-AC-3BØP
Special Operating Procedure for Care and Use of Volumetric Glassware	ØB-AC-3BØR
Use of Pipets	ØB-AC-3BØS
Ordering, Receipt, Recording Use and Returning Chemicals	ØB-AC-3EØ5
Labeling of Reagents and Chemicals	ØB-AC-3B12
Dispensing Test Material to Exposure Suite Control Center	ØB-AC-3B1H

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Operation of Toledo Scale (Model 2120) to Weigh Large  
Containers of Test Material

ØB-AC-3B1A

**ANIMAL RESOURCE CENTER**

Job Orientation and Training

ØB-QA-3BØ7

Barrier Procedures for LSL II Animal Facility

ØB-AR-3BØG

Operation and Maintenance of the Clean Corridor Area

ØB-AR-3BØ5

Operation of the Regulated Corridor

ØB-AR-3B1Y

Operation and Maintenance of the Street Corridor

ØB-AR-3BØ6

Moving Animals from LSL II Animal Resources Center

ØB-AR-3BØN

Management of Animal Feed

ØB-AR-3FØ5

**Pre-cleaning** Equipment and Operation of Cage,

Bottle and Rack Washers

ØB-AR-3GØ1

Operation of Steam, Gas and Bulk Sterilizers

ØB-AR-3GØ2

Kaye Digistrip-III Room-Temperature Recorder

ØB-AR-3GØ3

Operation of Garb-El Waste Disposal

ØB-AR-3GØ4

Operation of Clark-A-Matic Floor Scrubber

ØB-AR-3GØ5

Operating Procedures for Pathological Incinerator

ØB-AR-3GØ7

**Calibration/Service** of Balances

WØ-SL-3CØ1

Biweekly Deep Cleaning of Exposure Rooms

and Occupied Animal Rooms

ØB-AR-3HØ1

Deep-Cleaning and Sanitizing Empty

Animal and Exposure Rooms

ØB-AR-3HØ3

Processing Laundry for the LSL II Animal Facility

ØB-AR-3BØ7

Sanitizing **Operations** Monitoring

ØB-AR-3HØA

Handling and Changing Out Exposure Chamber and

Cage **Units**

ØB-AR-3BØ3

Handling, Changing and Storage of Animal Cages and Racks

ØB-AR-3BØD

Cage and Rack Change-Out and Rotation for LSL II

ØB-AR-3B1U

Changing Out Racks Having Individual-Compartment Cage Units

ØB-AR-3B1V

Pre-exposure Health Screening for Rodents

ØB-AR-3FØ2

Quarantine of Animals

ØB-AR-3FØ3

**Daily** Care of Bioassay Animals

and Cleaning of Exposure Rooms

ØB-AR-3FØA

Daily Care of Rodents Housed in Cage Units

and Cleaning of Animal Holding or Exposure Rooms

ØB-AR-3FØN

Daily Care of Animals Housed in Holding Cages and

Cleaning of Animal Holding Rooms

ØB-AR-3BØC

Handling Escaped Small Animals

ØB-AR-3BØ8

Determination of Ammonia Levels Within the

Exposure Chambers

ØB-AR-3AØ1

Handling of Animal Death Records and ARC Daily

Observation Records

ØB-AR-3FØ6

Moribund Sacrifice

ØB-AR-3FØB

Weighing Rodents with Toledo Semi-Automatic Weighing

System Using the 733 ASR Terminal

ØB-AR-3GØ6

**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 of Dead and

Moribund Animals

ØB-DT-3BØF

n-Hexane Rat Teratology Study  
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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 Acquisition and Transfer with a Microcomputer	ØB-DT-3BØK
Data <b>Handling</b> and Storage	ØB-DT-3BØL
Sample <b>Storage/Shipment</b>	ØB-DT-3BØM
Examination of Fetal Skeletons Stained <b>with</b> <b>Alcian Blue/Alizarin Red</b>	ØB-DT-3BØY
Preparation of the Reproductive System for Histologic Evaluation	ØB-DT-3B1J
<b><u>HEALTH AND SAFETY</u></b>	
Biohazard Protocol n-Hexane	ØB-HS-3S1S
Bioassay Studies: Health and Safety Plan	ØB-HS-3S1C
The 3M Brand <b>W-2869 Hardcap</b> , Continuous-Flow Air-line Respirator	ØB-HS-3S19
<b>Scott-Presur Pak II</b> Self-contained Breathing Apparatus	ØB-HS-3S1A
Respiratory Protection Program	ØB-HS-3S1B

TERATOLOGY STUDY ON N-HEXANE

Group	Sperm-positive Female Rats*	Virgins	Body Weights	Daily Obs.	Litters Examined
Control (0 ppm)	30	10	40	40	23
200 ppm	30	10	40	40	24
1000 ppm	30	10	40	40	27
5000 ppm	30	10	40	40	28

\* The study protocol requires a minimum of 30 sperm-positive females (to obtain 20 pregnant females).

Five additional rats of each sex were used for health screening.



# EXPOSURE CHAMBER CAGE LOCATION

SPONSOR: NTP-IRT

CHEMICAL: n-Hexane

STUDY: RAT TERATOLOGY/BEHAVIOR PILOT CHAMBER: 1

ROOM: 436

CONCENTRATION: 0ppm

DATE: 5/17/86 *BSR*

## LEVEL 1

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7		19
	6		18
	5		17
	4		16
	3		15
	2		14
FRONT	1		13

## LEVEL 2

		CAGE#		CAGE t	
BACK	12	512 (B)	695 (C)	24	
	11	450 (B)	676 (C)	23	
	10		604 (C)	22	
	9	976 (A)		21	
	8	969 (A)	963 (B)	20	
	7	620 (A)	926 (B)	19	
	6	612 (A)	882 (B)	18	
	5	553 (A)	681 (B)	17	
	4	550 (A)	579 (B)	16	
	3	548 (A)	568 (B)	15	
FRONT	2	519 (A)	567 (B)	14	
	1	507 (A)	514 (B)	13	

## LEVEL 3

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8	936 (D)	20
	7	805 (D)	19
	6	785 (D)	18
	5	746 (D)	17
	4	647 (D)	16
	3	646 (D)	15
	2	632 (D)	14
FRONT	1	566 (D)	13

## LEVEL 4

		CAGE#		CAGE#	
BACK	12	669 (A)	802 (C)	24	
	11	668 (A)	749 (C)	23	
	10	645 (A)	748 (C)	22	
	9	643 (A)	740 (C)	21	
	8	616 (A)	682 (C)	20	
	7	602 (A)	594 (C)	19	
	6	581 (A)	559 (C)	18	
	5	563 (A)	496 (C)	17	
	4	527 (A)		16	
	3	471 (A)	967 (A)	15	
	2	466 (A)	698 (A)	14	
FRONT	1	463 (A)	675 (A)	13	

## LEVEL 5

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7	651 (D)	19
	6	804 (D)	18
	5	798 (D)	17
	4	742 (D)	16
	3	732 (D)	15
	2	502 (D)	14
FRONT	1	449 (D)	13

## LEVEL 6

	CAGE#		CAGE #
BACK	12		24
	11		23
	10	883	22
	9	878	21
	8	771	20
	7	708	19
	6	630	18
	5	610	17
	4	609	16
	3	595	15
	2	551	14
FRONT	1	498	13

LEVEL 2 & 3 TERATOLOGY  
LEVEL 4 & 5 BEHAVIOR PILOT  
LEVEL 6 VIRGINS

\* A rat behavioral pilot study was conducted concurrently in the same chambers.

n-Hexane Rat Teratology Study  
Appendix F - Study Protocol

EXPOSURE CHAMBER CAGE LOCATION

SPONSOR: NTP-IRT

STUDY: RAT TERATOLOGY/BEHAVIOR PILOT

ROOM: 436

DATE: 5/17/86 *GJR*

\* CHEMICAL: n-Hexane

CHAMBER: 2

CONCENTRATION: 200ppm

LEVEL 1

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7		19
	6		18
	5		17
	4		16
	3		15
	2		14
WONT	1		13

LEVEL 2

	CAGE#		CAGE #	
BACK	12	516 (B)	777 (C)	24
	11	499 (B)	770 (C)	23
	10		640 (C)	22
	9	942 (A)	570 (C)	21
	8	931 (A)		20
	7	652 (A)	696 (B)	19
	6	629 (A)	823 (B)	18
	5	614 (A)	688 (B)	17
	4	613 (A)	671 (B)	16
	3	601 (A)	662 (B)	15
	2	561 (A)	590 (B)	14
	FRONT	1	453 (A)	562 (B)

LEVEL 3

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8	933 (D)	20
	7	843 (D)	19
	6	763 (D)	18
	5	716 (D)	17
	4	696 (D)	16
	3	534 (D)	15
	2	448 (D)	14
FRONT	1	445 (D)	13

LEVEL 4

CAGE#		CAGE #		
BACK	12	939 (A)	856 (C)	24
	11	930 (A)	743 (C)	23
	10	928 (A)	741 (C)	22
	9	924 (A)	728 (C)	21
	8	699 (A)	663 (C)	20
	7	661 (A)	619 (C)	19
	6	638 (A)	593 (C)	18
	5	633 (A)	490 (C)	17
	4	599 (A)		16
	3	515 (A)	977 (A)	15
	2	484 (A)	966 (A)	14
FRONT	1	467 (A)	943 (A)	13

LEVEL 5

	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7	971 (D)	19
	6	945 (D)	18
	5	908 (D)	17
	4	850 (D)	16
	3	835 (D)	15
	2	733 (D)	14
FRONT	1	714 (D)	13

LEVEL 6

	CAGE#		CAGE #
BACK	12		24
	11		23
	10	923	22
	9	888	21
	8	724	20
	7	712	19
	6	618	18
	5	575	17
	4	569	16
	3	564	15
	2	500	14
FRONT	1	495	13

LEVEL 2 & 3 TERATOLOGY  
LEVEL 4 & 5 BEHAVIOR PILOT  
LEVEL 6 VIRGINS

\* A rat behavioral pilot study was conducted concurrently in the same chambers.

EXPOSURE CHAMBER CAGE LOCATION

SPONSOR: NTP-IRT

STUDY: RAT TERATOLOGY/BEHAVIOR PILOT \*

ROOM: 436

DATE: 5/17/86

CHEMICAL: n-Hexane  
CHAMBER: 3

CONCENTRATION: 1000ppm

LEVEL 1			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7		19
	6		18
	5		17
	4		16
	3		15
	2		14
	1		13
FRONT			

LEVEL 2			
	CAGE#		CAGE #
BACK	12	510 (B)	24
	11	481 (B)	23
	10	470 (B)	22
	9		21
	8	925 (A)	20
	7	691 (A)	19
	6	664 (A)	18
	5	635 (A)	17
	4	555 (A)	16
	3	544 (A)	15
	2	520 (A)	14
	1	460 (A)	13
FRONT			

LEVEL 3			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9	965 (D)	21
	8	918 (D)	20
	7	911 (D)	19
	6	905 (D)	18
	5	768 (D)	17
	4	697 (D)	16
	3	689 (D)	15
	2	591 (D)	14
	1	549 (D)	13
FRONT			

LEVEL 4			
	CAGE#		CAGE #
BACK	12	935 (A)	24
	11	654 (A)	23
	10	644 (A)	22
	9	11g (A)	21
	8	587 (A)	20
	7	562 (A)	19
	6	571 (A)	18
	5	557 (A)	17
	4	547 (A)	16
	3	545 (A)	15
	2	504 (A)	14
	1	446 (A)	13
FRONT			

LEVEL 5			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8	822 (D)	20
	7	767 (D)	19
	6	731 (D)	18
	5	713 (D)	17
	4	687 (D)	16
	3	621 (D)	15
	2	611 (D)	14
	1	597 (D)	13
FRONT			

LEVEL 6			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9	973	21
	8	302	20
	7	895	19
	6	876	18
	5	784	17
	4	642	16
	3	585	15
	2	529	14
	1	522	13
FRONT			

LEVEL 2 & 3 TERATOLOGY  
LEVEL 4 & 5 BEHAVIOR PILOT  
LEVEL 6 VIRGINS

\* A rat behavioral pilot study was conducted concurrently in the same chambers.

EXPOSURE CHAMBER CAGE LOCATION

SPONSOR: NTP-IRT  
STUDY: RAT TERATOLOGY/BEHAVIOR PILOT \*  
ROOM: 436  
DATE: 5/17/86 *BR*

CHEMICAL: n-Hexane  
CHAMBER: 4  
CONCENTRATION: 5000ppm

LEVEL 1			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8		20
	7		14
	6		18
	5		17
	4		16
	3		15
FRONT	2		14
	1		13

LEVEL 2				
	CAGE#			CAGE #
BACK	12	536 (B)	951 (C)	24
	11	457 (B)	938 (C)	23
	10		762 (C)	22
	4	948 (A)	505 (C)	21
	8	690 (A)		20
	7	636 (A)	964 (B)	19
	6	586 (A)	922 (B)	18
	5	574 (A)	868 (B)	17
	4	538 (A)	814 (B)	16
	3	488 (A)	806 (B)	15
FRONT	2	472 (A)	658 (B)	14
	1	458 (A)	622 (B)	13

LEVEL 3			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8	880 (D)	20
	7	863 (D)	14
	6	800 (D)	18
	5	641 (D)	17
	4	623 (D)	16
	3	608 (D)	15
FRONT	2	542 (D)	14
	1	451 (D)	13

LEVEL 4				
	CAGE#			CAGE #
BACK	12	626 (A)		24
	11	605 (A)	954 (C)	23
	10	588 (A)	940 (C)	22
	9	554 (A)	792 (C)	21
	8	535 (A)	784 (C)	20
	7	531 (A)	774 (C)	19
	6	523 (A)	761 (C)	18
	5	517 (A)	456 (C)	17
	4	497 (A)		16
	3	492 (A)	956 (A)	15
FRONT	2	468 (A)	701 (A)	14
	1	454 (A)	650 (A)	13

LEVEL 5			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10		22
	9		21
	8	937 (D)	20
	7	854 (D)	19
	6	819 (D)	18
	5	799 (D)	17
	4	782 (D)	16
	3	730 (D)	15
FRONT	2	630 (D)	14
	1	486 (D)	13

LEVEL 6			
	CAGE#		CAGE #
BACK	12		24
	11		23
	10	906	22
	9	824	21
	8	803	20
	7	773	19
	6	754	18
	5	660	17
	4	543	16
	3	491	15
FRONT	2	480	14
	1	459	13

LEVEL 2 & 3 TERATOLOGY  
LEVEL 4 & 5 BEHAVIOR PILOT  
LEVEL 6 VIRGINS

\* A rat behavioral pilot study was conducted concurrently in the same chambers.

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