

Final Report

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

T. J. Mast

December 1987

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

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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 **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 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 ¹⁴C-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 morphologic 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 m³ (1.7 m³ 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°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-

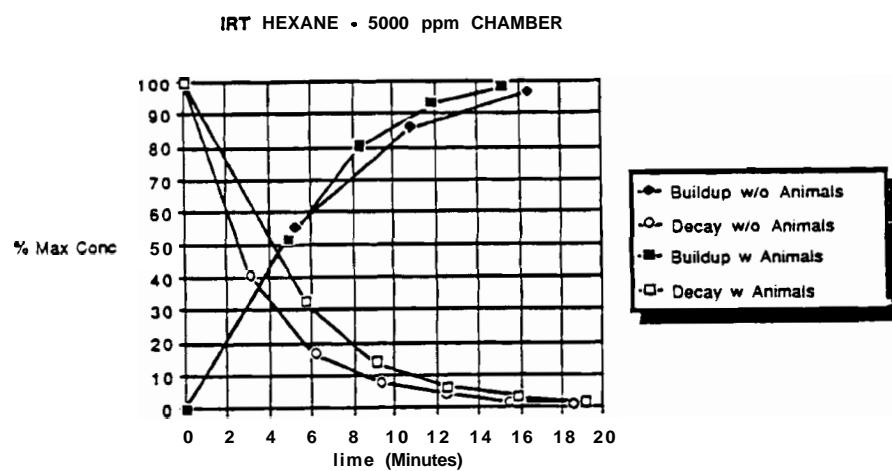
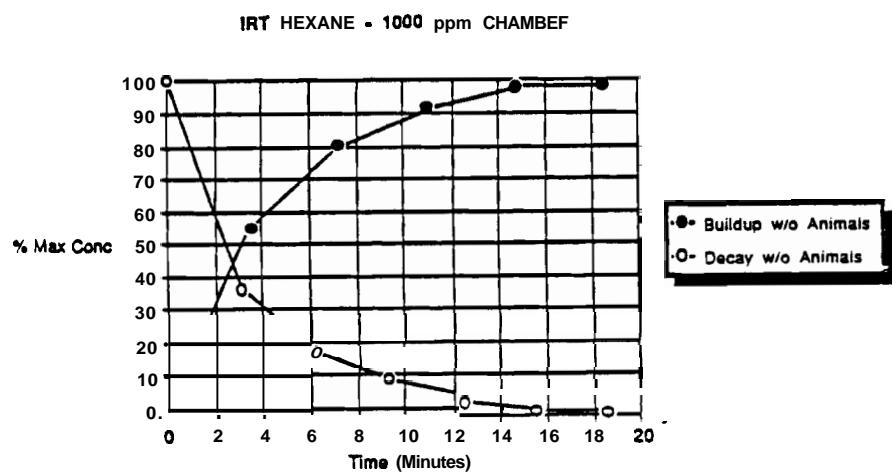
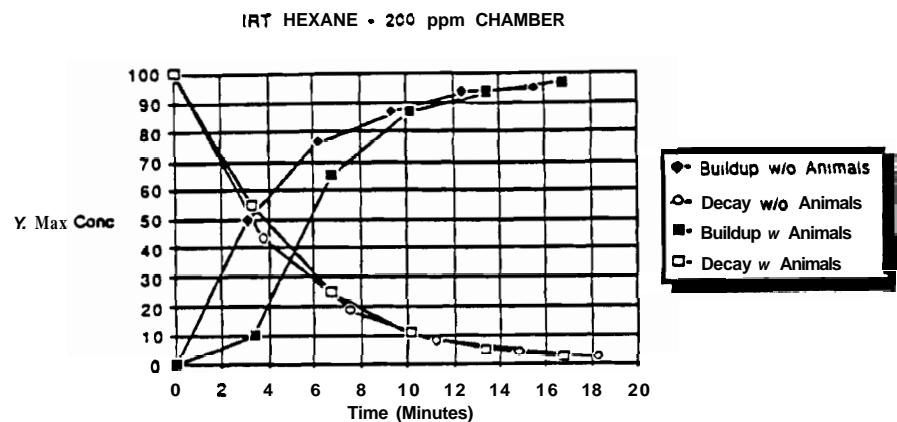


Figure 1. Buildup and decay of vapor concentrations in the 200 and 5000 ppm chambers (with and without animals present), and in the 1000 ppm chamber (without animals present).

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 CO₂ 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 14th 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
NUMBER OF:				
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
PERCENT OF:				
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	N	Mean \pm STD	N	Mean \pm STD	N	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	a 252.7 \pm 33.7	a		

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

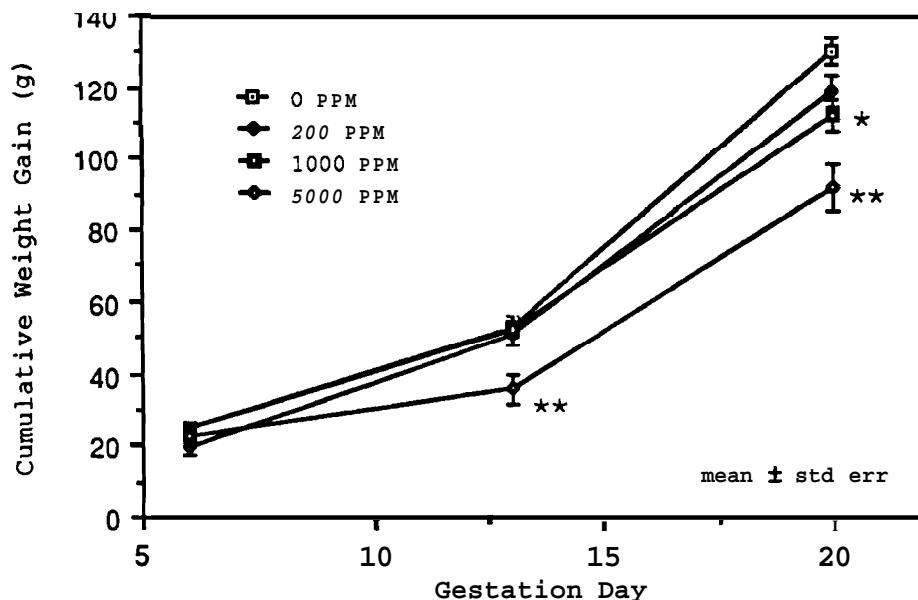
Table 5. N-Hexane Rat Teratology Study: Mean Body, Uterine, and Extra-gestational Weights (g \pm std) for Pregnant Dams.

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

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

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

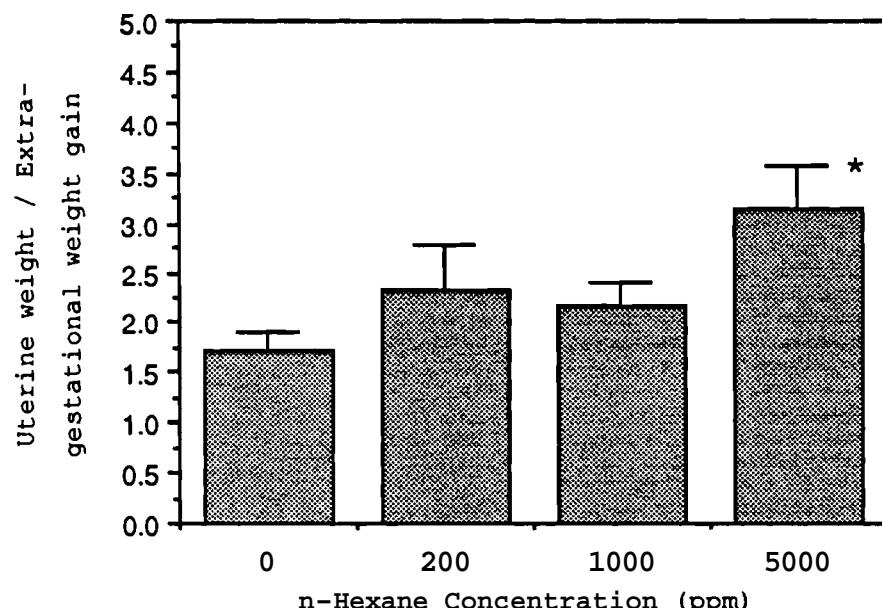
c = Uterine weight for animal 690 missed, n = 27.



• 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 1-4¹, 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

¹ 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.

n-Hexane (ppm)	Fetuses *				Litters				
	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)
Supernumerary 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)	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	n-Hexane Concentration (ppm)			
	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
Supernumerary 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
Reduced Ossification:				
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 4th 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 8th day of exposure as compared to controls (The

8th 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.

REFERENCES

Andersen, ME. Pharmacokinetics of inhaled gases and vapors. Neurobehav. Toxicol. Teratol. 3:383-389, 1981.

Baker, TS, DE Rickert. Dose-dependent uptake, distribution and elimination of inhaled n-hexane in the Fischer-344 rat. Toxicol. Appl. Pharmacol. 61:414-422, 1981.

Bohlen, R, UP Schlunegger, and E Lauppi. Uptake and distribution of hexane in rat tissues. Toxicol. Appl. Pharmacol. 25:242-249, 1973.

Brown, MG and OR Moss. An inhalation exposure chamber designed for animal handling. Labor. Anim. Sci. 31:717-720, 1981.

Bus, JS, EL White, PJ Gillies, and CS Barrow. Tissue distribution of n-hexane, methyl-n-butylketone and 2,5-hexanedione in rats after single or repeated inhalation exposure to n-hexane. Drua Metab. Dispos. 9:386-387, 1981.

Bus, JS, EL White, RW Tyl, and CS Barrow. Perinatal toxicity and metabolism of n-hexane in Fischer-344 rats after inhalation exposure during gestation. Toxicol. Appl. Pha. 51:295-302, 1979.

Graham, DG, and MR Gottfried. Cross-species extrapolation in hydrocarbon neuropathy. Neurobehav. Toxicol. Teratol. 6:433-435, 1984.

Howd, RA, CS Rebert, J Dickinson, and GT Pryor. A comparison of the rates of development of functional hexane neuropathy in weanling and young adult rats. Neurobehav. Toxicol. Teratol. 5:63-68, 1983.

Howell, WE and GP Cooper. Neurophysiological evaluation of prenatal n-hexane toxicity. Toxicologist, 1981.

Howell, WE. A neurobehavioral evaluation of the prenatal toxicity of n-hexane in rats. PhD Thesis, Univ. of Cincinnati, 1979. Available from University Microfilm International, Ann Arbor, MI #7922602.

Kimura, ET, DM Ebert, and PW Dodge. Acute toxicity and limits of solvent residue for sixteen organic solvents. Toxicol. Appl. Pharm. 19:699-704, 1971.

Moss, OR, JR Decker and WC Cannon. Aerosol mixing in an animal exposure chamber having three levels of caging with excreta pans. Amer. Ind. Hyg. Assoc. J. 43:244-249, 1982.

Marks, TA, PW Fisher, and RE Staples. Influence of n-hexane on embryo and fetal development in mice. Drugs Chem. Toxicol. 3(4):393-406, 1980.

National Institute Occupational Health and Safety. Pocket Guide to Chemical Hazards. Mackison, Stricoff, and Partridge, Eds., 1980, p108.

Spencer, PS and HH Schaumberg. Experimental and Clinical Neurotoxicology. Williams and Wilkins, NY. 1980.

Winer, BJ. Statistical Principles in Experimental Design, McGraw-Hill Book Co., NY, 1971, pp 170-185.

APPENDIX A

ANALYTICAL CHEMISTRY NARRATIVE AND DATA FOR N-HEXANE

1980-1981

1981-1982

n-Hexane Rat Teratology Study
Appendix A - Chemistry

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 CarboPak 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 CarboPak 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 \times 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

n-Hexane Rat Teratology Study
Appendix A - Chemistry

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 ± 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 Porapack Q 100/120

TEMP1 400 200 200
 TIME1 15.88
 INJ TEMP 400 200 200
 FID TEMP 400 250 250

CHT SPD 8.50
 ZEPO 18.0
 ATTN 2+ 8
 FID SGNL +8
 SLP SENS 0.10
 APER PEJ 1.0
 FLOW A 0.8 38.7
 FLOW B 8.1 3.8

DELETE CHANGE RUM 0

CHANGE RUM 0

OPTN 0 3

INJ/BTL,STROKE 1,2 200 ppm Front(next to glass wool)

START 0:07

1.672 CS₂

1 minute sample

•••

n-Hexane

HP RUN # 1
 ID: 18786
 AREA %

JUN/11/86
 BOTTLE 1

TIME 17:21:01

RT	AREA	AREA %
8.03	384	8.821
8.27	674	8.846
8.40	135	8.889
8.52	278	8.818
1.12	32478	2.283
1.32	28998	19.673
1.61	96846	6.572
2.98	1853888	71.458

DIL FACTOR: 1.8800 E+ 0

START 0:07

200 ppm Back(between foam plugs)

1 minute sample

3.49

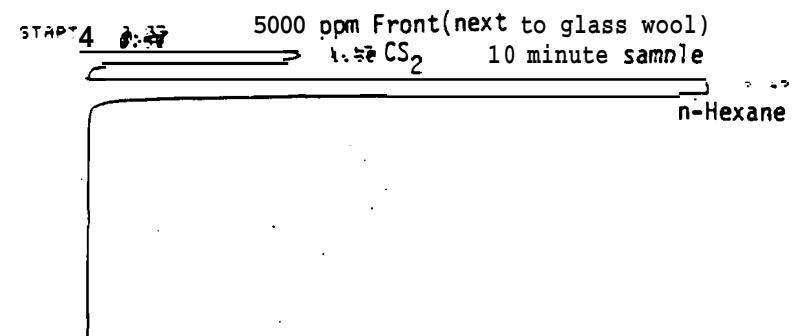
HP RUN # 2
 IS: 18786
 AREA %

JUN/11/86
 BOTTLE 3

TIME 17:37:34

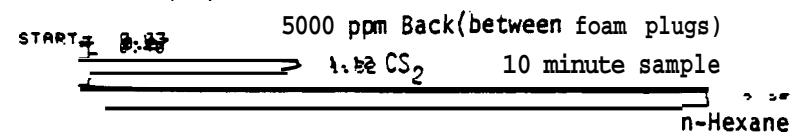
RT	AREA	AREA %
8.03	261	8.868
8.27	786	8.182
8.40	143	8.833
8.52	298	8.869
1.12	27668	6.392
1.31	291288	67.297
1.61	181408	23.434
3.49	18968	2.533

n-Hexane Rat Teratology Study
Appendix A - Chemistry



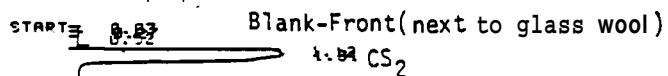
HP RUN # 13 JUN/11/86 TIME 20:38:49
ID: 18706 BOTTLE 25
AREH %

RT	AREA	ARER %
0.03	189	0.001
0.27	670	0.002
0.40	182	0.000
0.52	160	0.000
1.13	25330	0.074
1.30	284400	1.112
2.92	33930000	US. 804



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

RT	AREA	ARER %
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
2.35	19840000	97.337



HP RUN # 18 JUN/11/86 TIME 22:00:52
ID: 18706 BOTTLE 35
RRER %

RT	AREA	ARER %
0.03	210	0.051
0.27	822	0.208
0.52	235	0.057
1.12	24850	5.847
1.31	373780	98.858
3.50	12070	2.934
10.50	249	0.861

n-Hexane Rat Teratology Study
Appendix A - Chemistry

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 MRI, 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 Carbo Pak 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

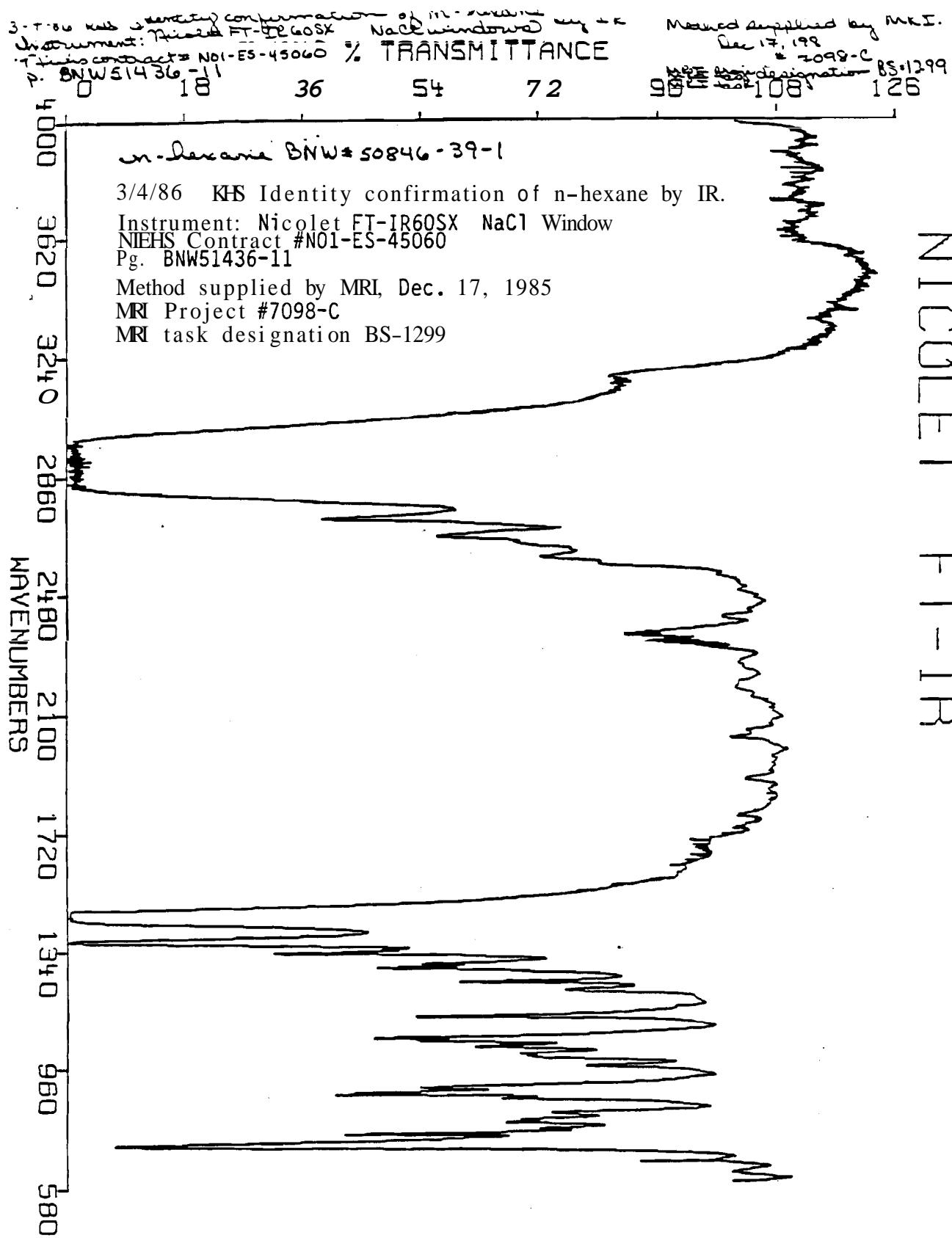
Test material sample was taken from bottle 1.

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⁻¹ and 600cm⁻¹. The spectra was similar to that provided by MRI.

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

Signature of Chemist: R. D. Schubert Date: 2/23/86

n-Hexane Rat Teratology Study
Appendix A - Chemistry



NICOLET FT-IR

n-Hexane Rat Teratology Study Appendix A - Chemistry

3-6-82 ~~test~~
7-secane survey analysis - p. 8NW 143L (60-11) (1)

447599-3
NCE Thermoanemometer 85-199
Jan. 17, 1994

TEMP1	158	158
TEMP1	158	158
ABOVE	158	158
TEMP2	157	157
TIME2	158	158
TIME2	158	158
TEMP	zaa	282
FID TEMP	258	258
OVEN MAX	488	488

CHT SPD	8.38
ATTM 2t	13
FID SGHL	+8
SLP SENS	8.18
AREA REJ	1
FLOW A	3
FLOW B	62
CPTH	22

ST	RT	AREA	AREA %
34	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 Carbopack C/0.1% SP1000(1.8 m * 4 mm Id. glass)
(BNW 50846 - 146)
Method supplied by MRI: NIEIIS Contract #N01-ES-45060
MRI Protocol #7038-C

Millask 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 Carbpak 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 Carbpak C.**

Instrument: HP5840A

RESULTS: **Impurity Profile**

Date **Area %**

5/86	-RT	Reference	Test
		Material	Material
	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%.

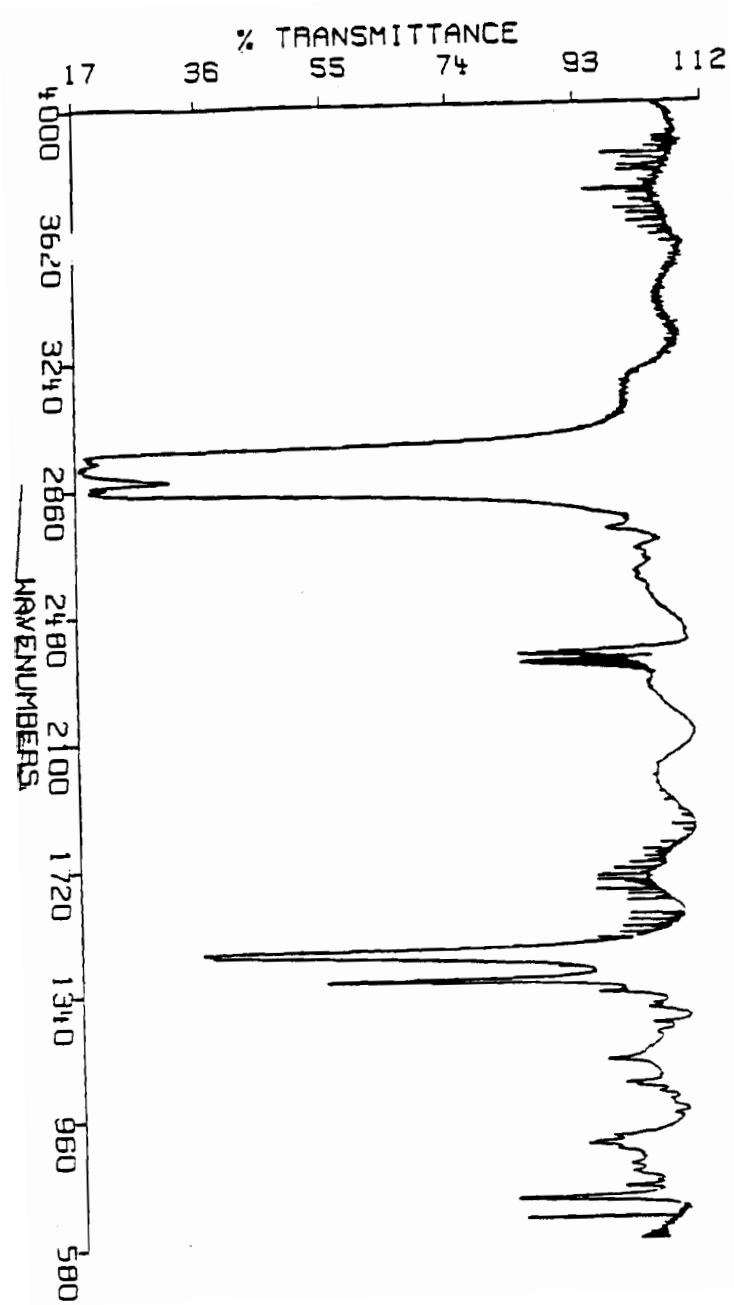
n-Hexane Rat Teratology Study
Appendix A - Chemistry

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 cm⁻¹ and 600 cm⁻¹. The spectrum was similar to previous BNW analysis.

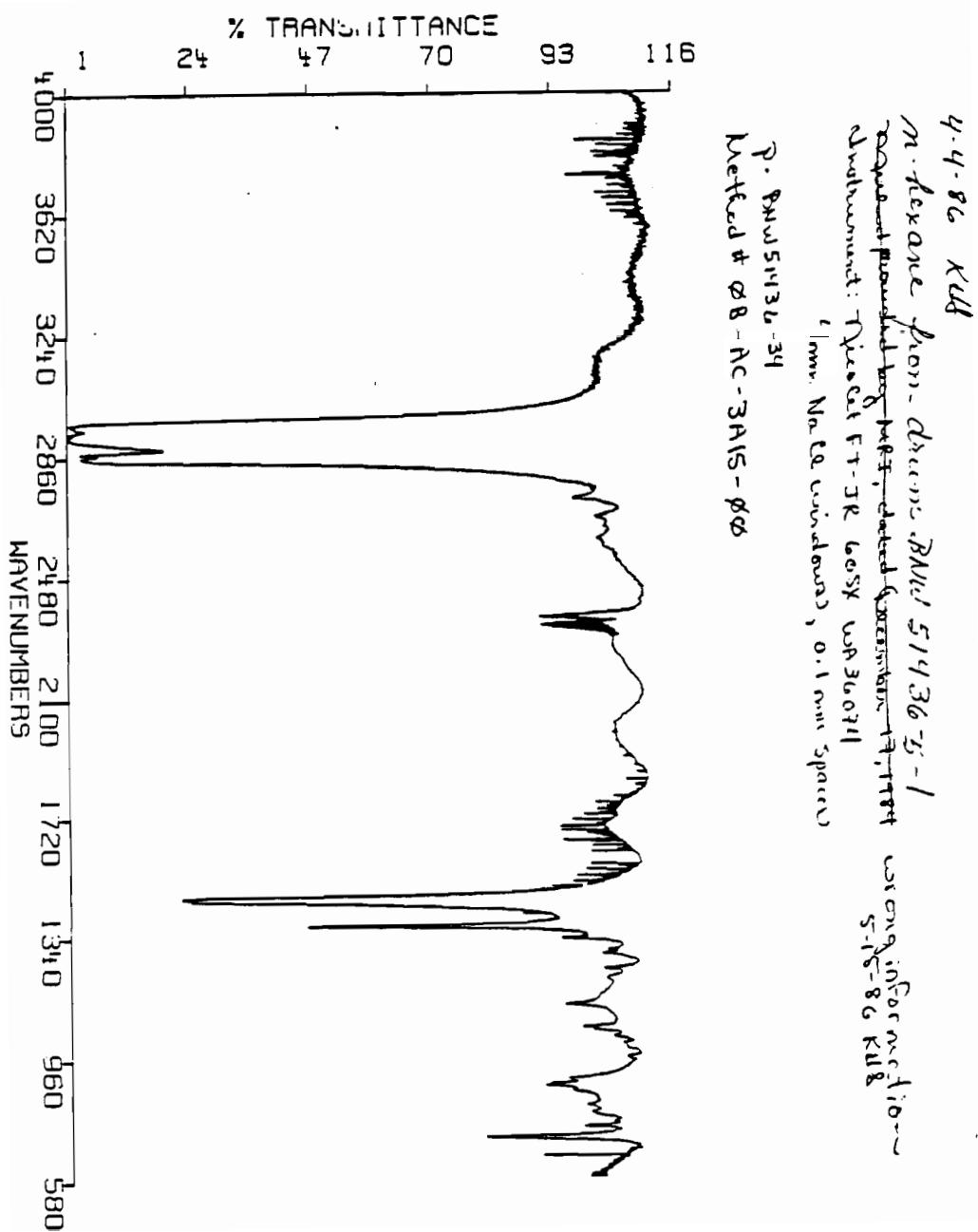
Signature of Technician: KH Stone Date: 5/15/86

Signature of Chemist: RBW Date: 5/15/86

n-Hexane Rat Teratology Study
Appendix A - Chemistry



n-Hexane Rat Teratology Study
Appendix A - Chemistry



n-Hexane Rat Teratology Study
Appendix A - Chemistry

4-3-86 KHD

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

Analyst: Not E5 45060

APR Project no: 7097-2

NRI Job designation: 651299

wrong information
S-15-86 KHD

ESCAPE Method # 03-AC-3A15-09

TEMP1 488 158 158

TIME1 15.88

INJ TERP 400 200 208

FID TEMP 400 250 250

DC: HPS840A WA10706

Column: 1.8x4mm ID glass

3% Carbowax 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

FLOU A 8.8 71.5

FLOU B 8.0 3.7

3. BNW51436 - 33

DELETE CHANGE RUN 2
CHANGE RUN 0 3

OPTN # 3 2

INJ/BTL, STROKE: 1 2 3

CHANGE RUN 2 1 STOP

DIL FACTOR: 1.8000 E+ 0 Ref # 1

Reference material BNW50846-145-1

START 0.04 0.35 0.47

0.51 0.62 0.75

0.73 0.80 0.81

0.84 0.95 0.96

0.98 1.05 1.06

1.12 1.20 1.21

1.25 1.32 1.33

1.38 1.45 1.46

1.52 1.60 1.61

1.68 1.75 1.76

1.84 1.91 1.92

1.98 2.05 2.06

2.14 2.21 2.22

2.28 2.35 2.36

2.44 2.51 2.52

2.60 2.67 2.68

2.76 2.83 2.84

2.94 3.01 3.02

3.12 3.19 3.20

3.31 3.38 3.39

3.50 3.57 3.58

3.68 3.75 3.76

3.86 3.93 3.94

4.04 4.11 4.12

4.22 4.29 4.30

4.40 4.47 4.48

4.58 4.65 4.66

4.76 4.83 4.84

4.94 5.01 5.02

5.12 5.19 5.20

5.30 5.37 5.38

5.48 5.55 5.56

5.66 5.73 5.74

5.84 5.91 5.92

6.02 6.09 6.10

6.20 6.27 6.28

6.38 6.45 6.46

6.56 6.63 6.64

6.74 6.81 6.82

6.92 6.99 7.00

7.10 7.17 7.18

7.28 7.35 7.36

7.46 7.53 7.54

7.64 7.71 7.72

7.82 7.89 7.90

8.00 8.07 8.08

8.18 8.25 8.26

8.36 8.43 8.44

8.54 8.61 8.62

8.72 8.79 8.80

8.90 8.97 8.98

9.08 9.15 9.16

9.26 9.33 9.34

9.44 9.51 9.52

9.62 9.69 9.70

9.80 9.87 9.88

9.98 10.05 10.06

10.16 10.23 10.24

10.34 10.41 10.42

10.52 10.59 10.60

10.70 10.77 10.78

10.88 10.95 10.96

11.06 11.13 11.14

11.24 11.31 11.32

11.42 11.49 11.50

11.60 11.67 11.68

11.78 11.85 11.86

11.96 12.03 12.04

12.14 12.21 12.22

12.32 12.39 12.40

12.50 12.57 12.58

12.68 12.75 12.76

12.86 12.93 12.94

13.04 13.11 13.12

13.22 13.29 13.30

13.40 13.47 13.48

13.58 13.65 13.66

13.76 13.83 13.84

13.94 14.01 14.02

14.12 14.19 14.20

14.30 14.37 14.38

14.48 14.55 14.56

14.66 14.73 14.74

14.84 14.91 14.92

15.02 15.09 15.10

15.20 15.27 15.28

15.38 15.45 15.46

15.56 15.63 15.64

15.74 15.81 15.82

15.92 16.09 16.10

16.10 16.17 16.18

16.28 16.35 16.36

16.46 16.53 16.54

16.64 16.71 16.72

16.82 16.89 16.90

16.99 17.06 17.07

17.17 17.24 17.25

17.35 17.42 17.43

17.53 17.60 17.61

17.71 17.78 17.79

17.89 17.96 17.97

18.07 18.14 18.15

18.25 18.32 18.33

18.43 18.50 18.51

18.61 18.68 18.69

18.79 18.86 18.87

18.97 19.04 19.05

19.15 19.22 19.23

19.33 19.40 19.41

19.51 19.58 19.59

19.69 19.76 19.77

19.87 19.94 19.95

20.05 20.12 20.13

20.23 20.30 20.31

20.41 20.48 20.49

20.59 20.66 20.67

20.77 20.84 20.85

20.95 21.02 21.03

21.13 21.20 21.21

21.31 21.38 21.39

21.49 21.56 21.57

21.67 21.74 21.75

21.85 21.92 21.93

22.03 22.10 22.11

22.21 22.28 22.29

22.39 22.46 22.47

22.57 22.64 22.65

22.75 22.82 22.83

22.93 23.00 23.01

23.11 23.18 23.19

23.29 23.36 23.37

23.47 23.54 23.55

23.65 23.72 23.73

23.83 23.90 23.91

23.91 23.98 23.99

24.09 24.16 24.17

24.27 24.34 24.35

24.35 24.42 24.43

24.53 24.60 24.61

24.71 24.78 24.79

24.89 24.96 24.97

25.07 25.14 25.15

25.25 25.32 25.33

25.43 25.50 25.51

25.61 25.68 25.69

25.79 25.86 25.87

25.97 26.04 26.05

26.15 26.22 26.23

26.33 26.40 26.41

26.51 26.58 26.59

26.69 26.76 26.77

26.87 26.94 26.95

27.05 27.12 27.13

27.23 27.30 27.31

27.41 27.48 27.49

27.59 27.66 27.67

27.77 27.84 27.85

27.95 28.02 28.03

28.13 28.20 28.21

28.31 28.38 28.39

28.49 28.56 28.57

28.67 28.74 28.75

28.85 28.92 28.93

29.03 29.10 29.11

29.21 29.28 29.29

29.39 29.46 29.47

29.57 29.64 29.65

29.75 29.82 29.83

29.93 30.00 30.01

30.11 30.18 30.19

30.29 30.36 30.37

30.47 30.54 30.55

30.65 30.72 30.73

30.83 30.90 30.91

30.91 30.98 30.99

31.09 31.16 31.17

31.27 31.34 31.35

31.45 31.52 31.53

31.63 31.70 31.71

31.81 31.88 31.89

31.99 32.06 32.07

32.17 32.24 32.25

32.35 32.42 32.43

32.53 32.60 32.61

32.71 32.78 32.79

32.89 32.96 32.97

33.07 33.14 33.15

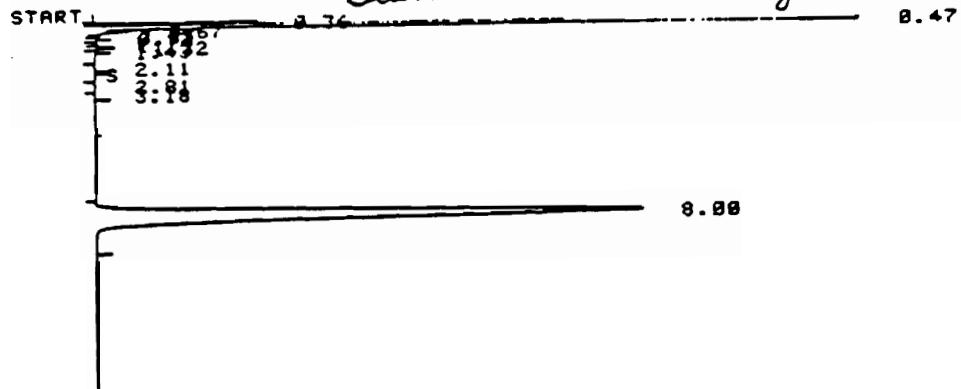
33.25 33.32 33.33

33.43 33.50 33.51

33.61 33.68 33.69

n-Hexane Rat Teratology Study
Appendix A - Chemistry

Blank - toluene / methylene chloride

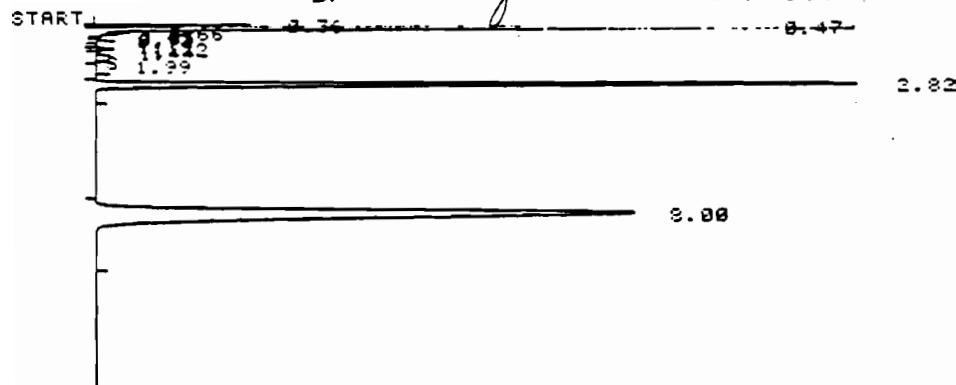


HP RUN # 19 APR/03/86 TIME 22:15
ID: 16786 BOTTLE 37

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 FACTOP: 1.0000 E+ 0

7 n-hexane from drum BNWS143G-5-1



HP RUN # 14 APR/03/86 TIME 20:51:25
ID: 16786 BOTTLE 27

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	729	0.001
1.19	4300	0.004
1.32	46930	0.035
1.44	11820	0.009
1.99	5383	0.004
2.82	4234000	3.591
8.00	8328000	6.186

DIL FACTOP: 1.0000 E+ 0

n-Hexane Rat Teratology Study
Appendix A - Chemistry

HP RUN # 34
ESCAPE
ESCAPE

TEMP1 400 50 55

TIME1 5.08

RATE 10.00

TEMP2 488 225

TIME2 5.08

INJ TEMP 400 200 199

FID TEMP 400 250 250

CHT SPD 0.50

ZERO 10.0

ATTN 2↑ 18

FID SCNL +8

SLP SENS 0.18

FLOW REJ 0.8 31.6

FLOW B 0.0 3.7

TEMP1 400 50 49

MAY/85/86

TIME 10:45:08

5-5-86 KAL

Purity Analysis of n-Hexane by H.C. Gas Chromatography Profile

Method# 08-AC-3A15-08

C. HPS840P WAT10706

Column: 2mm x 1.8m 10

1/86 CarboPack C/0.1% SP-1000

BNW51436-38-1

Samples: n-hexane

1/86 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

1.54

3.66

6.47

8.54

9.60

10.84

11.96

12.97

13.72

16.92

19.82

21.28

23.47

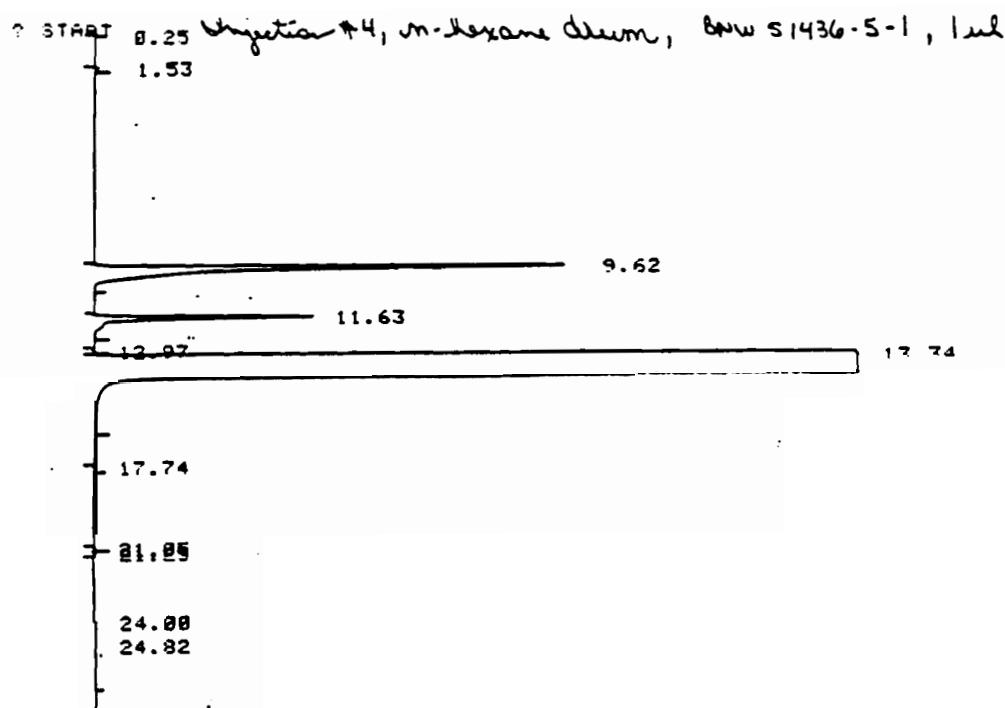
HP RUN # 36
ID: 10706
AREA %

MAY/85/86

TIME 11:34:26

RT	AREA	APEA %
1.54	234	0.000
3.66	133	0.000
6.47	225	0.000
8.54	2050	0.000
8.82	1388	0.000
9.60	599200	0.113
10.43	547	0.000
10.84	1393	0.000
11.62	229900	0.043
11.96	17910	0.003
12.97	23	0.000
13.32	528900000	99.836
15.92	3203	0.001
19.02	188	0.000
21.18	351	0.000
21.26	207	0.000
23.47	14950	0.003

n-Hexane Rat Teratology Study
Appendix A - Chemistry



HP RUN # 38 MAY/05/86 TIME 13:29:58
ID:10706
AREA %

RT	AREA	AREA %
0.25	6	0.000
1.53	2316	0.000
9.62	935600	0.182
11.63	325200	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

n-Hexane Rat Teratology Study
Appendix A - Chemistry

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

<u>Date</u>	<u>Bulk</u>
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

<u>Date</u>	<u>Area %</u>	Reference <u>Material</u>	Test <u>Material</u>
5/86	<u>-RT</u>		
	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

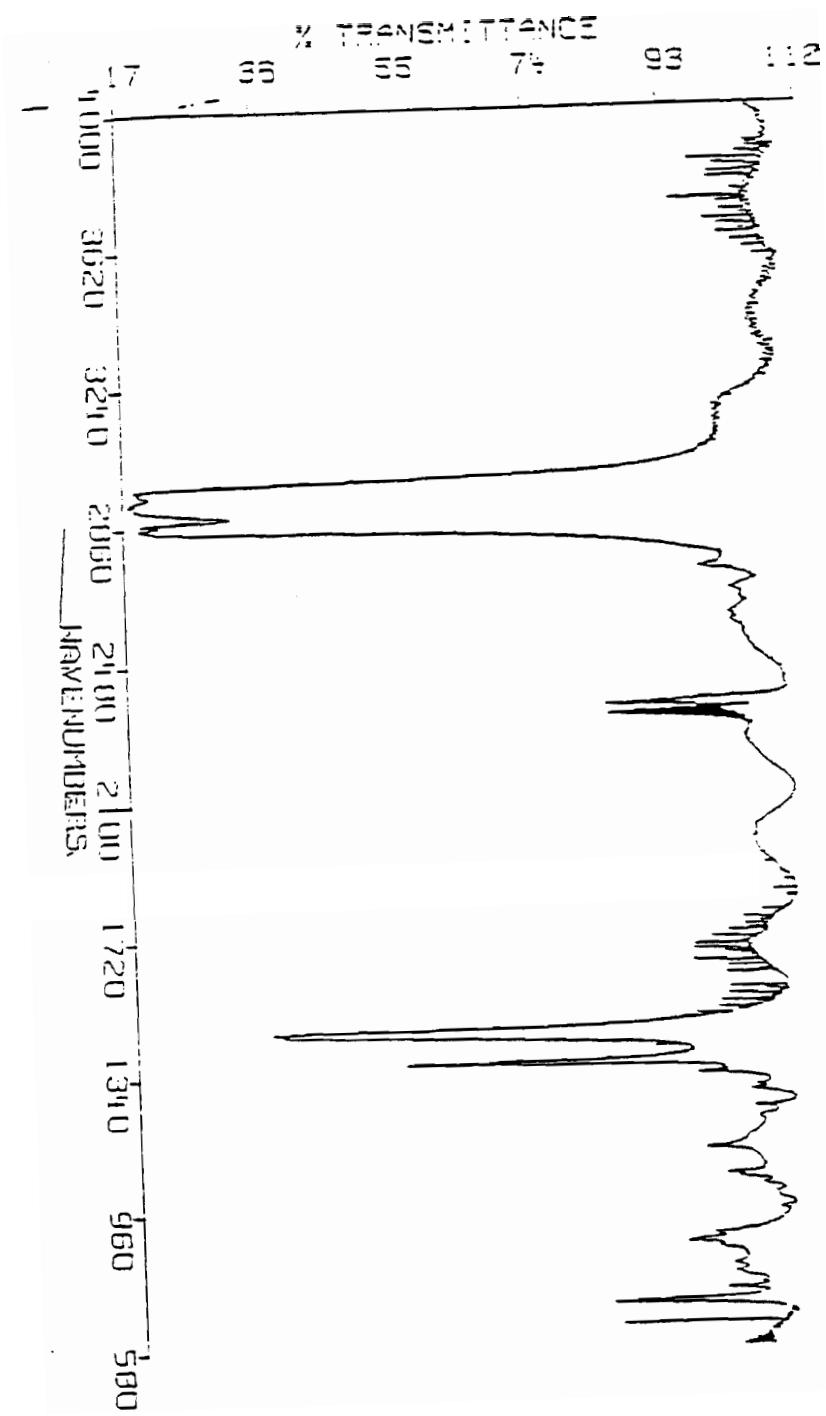
A major peak of 99.84% **area** was **observed** at a retention time of -13.3 **minutes** for both the reference and **test** material. The reference material showed 5 impurity peaks and the test material showed 4 impurity **peaks** all \geq 0.001%.

n-Hexane Rat Teratology Study
Appendix A - Chemistry

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 cm⁻¹ and 600 cm⁻¹. The spectrum was similar to previous BNW analysis.

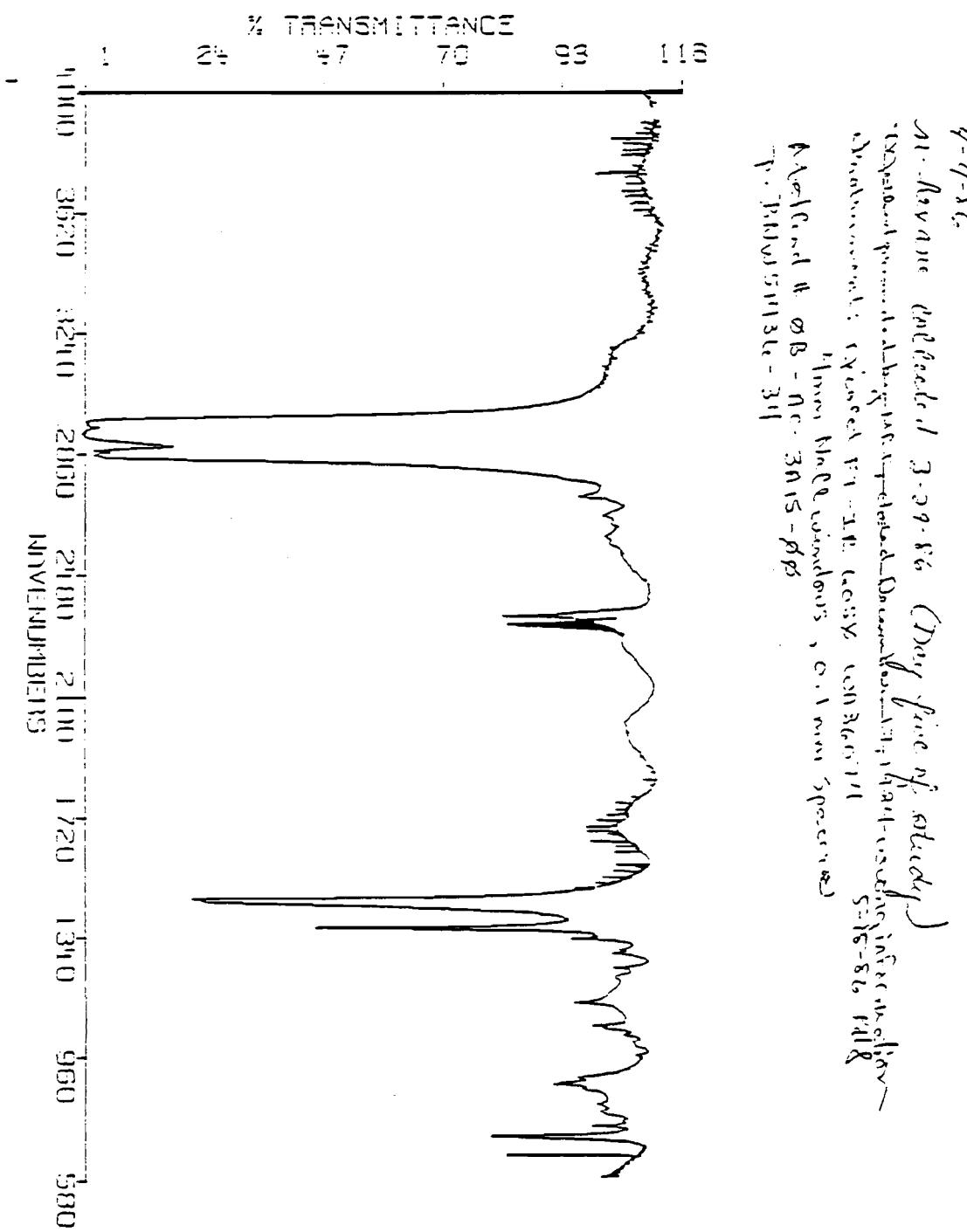
Signature of Technician: KH Stoner Date: 5/8/86
Signature of Chemist: RL Schuberg Date: 5/8/86

n-Hexane Rat Teratology Study
Appendix A - Chemistry



11/16/86 KdR
Reference: n-Hexane 36050846-195-1
Instrument: Nicolet 1710R 605K with 360711 / 11000 NCOE accessories
Date recorded: 11-19-86 - Determined 11-19-86 -
Sample: n-hexane - 36050846-195-1
V. BAW 5/13/86 - 361

n-Hexane Rat Teratology Study
Appendix A - Chemistry



n-Hexane Rat Teratology Study
Appendix A - Chemistry

• 41 400 50 65

STOP

HP RIJN # 34
ESCAPE
ESCAPE

MAY/05/86
5-5-96 KB
TIME 10:45:08

400 50 56

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

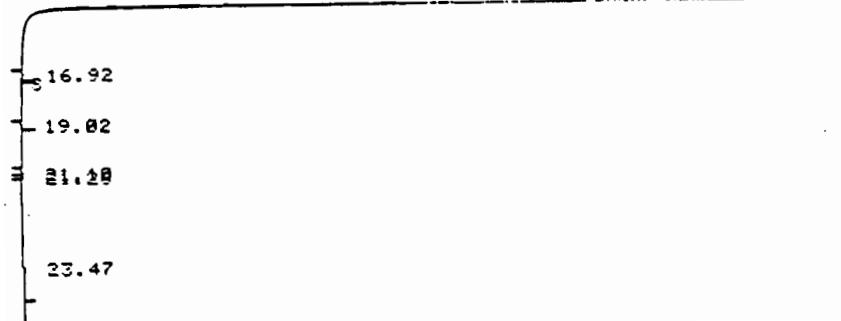
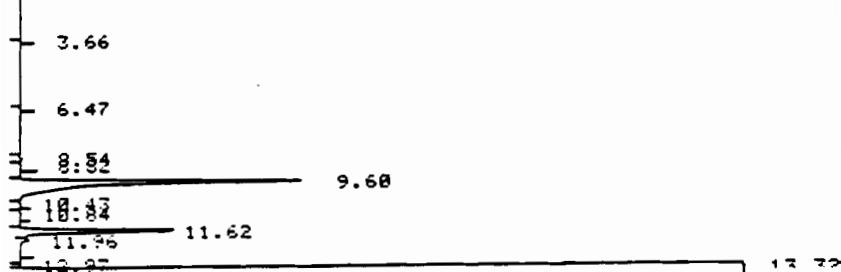
TIME1 5.00
RHTE 10.80
TEMP2 400 225
TIME2 5.00
INJ TEMP 400 200 199
FID TEMP 400 250 250
CHT SPD 0.50
ZERO 18.0
ATTN 2+ 10
F13 SGNL +8
SLC SENS 0.10
BREW REJ 3.0 31.6
FLOW B 5.0 3.7
TEMP1 400 50 49
TEMP1 400 50 49
TEMP1 400 50 50

Method# DB-AC-3A15-08
H.C. HP5840R ID 10706
Column: 2mm x 1.8m 1D glass
% CarboPac C/0.1% SP-1000
BNW51436-38-1

Samples: n-hexane
ref BNW50846-145-1
Last day 3-29-86
drum BNW51436-5-1

P BNW51436-45

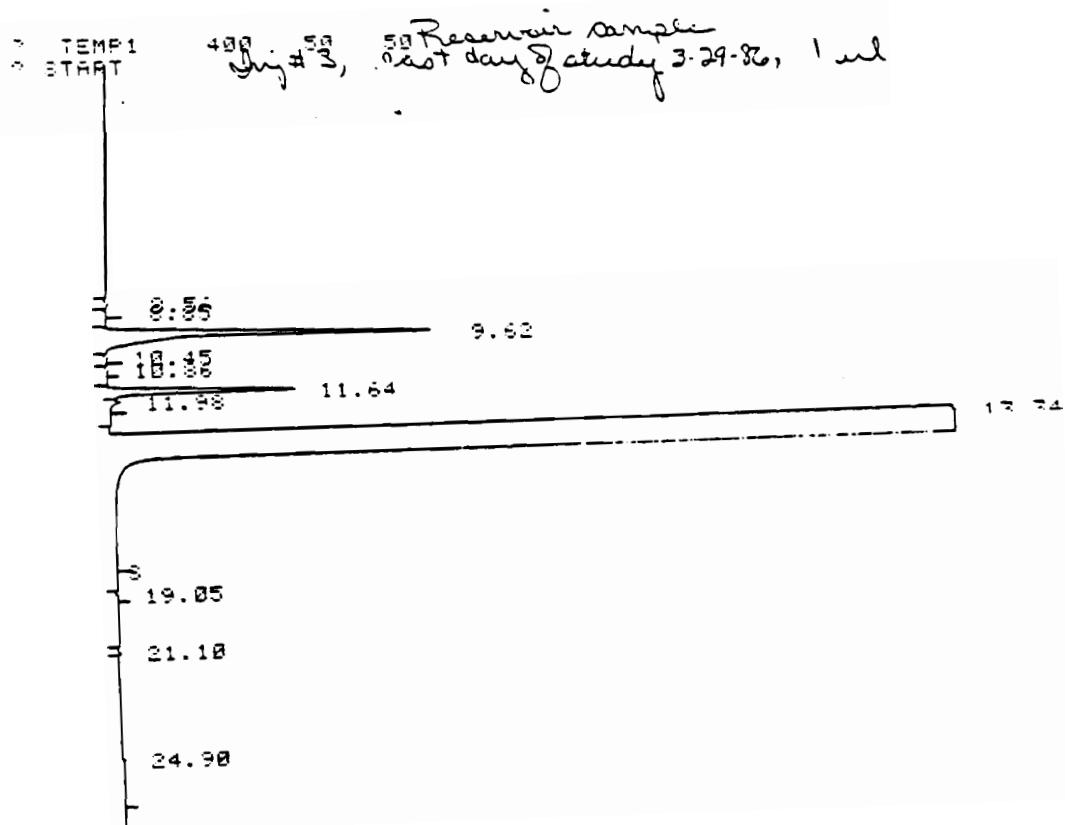
3 TEMP1 400 50 58
? START 1.54
Injection #2, Reference n-hexane BNW51436-145-1, 1 μl



HP RIJN # 36
ID: 10706
AREA %

PT	AREA	HPEA %
1.54	234	0.000
3.66	133	0.000
6.47	225	0.000
8.54	2050	0.000
8.82	1388	0.000
9.68	593200	0.113
10.43	547	0.000
10.84	1393	0.000
11.52	229900	0.043
11.96	17910	0.003
12.97	28	0.000
13.32	520900000	99.836
14.00	7000	0.000

n-Hexane Rat Teratology Study
Appendix A - Chemistry



HP RUN # 37 MAY/05/86 TIME 12:23:24
10:19706
AREA %

PT	AREA	AREA %
8.56	3417	0.000
9.06	435	0.000
9.62	594900	0.112
10.48	543	0.000
10.96	725	0.000
11.34	273000	0.044
11.58	16420	0.003
13.74	52820000	99.825
14.05	196	0.000
21.18	474	0.000
24.98	16420	0.005

DIL FACTOR: 1.0000 E+ 0

TEMP1 400 50 50

n-Hexane Rat Teratology Study
Appendix A - Chemistry

4-3-86 Ktd

Purity Analysis of n-hexane by H.C. major peak
~~Method supplied by NRI: December 17, 1984 Comparison~~
~~Method number: NRI-ES-45060~~
~~NRI Project no: 7093-C wrong information~~
~~NRI Task designation: 851299 5-86 Ktd~~

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ESCAPE

TEMP1	400	150	150
TIME1	15.00		
INJ TEMP	400	300	300
FID TEMP	400	250	250
CHT SPD	0.50		
ZERO	10.0		
RTTN \uparrow	14		
FID SGNL	+B		
SUP SENS	8.18		
AREA REG	1		
FLOW A	0.0	71.5	
FLOW B	0.0	4.4	

Method # 8B-AC-3A15-88

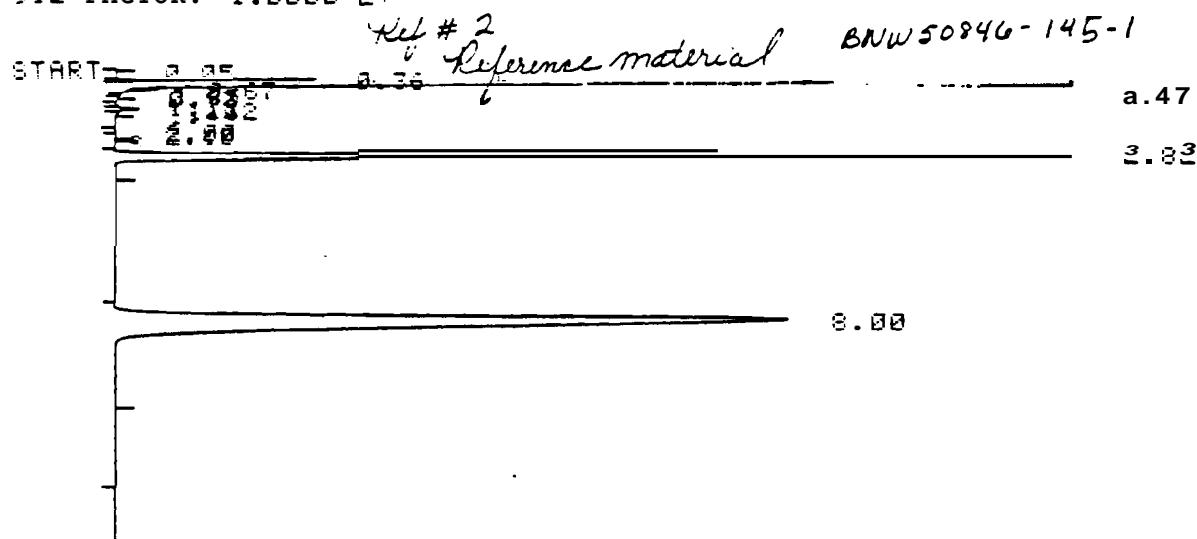
GC: HPS840 A WA10706

Column: 1.8m x 4mm ID glass

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

P. BNW51436 - 33

REL FACTOR: 1.0000 E+



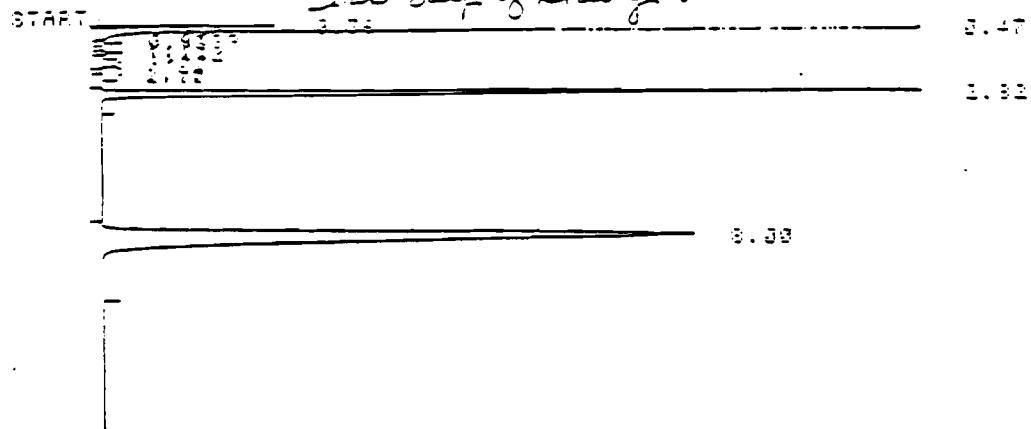
132

HP RUN # 4 APR/03/86 TIME 18:02:52
ID: 10706 BOTTLE 7
AREA %

RT	AREA	AREA %
0.36	7	0.000
0.36	155100	0.115
0.47	121100000	90.098
0.57	29430	0.022
0.67	0.0000	0.000
0.77	0.0000	0.001
0.87	0.0000	0.004
0.97	0.0000	0.005
1.07	0.0000	0.000
1.17	0.0000	0.000
1.27	0.0000	0.001
1.37	0.0000	0.000
1.47	0.0000	0.000
1.57	0.0000	0.000
1.67	0.0000	0.000
1.77	0.0000	0.000
1.87	0.0000	0.000
1.97	0.0000	0.000
2.07	0.0000	0.000
2.17	0.0000	0.000
2.27	0.0000	0.000
2.37	0.0000	0.000
2.47	0.0000	0.000
2.57	0.0000	0.000
2.67	0.0000	0.000
2.77	0.0000	0.000
2.87	0.0000	0.000
2.97	0.0000	0.000
3.07	0.0000	0.000
3.17	0.0000	0.000
3.27	0.0000	0.000
3.37	0.0000	0.000
3.47	0.0000	0.000
3.57	0.0000	0.000
3.67	0.0000	0.000
3.77	0.0000	0.000
3.87	0.0000	0.000
3.97	0.0000	0.000
4.07	0.0000	0.000
4.17	0.0000	0.000
4.27	0.0000	0.000
4.37	0.0000	0.000
4.47	0.0000	0.000
4.57	0.0000	0.000
4.67	0.0000	0.000
4.77	0.0000	0.000
4.87	0.0000	0.000
4.97	0.0000	0.000
5.07	0.0000	0.000
5.17	0.0000	0.000
5.27	0.0000	0.000
5.37	0.0000	0.000
5.47	0.0000	0.000
5.57	0.0000	0.000
5.67	0.0000	0.000
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5.87	0.0000	0.000
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6.67	0.0000	0.000
6.77	0.0000	0.000
6.87	0.0000	0.000
6.97	0.0000	0.000
7.07	0.0000	0.000
7.17	0.0000	0.000
7.27	0.0000	0.000
7.37	0.0000	0.000
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7.87	0.0000	0.000
7.97	0.0000	0.000
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13.97	0.0000	0.000
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15.47	0.0000	0.000
15.57	0.0000	0.000
15.67	0.0000	0.000
15.77	0.0000	0.000
15.87	0.0000	0.000
15.97	0.0000	0.000
16.07	0.0000	0.000
16.17	0.0000	0.000
16.27	0.0000	0.000
16.37	0.0000	0.000
16.47	0.0000	0.000
16.57	0.0000	0.000
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20.77	0.0000	0.000
20.87	0.0000	0.000
20.97	0.0000	0.000
21.07	0.0000	0.000
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21.47	0.0000	0.000
21.57	0.0000	0.000
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21.77	0.0000	0.000
21.87	0.0000	0.000
21.97	0.0000	0.000
22.07	0.0000	0.000
22.17	0.0000	0.000
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22.77	0.0000	0.000
22.87	0.0000	0.000
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23.77	0.0000	0.000
23.87	0.0000	0.000
23.97	0.0000	0.000
24.07	0.0000	0.000
24.17	0.0000	0.000
24.27	0.0000	0.000
24.37	0.0000	0.000
24.47	0.0000	0.000
24.57	0.0000	0.000
24.67	0.0000	0.000
24.77	0.0000	0.000
24.87	0.0000	0.000
24.97	0.0000	0.000
25.07	0.0000	0.000
25.17	0.0000	0.000
25.27	0.0000	0.000
25.37	0.0000	0.000
25.47	0.0000	0.000
25.57	0.0000	0.000
25.67	0.0000	0.000
25.77	0.0000	0.000
25.87	0.0000	0.000
25.97	0.0000	0.000
26.07	0.0000	0.000
26.17	0.0000	0.000
26.27	0.0000	0.000
26.37	0.0000	0.000
26.47	0.0000	0.000
26.57	0.0000	0.000
26.67	0.0000	0.000
26.77	0.0000	0.000
26.87	0.0000	0.000
26.97	0.0000	0.000
27.07	0.0000	0.000
27.17	0.0000	0.000
27.27	0.0000	0.000
27.37	0.0000	0.000
27.47	0.0000	0.000
27.57	0.0000	0.000
27.67	0.0000	0.000
27.77	0.0000	0.000
27.87	0.0000	0.000
27.97	0.0000	0.000
28.07	0.0000	0.000
28.17	0.0000	0.000
28.27	0.0000	0.0

n-Hexane Hat Teratology Study
Appendix A - Chemistry

DIL FACTOR: 1.2222 E- 4
6 n-hexane collected from receiver 3-29-86
last day of study!



HP RUN # 11
10:18786 AREA %
APR/03/86 BOTTLE 31 TIME 20:01:00

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

JPM
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 m³ (1.7 m³ 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.

n-Hexane Rat Teratology Study
Appendix B - Exposure

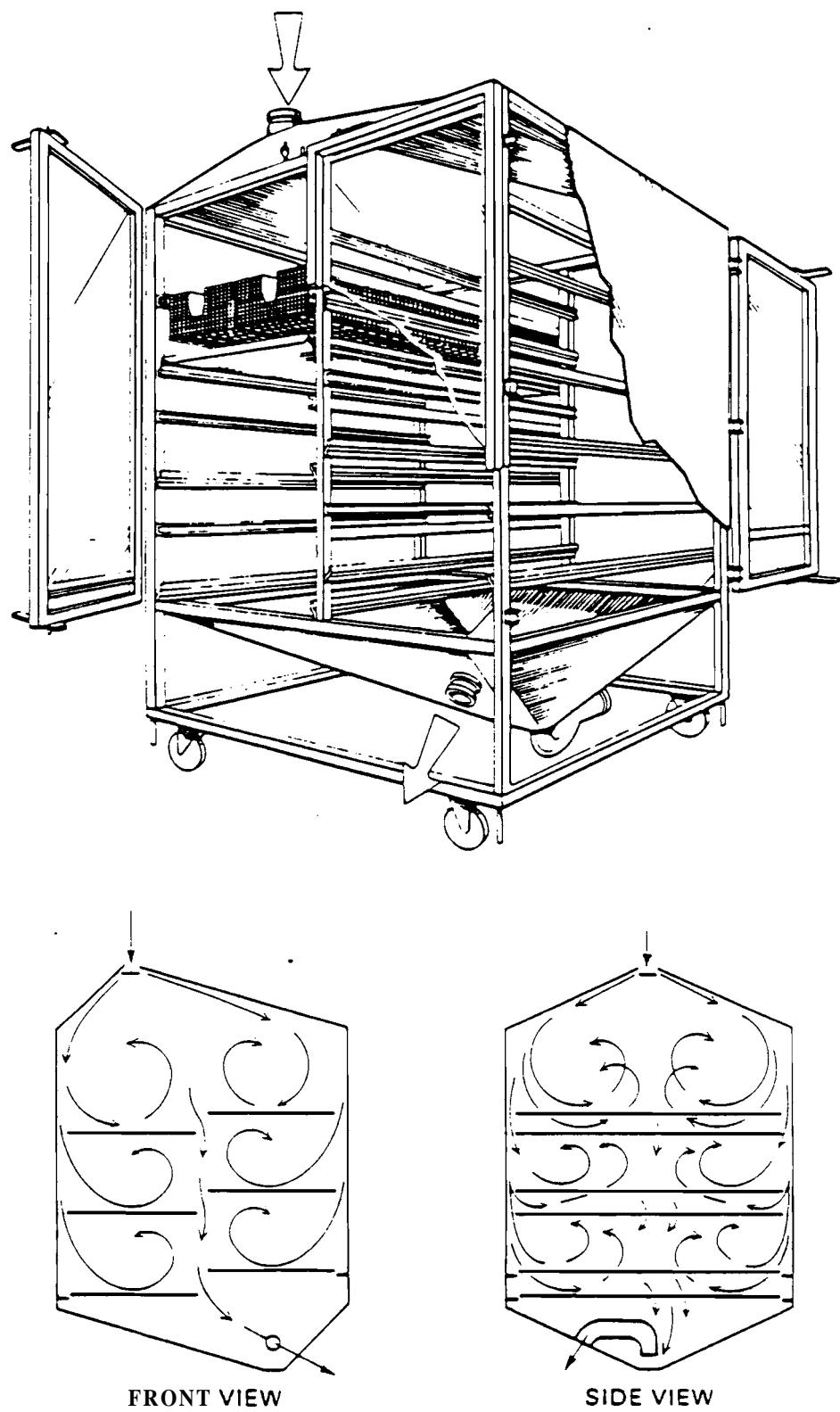


Figure B1. Inhalation Exposure Chamber.

n-Hexane Rat Teratology Study
Appendix B - Exposure

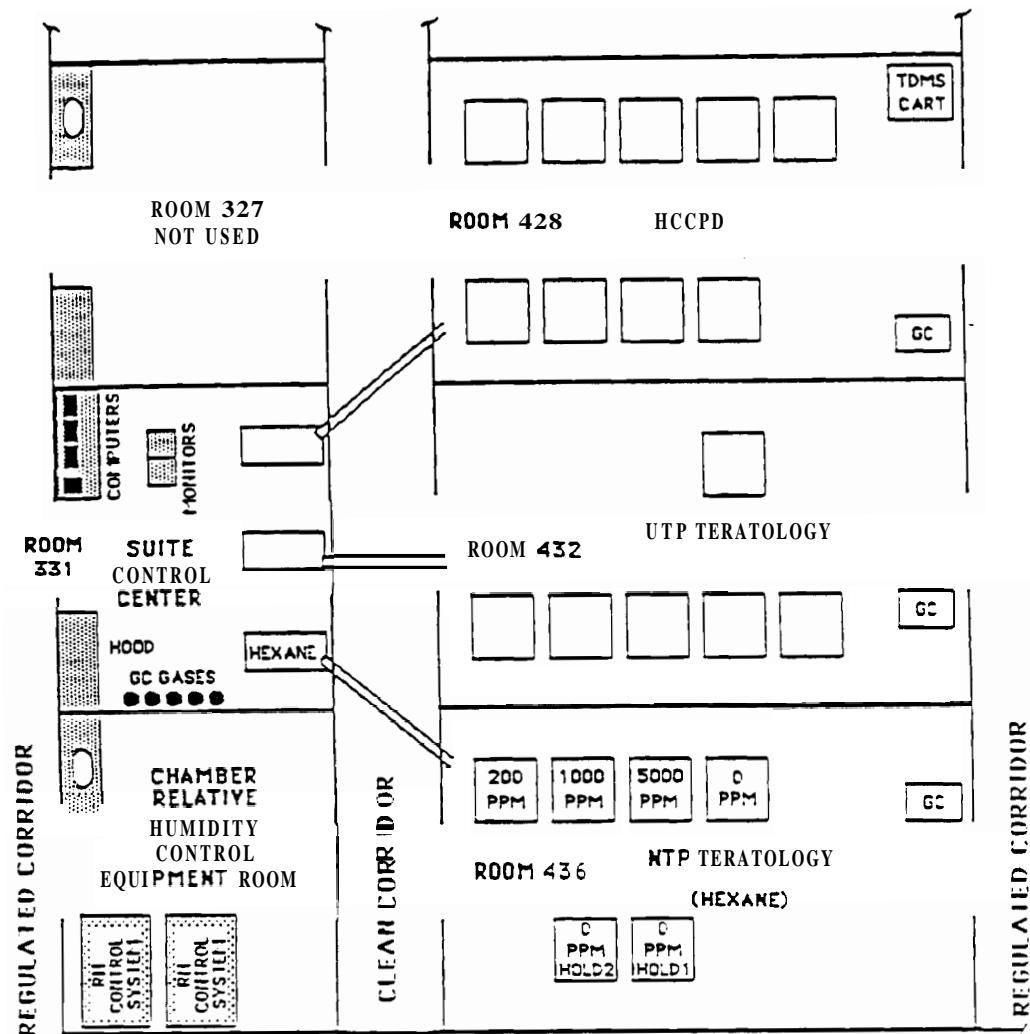


Figure B 2. Hexane Exposure Suite.

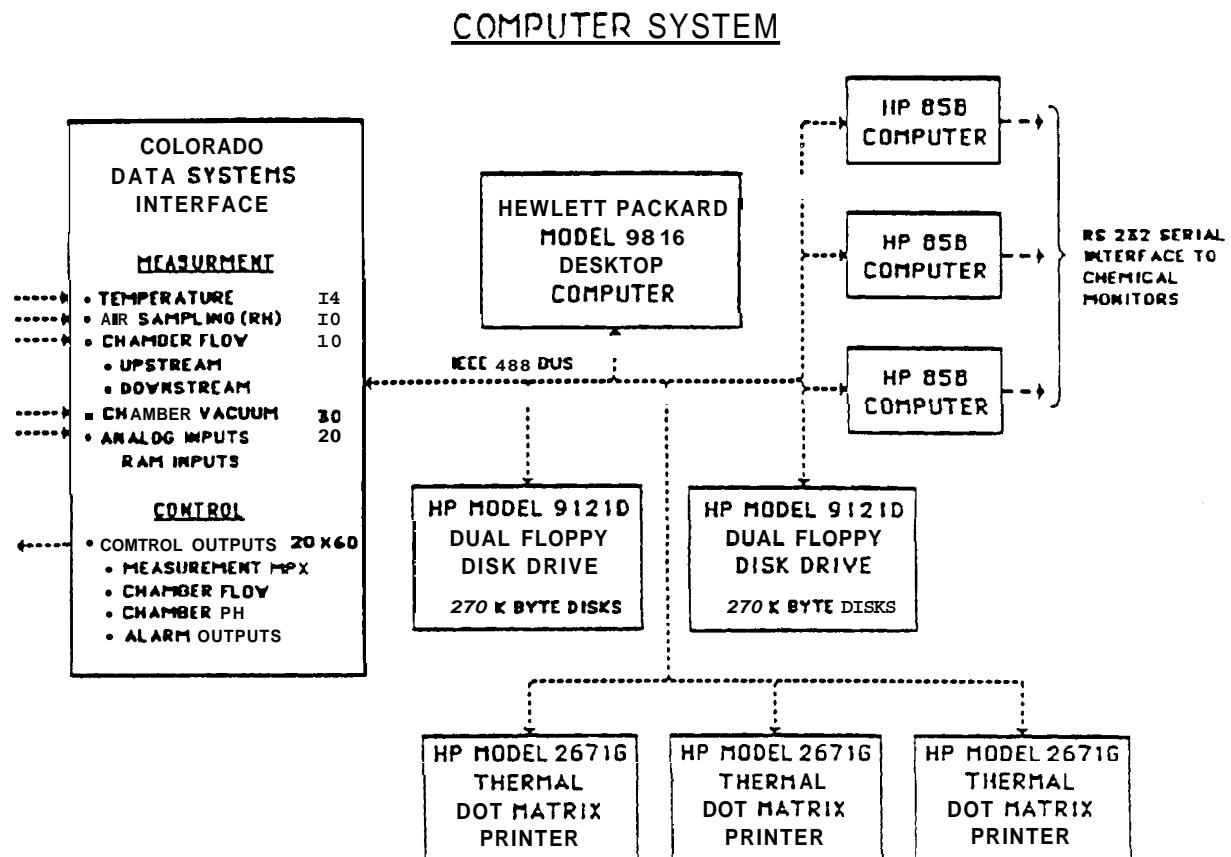


Figure E3. Data Acquisition System For n-Hexane Exposures.

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.

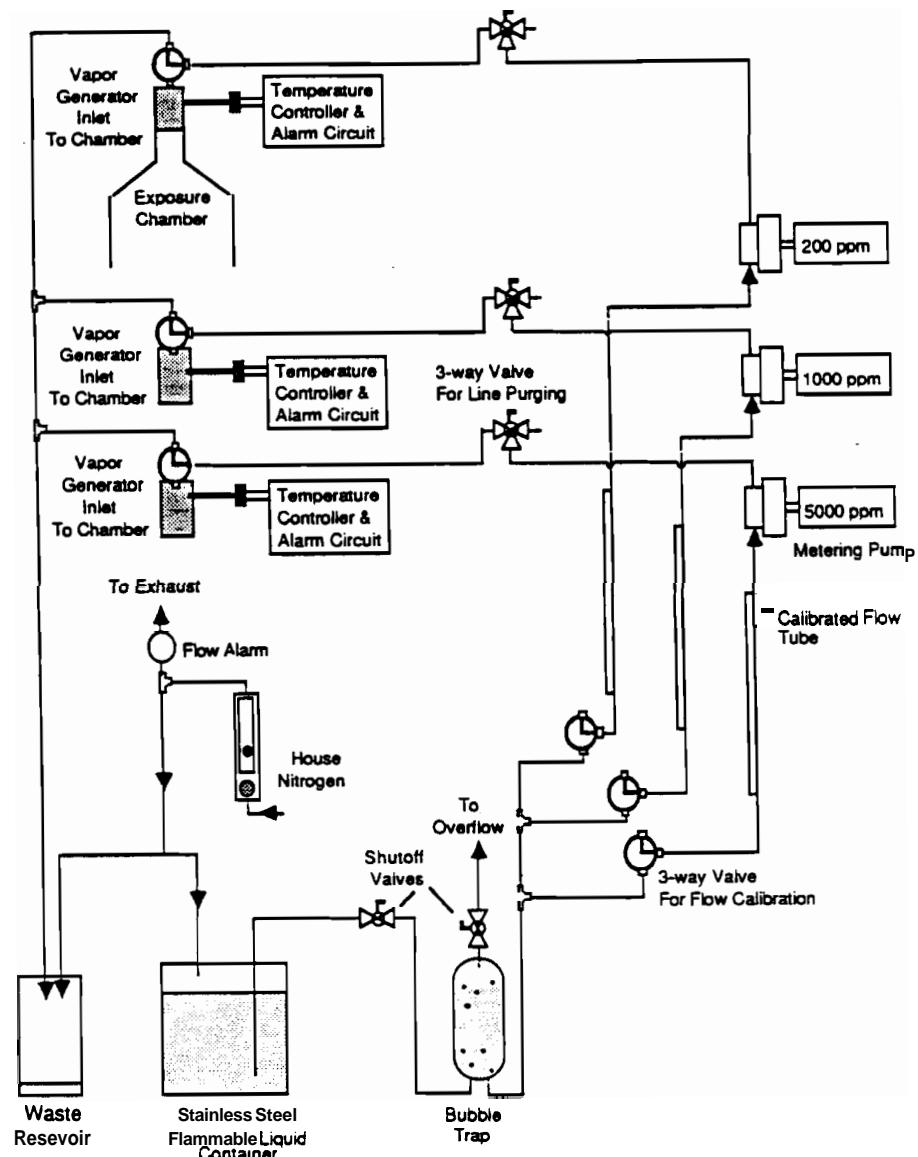
Chamber air flow is calculated with an accuracy of approximately ± 15 liters/min by measurement of the pressure drop across calibrated orifices located at the inlet and exhaust of each chamber. The desired flow orifice is attached by means of a multiplexed valve system to a calibrated pressure transducer 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 ± 0.2 cm H₂O using the same pressure transducer system which measures chamber air flows. Chamber vacuum is maintained at approximately (-)1" H₂O 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 1×10^{-3} to greater than 20 ml per minute are used.



Hexane Generation And Delivery System

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

n-Hexane Rat Teratology Study
Appendix B - Exposure

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.

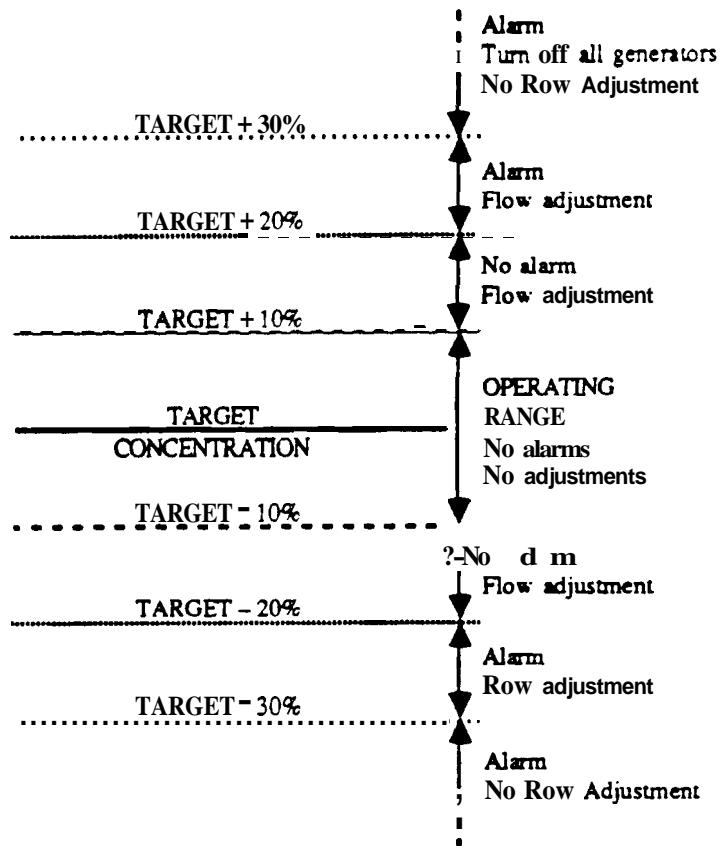
Adjustments are made to the air flow only if the concentration is beyond the Non-Critical Limit ($\pm 10\%$ of target concentration). The concentration adjustment is limited to assure that the chamber dilution air flow is not adjusted beyond the non-critical flow limits (12 to 18 air changes per hour). 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.

n-Hexane Rat Teratology Study
Appendix B - Exposure

The following conditions for alarms and concentration adjustments will apply:

- Concentration $<$ Target + 10% and $>$ Target - 10%
No action necessary-
- Concentration $>$ Target + 10% and \leq Target + 20%
or
 $<$ Target - 10% and \geq Target - 20%
Set no alarms.
Adjust chamber air flow rate to bring concentration as close to target as possible within air flow limits (12 to 18 air changes per hour).
- Concentration $>$ Target + 20% and \leq Target + 30%
 $<$ Target - 20% and \geq Target - 30%
Set audible alarm in control room and exposure room. **If** after normal working hours or **if** weekend, also set power operator alarm. Adjust chamber air flow rate to bring concentration as close to target as possible within air flow limits (12 to 18 air changes per hour).
- Concentration $>$ Target + 30%
Turn off all generators.
Set audible alarm in control room and exposure room. **If** after normal working hours or **if** weekend, also set power operator alarm. Make no adjustment of chamber air flow.
- Concentration $<$ Target - 30%
Set audible alarm in control room and exposure room. **If** after normal working hours or **if** weekend, also set power operator alarm. Make no adjustment of chamber air flow.

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



The time (T_{90}), following the start of generation, for the concentration to build up to 90% of the final stable concentration in the chamber and the time (T_{10}), following the stop of generation for the vapor concentration to decay to 10% of the stable concentration were determined before animals were placed in the chambers. The resulting curves for all chambers are shown in Figure 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

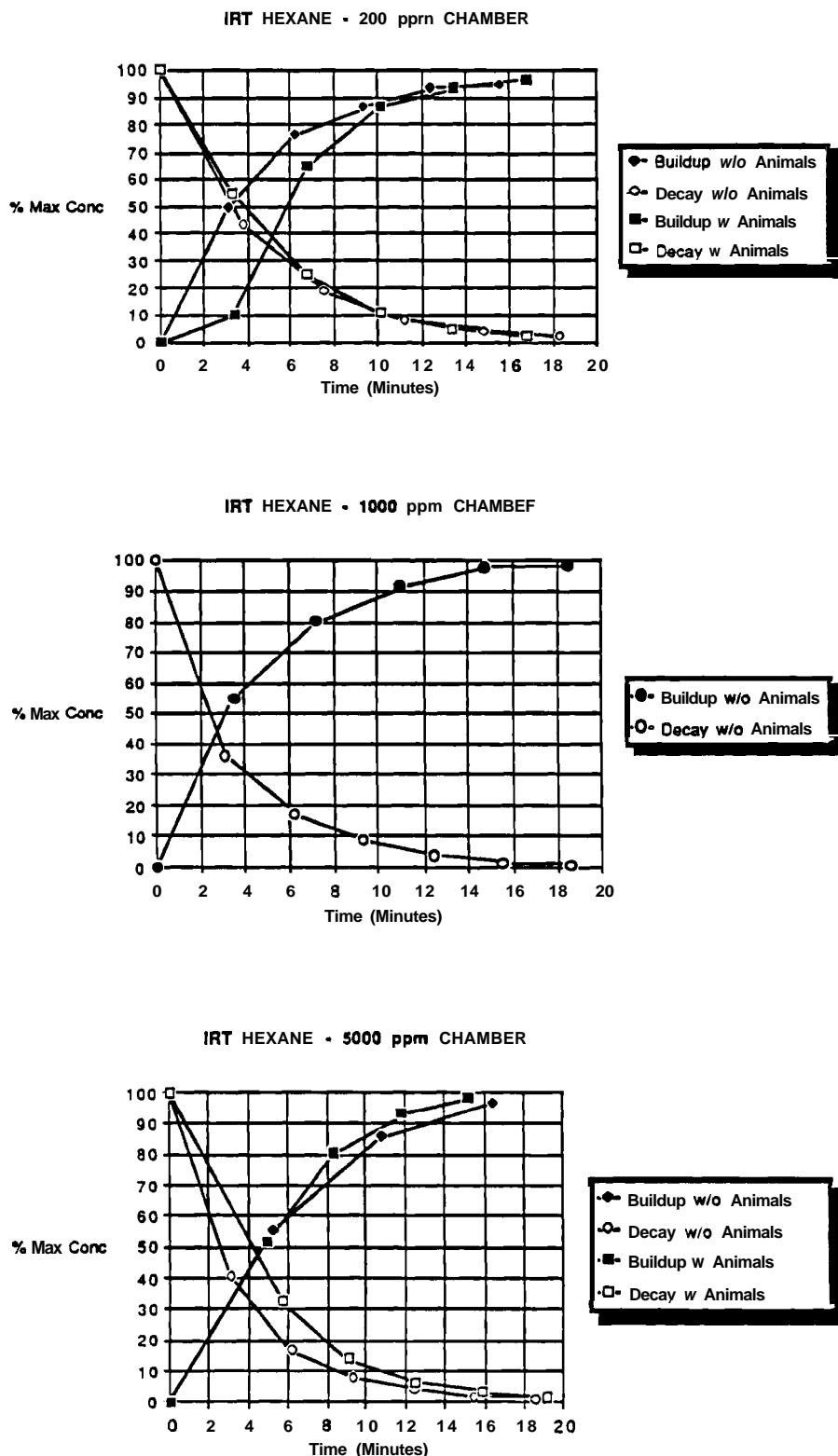


Figure B 5. Buildup and Decay of Vapor Concentrations With and Without Animals Present.

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	Percent of	Number of	% Samples			
<u>Conc. (ppm)</u>	<u>Mean ± SD</u>	<u>Target ±%RSD</u>	<u>Samples</u>	<u>in Range</u>		
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
1 200	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	Percent of	Number of	% Samples			
<u>Conc. (ppm)</u>	<u>Mean ± SD</u>	<u>Target ±%RSD</u>	<u>Samples</u>	<u>in Range</u>		
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	Percent of	Number of	% Samples			
<u>Conc. (ppm)</u>	<u>Mean ± SD</u>	<u>Maximum</u>	<u>Minimum</u>	<u>Samples</u>	<u>in Range</u>	
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
1 200	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

n-Hexane Rat Teratology Study
Appendix B - Exposure

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

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

Target <u>Conc. (ppm)</u>	<u>Mean \pm SD</u>	<u>Percent</u>	Maximum	Minimum	<u>Number Samples</u>	<u>Number In Range</u>	<u>% Samples In Range</u>
Room	0.07 \pm 0.5	_____	4	0	658	*643	*98
0	0.00 \pm 0.00	_____	0	0	631	*631	*100
Hold 1 1	0.00 \pm 0.01	_____	0.1	0	99	*99	*100
Hold 2 1	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 - IRT (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

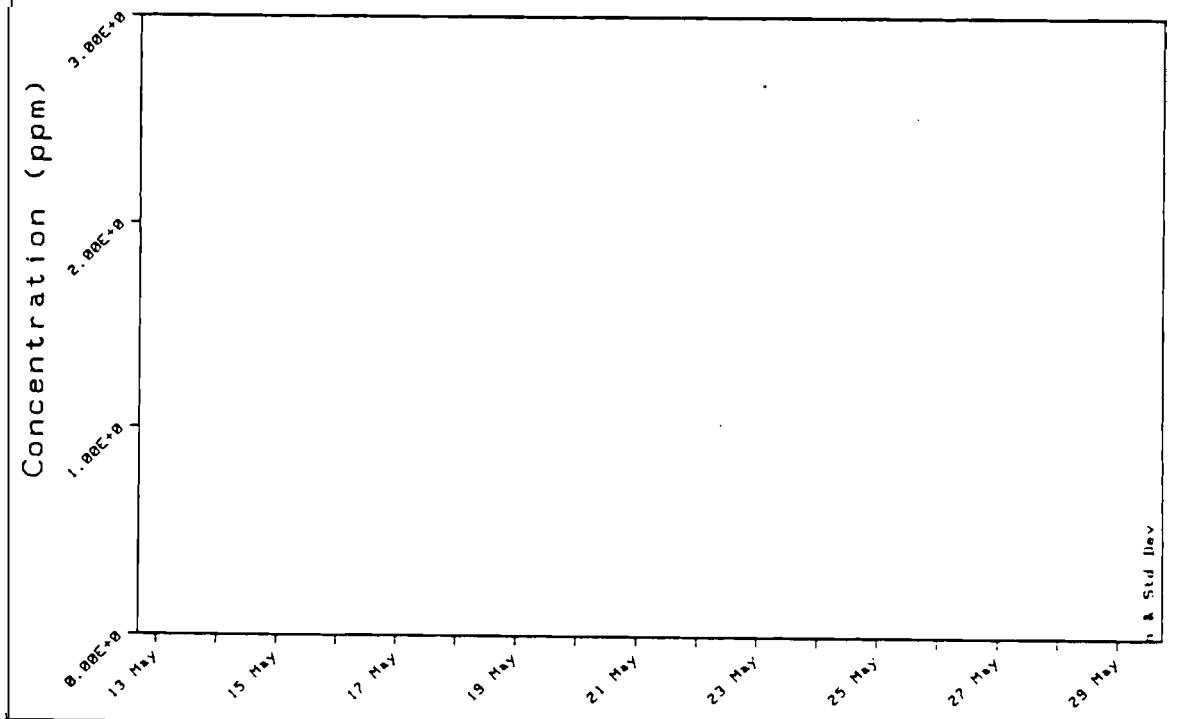
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N ir	% N ir
13 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	33.	33.	100%
14 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	35.	35.	100%
15 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	3.	3.	100%
16 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	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	€31.	631.	100%

Hexane - IRT (Rats)

Hexane - 0 ppm-R/M

Mean & Standard Deviation

From 13 May 1986 through 29 May 1986

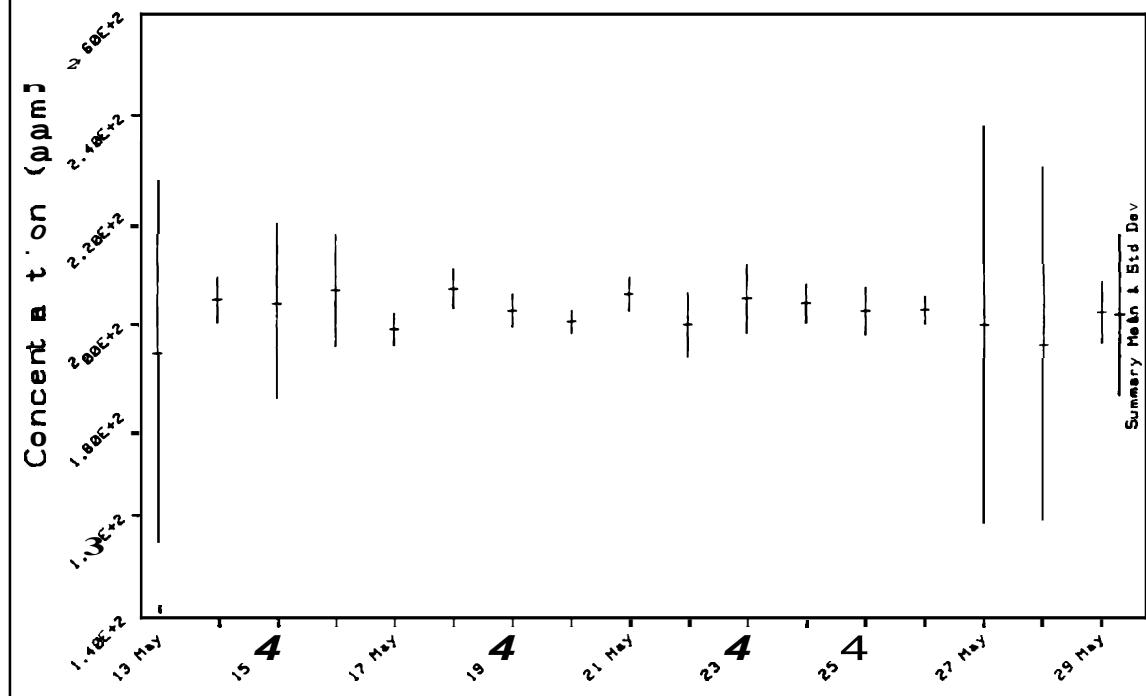


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

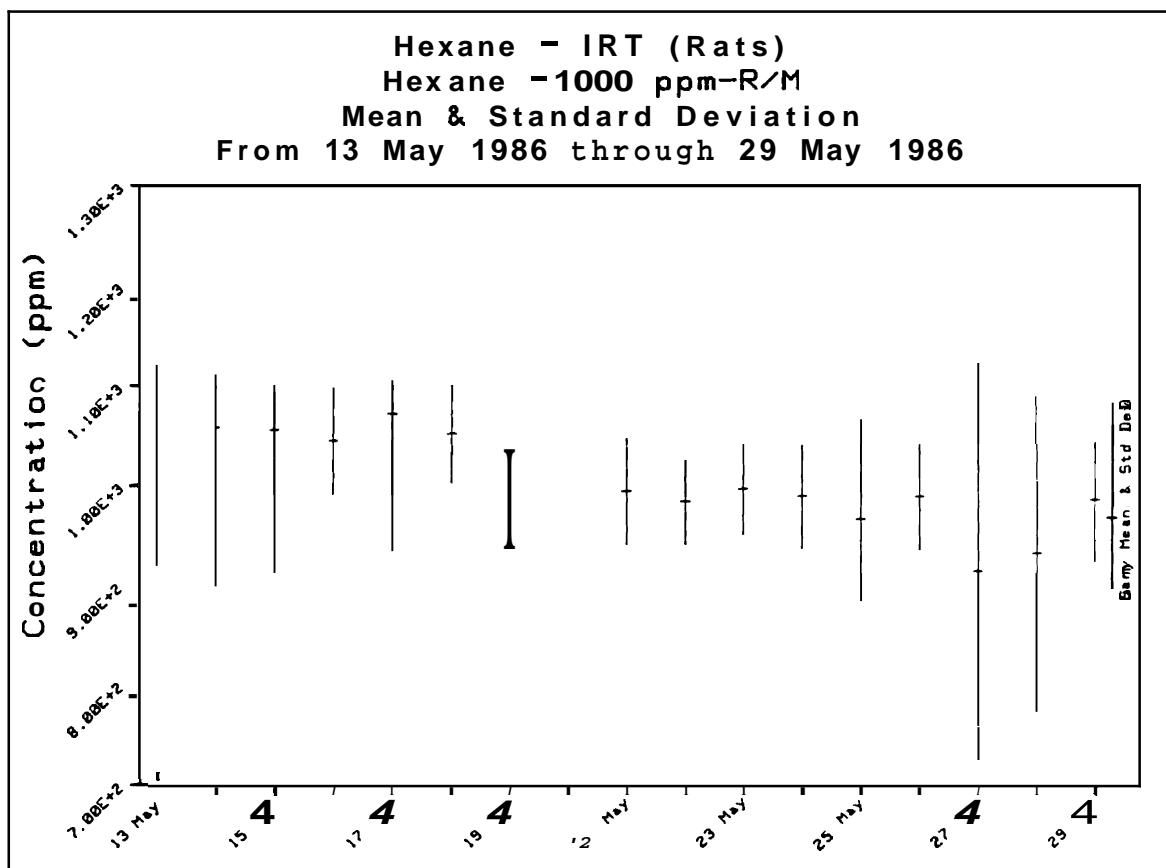
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	1.80E+2 to 2.20E+2		
								N in	% N in	
13 May 1986	1.91E+2	95%	3.616E+1	19%	2.05E+2	7.14E-1	30.	29.	97%	
14 May 1986	2.02E+2	101%	4.529E+0	2%	2.08E+2	1.89E+2	32.	32.	100%	
15 May 1986	2.01E+2	100%	1.756E+1	9%	2.76E+2	1.73E+2	35.	32.	91%	
16 May 1986	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%	

Hexane - IRT (Rats)
Hexane - 288 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



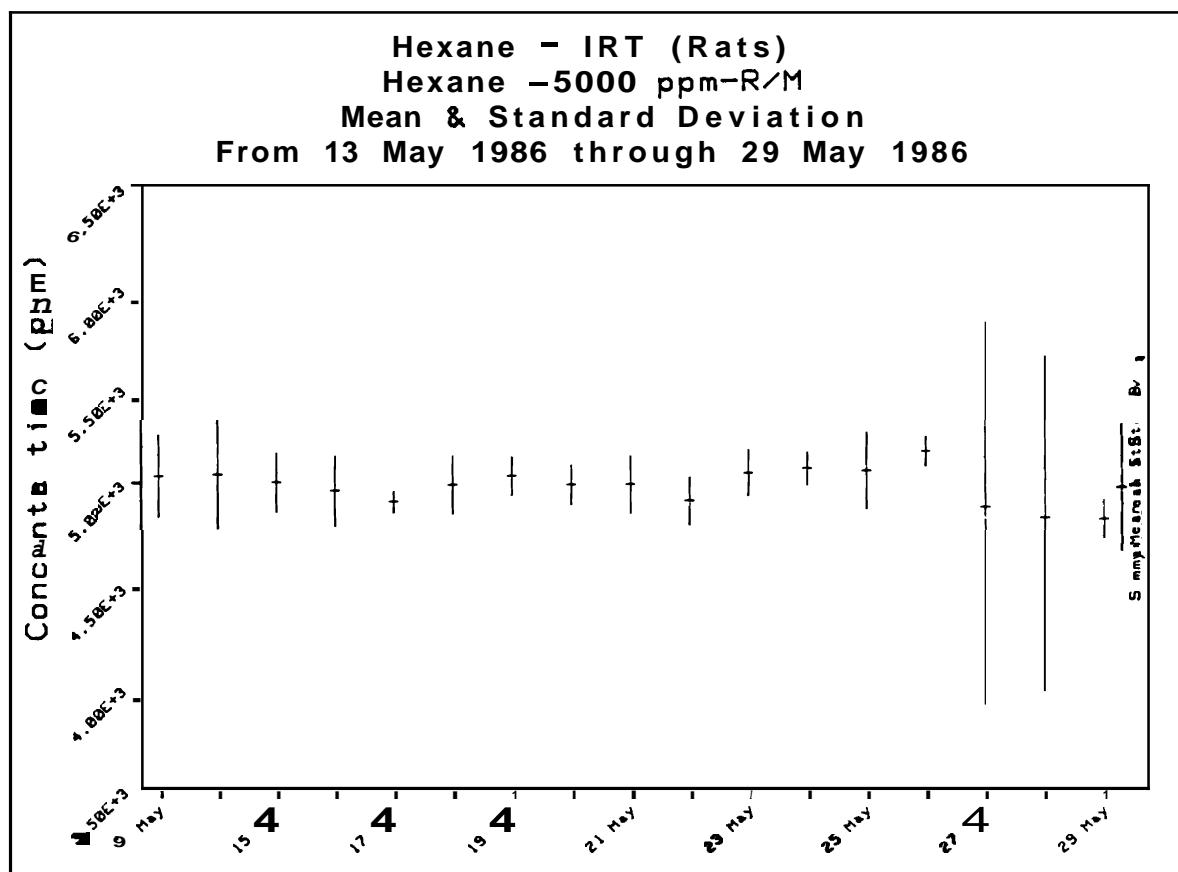
n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							9.00E+2 to 1.10E+3		
Sumry Data for: Hexane -1000 ppm-R/M/Concentration									
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%
Sumry	9.94E+2	99%	8.891E+1	9%	1.47E+3	2.70E+1	629.	560.	89%



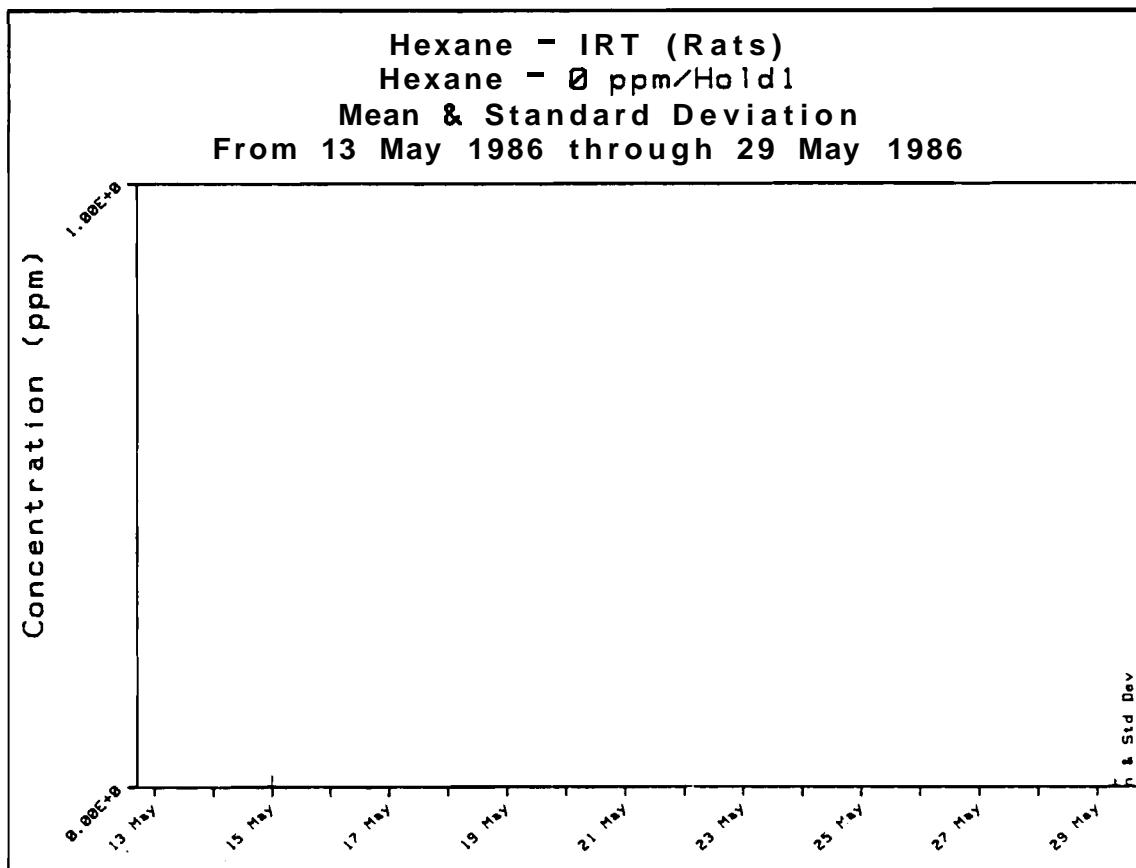
n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							4.50E+3 to 5.50E+3		
Summary Data for: Hexane -5000 ppm-R/M/Concentration									
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%



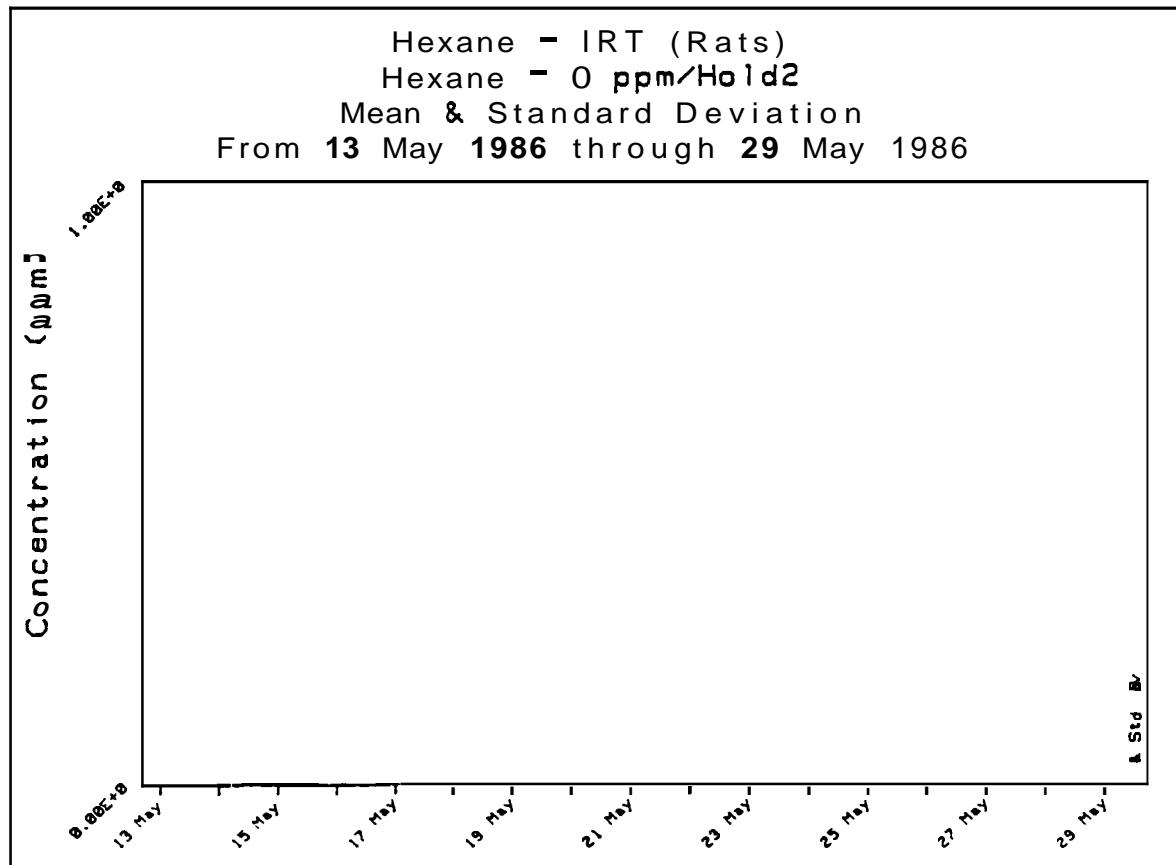
n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							0.00E+0 to 1.00E+0		
Summary Data for: Hexane - 0 ppm/Hold1/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	0%	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							0.00E+0 to 1.00E+0		
Summary Data for: Hexane - 0 ppm/Hold2/Concentration									
Date	Mean	X Taraet	Std Dev	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%

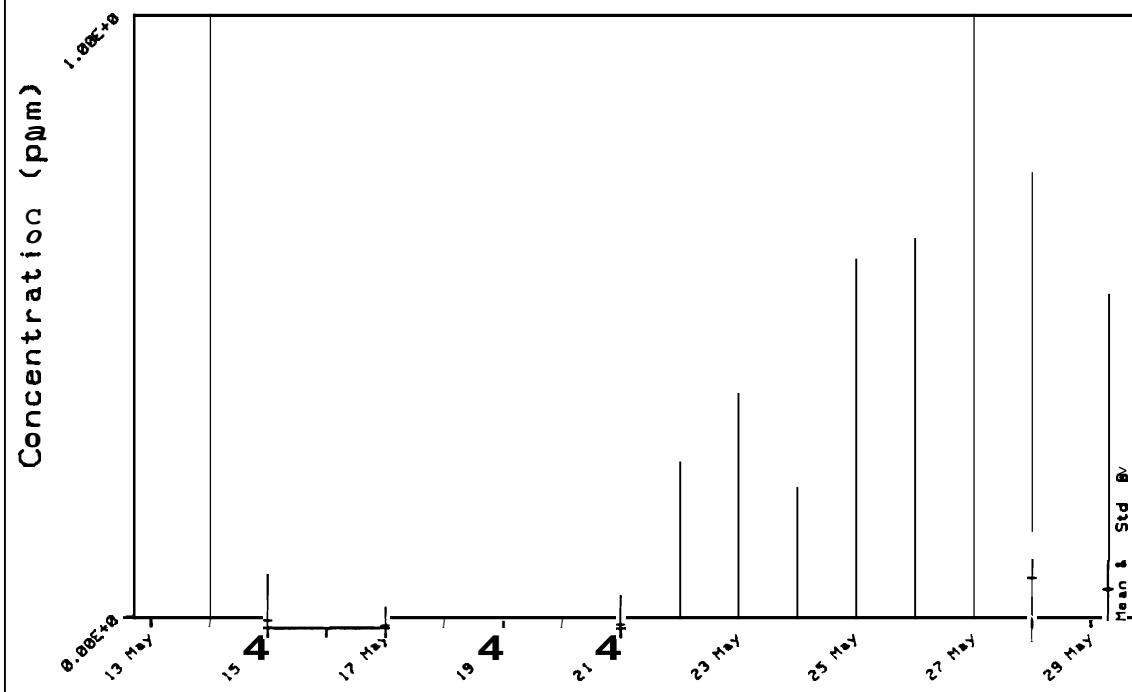


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

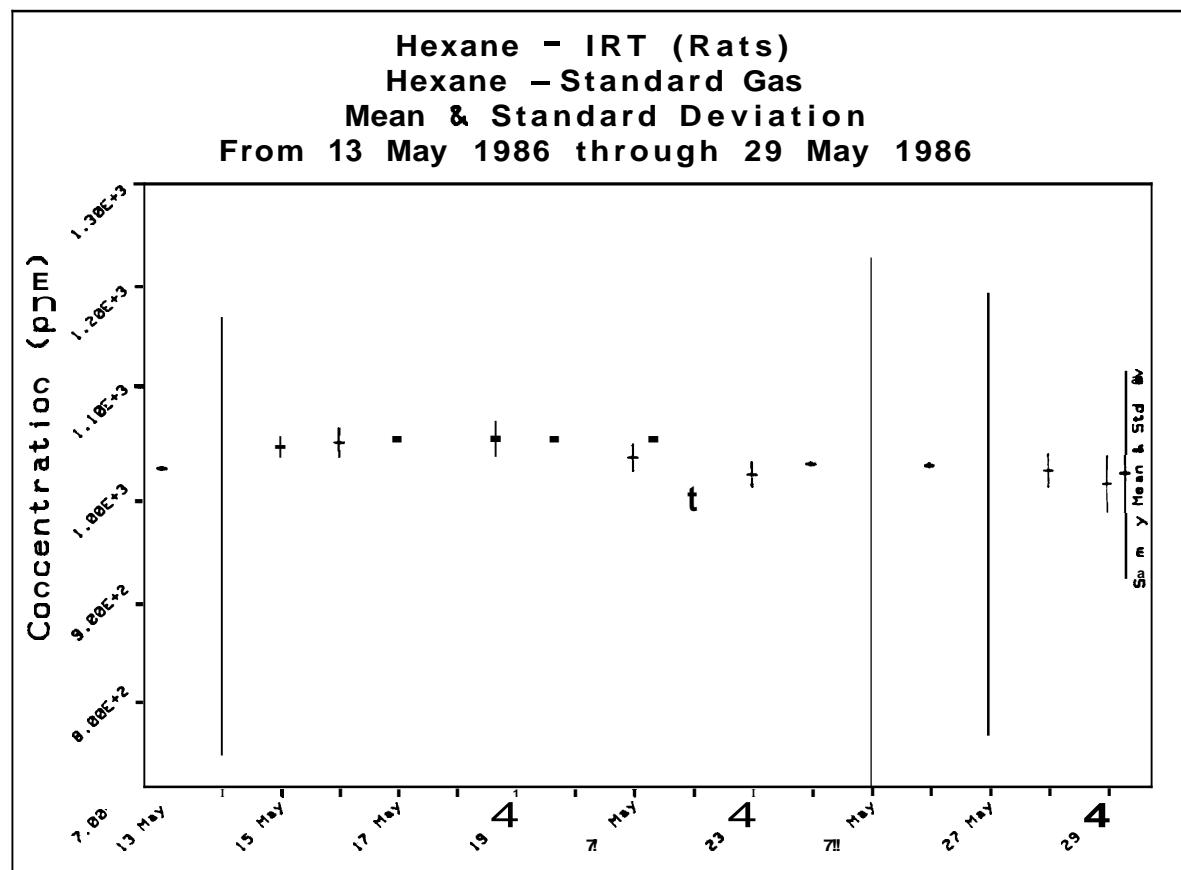
Date	Mean	% Target	Room/Concentration			0.00E+0 to 1.00E+0		
			Std Dev	% RSD	Maximum	Minimum	N	N in
13 May 1986	0.00E+0	0%	0.000E+0	0%	0.00E+0	0.00E+0	31.	31. 100%
14 May 1986	4.81E-1	0%	1.338E+0	278%	4.18E+0	0.00E+0	34.	30. 88%
15 May 1986	1.27E-2	0%	7.428E-2	583%	4.33E-1	0.00E+0	34.	34. 100%
16 May 1986	0.00E+0	0%	0.000E+0	0%	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	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	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	0%	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%	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%

Hexane - IRT (Rats)
Hexane - Room
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



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%

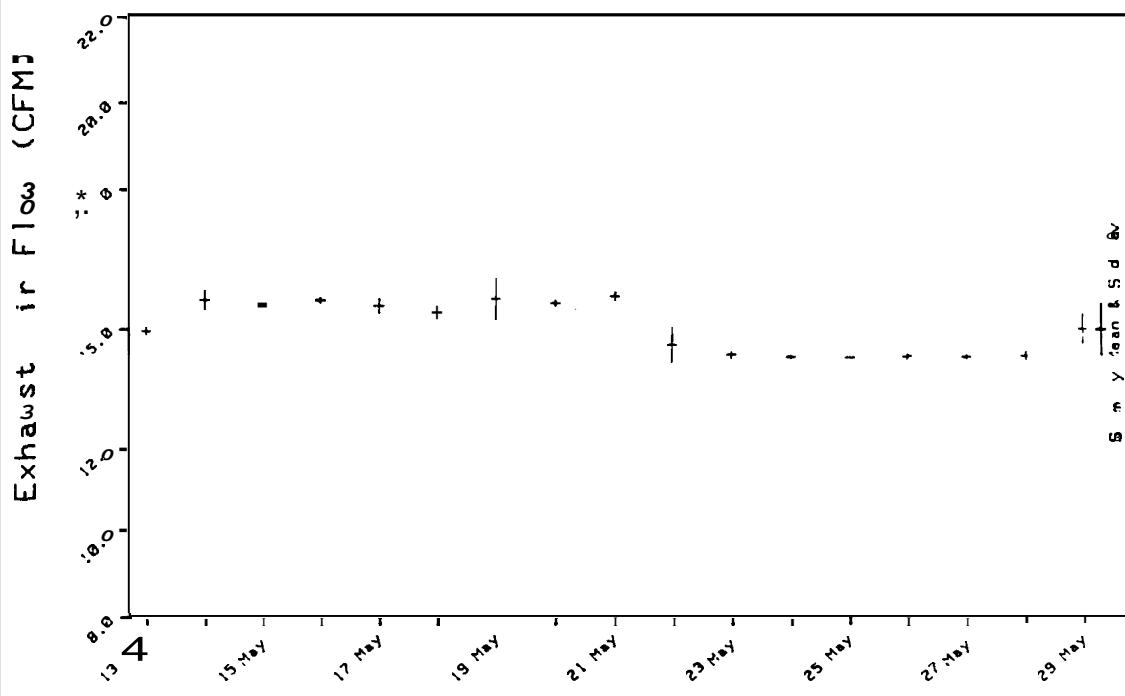


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	12.0 to 18.0	
								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%

Hexane - IRT (Rats)
Hexane - 0 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986

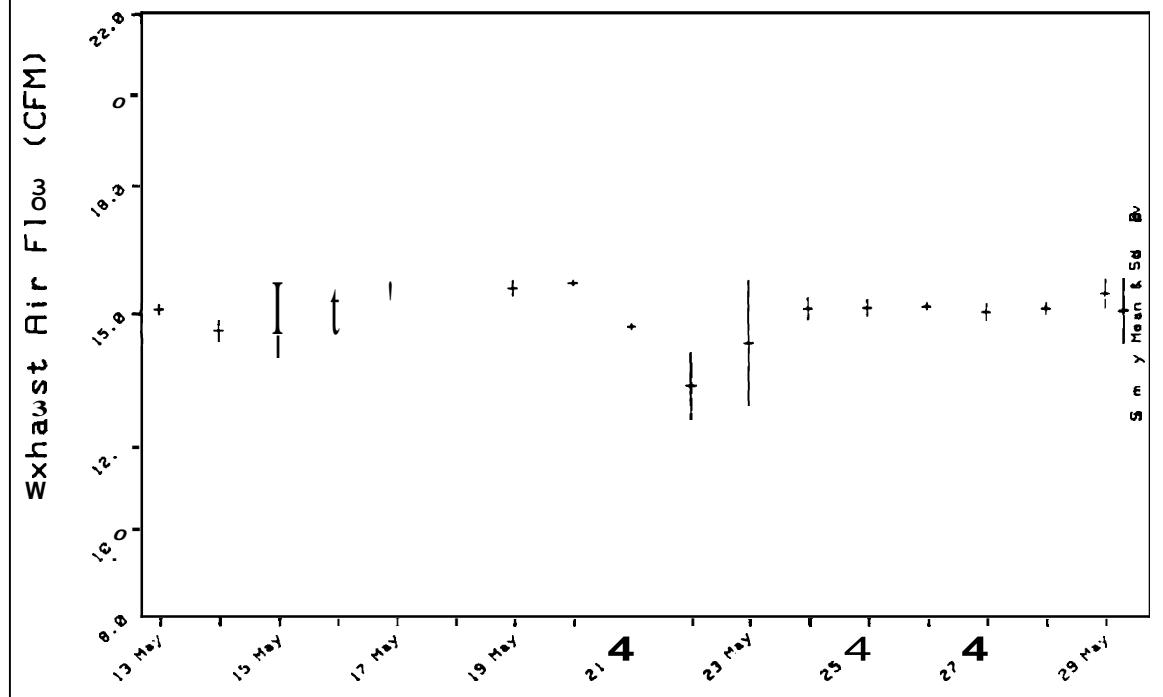


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Date	Mean	% Target	Std Dev	X RSD	Maximum	Minimum	12.0 to 18.0	
							N	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	0%	15.3	15.1	7.	7. 100%
19 May 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%

Hexane - IRT (Rats)
Hexane - 200 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986

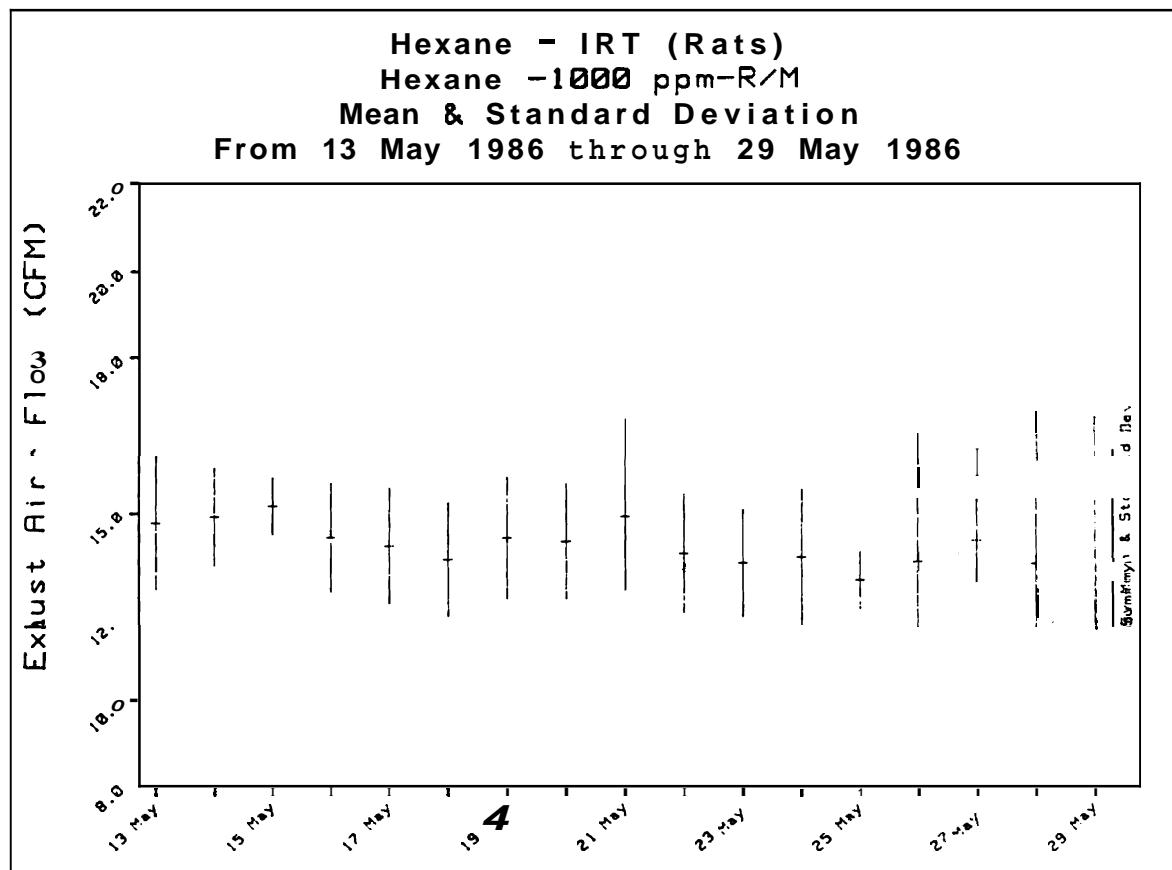


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

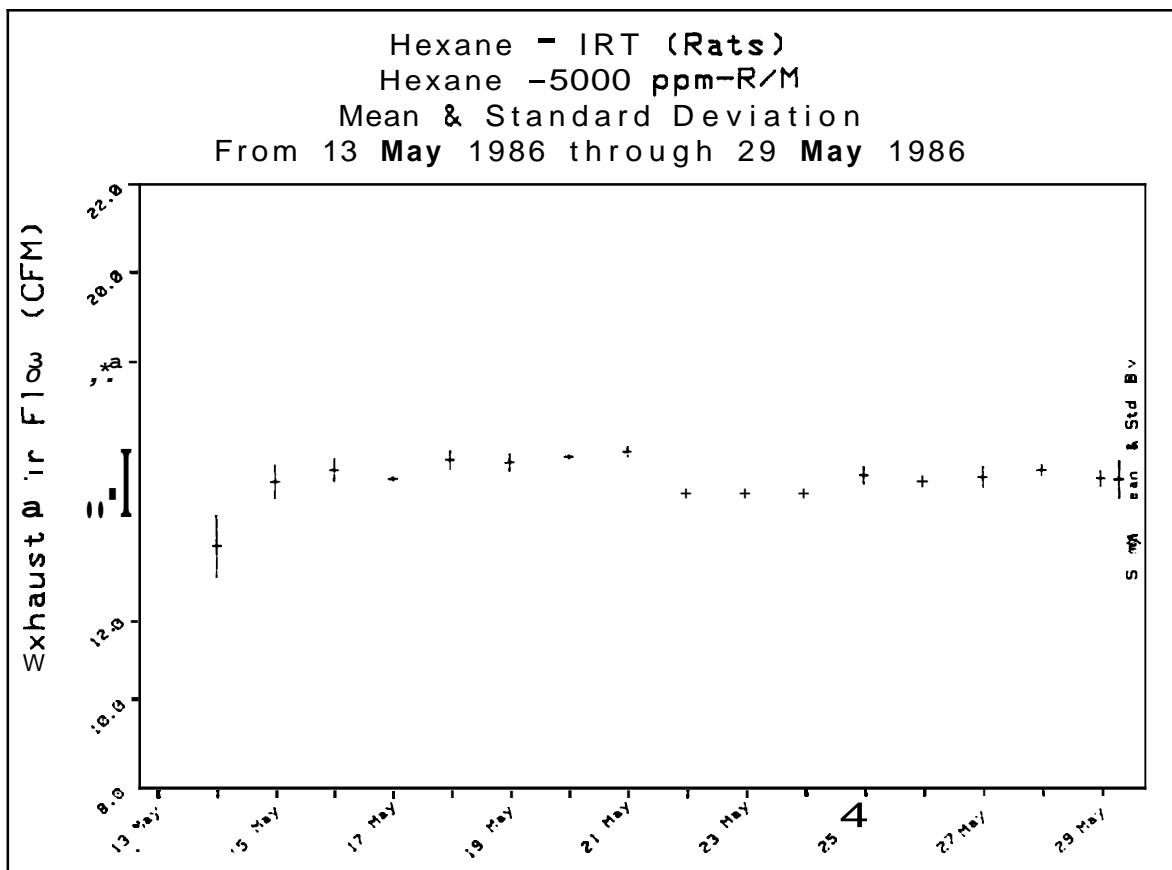
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	14.8	99%	1.56	11%	16.6	12.5	5.	5.	100%
14 May 1986	14.9	99%	1.14	8%	16.8	13.8	5.	5.	100%
15 May 1986	15.2	101%	.66	4%	15.8	14.0	6.	6.	100%
16 May 1986	14.4	96%	1.26	9%	15.8	12.8	6.	6.	100%
17 May 1986	14.2	95%	1.35	9%	15.8	12.7	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

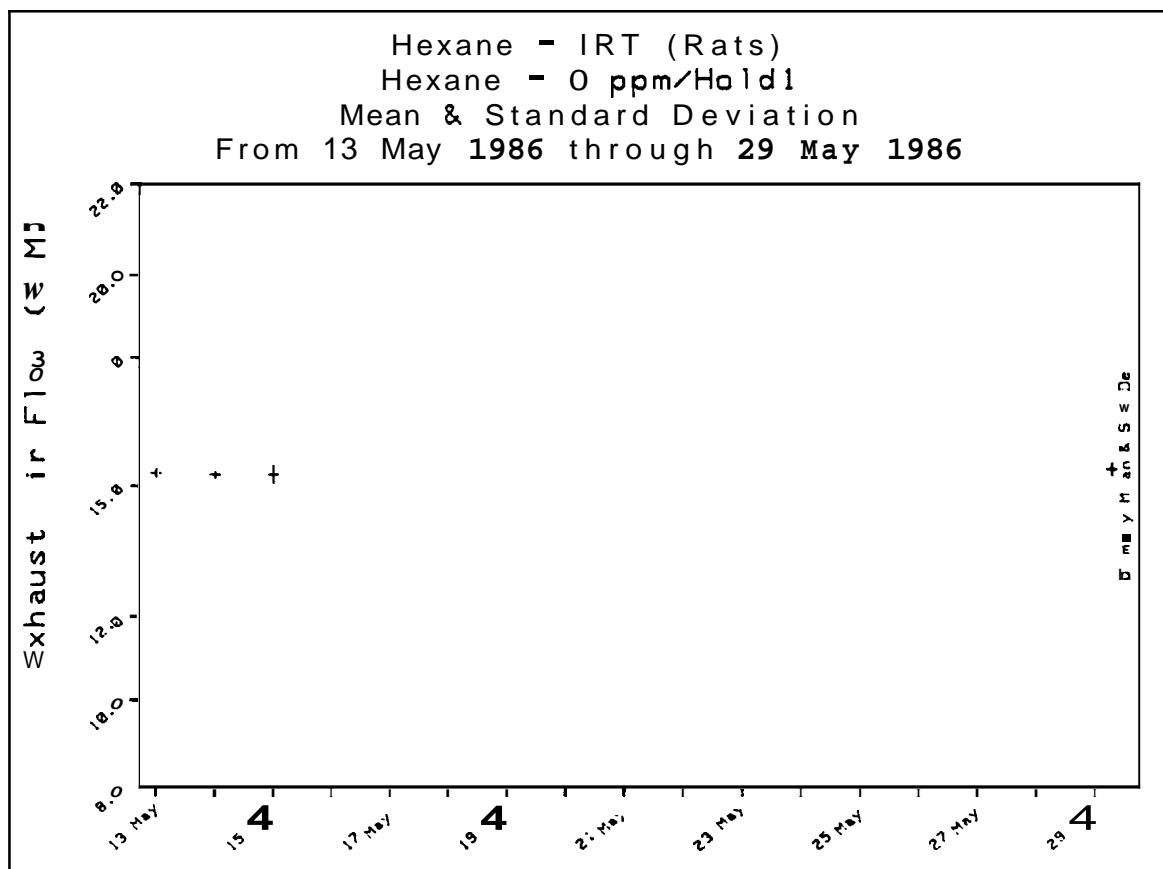
Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	12.0 to 18.0		
							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%



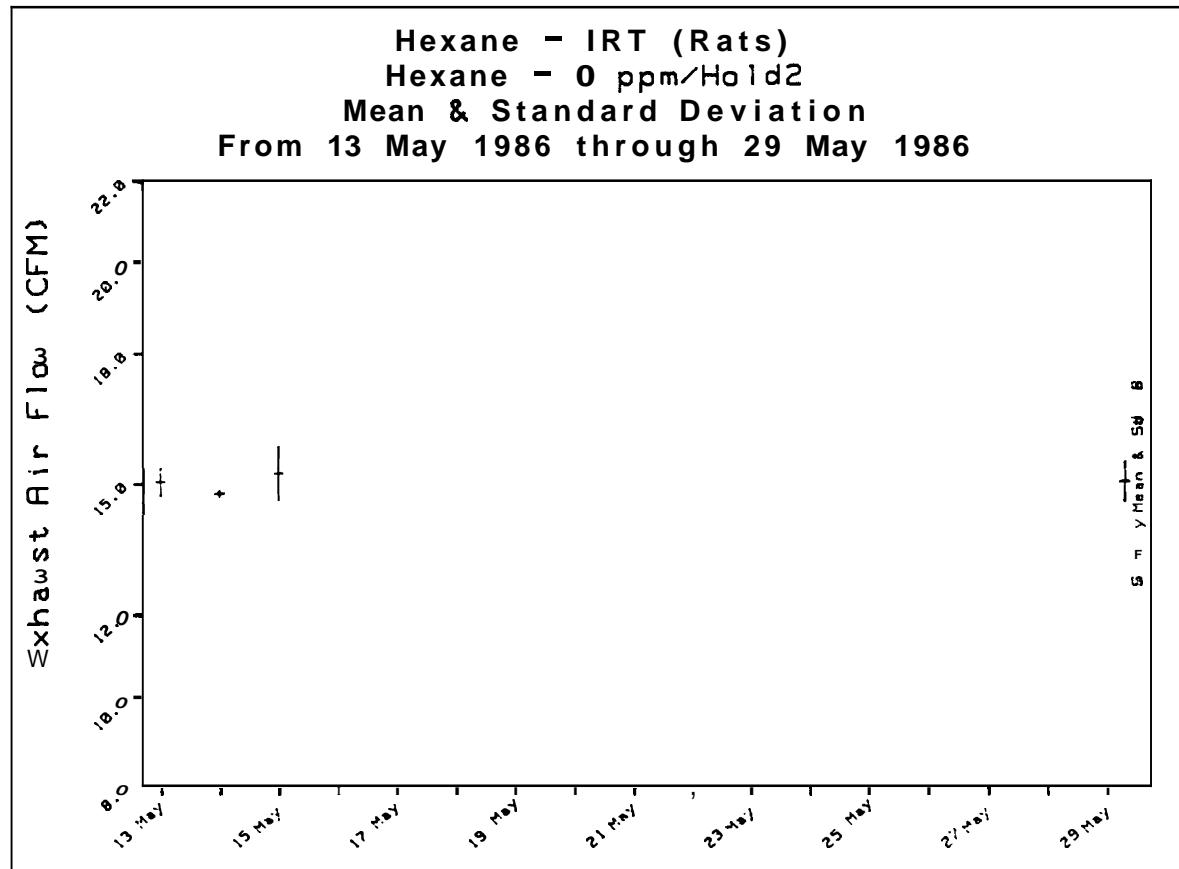
n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							12.0 to 18.0		
Summary Data for: Hexane - 0 ppm/Hold1/Exhaust Air Flow									
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							12.0 to	18.0	
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%

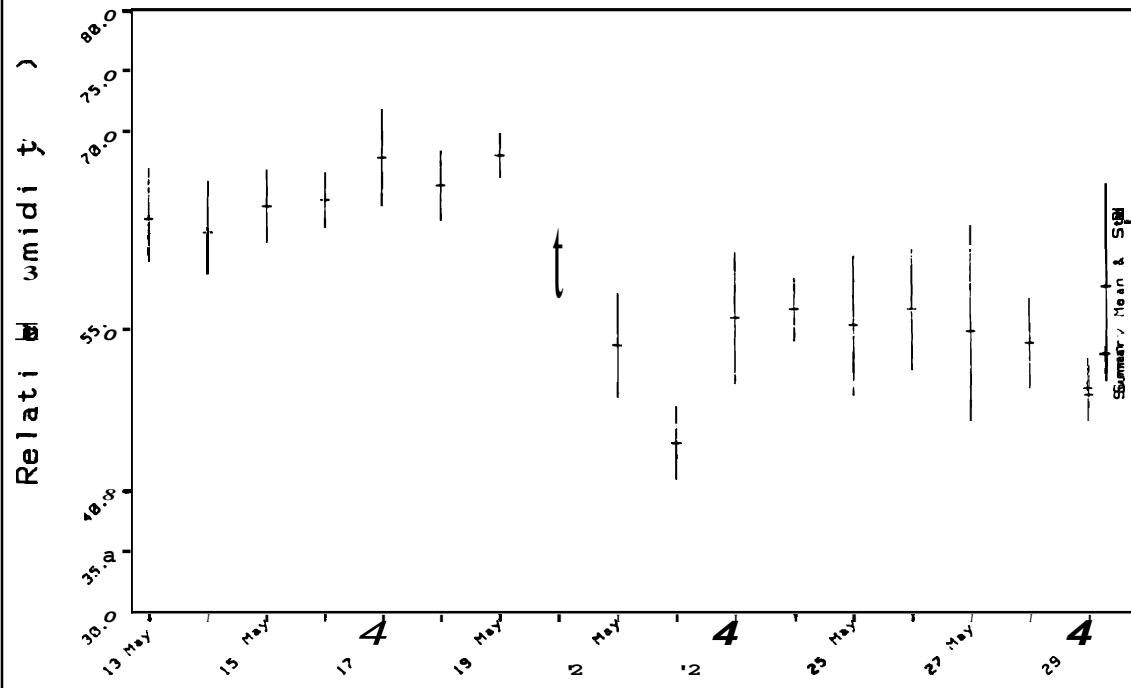


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	40.0 to	70.0
								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%

Hexane - IRT (Rats)
Hexane - 0 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



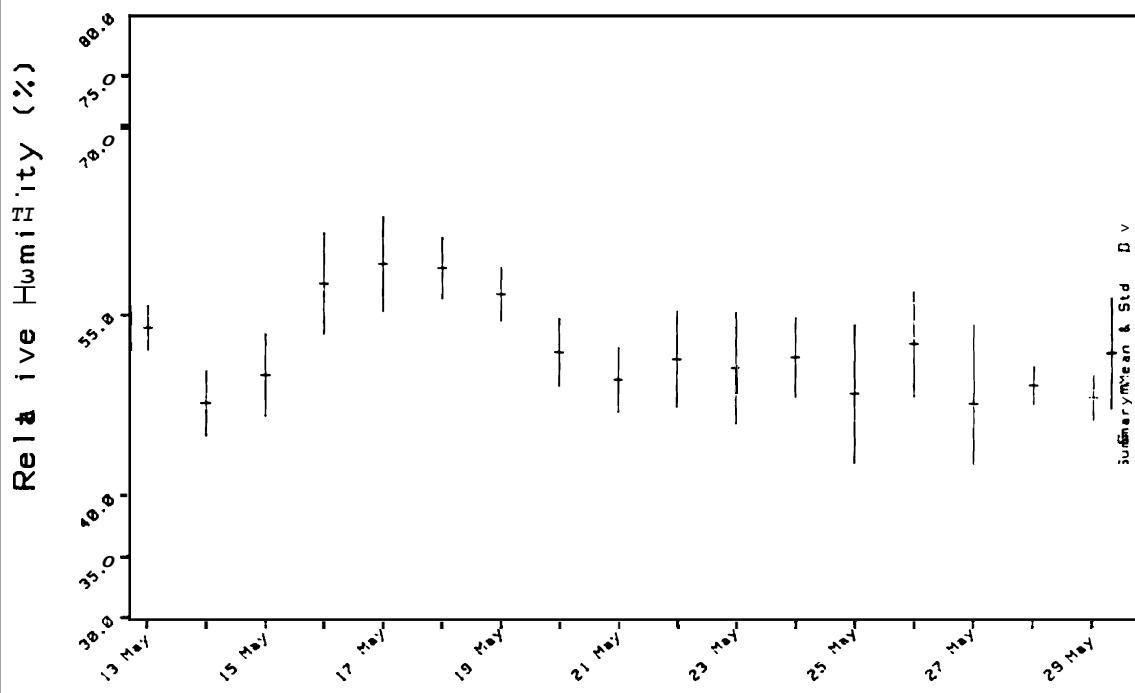
n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Summary Data for: Hexane - 200 ppm-R/M/Relative Humidity

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	40.0 to 70.0	% 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%

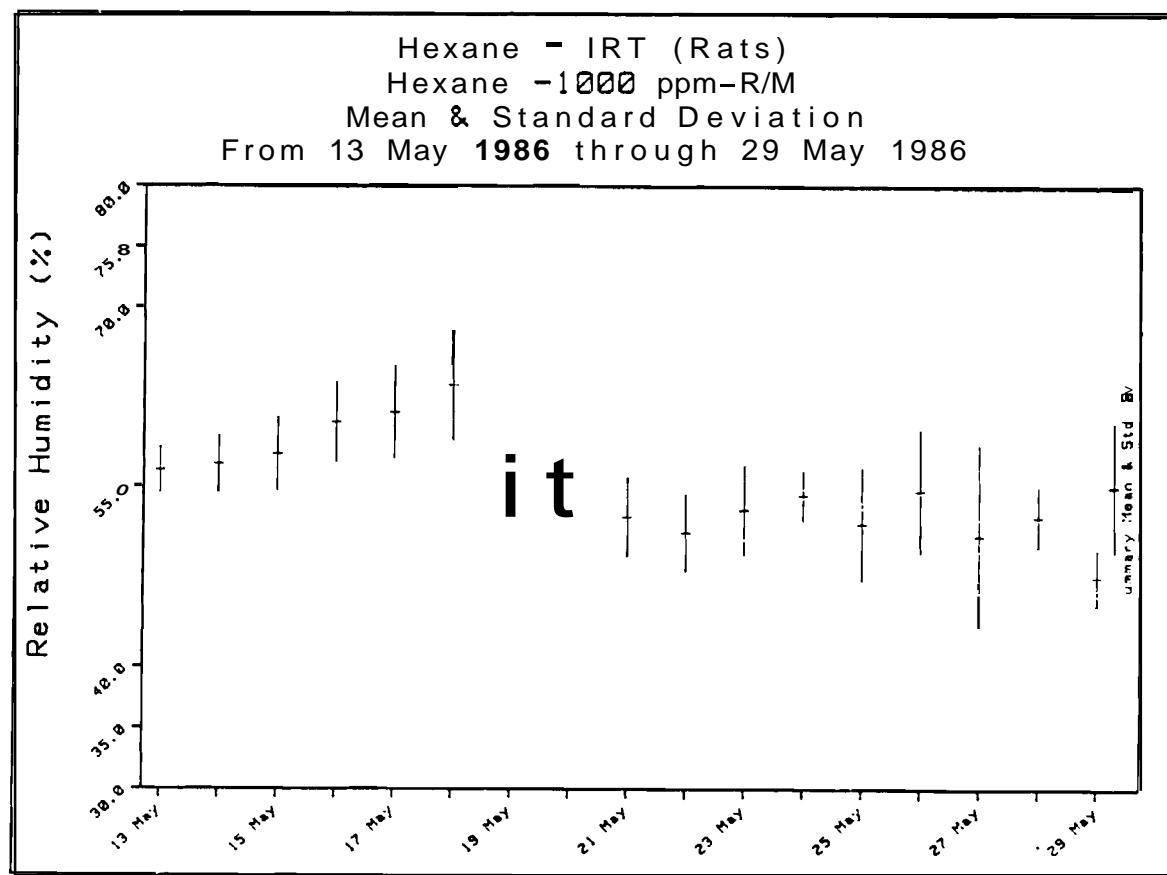
Hexane - IRT (Rats)
Hexane - 200 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



n-Hexane Rat Teratology Study
Appendix B - Exposure

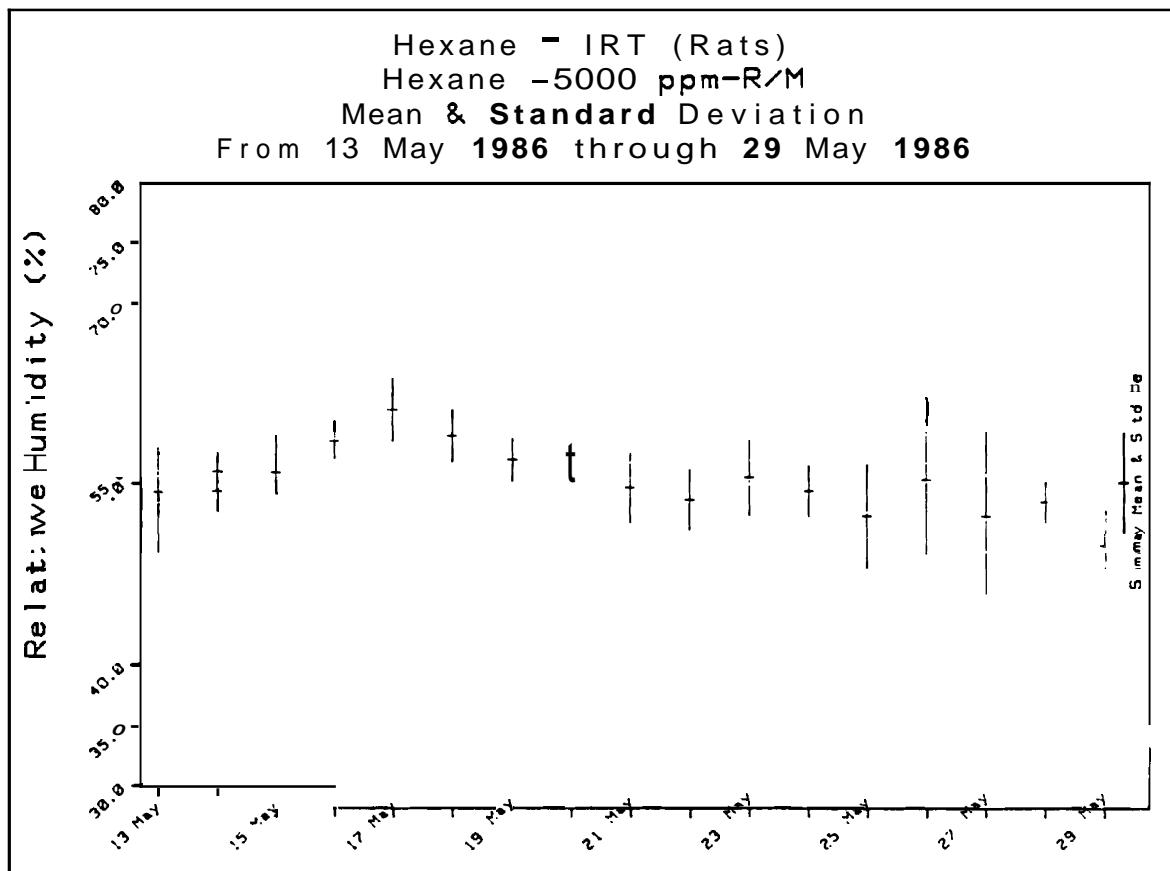
Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	40.0 to 70.0		
							N	N in	% N in
13 May 1986	56.5	103%	1.91	3%	59.0	55.0	4.	4.	100%
14 May 1986	57.0	104%	2.35	4%	59.0	53.0	5.	5.	100%
15 May 1986	57.8	105%	3.06	5%	61.0	52.0	6.	6.	100%
16 May 1986	60.5	110%	3.33	6%	65.0	57.0	6.	6.	100%
17 May 1986	61.3	112%	3.83	6%	65.0	56.0	6.	6.	100%
18 May 1986	63.6	116%	4.54	7%	69.0	59.0	7.	7.	100%
19 May 1986	56.2	102%	2.56	5%	59.0	53.0	6.	6.	100%
20 May 1986	55.7	101%	2.36	4%	59.0	52.0	7.	7.	100%
21 May 1986	52.6	96%	3.26	6%	56.0	46.0	7.	7.	100%
22 May 1986	51.3	93%	3.20	6%	54.0	46.0	7.	7.	100%
23 May 1986	53.1	97%	3.72	7%	57.0	47.0	7.	7.	100%
24 May 1986	54.3	99%	2.07	4%	56.0	51.0	6.	6.	100%
25 May 1986	52.0	95%	4.69	9%	58.0	44.0	6.	6.	100%
26 May 1986	54.7	99%	5.09	9%	62.0	48.0	7.	7.	100%
27 May 1986	51.0	93%	7.54	15%	58.0	40.0	6.	6.	100%
28 May 1986	52.6	96%	2.51	5%	56.0	49.0	7.	7.	100%
29 May 1986	47.6	86%	2.30	5%	52.0	45.0	7.	7.	100%
Summary	55.0	100%	5.33	10%	69.0	40.0	107.	107.	100%



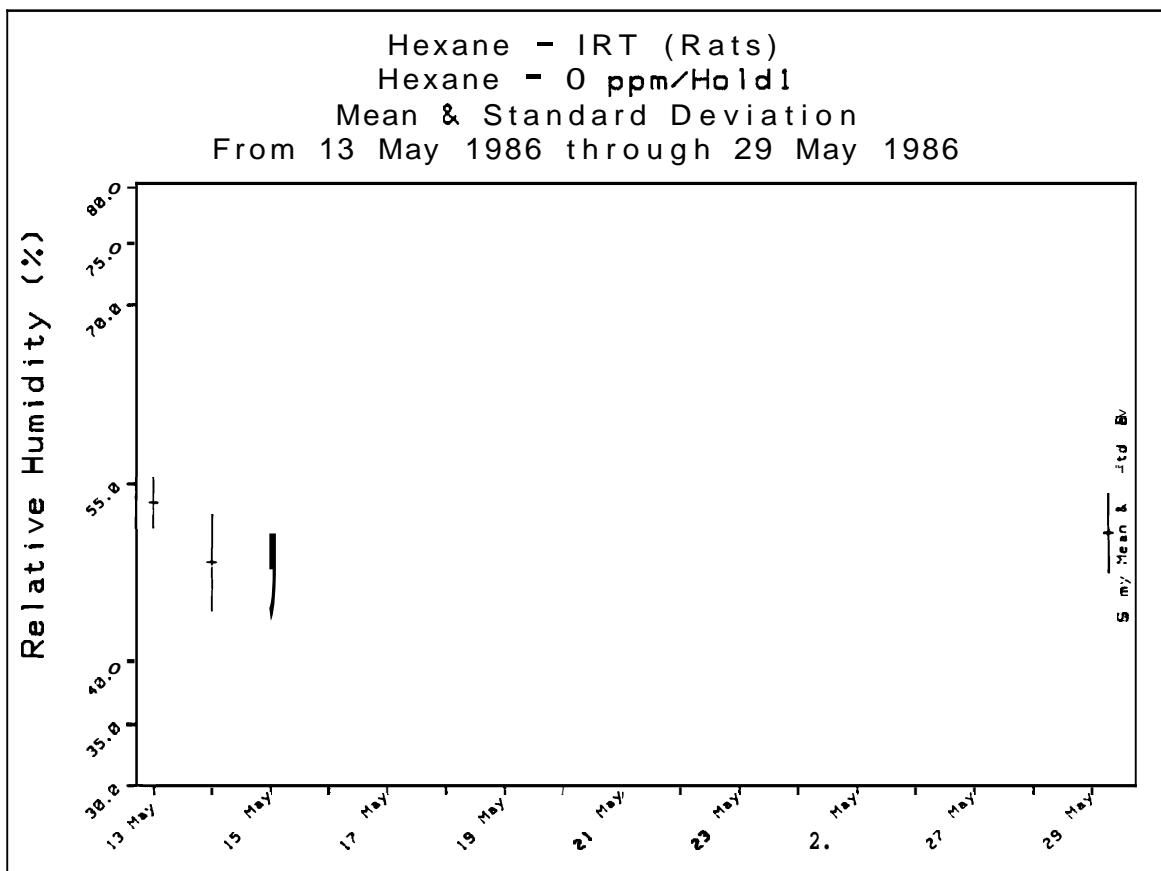
n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							40.0 to 70.0	
Summary Data for: Hexane -5000 ppm-R/M/Relative Humidity							N in	X N in
Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum		
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							40.0 to 70.0	
Summary Data for: Hexane - 0 ppm/Hold1/Relative Humidity							N in	% N in
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum		
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

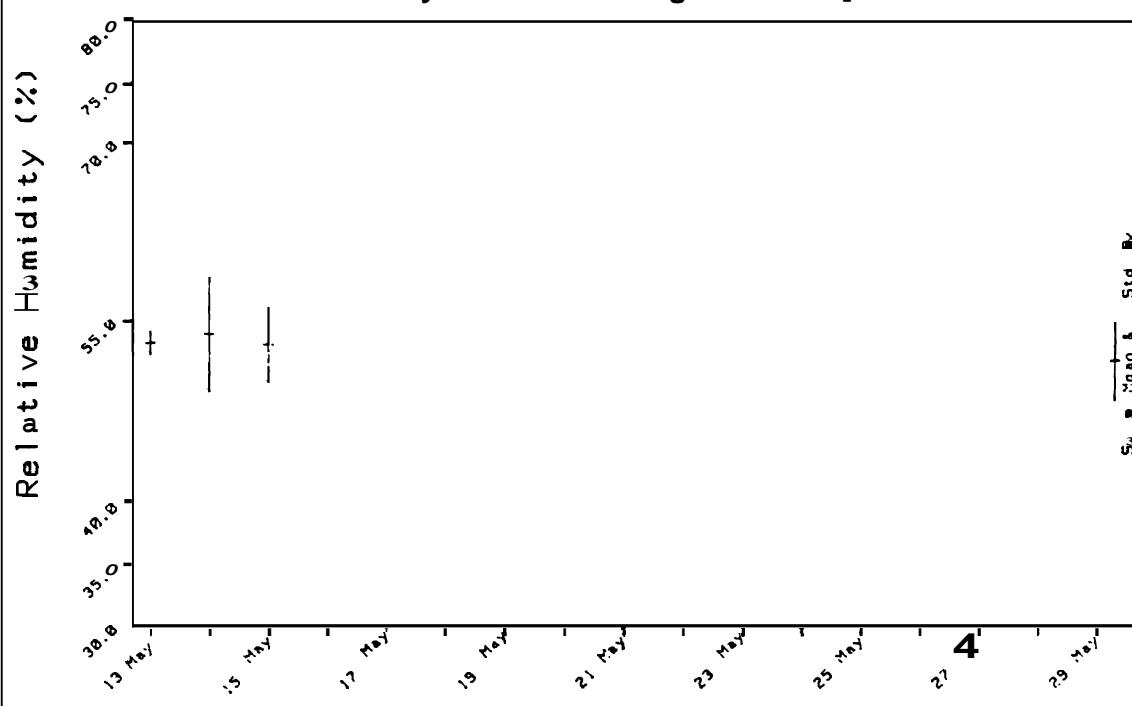
Date	Mean	X Target	Std Dev	X RSD	Maximum	Minimum	N	40.0 to 70.0
							N in	X N in
13 May 1986	53.2	97%	.96	2%	54.0	52.0	4.	4. 100%
14 May 1986	54.0	98%	4.74	9%	59.0	48.0	5.	5. 100%
15 May 1986	53.2	97%	3.13	6%	57.0	50.0	6.	6. 100%
16 May 1986								
17 May 1986								
18 May 1986								
19 May 1986								
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%

Hexane - IRT (Rats)

Hexane - 0 ppm/Hold2

Mean & Standard Deviation

From 13 May 1986 through 29 May 1986

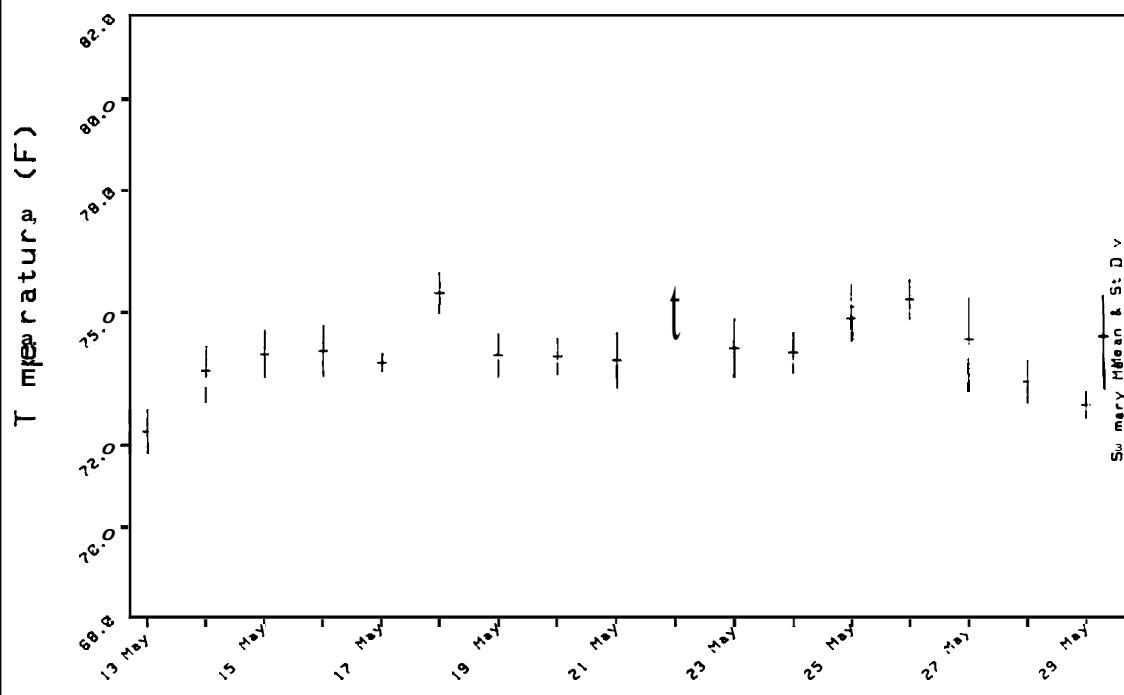


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Date	Summary Data for: Hexane - 0 ppm-R/M/Temperature						72.0 to 78.0		
	Mean	% Target	Std Dev	% RSD	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%

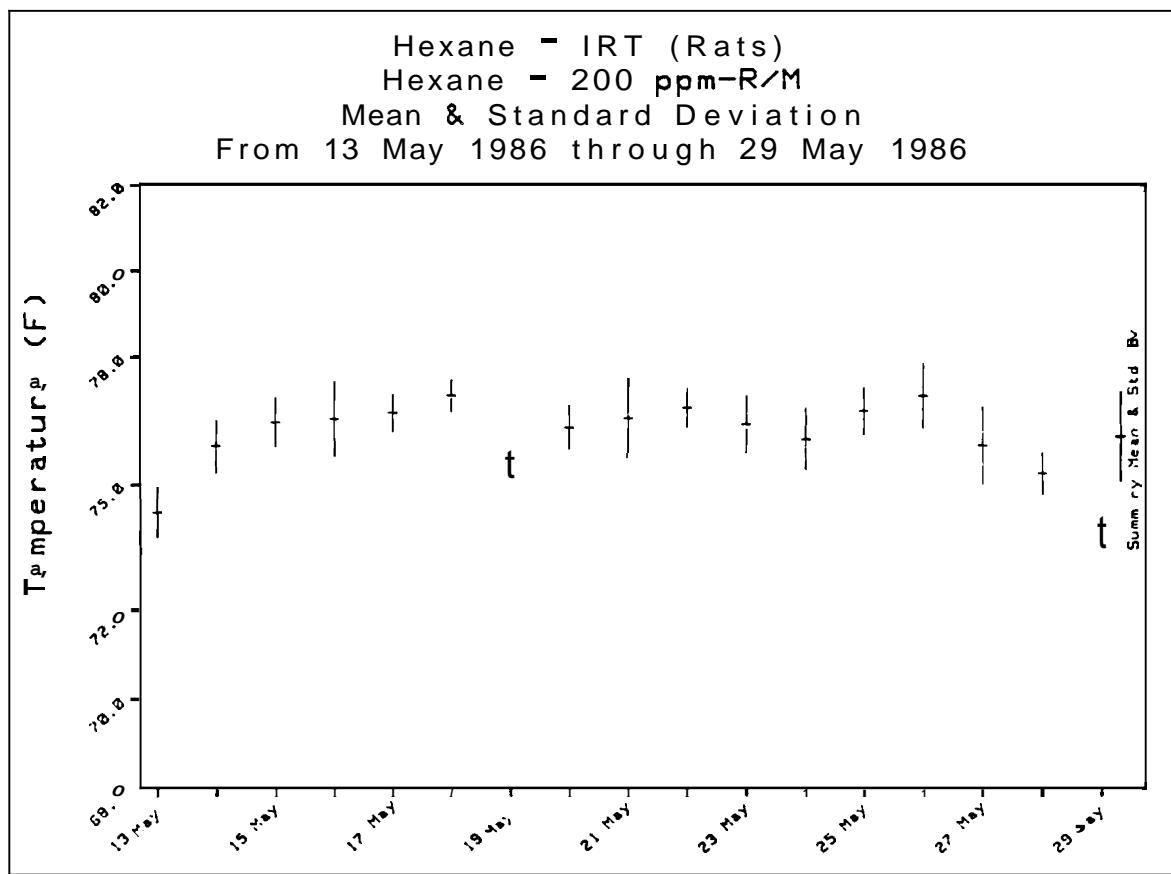
Hexane - IRT (Rats)
Hexane - 0 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



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

Summary Data for: Hexane - 200 ppm-R/M/Temperature

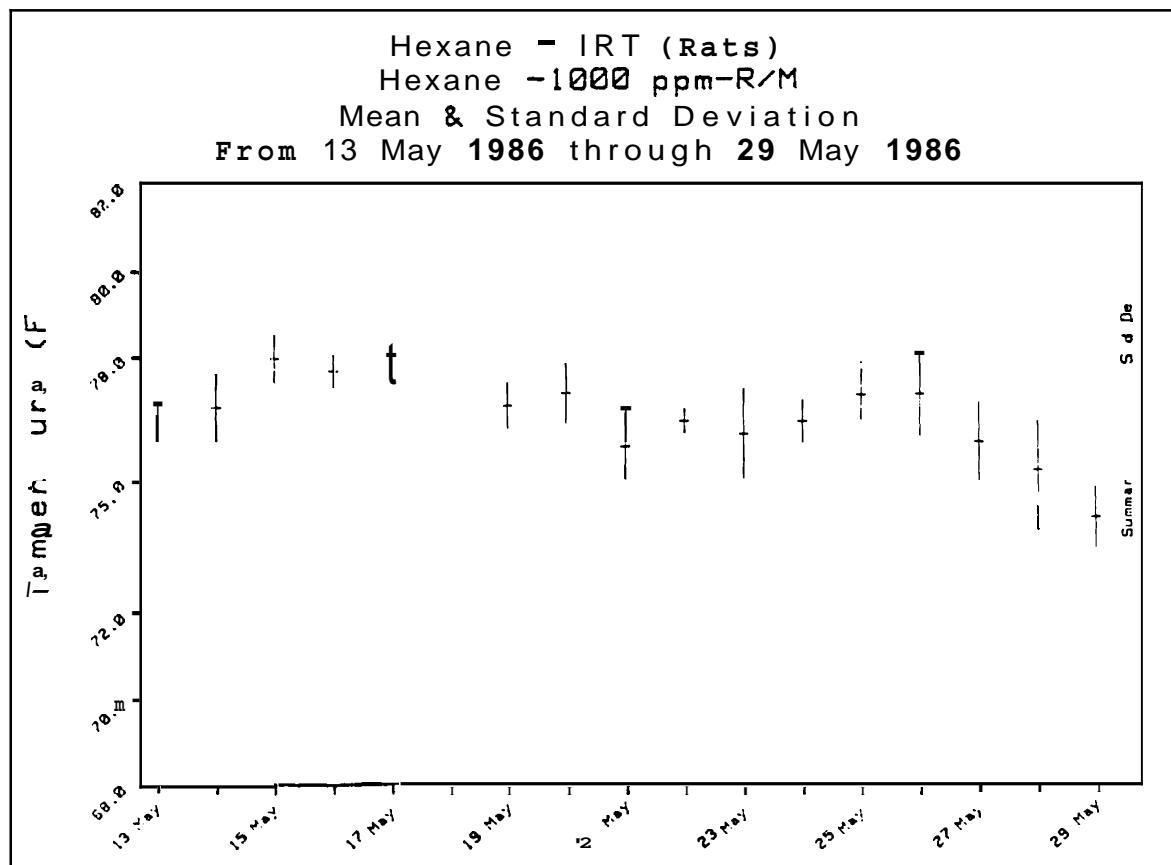
Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	72.0 to 78.0 % N in
13 May 1986	74.4	99%	.58	1%	75.3	73.7	5.	5.	100%
14 May 1986	75.9	101%	.62	1%	76.6	75.2	5.	5.	100%
15 May 1986	76.5	102%	.57	1%	77.0	75.4	6.	6.	100%
16 May 1986	76.5	102%	.88	1%	77.4	75.5	5.	5.	100%
17 May 1986	76.7	102%	.43	1%	77.1	75.9	6.	6.	100%
18 May 1986	77.1	103%	.37	0%	77.4	76.5	7.	7.	100%
19 May 1986	75.5	101%	.34	0%	76.1	75.1	6.	6.	100%
20 May 1986	76.4	102%	.50	1%	77.0	75.6	6.	6.	100%
21 May 1986	76.6	102%	.93	1%	77.4	74.7	7.	7.	100%
22 May 1986	76.8	102%	.45	1%	77.4	76.1	6.	6.	100%
23 May 1986	76.4	102%	.67	1%	77.2	75.6	7.	7.	100%
24 May 1986	76.1	101%	.72	1%	77.1	75.0	7.	7.	100%
25 May 1986	76.7	102%	.54	1%	77.2	75.8	6.	6.	100%
26 May 1986	77.1	103%	.75	1%	78.3	76.1	7.	6.	86%
27 May 1986	75.9	101%	.89	1%	76.7	74.0	7.	7.	100%
28 May 1986	75.3	100%	.48	1%	75.9	74.5	7.	7.	100%
29 May 1986	73.9	99%	.40	1%	74.5	73.3	6.	6.	100%
Summary	76.1	102%	1.03	1%	78.3	73.3	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

Date	Summary Data for: Hexane -1000 ppm-R/M/Temperature						72.0 to 78.0		
	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%

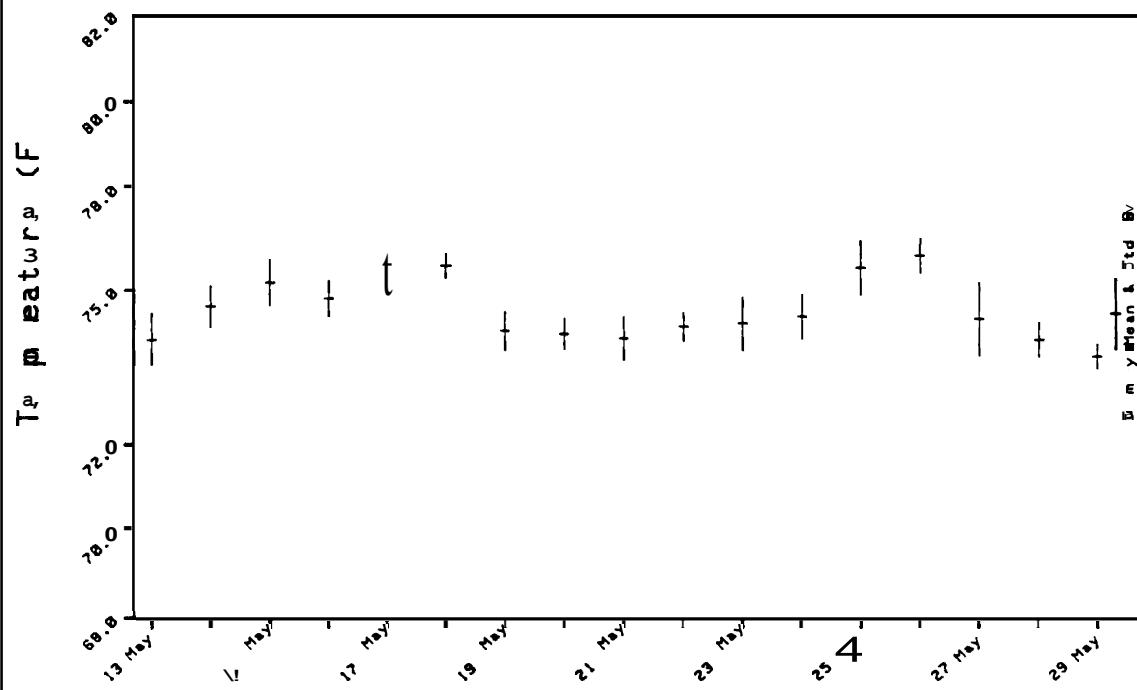


n-Hexane Rat Teratology Study
Appendix B - Exposure

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

Date	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	72.0 to 78.0	
								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%

Hexane - IRT (Rats)
Hexane - 5888 ppm-R/M
Mean & Standard Deviation
From 13 May 1986 through 29 May 1986



n-Hexane Rat Teratology Study
 Appendix B - Exposure

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

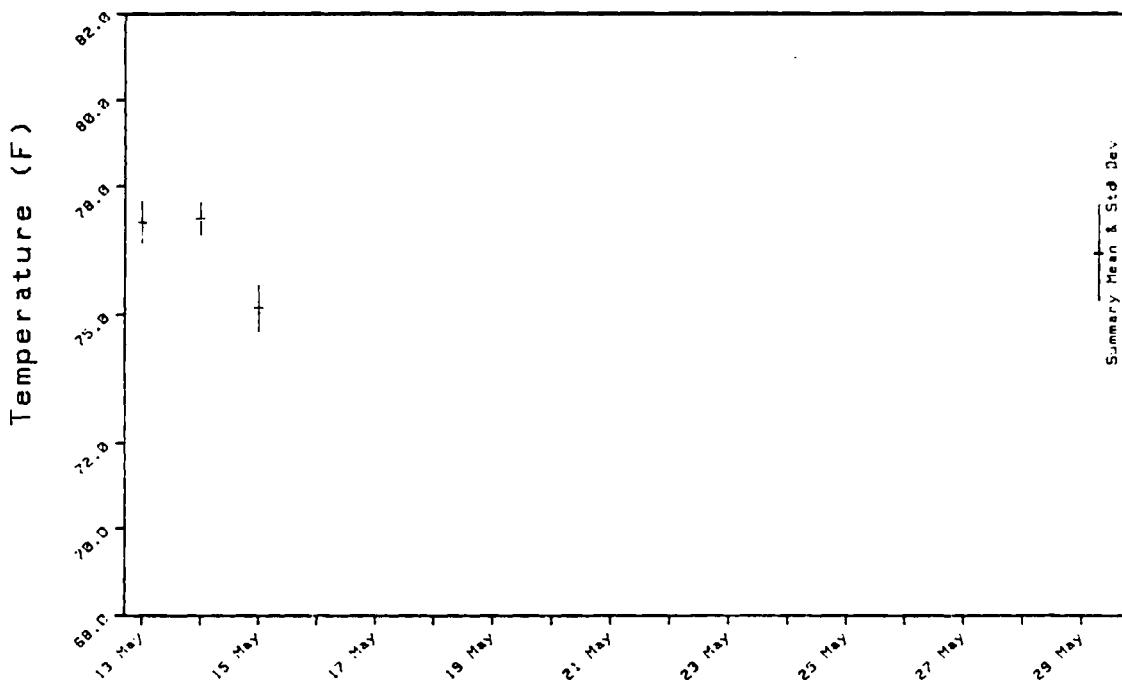
Date	Summary Data for: Hexane - 0 ppm/Hold1/Temperature						72.0 to 78.0		
	Mean	% Target	Std Dev	% RSD	Maximum	Minimum	N	N in	% N in
13 May 1986	77.2	103%	.48	1%	77.7	76.5	5.	5.	100%
14 May 1986	77.3	103%	.38	0%	77.7	76.9	5.	5.	100%
15 May 1986	75.2	100%	.55	1%	75.9	74.3	6.	6.	100%
16 May 1986									
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%

Hexane - IRT (Rats)

Hexane - 0 ppm/Hold1

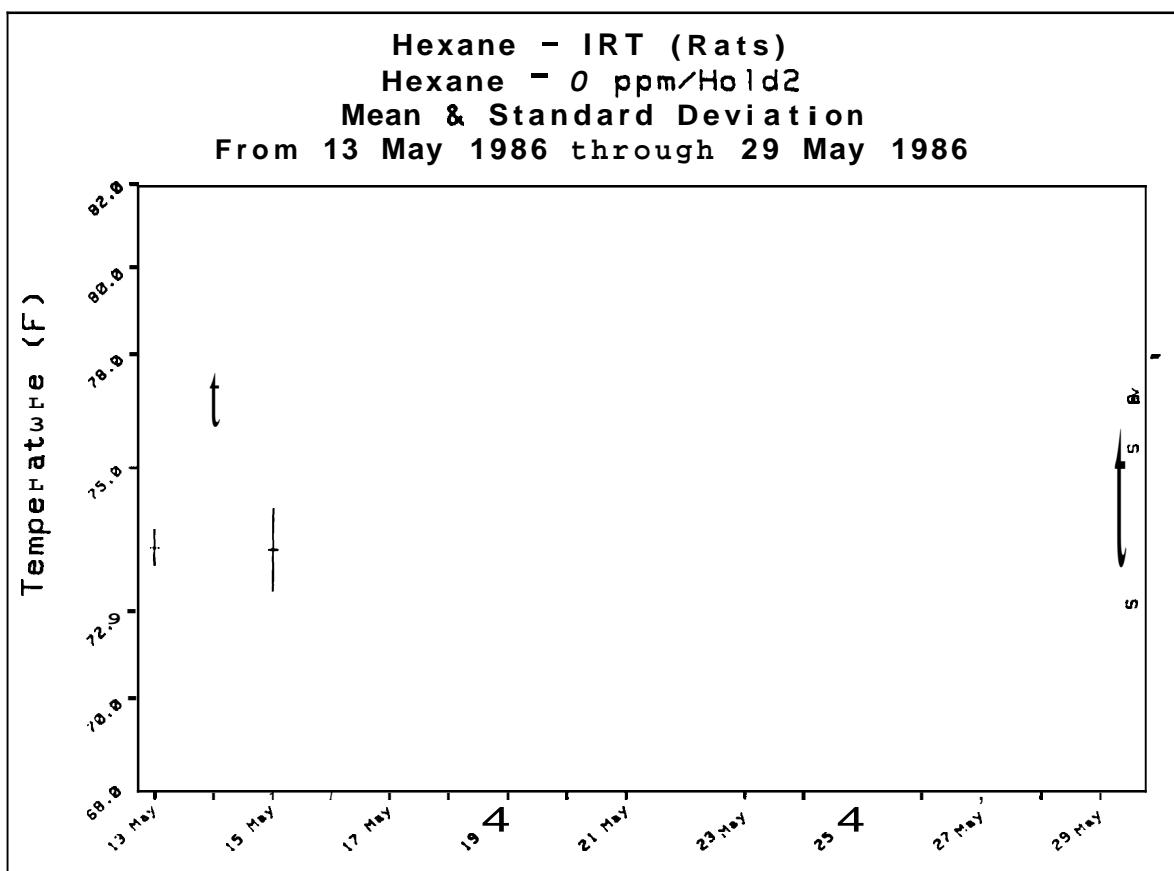
Mean & Standard Deviation

From 13 May 1986 through 29 May 1986



n-Hexane Rat Teratology Study
Appendix B - Exposure

Daily Summation For Hexane - IRT (Rats) From 13 May 1986 through 29 May 1986							72.0 to 78.0		
Summary Data for: Hexane - 0 ppm/Hold2/Temperature									
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

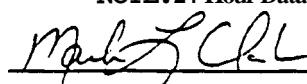
INCLUDES DISCUSSIONS AND/OR EXPLANATIONS OF PROBLEMS AFFECTING ANIMAL ENVIRONMENT AND EXPOSURES. EXPLANATIONS ARE INCLUDED FOR DATA IN WHICH THERE WERE EXCURSIONS OF DAILY MEAN OR STANDARD DEVIATION BEYOND ALLOWABLE OPERATING LIMITS OR EXCURSIONS OF INDIVIDUAL DATUM BEYOND CRITICAL LIMITS.

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:



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 ± 100 ppm).

The executive **computer** hung up at 01:18 and failed to trigger the security **alarm**, 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** pprn 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 pprn 1st reading = 212.7 ppm
1000 pprn 1st reading = 1030 pprn
5000 pprn 1st reading = 4962 pprn

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 pprn 1st reading = 1008 pprn
5000 pprn 1st reading = 4717 pprn

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 pprn 1st reading = 192.8 pprn
1000 pprn 1st reading = 975.1 pprn
5000 pprn 1st reading = 4753 pprn

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 pprn 1st reading = 207.8 ppm
1000 pprn 1st reading = 977.1 pprn
5000 pprn 1st **reading** = 5110 pprn

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 care 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 **5000** ppm 1st reading = 5105 ppm
Twenty-five minutes after expiration of the **T₉₀**, the exposure system shut off for **unknown** reasons. Generation resumed 11 minutes later, however chamber concentrations recorded during this period exceeded the lower critical operating limits. Reported values were: **1000** ppm chamber, 1 reading = 540 ppm; and **5000** ppm chamber, 1 reading = 735 ppm During the next sample cycle, concentration in the **1000** ppm chamber (1 reading = 1467 ppm) **exceeded** the upper critical operating limit (1200 ppm). The system was again shut off, resulting in low chamber readings the following sample cycle, **e.g.** 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 **21:58** the GC **stream** select valve **stuck** and failed to cycle. Mass balance measurements were used to predict chamber concentration throughout the remainder of the exposure **period**. These measurements indicated that the **1000** ppm chamber ran below the lower critical operating limit. No adjustments **were attempted**. Daily mean concentrations were within specs but standard deviations exceeded the **±10%** operating limit. Reported data are:

200 ppm mean = 198 ± 40 ppm
1000 ppm mean = 925 ± 198 ppm
5000 ppm mean = 4870 ± 954 ppm

5/28/86 The stream select valve to the GC was incorrectly connected and prevented the proper **determination** of chamber concentration for the 5000 ppm chamber. Mass balance (**i.e.** chemical pump delivery rate and chamber dilution air flow rate) was used to determine chamber concentration **after** 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 **~02:55** and chamber concentrations were reestablished by **03:11**. Low **concentrations** exceeding the lower critical operating limits were reported as follows:

200 ppm 2 readings: 5.1 and 85.0 ppm
1000 ppm 3 readings: **27.0, 570**, and 783 ppm
5000 ppm 1 reading: 16.6 ppm

Though daily mean concentrations were within specs, standard deviations exceeded the operating limit of $\pm 10\%$ because of the system shutdown.

TEMPERATURE & RELATIVE HUMIDITY

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

CHAMBER FLOW & VACUUM

DATE **DISCUSSION OR EXPLANATION**
5/15/86 Low vacuum was detected in the 0 ppm Hold 2 chamber (1 reading = 0.2" H₂O). Water **was** placed in the trap at the bottom of the chamber and vacuum returned to specs.

APPENDIX C

DEVELOPMENTAL TOXICOLOGY DATA

О. ХОДОЧЕВА

АТАС ЧЕЛОВЕЧЕСКОГО ПОДВИГА

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

1

0 ppm n-Hexane

MATNO	Pro-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
809	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	263.60

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

Females

2

200 ppm n-Hexane

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	273.60	291.20	297.90
618	305.60	311.80	327.20	327.30
712	226.00	232.40	239.40	242.40
724	264.60	276.40	301.20	308.30
888	282.00	308.00	327.60	335.60
923	259.00	261.60	272.00	266.40

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

1000 ppm n-Hexane

MATNO	Pro-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

-----6000 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	242.60	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

-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	.	.	1	0	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	0.80	0	.	.	1	0	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	1	0	0
550	265.00	285.40	307.80	333.80	393.20	89.30	1	18	17	1	0	0
553	255.20	259.60	287.40	326.80	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	282.80	276.00	0.50	0	.	.	0	0	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	.	.	0	0	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	268.60	284.00	333.40	401.40	74.70	1	15	14	1	0	0
681	274.00	287.80	307.20	339.40	414.00	84.40	1	18	15	0	1	0
695	229.00	239.00	241.60	247.00	256.40	0.90	0	.	.	0	0	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	82.40	1	13	11	2	0	0
882	230.00	238.40	258.60	275.60	249.10	0.60	0	.	.	0	0	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	2	0
976	257.60	266.60	295.80	329.60	385.40	74.70	1	14	12	2	0	0

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

-----TMT=200 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
445	266.2B	291.6B	325.8B	357.0B	415.3B	51.10	1	10	10	0	0	0
448	298.6B	296.4B	313.2B	342.8B	436.4B	99.60	1	18	18	0	0	0
453	271.8B	274.8B	287.4B	309.2B	361.1B	65.00	1	15	12	3	0	0
499	274.2B	284.4B	299.6B	320.0B	297.6B	0.60	0	.	.	0	0	0
516	289.0B	282.4B	303.6B	338.2B	436.5B	105.20	1	17	17	0	0	0
534	250.2B	258.2B	281.6B	294.8B	275.7B	0.70	0	.	.	0	0	0
561	245.8B	263.2B	275.0B	309.8B	378.0B	75.90	1	13	13	0	0	0
562	314.8B	324.4B	356.6B	392.2B	465.5B	61.80	1	14	13	1	0	0
570	302.4B	287.8B	308.6B	350.2B	418.4B	54.60	1	9	9	0	0	0
590	245.8B	259.0B	284.0B	310.4B	363.1B	69.30	1	15	13	0	0	0
601	237.2B	251.8B	273.0B	308.8B	361.5B	75.50	1	15	15	0	0	0
613	275.6B	286.0B	304.2B	335.2B	399.8B	75.40	1	15	13	0	0	0
614	284.2B	289.4B	323.8B	345.6B	409.5B	88.80	1	19	17	2	0	0
629	282.8B	264.0B	293.4B	333.6B	402.8B	84.10	1	16	16	0	0	0
640	246.4B	263.6B	274.8B	315.0B	375.5B	77.50	1	17	17	0	0	0
652	261.2B	256.4B	284.2B	305.2B	375.7B	76.20	1	16	15	1	0	0
662	239.8B	252.0B	261.8B	290.6B	366.4B	81.60	1	16	15	0	0	0
671	264.4B	273.6B	307.6B	333.4B	423.0B	95.90	1	17	17	0	0	0
688	289.2B	279.0B	306.0B	342.2B	416.4B	89.20	1	13	13	0	0	0
698	242.0B	277.6B	261.4B	284.4B	351.8B	79.40	1	15	15	0	0	0
716	247.8B	253.2B	283.6B	298.6B	251.1B	0.50	0	.	.	0	0	0
763	286.0B	302.8B	317.0B	327.8B	404.1B	93.30	1	17	17	0	0	0
770	269.8B	275.6B	301.4B	331.8B	398.6B	74.20	1	15	15	0	0	0
777	239.8B	281.6B	277.2B	312.8B	376.3B	67.00	1	13	13	0	0	0
823	258.2B	282.8B	285.0B	294.2B	277.7B	0.60	0	.	.	0	0	0
843	261.2B	276.4B	300.8B	334.8B	412.5B	84.00	1	18	15	3	0	0
898	233.0B	242.4B	255.0B	266.8B	261.0B	1.00	0	.	.	0	0	0
931	284.0B	294.6B	307.4B	348.4B	423.7B	94.60	1	18	18	0	0	0
933	265.8B	267.0B	294.0B	307.4B	287.7B	0.70	0	.	.	2	0	0
942	229.8B	234.6B	244.8B	276.8B	303.2B	65.40	1	16	14	0	0	0

n-Hexane Rat Teratology Study: ~~69~~65 Weights (g) for Sperm-positive Females

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	278.00	309.20	361.80	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	1	0
478	248.00	254.80	268.60	284.80	338.30	82.20	1	15	14	1	0	0
481	260.00	261.00	278.60	309.80	378.10	66.90	1	15	13	1	0	0
510	274.40	280.40	311.80	345.20	423.40	78.50	1	16	16	2	0	0
520	288.40	290.80	319.40	340.40	358.80	12.40	1	4	16	16	0	0
544	272.60	281.00	306.00	315.00	373.30	76.60	1	17	15	2	1	0
549	285.60	288.80	310.20	333.00	397.10	78.30	1	17	15	1	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	292.80	337.40	408.30	78.40	1	17	16	1	0	0
591	242.00	260.00	281.80	310.20	379.30	68.80	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	295.80	338.20	397.90	81.50	1	15	15	0	0	0
653	249.80	271.20	291.20	326.40	410.90	85.80	1	18	18	1	0	0
664	237.80	248.00	270.80	295.40	350.30	89.50	1	14	13	1	5	0
689	282.80	277.00	302.40	325.80	368.80	48.10	1	14	9	0	0	0
691	287.40	284.40	315.20	333.20	317.40	0.70	0	.	.	0	0	0
697	240.40	254.80	279.00	297.80	375.90	78.40	1	14	13	1	1	1
788	288.40	300.80	319.00	344.40	378.80	86.30	1	17	18	0	0	1
807	260.00	268.00	295.80	338.80	375.80	51.10	1	11	.	0	0	0
836	270.40	286.80	298.80	311.80	288.00	0.70	0	.	.	3	1	0
855	321.60	336.80	353.40	387.00	458.70	87.80	1	21	18	0	0	0
905	241.80	268.20	303.80	336.00	400.50	81.80	1	16	15	1	0	0
911	285.00	277.00	307.80	328.00	430.70	83.20	1	17	17	0	0	0
918	273.80	275.80	309.80	324.80	420.70	97.20	1	18	18	0	0	0
921	253.80	255.20	278.00	298.40	362.00	81.70	1	15	15	0	0	0
925	277.80	291.80	303.80	329.40	307.50	0.60	0	.	.	0	0	0
944	287.80	274.80	298.40	327.80	388.30	85.40	1	17	17	0	0	0
965	278.40	306.20	340.80	369.00	369.10	85.50	1	16	16	1	0	0
972	278.60	283.20	313.00	346.80	400.80	81.20	1	16	16	0	0	0

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

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	280.80	284.00	286.80	305.80	366.00	67.10	1	16	14	2	1	0
457	292.80	297.20	319.00	317.00	413.90	67.90	1	17	16	0	0	0
458	244.80	261.40	270.80	268.80	269.60	0.60	0	.	.	0	0	0
472	252.20	284.40	276.80	304.60	376.70	80.60	1	17	17	0	0	0
488	248.20	252.00	261.80	284.00	320.00	60.80	1	15	15	0	0	0
505	246.80	251.60	279.80	303.20	278.70	0.80	0	.	.	0	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	245.80	244.40	256.80	297.80	339.10	29.90	1	8	6	0	0	0
586	302.20	317.40	353.80	361.80	415.90	69.70	1	16	15	1	0	0
608	287.00	270.40	308.80	251.20	345.90	63.40	1	15	15	0	0	0
622	248.80	258.40	277.20	297.20	336.20	69.80	1	18	18	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	328.80	360.60	68.40	1	18	15	3	0	0
641	231.80	238.80	269.80	261.60	327.40	69.20	1	15	15	0	0	0
658	241.80	252.40	275.80	305.40	352.50	64.40	1	15	14	1	0	0
690	284.20	282.80	303.40	244.40	202.10	.	(a)	1	14	12	2	2
762	242.80	263.40	288.40	303.80	361.60	61.70	1	17	14	1	0	0
800	264.20	279.40	297.40	302.20	378.20	83.10	1	18	17	1	0	0
806	229.00	242.40	248.00	269.00	342.00	83.90	1	18	18	0	0	0
814	279.80	284.00	313.00	348.20	372.10	41.00	1	10	8	0	0	0
863	275.80	301.40	332.00	341.20	392.20	70.00	1	14	14	0	0	0
888	287.80	263.80	283.00	243.80	307.20	49.50	1	11	10	1	0	0
889	278.40	311.00	328.40	340.60	419.50	91.30	1	19	19	0	0	0
922	285.00	277.60	295.20	320.40	371.70	66.90	1	14	14	0	0	0
938	257.80	274.60	300.80	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	1
951	278.20	278.80	317.80	345.00	424.80	78.70	1	17	16	0	0	0
984	259.80	281.60	308.20	328.20	374.40	72.40	1	17	15	2	0	0

a) Uterus inadvertently not weighed.

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					
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					
514	1	1	2	3.19	0.49	DIUR				
514	2	1	2	3.10	0.40					
514	3	1	2	2.83	0.34					
514	4	1	2	3.24	0.45					
514	5	1	2	3.17	0.50	ROST				
514	6	1	1	3.19	0.38					
514	7	1	2	3.00	0.31					
514	8	1	1	3.35	0.47					
514	9	1	1	2.98	0.29					
514	10	1	1	3.31	0.42	ROST				
514	11	1	2	2.98	0.36					
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					
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					
548	3	1	1	3.79	0.46					
548	4	1	2	3.53	0.38					
548	5	1	2	3.60	0.38					
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					
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

0 ppm n-Hexane

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	■	.	.					
663	7	1	■	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					
568	1	1	1	3.77	0.55					
568	2	1	1	3.63	0.57					
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					
568	7	1	1	3.03	0.42					
568	8	1	2	3.69	0.53					
568	9	1	1	3.98	0.43					
568	10	1	1	3.92	0.58					
568	11	1	1	3.93	0.44					
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	0.66					
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					
579	9	1	1	3.58	0.47					
579	10	1	2	1.93	0.34					
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	3.66	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					
604	3	1	1	3.39	0.40					
604	4	1	2	3.28	0.41					
604	5	1	1	3.69	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					
604	8	1	1	3.10	0.43					
604	9	1	2	2.98	0.40					
604	10	1	1	3.39	0.40					
604	11	1	2	3.21	0.35					
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					
612	2	1	2	3.59	0.38					
612	3	2	2	.	.					
612	4	1	2	3.45	0.47					
612	5	1	1	3.86	0.42					
612	6	1	1	3.80	0.40					
612	7	1	1	3.32	0.41					
612	8	1	1	3.97	0.45					
612	9	1	1	3.76	0.41					
612	10	1	2	3.24	0.43					
612	11	1	2	3.54	0.36					
612	12	1	2	3.48	0.40					
612	13	2	2	.	.					
612	14	1	1	3.94	0.47					
612	15	1	1	3.97	0.51					
612	16	1	2	3.58	0.42					
612	17	1	1	4.29	0.41					
612	18	1	1	4.17	0.50					
632	1	1	1	3.63	0.36					
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	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					
632	10	2	2	.	.					
632	11	1	2	3.27	0.33					
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					
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

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	3.42	0.38					
646	1	1	1	3.74	0.46					
646	2	1	2	3.83	0.56					
646	3	1	1	3.86	0.48					
646	4	1	1	3.42	0.41					
646	5	1	1	3.68	0.40					
646	6	1	1	4.14	0.41					
646	7	1	1	3.90	0.41					
646	8	1	2	3.86	0.42					
646	9	1	2	4.09	0.38					
646	10	1	1	4.18	0.47					
646	11	1	2	3.79	0.49					
646	12	1	2	3.67	0.39					
646	13	1	2	3.87	0.51					
646	14	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					
676	15	1	2	3.13	0.43	DIUR				

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

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	2.56	0.42					
681	3	1	2	3.32	0.39					
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					
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	3.89	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					
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	3.28	0.44					
785	4	1	2	3.02	0.37					
785	5	1	2	2.91	0.38					
785	6	1	2	2.98	0.34					
785	7	1	2	3.03	0.39					
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					
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]

n-Hexane Rat Teratology Study: Raw Fetal Data

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					
785	17	1	1	3.02	0.27	ROVE				
805	1	1	1	4.02	0.63	ROSK	ROVE			
805	2	2								
805	3	1	2	3.39	0.41					
805	4	1	1	3.51	0.46					
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					
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					
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]

n-Hexane Rat Teratology Study: Raw Fatal Data

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

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
936	14	1	2	3.46	0.43					
936	15	1	1	3.57	0.61					
936	16	1	1	3.54	0.49					
936	17	1	2	2.91	0.34					
936	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	3.83	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	3.78	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	ROPB	ROVE	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			
976	1	1	2	2.75	0.64					
976	2	1	1	4.06	0.68	SRRR	ROVE			
976	3	1	1	4.33	0.68	ROVE				
976	4	2	.	.	.					
976	6	1	2	3.93	0.46					
976	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	3.76	0.53	ROVE				

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

n-Hexane Rat Teratology Study: Raw Fetal Data

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

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
976	11	1	1	4.33	0.56					
976	12	1	1	4.28	0.46	ROVE				
976	13	1	1	4.41	0.51	DIUR	ROVE			
976	14	1	1	4.22	0.50	DIUR	ROVE			

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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	.	.	.					
518	1	1	2	4.17	0.35					
518	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]

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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					
561	1	1	2	3.80	0.50	ROVE				
561	2	1	1	3.90	0.66					
561	3	1	1	3.83	0.60					
561	4	1	2	3.78	0.60					
561	5	1	1	4.16	0.66					
561	6	1	1	3.79	0.47					
561	7	1	2	3.86	0.66					
561	8	1	2	3.61	0.63					
561	9	1	1	3.86	0.63					
561	10	1	2	3.66	0.48					
561	11	1	2	3.69	0.49					
561	12	1	1	3.98	0.61					
561	13	1	1	4.13	0.66					
562	1	1	2	2.80	0.44	ROST				
562	2	1	1	3.08	0.46					
562	3	1	2	2.88	0.36					
562	4	1	1	3.27	0.32					
562	5	1	1	3.09	0.32		ROST	ROPB		
562	6	2	.	.	.					
562	7	1	2	2.71	0.31		ROST	ROPB		
562	8	1	1	3.12	0.38					
562	9	1	1	2.83	0.39					
562	10	1	1	3.32	0.31					
562	11	1	2	2.86	0.32					
562	12	1	1	3.46	0.36					
562	13	1	1	3.46	0.34					
562	14	1	1	3.47	0.41					
570	1	1	2	3.12	0.60	ROST				
570	2	1	2	3.24	0.46					
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

-----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					
670	6	1	2	3.30	0.69					
570	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					
690	1	1	2	2.81	8.36	ROVE				
690	2	4	2	3.58	0.40	ROST				
590	3	1	2	3.28	0.40					
690	4	1	2	2.30	0.31	ROST				
690	6	1	2	3.32	0.41					
590	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				
690	10	1	2	3.32	0.41	ROST				
690	11	1	1	3.67	0.39					
690	12	1	1	3.66	0.40					
690	13	1	1	3.40	0.43	ROST				
690	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					
601	6	1	2	3.66	8.43	DIUR				
601	6	1	2	3.36	0.36	ROST				
601	7	1	1	3.40	0.41	ROST				
601	8	1	2	3.32	0.37					
601	9	1	2	3.28	0.40					
601	10	1	1	3.47	0.40					
601	11	1	1	3.31	0.39					
601	12	1	1	3.16	0.33	DIUR				
601	13	1	2	3.36	0.36	ROVE				
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					
613	6	1	2	3.98	0.62	DIUR				
813	6	1	2	3.80	0.46	ROST				
613	7	1	2	3.81	0.47					
613	8	1	2	3.84	0.47					
613	9	1	1	4.16	0.60	SRRR				
						DIUR				

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
200 ppm n-Hexane										
613	10	1	1	3.59	0.42					
613	11	1	2	3.76	0.60					
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					
614	1	1	1	2.73	0.38					
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					
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					
614	16	1	1	3.73	0.38					
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	3.60	0.37					
629	3	1	1	3.86	0.35					
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					
629	8	1	1	3.33	0.34					
629	9	1	2	3.31	0.39					
629	10	1	2	3.27	0.41					
629	11	1	1	3.49	0.37					
629	12	1	2	3.20	0.32					
629	13	1	1	3.57	0.37					
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					
640	3	1	1	2.91	0.43					
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]

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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	3.60	0.36					ROVE
662	4	1	1	3.60	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	3.60	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	3.46	0.36					
662	14	1	1	4.03	0.47					
662	15	1	1	2.17	0.28					ROSK
662	16	1	1	4.13	0.36					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]

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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	0.48					
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	0.66	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				
698	1	1	1	3.69	0.52					
698	2	1	2	3.34	0.46					
698	3	1	2	3.34	0.41	ROST				
698	4	1	2	3.70	0.38					
698	5	1	2	3.42	0.43					
698	6	1	2	3.33	0.38					
698	7	1	2	3.38	0.39					
698	8	1	1	8.66	0.34					
698	9	1	1	3.82	0.37					
698	10	1	1	3.57	0.43					
698	11	1	1	3.94	0.48					
698	12	1	1	3.31	0.34	ROST				
698	13	1	1	3.83	0.39					
698	14	1	2	3.39	0.24					
698	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]

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
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	1	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					
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]

n-Hexane Rat Teratology Study: Raw Fetal Data

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

Mat No	Site	Status	Sex	Fetal Wt(g)	Placenta Wt(g)	ABN1	ABN2	ABN3	ABN4	ABN5
843	1	2	.	3.94	0.45					
843	2	1	1	3.49	0.40	DIUR				
843	3	1	1	3.97	0.41	ROST				
843	4	1	1	3.76	0.45	DIUR	ROST			
843	5	2	.	3.33	0.42					
843	6	1	2	3.54	0.42	DIUR				
843	7	1	2	3.75	0.41	ROST				
843	8	2	.	3.68	0.51					
843	9	1	2	3.86	0.48	ROST				
843	10	1	1	4.41	0.54	DIUR				
843	11	1	2	3.78	0.36					
843	12	1	2	3.96	0.40					
843	13	1	1	3.66	0.45					
843	14	1	1	3.82	0.43					
843	15	1	1	3.87	0.43					
843	16	1	2	3.38	0.39					
843	17	1	2	3.68	0.35					
843	18	1	2	3.62	0.41	DIUR				
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					
931	8	1	1	3.76	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	3.66	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

-----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	.	.	.					

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					
460	2	1	2	2.82	0.35					
460	3	1	1	2.78	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	0.46					
460	8	1	1	2.84	0.44					
460	9	1	1	3.03	0.46					
460	10	1	2	2.60	0.39	ROST				
460	11	1	2	2.74	0.44					
460	12	1	1	3.17	0.46					
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	3.64	0.46					
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	2.68	0.43	ROST				
470	10	1	2	2.83	0.33	ROST				
470	11	1	1	3.28	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	0.36	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	0.36	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

-----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	1	3.10	0.39	ROST				
481	2	1	2	3.66	0.36	ROST				
481	3	1	2	3.26	0.34	ROST				
481	4	1	2	3.11	0.32	ROST				
481	5	1	2	3.46	0.44					
481	6	1	1	3.46	0.39					
481	7	1	2	3.46						
481	8	2	1	3.62	0.40	ROST				
481	9	1	2	3.13	0.36	ROVE				
481	10	1	1	3.64	0.43	ROST				
481	11	1	1	3.49	0.41	ROST				
481	12	1	1	3.66	0.40	ROST				
481	13	1	2	3.33	0.38	ROST				
481	14	1	1	3.19	0.46					
481	16	1	1	2.98	0.39	ROSK	ROVE			
610	1	1	1	2.89	0.37	ROST				
610	2	1	2	2.66	0.39	ROSK	ROPB			
610	3	1	2	3.34	0.46					
610	4	1	1	3.71	0.42					
610	6	1	2	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	2	3.07	0.39	ROST				
544	2	1	2	3.17	0.33	DIUR				
544	3	1	2	3.30	0.41	ROST				
544	4	1	1	3.51	0.37					
544	5	1	1	3.26	0.39	ROST				
544	6	1	2	3.38	0.36	ROST				
544	7	1	2	3.33	0.23	ROST				
544	8	1	2	3.32		ROST				
544	9	1	1							

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

-----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	18	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	.	.	.					
549	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	■	.	.					
549	12	1	2	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	3.68	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	18	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	0.36					
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]

n-Hexane Rat Teratology Study: Raw Fatal Data

-----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					
580	5	1	1	3.32	0.33					
580	6	1	1	3.38	0.32					
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					
580	16	1	2	3.13	0.33					
580	17	1	1	3.04	0.27					
591	1	1	1	3.03	0.63					
591	2	1	2	3.02	0.36					
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					
591	10	1	2	3.20	0.48					
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					
635	8	1	2	3.26	0.46					
635	9	1	1	3.06	0.44					
635	10	1	2	3.60	0.27					
635	11	1	1	3.41	0.36					
635	12	1	2	3.08	0.42					
635	13	1	2	3.37	0.40					
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

-----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	3.06	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]

n-Hexane Rat Teratology Study: Raw Fetal Data

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n-Hexane Rat Teratology Study
 Appendix C - Toxicology Data

-----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	1	1	3.50	0.57	ROVE				
689	4	2	2	3.24	0.50	ROST				
689	6	1	2	3.36	0.45	ROST	ROVE			
689	7	1	2	3.48	0.53					
689	8	1	2	2.57	0.47	ROST	ROVE			
689	9	2	1	3.65	0.45					
689	10	1	1	3.51	0.49					
689	11	1	1	3.88	0.49					
689	12	1	2	4.25	0.48					
689	13	2	1	3.85	0.36					
689	14	1	2	3.85	0.47					
697	1	1	1	4.01	0.44					
697	2	2	1	3.73	0.40					
697	3	1	1	3.83	0.44					
697	4	1	1	4.09	0.47					
697	6	1	2	3.85	0.47					
697	7	1	2	3.73	0.40					
697	8	1	1	3.83	0.44					
697	9	1	1	3.75	0.40					
697	10	1	1	3.83	0.61	ROST	ROPB			
697	11	1	2	3.60	0.44					
697	12	1	2	3.60	0.44					
697	13	1	2	3.98	0.37					
697	14	1	2	3.87	0.46					
768	1	1	1	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	0.36	ROPB				
768	6	1	1	2.73	0.44					
768	6	1	2	2.44	0.40	ROPB				
768	7	1	2	2.24	0.33	ROPB				
768	8	2	1	2.42	0.26	ROST				
768	9	1	2	2.31	0.40	ROST				
768	10	1	2	2.19	0.29	ROST	ROPB			
768	11	1	2	2.67	0.41	ROST	ROPB			
768	12	1	2	2.37	0.34					
768	13	1	2	2.27	0.32	ROST	ROPB			
768	14	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

-----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	I7	I	I	2.65	0.38	ROSK	ANON	ROPH	ROPB	
807	I	I	I	3.32	0.47					
807	23	I	2	3.47	0.54	SRRR	ROPB			
807	4	I	2	3.09	0.49	ROSK	SRRR			
807	6	I	I	3.84	0.45					
807	6	I	I	3.65	0.66					
807	6	I	I	3.61	0.47					
807										
807	2	I	I							
807	4	I	I							
807	10	I	I	3.31	0.37	ROPB				
807	11	I	I	3.49	0.44	DIUR				
807										
866	I	I	I	3.80	0.48					
855	2	I	2	2.98	0.42					
866	3	I	1	2.63	0.28	DIUR	RPCA			
866	4	I	1	3.20	0.37					
866	6	I	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										
866	9	I	I	3.04	0.49					
866	10	I	I	3.37	0.39	DIUR	RPCA			
866	11	I	I	2.39	0.37	ROST				
855	12	I	I	3.47	0.44	DIUR				
866	13	I	I	3.39	0.52					
866	14	I	2	2.83	0.36					
866	15	I	2	3.03	0.43					
866	16	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	I	2							
866	21	I	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	I	I							
906	10	I	2	3.84	0.47	DIUR				
906	11	I	I	3.52	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]

n-Hexane Rat Teratology Study: Raw Fetal Data

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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	1	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	1	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	1	3.24	0.48					
918	4	1	2	3.66	0.60					
918	6	1	1	3.62	0.48	DIUR	RPCA			
918	6	1	2	3.34	0.44					
918	7	1	1	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	1	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

-----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					
921	7	1	2	2.84	0.31	ROVE				
921	8	1	1	4.03	0.46	DIUR				
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	3.83	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

-----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					
972	4	1	2	3.46	0.40					
972	6	1	1	3.24	0.28					
972	6	1	1	2.94	0.29	DIUR		ROVE		
972	7	1	2	2.97	0.38					
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	18	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

29

-----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					
451	2	1	1	3.21	0.37					
451	3	1	2	3.23	0.44					
451	4	1	1	2.87	0.44					
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					
451	10	2								
451	11	1	1	3.34	0.42					
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					
457	3	1	2	2.82	0.37					
457	4	1	1	2.83	0.38					
457	5	1	1	2.81	0.38					
457	6	1	2	2.76	0.41					
457	7	1	2	2.57	0.34					
457	8	1	1	2.60	0.32					
457	9	1	2	2.87	0.34					
457	10	1	2	2.46	0.38					
457	11	4								
457	12	1	2	2.41	0.30					
457	13	1	2	2.48	0.25					
457	14	1	2	2.51	0.38					
457	15	1	1	2.88	0.34					
457	16	1	1	2.82	0.39					
457	17	1	1	2.73	0.35					
472	1	1	2	3.00	0.36					
472	2	1	1	3.25	0.34					
472	3	1	2	2.93	0.37					
472	4	1	2	2.61	0.33					
472	5	1	1	3.05	0.41					
472	6	1	1	3.18	0.48					
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					
472	12	1	1	2.96	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

-----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					
472	15	1	1	3.01	0.28					
472	16	1	2	3.29	0.29					
472	17	1	1	3.31	0.40					
488	1	1	1	2.69	0.30					
488	2	1	2	2.52	0.29					
488	3	1	1	2.78	0.32					
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					
488	8	1	1	2.22	0.29					
488	9	1	2	2.48	0.28					
488	10	1	2	2.27	0.26					
488	11	1	1	2.78	0.31					
488	12	1	1	2.68	0.33					
488	13	1	1	2.68	0.25					
488	14	1	1	2.67	0.33					
488	15	1	1	2.68	0.29					
538	1	1	1	3.08	0.31					
538	2	1	2	2.77	0.36					
538	3	1	2	2.84	0.31					
538	4	1	2	2.79	0.38					
538	5	1	2	2.65	0.40					
538	6	1	2	2.83	0.28					
538	7	1	2	2.88	0.30					
538	8	1	1	3.00	0.28					
538	9	1	1	2.77	0.28					
538	10	1	1	2.31	0.31					
538	11	1	2	2.88	0.31					
538	12	1	2	2.95	0.33					
538	13	1	2	3.03	0.35					
538	14	1	2	2.95	0.31					
538	1	1	2	2.65	0.38					
538	2	1	1	3.21	0.39					
538	3	1	2	3.03	0.38					
538	4	1	1	2.98	0.42					
538	5	1	2	3.28	0.52					
538	6	1	2	3.29	0.42					
538	7	1	1	3.16	0.43					
538	8	1	2	3.24	0.37					
538	9	1	2	2.91	0.38					
538	10	1	2	3.09	0.43					
538	11	1	2	2.69	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]

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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					
638	13	1	1	3.29	0.43	ROST	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					
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	0.38					
586	9	1	1	3.22	0.32					
586	10	1	2	3.00	0.37		ROST			
586	11	1	2	3.17	0.38		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		ROST		ROPB	
608	1	1	1	2.16	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

-----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					
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					
608	14	1	2	2.62	0.38					
608	15	1	2	2.15	0.36					
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					
622	5	1	2	2.85	0.30					
622	6	1	1	2.82	0.31					
622	7	1	1	3.19	0.32					
622	8	1	1	3.23	0.34					
622	9	1	2	2.81	0.29					
622	10	1	2	2.84	0.29					
622	11	1	1	2.94	0.29					
622	12	1	1	2.98	0.30					
622	13	1	2	2.82	0.29					
622	14	1	1	2.98	0.30					
622	15	1	1	3.19	0.30					
622	16	1	1	3.04	0.31					
623	1	1	1	2.99	0.39					
623	2	1	2	2.92	0.44					
623	3	1	1	3.37	0.42					
623	4	1	2	3.04	0.43					
623	5	1	1	3.35	0.48					
623	6	1	1	3.38	0.43					
623	7	1	2	3.92	0.44					
623	8	1	2	3.15	0.36					
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					
623	14	1	2	2.78	0.38					
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

-----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	2.58	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]

n-Hexane Rat Teratology Study: Raw Fetal Data

-----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	2	3.00	0.31					
658	14	1	2	2.89	0.35					
658	15	1	2	1.79	0.37	ROST				
690	1	1	2	1.82	0.32	ROST	SRRR			
690	2	1	2	1.39	0.27	ROSK	ROST	ROPE	ROPH	
690	3	1	2	1.54	0.28	ROST	ROPE			
690	4	1	1	1.53	0.30	ROSK	ROST	ROPE		
690	5	1	1	1.48	0.27	ROST	ROPE			
690	6	1	2	1.19	0.27	ROSK	ROST	ROVE	ROPE	ROPH
690	7	1	2	1.40	0.28	ROST	ROVE	ROPE	ROPH	
690	8	1	2	1.81	0.32	ROSK	ROST	ROPE		
690	9	2	1	1.26	0.34					
690	10	1	1	1.33	0.26	ROST	ROVE	ROPH		
690	11	2	1	1.84	0.30	ROST	ROPE	ROVE	ROPH	
690	12	1	1	2.83	0.39					
690	13	1	1	2.79	0.49	DIUR				
782	1	4	2	2.45	0.30					
782	2	2	1	2.75	0.34					
782	3	1	1	2.67	0.41					
782	4	1	2	2.67	0.32					
782	5	2	2	2.51	0.34					
782	6	1	2	2.86	0.36					
782	7	1	2	2.80	0.34					
782	8	1	1	2.67	0.36					
782	9	1	2	2.67	0.36					
782	10	1	2	2.89	0.36					
782	11	1	1	2.95	0.46					
782	12	1	2	2.76	0.36					
782	13	1	1	2.90	0.36					
782	14	1	1	2.95	0.46					
782	15	1	1	2.86	0.36					
782	16	1	2	2.90	0.36					
782	17	1	2	2.90	0.36					
800	1	1	1	3.10	0.38					
800	2	1	1	3.31	0.36					
800	3	4	2	3.00	0.43					
800	4	1	2	3.25	0.43					
800	5	1	2	3.44	0.43					
800	6	1	1	3.50	0.33	ROST				
800	7	1	2	2.89	0.38	ROST				
800	8	1	1	3.37	0.46					
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]

Sex: Male = 1; Female = 2 See Code Sheet 39 for identification of abnormalities (ABN)

No.	Site	Status	Sex	Fetal	Pi/centra	ABN1	ABN2	ABN3	ABN4	ABN5
-----5000 ppm n-Hexane-----										
800	11	1	1	3.43	0.36	ROVE	ROVE	ROVE	ROVE	ROVE
800	12	1	1	3.60	0.37	ROVE	ROVE	ROVE	ROVE	ROVE
800	13	1	1	3.29	0.37	ROVE	ROVE	ROVE	ROVE	ROVE
800	14	1	1	2.63	0.39	ROST	ROST	ROST	ROST	ROST
800	15	1	1	3.09	0.41	ROST	ROST	ROST	ROST	ROST
800	16	1	1	3.15	0.39	ROST	ROST	ROST	ROST	ROST
800	17	1	1	3.14	0.46	ROSK	ROSK	ROSK	ROSK	ROSK
800	18	1	1	3.12	0.39	ROST	ROST	ROST	ROST	ROST
800	19	1	1	2.41	0.44	ROBB	ROBB	ROBB	ROBB	ROBB
800	20	1	1	3.21	0.42					
800	21	1	1	3.33	0.39					
800	22	1	1	3.15	0.41					
800	23	1	1	3.10	0.38					
800	24	1	1	3.14	0.37					
800	25	1	1	3.14	0.47					
800	26	1	1	2.64	0.39					
800	27	1	1	3.27	0.40					
800	28	1	1	2.96	0.38					
800	29	1	1	3.27	0.37					
800	30	1	1	3.36	0.40					
800	31	1	1	3.36	0.37					
800	32	1	1	3.27	0.40					
800	33	1	1	3.10	0.34					
800	34	1	1	3.32	0.39					
800	35	1	1	3.36	0.45					
800	36	1	1	3.27	0.37					
800	37	1	1	2.69	0.35					
800	38	1	1	3.61	0.40					
800	39	1	1	3.27	0.37					
800	40	1	1	3.10	0.34					
800	41	1	1	3.27	0.40					
800	42	1	1	3.36	0.40					
800	43	1	1	3.27	0.37					
800	44	1	1	3.10	0.34					
800	45	1	1	3.32	0.39					
800	46	1	1	3.27	0.37					
800	47	1	1	3.10	0.34					
800	48	1	1	3.27	0.37					
800	49	1	1	3.36	0.45					
800	50	1	1	3.27	0.37					
800	51	1	1	3.10	0.34					
800	52	1	1	3.27	0.37					
800	53	1	1	3.36	0.45					
800	54	1	1	3.27	0.37					
800	55	1	1	3.10	0.34					
800	56	1	1	3.27	0.37					
800	57	1	1	3.36	0.45					
800	58	1	1	3.27	0.37					
800	59	1	1	3.10	0.34					
800	60	1	1	3.27	0.37					
800	61	1	1	3.36	0.45					
800	62	1	1	3.27	0.37					
800	63	1	1	3.10	0.34					
800	64	1	1	3.27	0.37					
800	65	1	1	3.36	0.45					
800	66	1	1	3.27	0.37					
800	67	1	1	3.10	0.34					
800	68	1	1	3.27	0.37					
800	69	1	1	3.36	0.45					
800	70	1	1	3.27	0.37					
800	71	1	1	3.14	0.37					
800	72	1	1	3.49	0.47					
800	73	1	1	3.14	0.37					
800	74	1	1	3.61	0.46					
800	75	1	1	3.22	0.32					
800	76	1	1	3.01	0.31					
800	77	1	1	2.46	0.29					
800	78	1	1	3.22	0.32					
800	79	1	1	3.01	0.31					
800	80	1	1	2.46	0.29					
800	81	1	1	3.22	0.32					
800	82	1	1	3.01	0.31					
800	83	1	1	2.46	0.29					
800	84	1	1	3.22	0.32					
800	85	1	1	3.01	0.31					
800	86	1	1	2.46	0.29					
800	87	1	1	3.22	0.32					
800	88	1	1	3.01	0.31					
800	89	1	1	2.46	0.29					
800	90	1	1	3.22	0.32					
800	91	1	1	3.01	0.31					
800	92	1	1	2.46	0.29					
800	93	1	1	3.22	0.32					
800	94	1	1	3.01	0.31					
800	95	1	1	2.46	0.29					
800	96	1	1	3.22	0.32					
800	97	1	1	3.01	0.31					
800	98	1	1	2.46	0.29					
800	99	1	1	3.22	0.32					
800	100	1	1	3.01	0.31					
800	101	1	1	2.46	0.29					
800	102	1	1	3.22	0.32					
800	103	1	1	3.01	0.31					
800	104	1	1	2.46	0.29					
800	105	1	1	3.22	0.32					
800	106	1	1	3.01	0.31					
800	107	1	1	2.46	0.29					
800	108	1	1	3.22	0.32					
800	109	1	1	3.01	0.31					
800	110	1	1	2.46	0.29					
800	111	1	1	3.22	0.32					
800	112	1	1	3.01	0.31					
800	113	1	1	2.46	0.29					
800	114	1	1	3.22	0.32					
800	115	1	1	3.01	0.31					
800	116	1	1	2.46	0.29					
800	117	1	1	3.22	0.32					
800	118	1	1	3.01	0.31					
800	119	1	1	2.46	0.29					
800	120	1	1	3.22	0.32					
800	121	1	1	3.01	0.31					
800	122	1	1	2.46	0.29					
800	123	1	1	3.22	0.32					
800	124	1	1	3.01	0.31					
800	125	1	1	2.46	0.29					
800	126	1	1	3.22	0.32					
800	127	1	1	3.01	0.31					
800	128	1	1	2.46	0.29					
800	129	1	1	3.22	0.32					
800	130	1	1	3.01	0.31					
800	131	1	1	2.46	0.29					
800	132	1	1	3.22	0.32					
800	133	1	1	3.01	0.31					
800	134	1	1	2.46	0.29					
800	135	1	1	3.22	0.32					
800	136	1	1	3.01	0.31					
800	137	1	1	2.46	0.29					
800	138	1	1	3.22	0.32					
800	139	1	1	3.01	0.31					
800	140	1	1	2.46	0.29					
800	141	1	1	3.22	0.32					
800	142	1	1	3.01	0.31					
800	143	1	1	2.46	0.29					
800	144	1	1	3.22	0.32					
800	145	1	1	3.01	0.31					
800	146	1	1	2.46	0.29					
800	147	1	1	3.22	0.32					
800	148	1	1	3.01	0.31					
800	149	1	1	2.46	0.29					
800	150	1	1	3.22	0.32					
800	151	1	1	3.01	0.31					
800	152	1	1	2.46	0.29					
800	153	1	1	3.22	0.32					
800	154	1	1	3.01	0.31					
800	155	1	1	2.46	0.29					
800	156	1	1	3.22	0.32					
800	157	1	1	3.01	0.31					
800	158	1	1	2.46	0.29					
800	159	1	1	3.22	0.32					
800	160	1	1	3.01	0.31					
800	161	1	1	2.46	0.29					
800	162	1	1	3.22	0.32					
800	163	1	1</td							

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	3.38	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	3.65	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	2.38	0.81	ROST				
868	7	1	2	3.58	0.40	SRRR				
868	8	1	2	3.83	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	3.80	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	3.18	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	3.28	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]

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	0.48					
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	3.08	0.34					
938	2	1	2	2.98	0.27					
938	3	1	1	3.49	0.32					
938	4	1	1	3.41	0.38					
938	5	1	2	3.18	0.28					
938	6	1	2	2.89	0.32					
938	7	1	1	3.44	0.37					
938	8	1	1	3.39	0.35					
938	9	1	1	2.90	0.29					
938	10	1	2	3.07	0.29					
938	11	1	2	2.93	0.27					
938	12	1	1	3.48	0.35					
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					
948	3	1	1	3.68	0.48					
948	4	1	1	3.33	0.39					
948	5	1	2	3.37	0.50					
948	6	1	1	3.93	0.44					
948	7	1	1	3.70	0.44					
948	8	1	1	3.20	0.43					
948	9	1	1	3.83	0.43					
948	10	1	1	3.49	0.41					
948	11	1	1	3.71	0.44					
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					
948	16	1	1	3.78	0.50					
948	17	1	1	3.80	0.49					
951	1	1	1	2.99	0.38					
951	2	1	1	2.55	0.33					
951	3	1	2	2.68	0.43					
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	2.82	0.42					
951	8	1	1	3.30	0.43					
951	9	1	2	2.78	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

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	0.48					
951	13	1	1	3.22	0.36					
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					
964	3	1	2	2.85	0.38					
964	4	1	1	3.58	0.38					
964	5	1	1	3.43	0.40					
964	6	1	1	3.41	0.37					
964	7	1	1	3.10	0.33					
964	8	1	1	2.70	0.38					
964	9	1	1	3.22	0.38					
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					
964	15	1	1	3.40	0.37					
964	16	1	1	3.04	0.38					
964	17	2	.	.	.					

C-46

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

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.

n-Hexane Rat Teratology Study
Appendix C - Toxicology Data

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 Pilo-Ectomy ^a	120
	---	---
		536
		536

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

608	pregnant
690	pregnant
716	non-pregnant
754	virgin

a) This study has been reported elsewhere.

APPENDIX D

ANIMAL HEALTH SCREEN

ARC DIAGNOSTIC LABORATORY REPORT

INVESTIGATOR Jackett/Mast
EXPERIMENT n-Hexane - Rat Teratology
COST CODE -
BUILDING LSL II
PEN, ROOM 429

LAB NO. 071
DATE 4/21/86
ANIMAL OR SHIP'NT NO. 360047
SOURCE Charles River REC'D 4-1-86
SPECIES & STRAIN RAT (C)
SEX SM/5F AGE ED. 2-6-86

SPECIMEN SUBMITTED AND CLINICAL HISTORY:

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

LABORATORY RESULTS

gross necropsy: No significant findings 282 5/14/86
Summary: A number of incidental lesions were seen in
the histopathology but none which considered a significant
indication for infectious disease. 282 5/14/86

Request for study on 4/29/86 - Spec. 108. Scr 2/23/86

n-Hexane Rat Teratology Study
Appendix D - Health Screen

RESULTS
ARC DIAGNOSTIC LABORATORY ELISA REPORT

LAB NO. 671
PAGE 2 OF 1

TEST: Sendai

Positive Control: - Lot: 07575

Negative Control: - Exp.: 12/86

Animal #	1	Result	-
	2		-
	3		-
	4		-
	5		-
	6		-
	7		-
	8		-
	9		-
	10		-

TEST: Vibram 141

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: 08C25

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: MRM

Positive Control: - Lot: 07787

Negative Control: - Exp.: 12/86

Animal #	1	Result	-
	2		-
	3		-
	4		-
	5		-
	6		-
	7		-
	8		-
	9		-
	10		-

Initial: REG

REG
Date dictated 4/22/86
4/22/86

HEALTH EVALUATION

HISTOPATHOLOGY

ARC Lab. # 071 Histo Lab. # 286-1166

Animal #	1	2	3	4	5	6	7	8	9	10
Lung	(1)	(1)	0	1,15	0	0	1	1,15	(1)	0
Trachea	NSC	NSC	NSC	NSC	NE	NSC	NSC	NSC	NSC	NSC
Harderian Gl.	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC
Salivary Gl.	NSC	NSC	1,5	0	NSC	NE	NSC	NSC	NSC	NSC
Submand. L.N.	NSC	NE	1,5	NSC	NE	NSC	NSC	NSC	NSC	NSC
Heart	NSC	VS	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NE
Liver	(1,3)	(3)	1,15	1,2	(-)	NSC	NSC	1	2,15	(2)
Kidney	NSC	1	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC
Ileum	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NSC
Colon	NSC	NSC	NSC	NSC	NSC	NSC	NSC	NE	NSC	NSC

NSC = N = Significant lesion

NE = NOT EXAMINED (tissue not submitted or not in slide).

(1) coarse granular lymphoid aggregate

(2) coarse fat 15 mm from right colic mesentery
with associated white infiltrate

(3) coarse pericholangial cutting with mixed type

(4) coarse pericholangial cutting with lymphoma

(5) coarse pericholangial cutting with white wiz

DEC 1/28/86

ARC DIAGNOSTIC LABORATORY ELISA REPORT

INVESTIGATOR Electra LAB NO. 8103
 EXPERIMENT 4-1-86 2Kt Recovery Study TEST: 5-28-86
 COST CODE — ANIMAL OR SHIPMENT NO. 340047
 BUILDING LSI SOURCE CR Recovery Box REC'3 U-1-36
 PEN, ROOM — SPECIES & STRAIN CD Rat
 SEX F AGE A.O. 2-06-86

TESTS REQUESTED

in rat blood specimens submitted for visual
examination
UJ

SEROLOGY RESULTS

TEST: <u>PVM</u>	TEST: <u>Ritom It/</u>	TEST: <u>LCV/SDA</u>
Positive Control: <u>+</u> Loc: 08025	Positive Control: <u>+</u> Loc: 08201	Positive Control: <u>+</u> Loc: 07175
Negative Control: <u>-</u> Exp.: 7/86	Negative Control: <u>-</u> Exp.: 3/87	Negative Control: <u>-</u> Exp.: 10/86
Animal # <u>1</u> Result <u>-</u>	Animal # <u>1</u> Result <u>-</u>	Animal # <u>1</u> Result <u>-</u>
<u>2</u>	<u>2</u>	<u>2</u>
<u>3</u>	<u>3</u>	<u>3</u>
<u>4</u>	<u>4</u>	<u>4</u>
<u>5</u>	<u>5</u>	<u>5</u>
<u>6</u>	<u>6</u>	<u>6</u>
<u>7</u>	<u>7</u>	<u>7</u>
<u>8</u>	<u>8</u>	<u>8</u>
<u>9</u>	<u>9</u>	<u>9</u>
<u>10</u>	<u>10</u>	<u>10</u>

TEST: <u>MRM</u>	TEST: <u>Sendai</u>
Positive Control: <u>-</u> Loc: 07387	Positive Control: <u>-</u> Loc: 08107
Negative Control: <u>-</u> Exp.: 12/86	Negative Control: <u>-</u> Exp.: 3/87
Animal # <u>1</u> Result <u>-</u>	Animal # <u>1</u> Result <u>-</u>
<u>2</u>	<u>2</u>
<u>3</u>	<u>3</u>
<u>4</u>	<u>4</u>
<u>5</u>	<u>5</u>
<u>6</u>	<u>6</u>
<u>7</u>	<u>7</u>
<u>8</u>	<u>8</u>
<u>9</u>	<u>9</u>
<u>10</u>	<u>10</u>

SCR 6/2/86
 Send copy to [unclear]
 D-4

Total: 28
 Date: 5/30/86
 test performed

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
Animal 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
Necropsy	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. Ruemmler
Quality Assurance Specialist

1/18/88
Date

R. H. Gelman
Quality Assurance Specialist

1/18/88
Date

APPENDIX F

PROTOCOL AND CAGE MAPS

2. КИЕВІЯ

закінчено від відомих

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 ¹⁴C-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 ($t_{1/2} = 1.2$ hr) and **2,5-hexanedione** ($t_{1/2} = 3.9$ hr) in maternal organs and fetuses exposed to n-hexane during gestation. Concentrations of n-hexane and its metabolites in fetuses were approximately equal to those in maternal blood. Nevertheless, they observed no statistically significant effects on intrauterine mortality, fetal body weights or the incidence of fetal anomalies following 6-hour daily inhalation exposures to 1000 ppm of n-hexane from 8-12, 12-16, or 8-16 dg. Growth of pups was impaired 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**

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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 ± 3 °F and relative humidities at 50 ± 15% during the quarantine, acclimation and exposure periods. These values will be measured and recorded twice daily.
3. During the quarantine period the animals **will** be housed by sex, **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 **eartagging** 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 1st Shipment: BNW 50846-39
- H. Date of Receipt: 1st Shipment 2/12/86
- I. Test Article Preparation and Storage Areas: 2-day reserve in Rm 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

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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 ± 3 **°F** and relative humidities at $55 \pm 15\%$. Air flow will be maintained at 15 ± 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 1st and 7th 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.

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C. Scheduled Necropsy: The rats are scheduled to be euthanized with CO₂ 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

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- 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	CHI- ANOVA	FISHER'S SQUARE	EXACT	TREND TESTS
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

P.L. Hackett
Co-Study Director

Date: 4/4/86

Co-Study Director

Date: 4/4/86

E.D. Crow
Quality Assurance Auditor

Date: 4-8-86

XVIII. APPROVAL BY NTP

B.A. Schweg
Co-Study Officer

Date: 20 May 86

Bryan D. Hansen
Co-Study Officer

Date: 20 May 1986

XIX. REFERENCES

Andersen, M.E. 1981. Pharmacokinetics of inhaled gases and vapors. *Neurobehavioral Toxicology and Teratology* 3: 383-389.

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Armitage, P. 1955. Tests for linear trends in proportions and frequencies. **Biometrics** 11: 375-386.

Baker, T.S. and D.E. **Rickert**. 1981. Dose-dependent uptake, distribution, and elimination of **inhaled** n-hexane in the Fischer-344 **rat**. **Toxicol. Appl. Pharmacol.** 61: 414-422.

Bohlen, P., **U.P.** Schlunegger and E. **Lauppi**. 1973. Uptake and distribution of hexane in rat tissues. **Toxicol. Appl. Pharmacol.** 25: 242-249.

Bus, J.S., D. Deyo **and** M. Cox. 1982. Dose-dependent disposition of n-hexane in F-344 rats after inhalation exposure. **Fund. and Appl. Toxicol.** 2: 226-229.

Bus, J.S., **E.L.** White, P.J. **Gillies** **and** C.S. Barrow. 1979. Tissue distribution of n-hexane, methyl n-butyl ketone and **2,5-hexanedione** in rats after single or repeated inhalation exposure to n-hexane. **Drug Metab. Disposit.** 9: 385-387.

Graham, D.G. and M.R. **Gottfried**. 1984. Cross-species extrapolation in hydrocarbon neuropathy. **Neurobehavioral Toxicol. and Teratol.** 6: 433-435.

Howd, R.A., C.S. Rebert, J. **Dickinson** and G.T. **Pryor**. 1983. A comparison of the rats of development of functional hexane neuropathy in **weanling** and young adult rats. **Neurobehavioral Toxicol. and Teratol.** 5: 63-68.

Howell, W.E. A **neurobehavioral** evaluation of the prenatal toxicity of n-hexane in rats. PhD Thesis, Univ. of Cincinnati, 1979. **Available** from University Microfilms International, Ann Arbor, MI #7922602.

Howell, W.E. and G. P. Cooper. 1981. Neurophysiological evaluation of prenatal n-hexane toxicity. **The Toxicologist** 1:1.

Kimura, E.T. D.M. **Ebert** and P.W. Dodge. 1971. Acute toxicity and **limits** of solvent residue for sixteen organic solvents. **Toxicol. Appl. Pharmacol.** 19: 699-704.

n-Hexane Rat Teratology Study
Appendix F - Study Protocol

Marks, T.A., P.W. Fisher and R.E. Staples. 1981. Influence of n-hexane on embryo and fetal development in rats. *Drug Chem. Toxicol.* 3: 393-406.

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

Singh, K.P., D. Dannan, S.K. Goel, K.P. Pandya and R. **Shanker**. 1983. **2,5-Hexane diol** induced thymic atrophy and **lymphocytotoxicity** in rats. *Indust. Health* 21: 235-242.

Spencer, P.S., D. **Couri** and H.H. Schaumburg. 1980. n-Hexane and methyl n-butyl ketone. In *Experimental and Clinical Neurotoxicology*, P.S. Spencer and H.H. Schaumburg J. (eds.), **Williams & Wilkins**, Baltimore, MD, pp. **456-475**.

Spencer, P.S., H.H. Schaumburg, M.I. **Sabri** and B. Veronesi. 1980. The enlarging view of **hexacarbon neurotoxicity**. *CRC Critical Reviews in Toxicology* 3: 279.

Staples, R.E. 1974. Detection of visceral alterations in **mammalian** fetuses. *Teratology* 9: **A37-A38**.

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

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

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

ATTACHMENT 1

**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^3 , the chamber has an active mixing volume of 1.7 m^3 , the remainder being the non-mixing inlet and exhaust volumes. There are three levels of caging, each level split into two tiers which are offset from each other and from the chamber walls (Figure 1B). Drawer-like, stainless steel cage units composed of individual animal cages, are suspended in the space above each tier. Stainless steel catch pans for collection of urine and feces are suspended below each cage unit. Catch pans are left in position during each exposure period. Instructions for maintenance of these chambers is detailed in SOP# 0B-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^2 and of a rat cage 270 cm^2 (representing dimensions 14.0 cm by 7.6 cm with height 15.0 cm, and 27.9 cm by 9.7 cm with height 20.0 cm, respectively). There are 60 mice or 24 rat individual cages per cage unit. Up to six cage units can fit in a chamber.

II EXPOSURE SUITE CONTROL CENTER

A computer located in the Suite Control Center interfaces with system monitors and controls the basic functions of chamber air flow, test chemical concentration, vacuum, temperature and relative humidity in each of three exposure rooms (Figure 2). The arrangement of computer control and interface instrumentation is shown in Figure 3. The executive computer is an Hewlett Packard Model 9816. All data acquisition and automated system control originates from this computer. All experimental protocols related to the data acquisition and control system (such as data channel assignments, monitoring frequencies, and alarm settings) reside in the executive computer and are entered into tables accessed by menus.

Data input to the executive computer is accomplished through several interface instruments. All gas chromatographic (GC) data is collected and preconditioned by Hewlett Packard Model 85B computers, one for each of the exposure rooms. Conditioned data is transferred to the executive computer for analysis, storage, printing and concentration control. Up to two GCs can be attached to each HP85B computer. Data from all monitoring equipment other than the GCs are inputted through a Colorado Data Systems (CDS) Model 53A-IBX Intelligent Interface System.

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

A complete description of the software for this system is contained in document #B-BE-5E01. Maintenance of the system is detailed in SOP #B-BE-3D0E. Routine operation of the computer system is detailed in SOP #B-BE-3G04. Routine daily operation of the system hardware is detailed in SOP #B-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 1×10^{-3} to greater than 20 ml per minute will be used.

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

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

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

Detailed operating instructions for this system are contained in SOP's QB-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 ~~IDs~~ 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 #OB-BE-3C0J and #OB-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:

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

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 (#OB-BE-3C0J and #OB-BE-3C0L). 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

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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 #0B-BE-3D0E.

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 #0B-BE-3D0E.

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 **ØB-BE-5EØ3**, **ØB-BE-3EØA**, and **ØB-BE-3EØB**.

H. EQUIPMENT OR POWER FAILURE PROTECTION SYSTEMS

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

Power is provided to the Battelle complex from two separate city substations through an automatic **switching** device. This significantly reduces the possibility of losing city power. Power from the city is routed to equipment in LSL-II through **two types** of motor control centers. One type can switch power to the equipment from either city power or emergency power from the LSL-II diesel generator. The other has access only to city power. The emergency-power-type motor control center has a low voltage detector on each leg of the three-phase input power. If the city-supplied power should fail or "brown out", these detectors automatically start the emergency power diesel generator, and route the emergency power to the 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.

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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.

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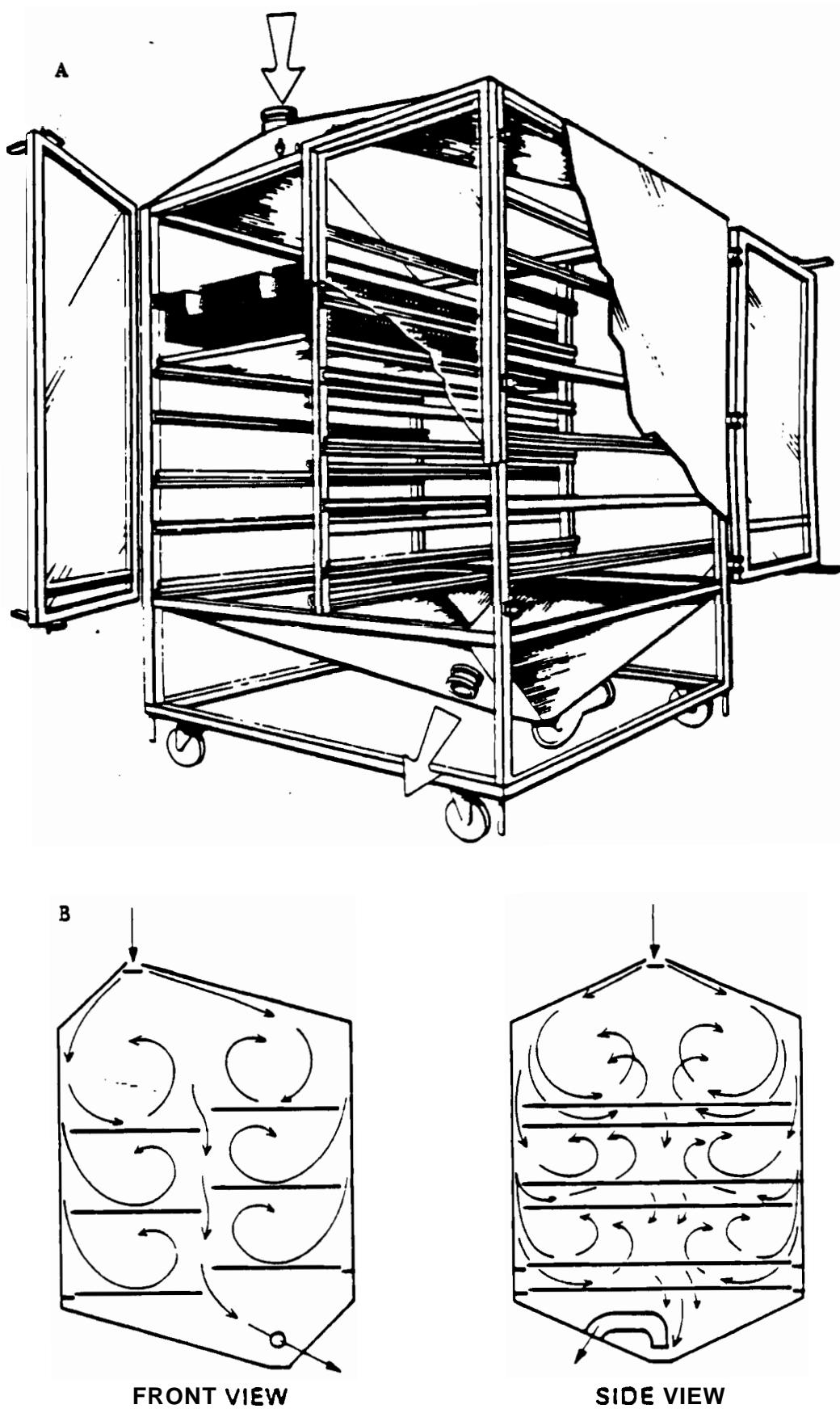


FIGURE 1. Inhalation Exposure Chamber Designed at BNW
(A. Oblique cutaway view of the chamber;
B. Airflow patterns)

EXPOSURE SUITE #1

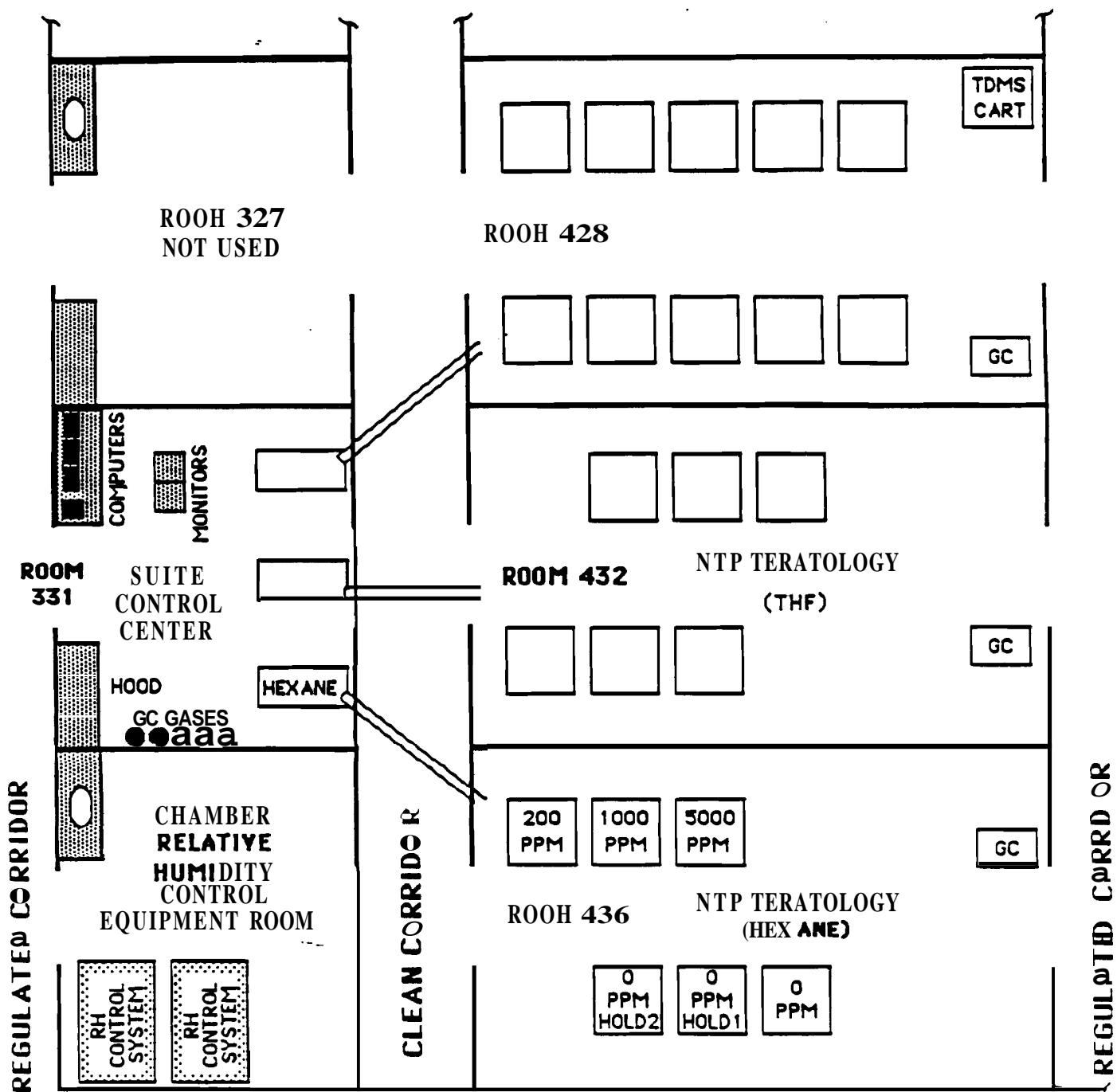


FIGURE 2. Schematic Diagram of the Three Exposure Rooms in the Automated Inhalation Exposure Suite.

COMPUTER SYSTEM

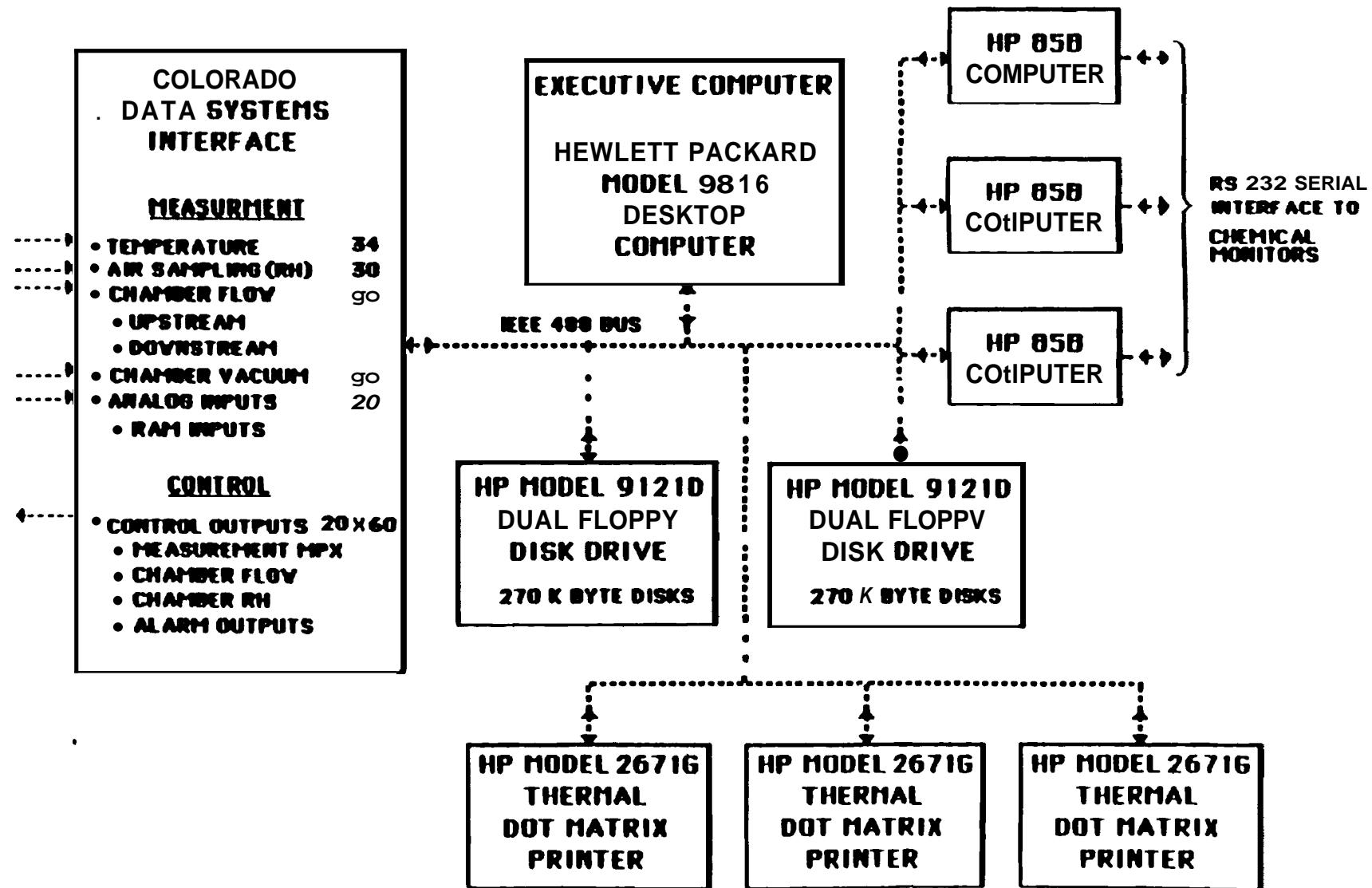


FIGURE 3. Block Diagram of Data Acquisition and Control Computers and Interface Instrumentation

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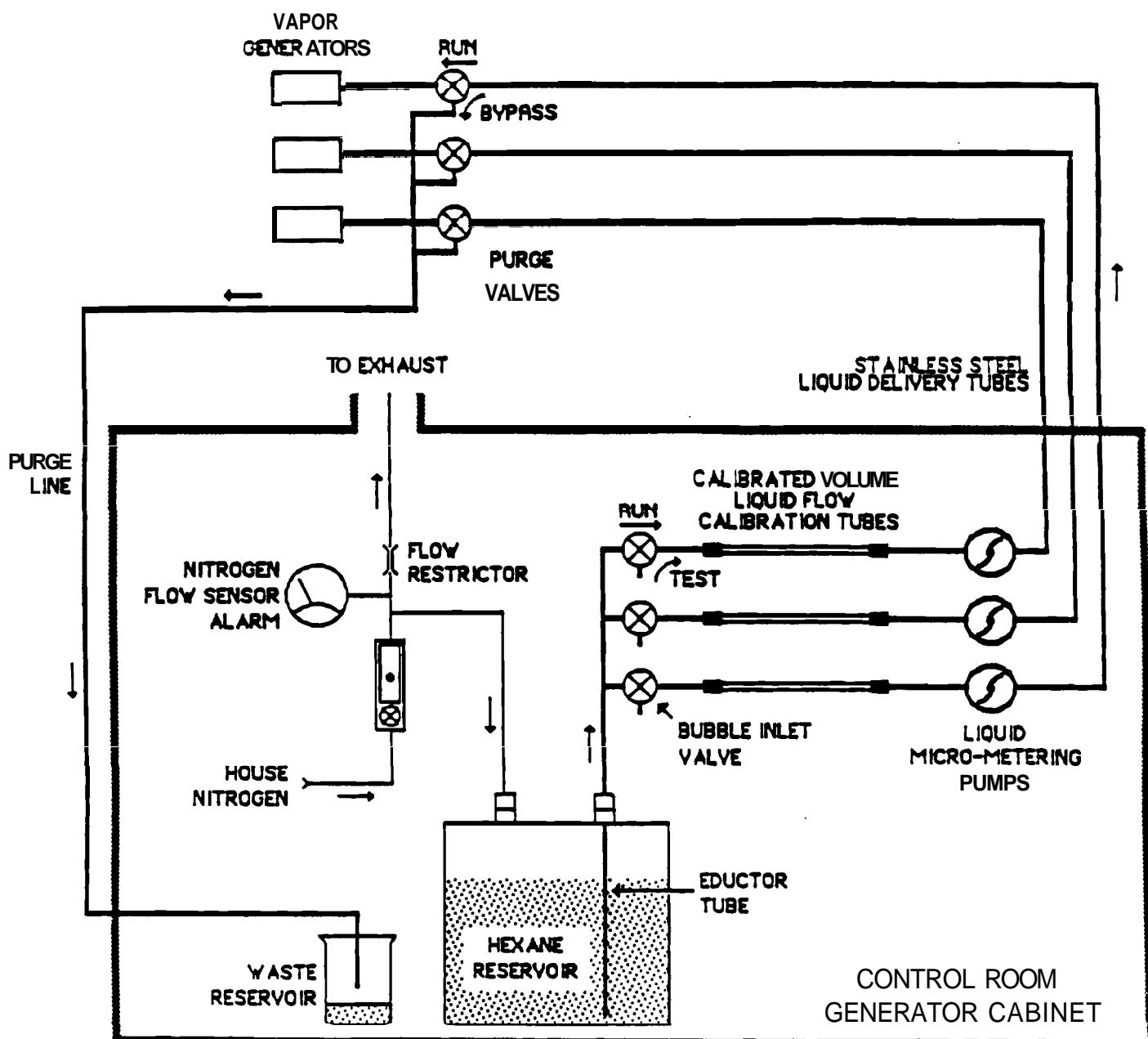


FIGURE 4. Schematic Diagram of the Hexane Vapor Generation System.

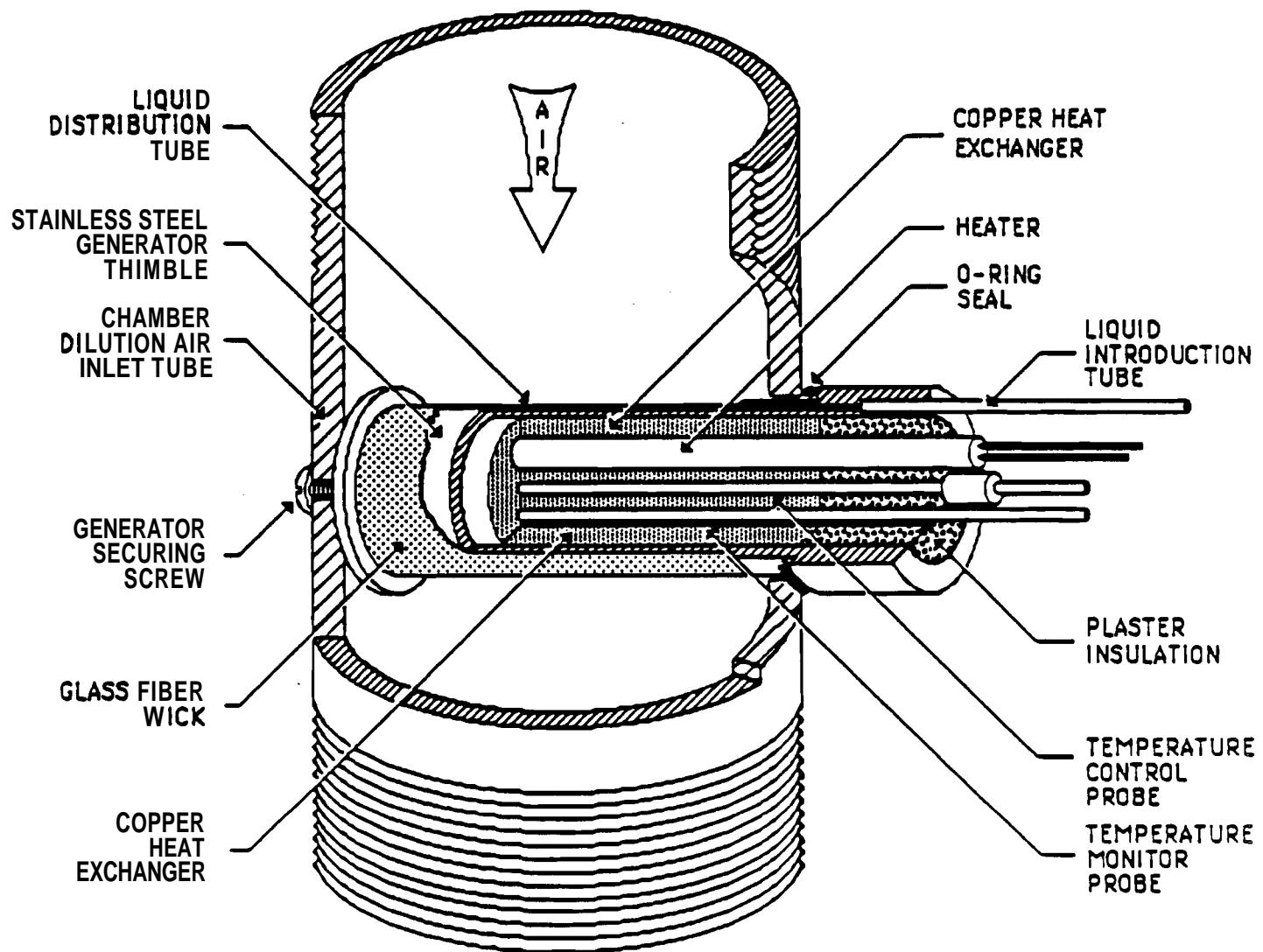


FIGURE 5. Cutaway Drawing of the Hexane Vapor Generator Located in the Fresh-Air Inlet Tube of the Exposure Chamber.

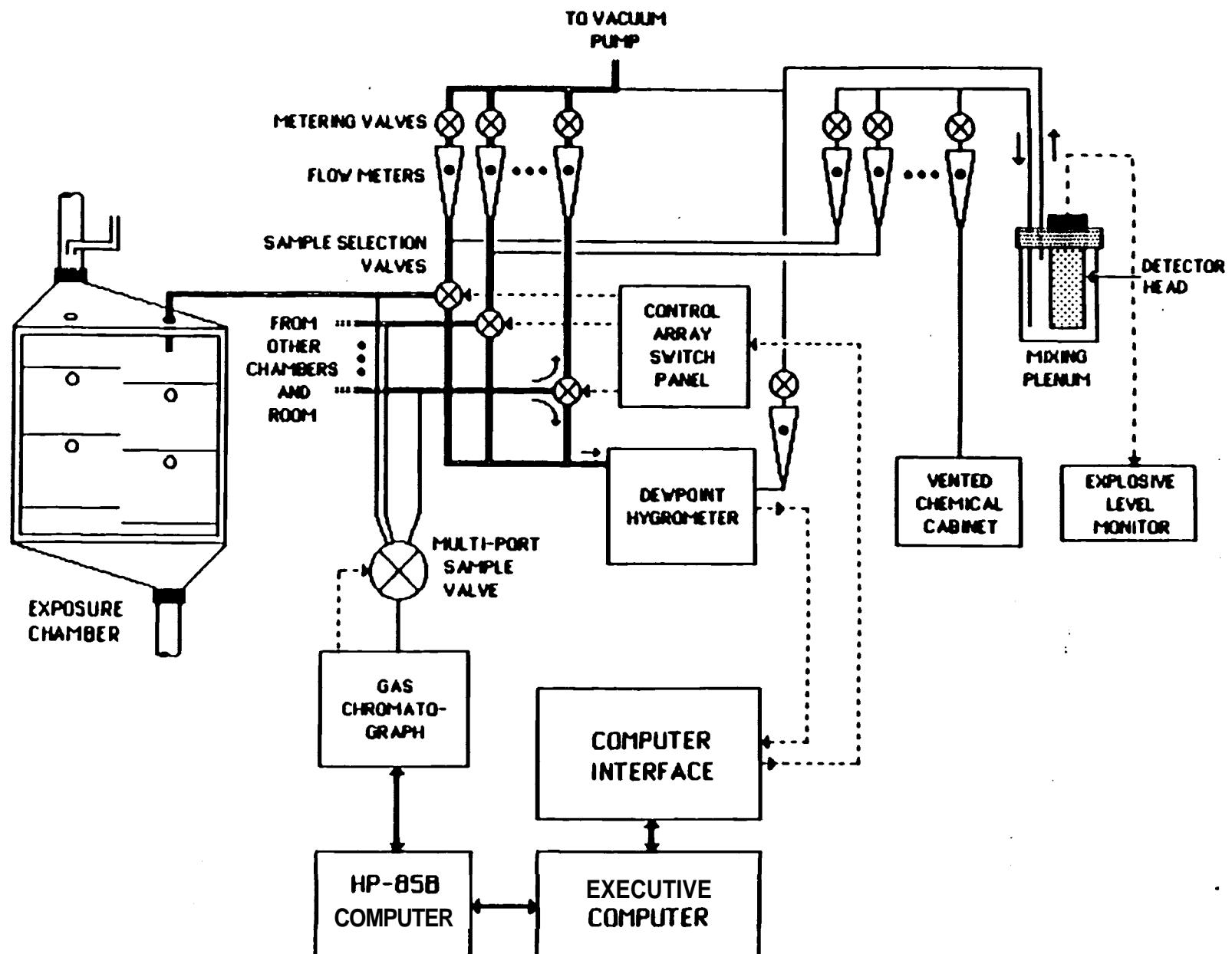


FIGURE 6. Schematic Diagram of the Dewpoint, Chemical Concentration, and Explosive Level Monitoring Systems

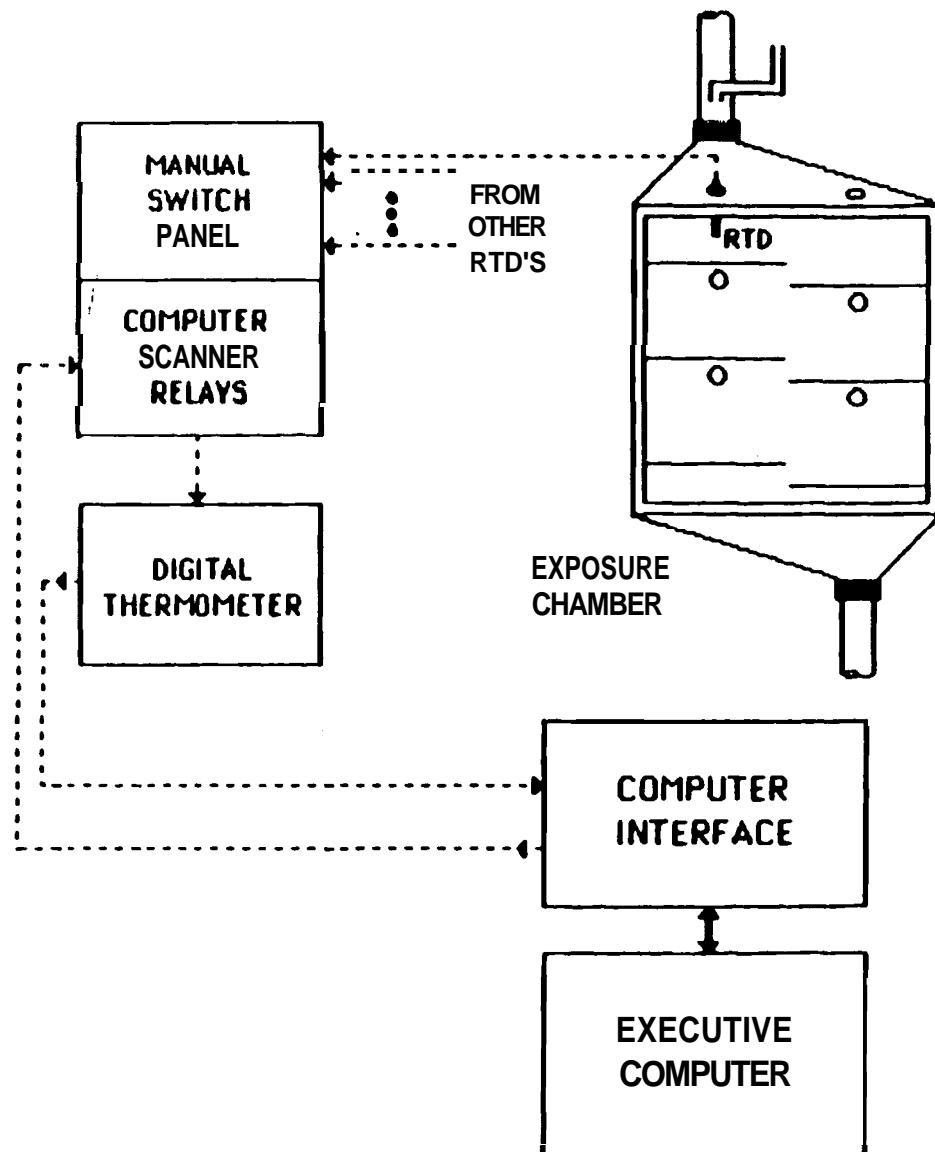


FIGURE 7. Schematic Diagram of Temperature Monitoring System

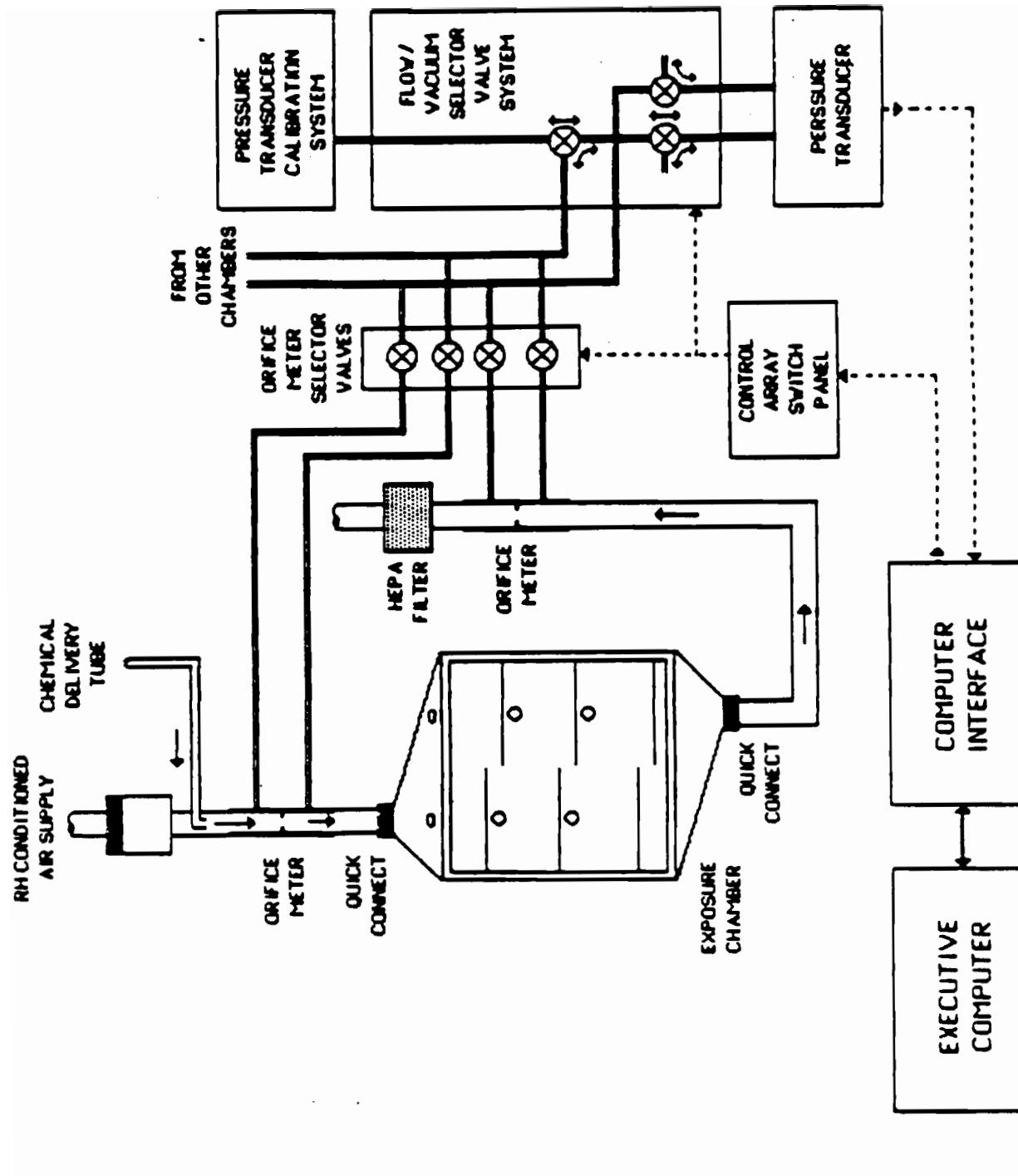


FIGURE 8. Schematic Diagram of the Chamber Flow and Vacuum Monitoring System

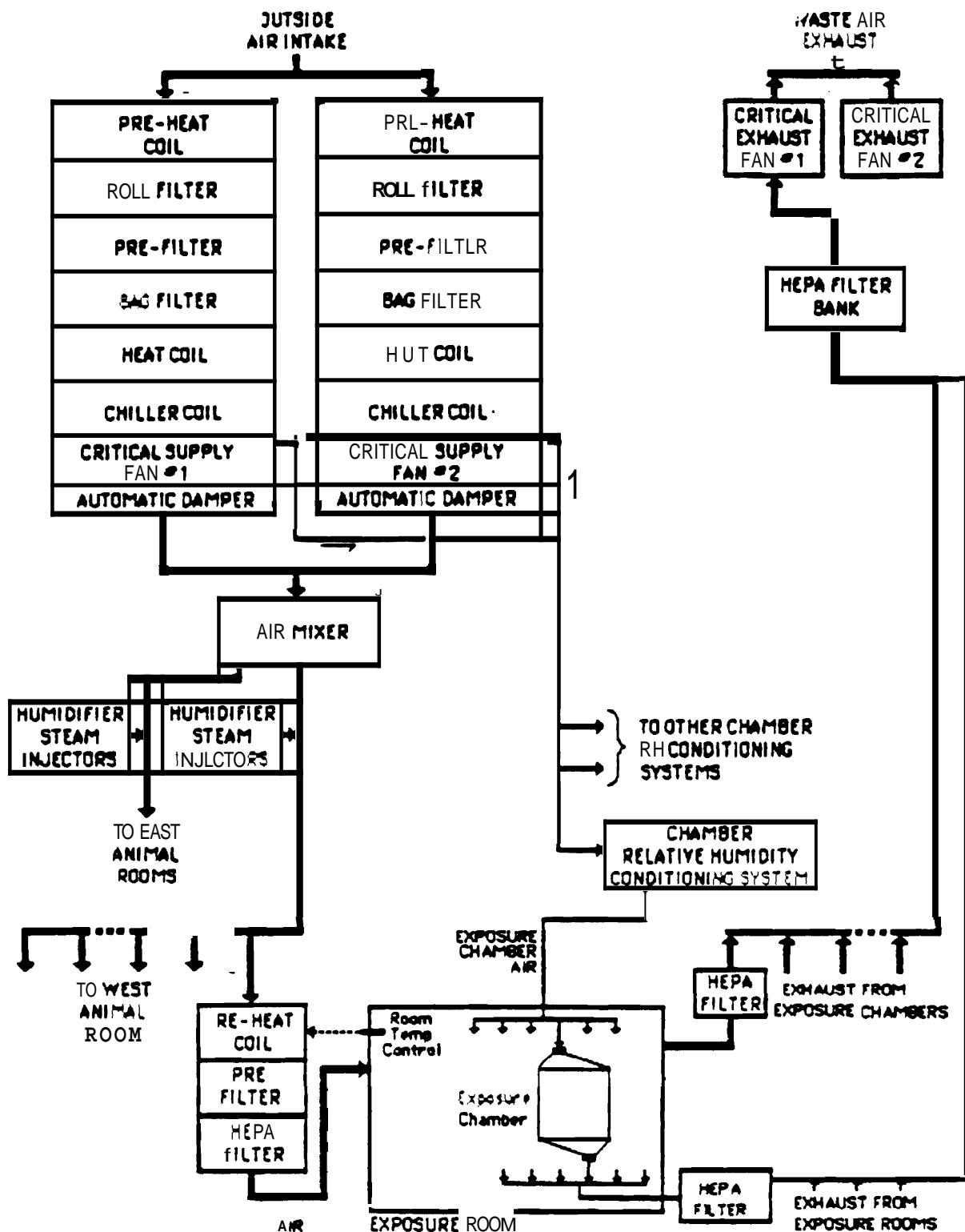


FIGURE 9. Air Handling System for Animal Rooms of Life Sciences II Building

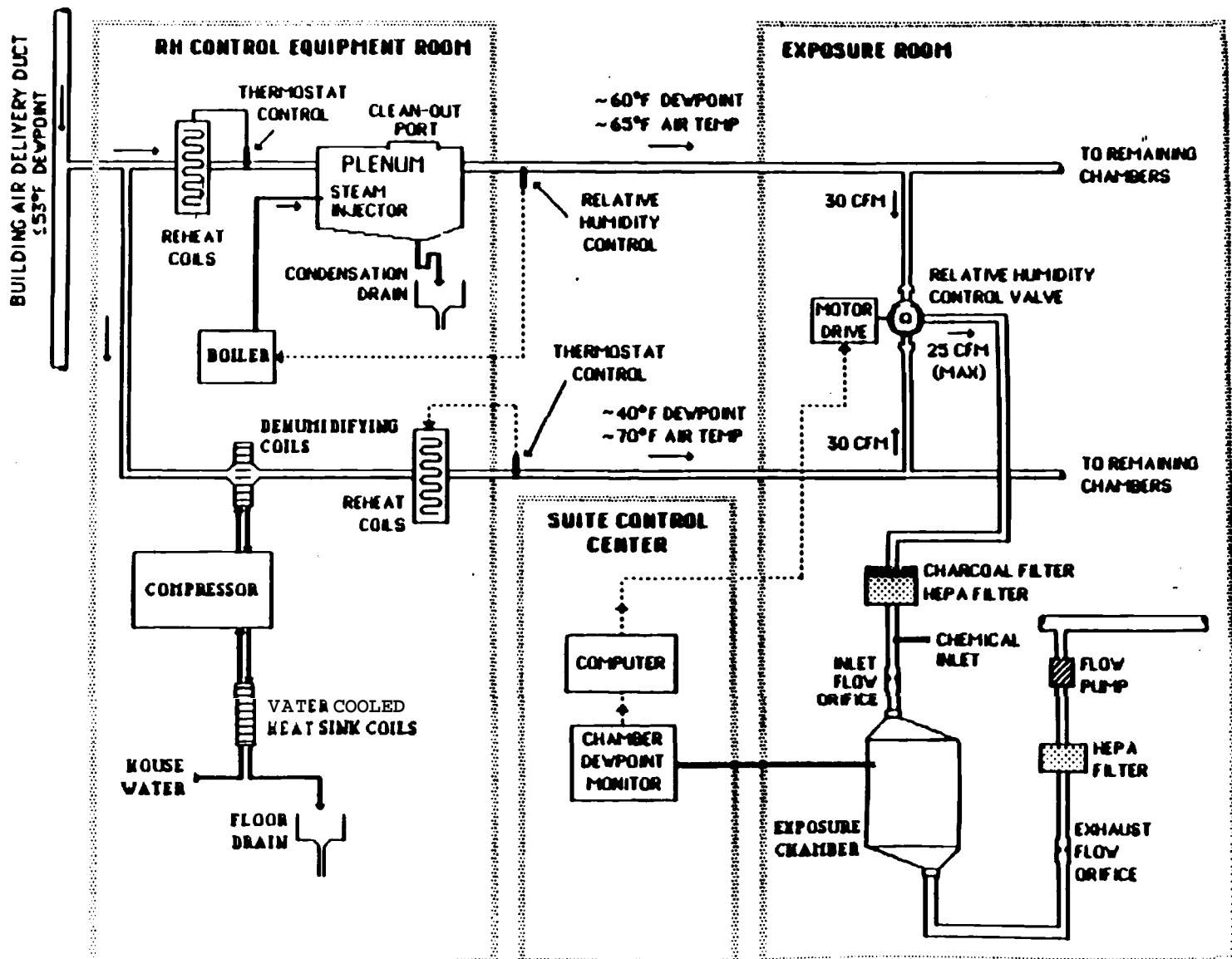


FIGURE 10. Schematic Diagram of Chamber Relative Humidity Control System

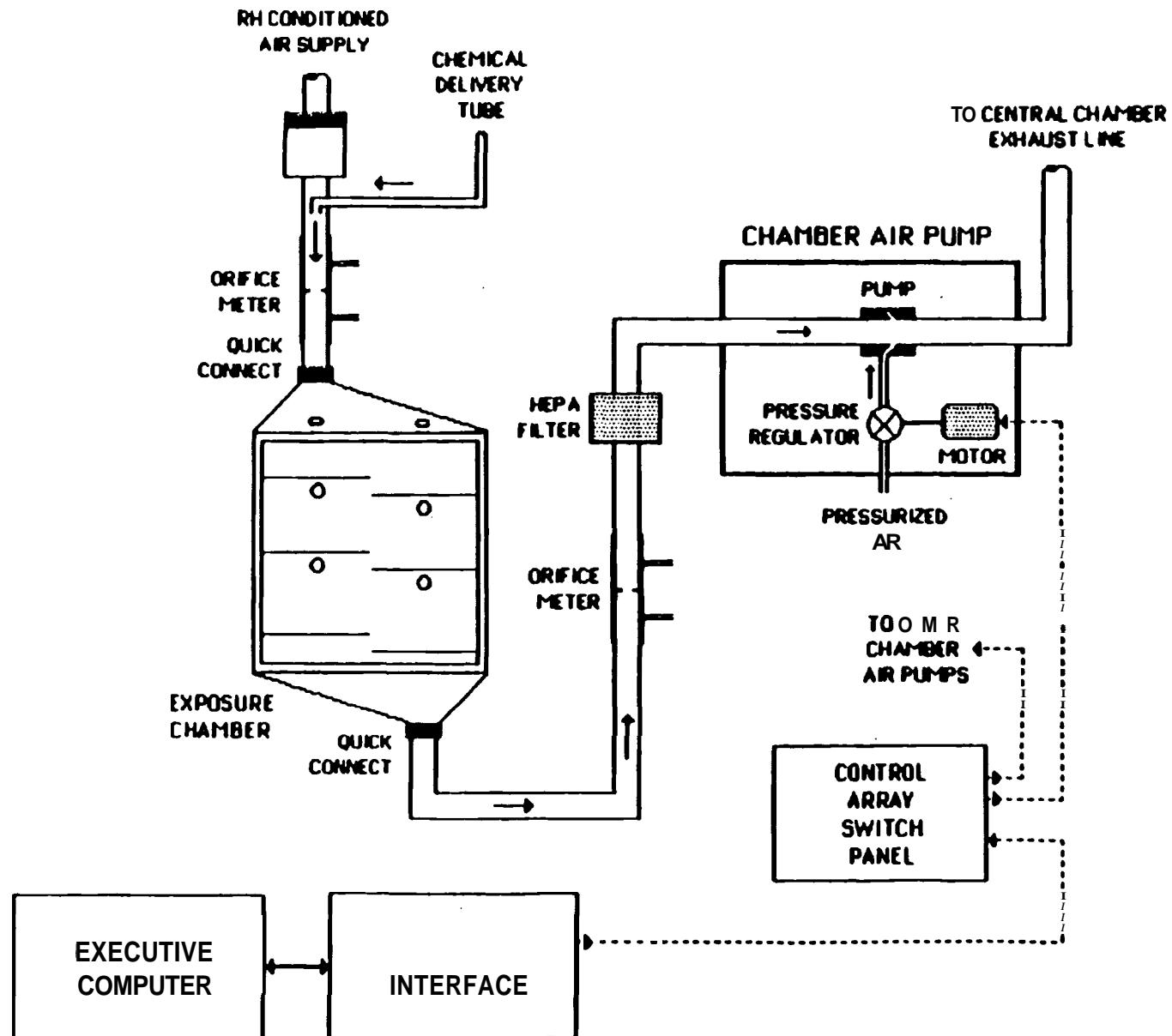


FIGURE 11. Schematic Diagram of the Chamber Air Flow Pump and Air Flow Control System

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 HOH
21:08	Ch #1 -- Room 324	Vacuum	(BSI .8 HOH
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 HOH
21:17	Ch #1 -- Room 324	Temperature	(BSI 81.1 F
21:18	Ch #2 -- Room 324	Relative Humidity	(OKI 46. %
21:18	Ch #3 -- Room 324	Flow	(OKI 16.3 CFM
21:19	Ch #2 -- Room 436	Relative Humidity	(BSE 65. %
21:20	Ch #2 -- Room 436	Vacuum	(OKE 4 HOH
21:21	Ch #1 -- Room 324	Vacuum	(BSI .8 HOH
21:25	Ch #2 -- Room 324	Relative Humidity	(OKI 35. X
21:26	Ch #3 -- Room 324	Concentration	(OKI 5.000E+1 PPM
21:26	Ch #2 -- Room 436	Relative Humidity	(BSE 65. %
21:26	Ch #2 -- Room 436	Vacuum	(OKE 1.3 HOH
21:27	LJF	This is a demonstration of the comment 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 HOH
21:48	Ch #1 -- Room 324	Vacuum	(BSI .8 HOH
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. %
:06	Ch #2 -- Room 436	Vacuum	(OKE 1.5 HOH

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 ~~nr.~~ ~~ver~~, 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: DODO.

 DDD.D

 DD.DD

 D.DDD

 .DDDD

 D.DDDESZ

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

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

FIGURE 12. (Continued)

Summation for the File: 23 July 1985

Exposure: Demonstration

Temperature	Mean	X Targ	Std Dev	% PSD	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	78.3	72.7	15	72.0
Ch #03	73.20	101	.134	3	75.3	70.7	15	72.0
Ch #04	3.20	55	.131	2	75.5	65.7	15	72.0
Ch #05	73.31	101	.131	2	76.3	68.7	15	72.0
Ch #06	73.40	102	.139	2	75.3	72.7	15	72.0
Ch #07	69.40	55	.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	% Targ	Std Dev	% PSD	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	% Targ	Std Dev	% PSD	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	53.	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.	46.	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	59.3	70.0	72.0	74.0
			16:48	59.2	70.0	72.0	74.0
			16:51	59.0	70.0	72.0	74.0
			16:55	59.1	70.0	72.0	74.0
			16:59	59.3	70.0	72.0	74.0
23 Jul		Ch #02	16:47	58.1	70.0	72.0	74.0
			16:49	58.3	70.0	72.0	74.0
		Ch #03	16:40	58.0	70.0	72.0	74.0
			16:59	75.1	70.0	72.0	74.0
			17:09	74.8	70.0	72.0	74.0
23 Jul		Ch #05	14:59	74.3	70.0	72.0	74.0
			16:01	57.1	70.0	72.0	74.0
		Ch #08	16:20	58.1	70.0	72.0	74.0
			16:23	59.0	70.0	72.0	74.0
			16:41	59.8	70.0	72.0	74.0
23 Jul	Flow	Ch #01	12:45	11.2	12.0	15.0	17.0
			15:23	18.1	12.0	15.0	17.0
		Ch #05	15:33	9.1	12.0	15.0	17.0
			10:23	20.1	12.0	15.0	17.0
			16:41	20.2	12.0	15.0	17.0
23 Jul	Concentration	Ch #03	10:45	4.550E+0	5.000E+0	7.500E+0	1.000E+1
			10:50	4.350E+0	5.000E+0	7.500E+0	1.000E+1
			11:01	4.200E+0	5.000E+0	7.500E+0	1.000E+1
			11:14	4.130E+0	5.000E+0	7.500E+0	1.000E+1
			11:28	4.580E+0	5.000E+0	7.500E+0	1.000E+1
		Ch #06	9:06	1.140E+1	5.000E+0	7.500E+0	1.000E+1
			9:21	1.194E+1	5.000E+0	7.500E+0	1.000E+1
23 Jul		Ch #08	9:46	1.053E+1	5.000E+0	7.500E+0	1.000E+1
			11:46	1.001E+1	5.000E+0	7.500E+0	1.000E+1
			12:07	1.003E+1	5.000E+0	7.500E+0	1.000E+1

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

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

n-Hexane Rat Teratology Study
Appendix F - Study Protocol

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

ØB-AC-3B1A

ANIMAL RESOURCE CF TER

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 Rotatation 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
Appendix F - Study Protocol

Necropsy and Developmental Evaluations for Teratology
Studies—Rodents and Rabbits
Examination of Fetal Heads Fixed in Bouin's Solution
Photography
Data Acquisition and Transfer with a Microcomputer
Data Handling and Storage
Sample Storage/Shipmet
Examination of Fetal Skeletons Stained with
Alcian Blue/Alizarin Red
Preparation of the Reproductive System for Histologic Evaluation

ØB-DT-3BØG
ØB-DT-3BØI
ØB-DT-3BØJ
ØB-DT-3BØK
ØB-DT-3BØL
ØB-DT-3BØM
ØB-DT-3BØY
ØB-DT-3B1J

HEALTH AND SAFETY

Biohazard Protocol n-Hexane
Bioassay Studies: Health and Safety Plan
The 3M Brand **W-2869 Hardcap**, Continuous-Flow Air-line Respirator
Scott-Presur Pak II Self-contained Breathing Apparatus
Respiratory Protection Program

ØB-HS-3S1S
ØB-HS-3S1C
ØB-HS-3S19
ØB-HS-3S1A
ØB-HS-3S1B

n-Hexane Rat Teratology Study
Appendix F - Study Protocol

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
STUDY: RAT TERATOLOGY/BEHAVIOR PILOT
ROOM: 436
DATE: 5/17/86 *BJS*

CHEMICAL: n-Hexane
CHAMBER: 1
CONCENTRATION: 0ppm

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

LEVEL 3		LEVEL 4	
CAGE #	CAGE #	CAGE #	CAGE #
BACK 12	24	BACK 12	669 (A) 802 (C)
11	23	11	668 (A) 749 (C)
10	22	10	645 (A) 748 (C)
9	21	9	643 (A) 740 (C)
8 936 (D)	20	8	616 (A) 662 (C)
7 805 (D)	19	7	602 (A) 594 (C)
6 785 (D)	18	6	581 (A) 559 (C)
5 746 (D)	17	5	563 (A) 496 (C)
4 647 (D)	16	4	527 (A)
3 646 (D)	15	3	471 (A) 967 (A)
2 632 (D)	14	2	466 (A) 698 (A)
FRONT 1 566 (D)	13	FRONT 1	463 (A) 675 (A)

LEVEL 5		LEVEL 6	
CAGE #	CAGE #	CAGE #	CAGE #
BACK 12	24	BACK 12	24
11	23	11	23
10	22	10	383
9	21	9	378
8	20	8	771
7 651 (D)	19	7	706
6 804 (D)	18	6	630
5 798 (D)	17	5	510
4 742 (D)	16	4	609
3 732 (D)	15	3	595
2 502 (D)	14	2	551
FRONT 1 449 (D)	13	FRONT 1	498

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 *GD*

* CHEMICAL: n-Hexane

CHAMBER: 2

CONCENTRATION: 200 ppm

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 #
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)	
	7 652 (A)	896 (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) 13

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)	726 (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)	
	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
	5 906 (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
	8 724	20
	7 713	19
	6 618	18
	5 575	17
	4 569	16
	3 564	15
	2 500	14
FRONT	1 495	13

LEVEL 3 & 4 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 * CHEMICAL: n-Hexane
STUDY: RAT TERATOLOGY/BEHAVIOR PILOT CHAMBER: 3
ROOM: 436 CONCENTRATION: 1000ppm
DATE: 5/17/86 (JL)

LEVEL 1		LEVEL 2	
BACK	CAGE #	BACK	CAGE #
	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 3		LEVEL 4	
BACK	CAGE #	BACK	CAGE #
	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
FRONT	1 549 (D)		13

LEVEL 5		LEVEL 6	
BACK	CAGE #	BACK	CAGE #
	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
FRONT	1 597 (D)		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 *BLR*

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

		LEVEL 1		LEVEL 2	
	CAGE #		CAGE #		CAGE #
BACK	12		24	12	536 (B)
	11		23	11	457 (B)
	10		22	10	762 (C)
	9		21	4	948 (A)
	8		20	8	690 (A)
	7		19	7	636 (A)
	6		18	6	586 (A)
	5		17	5	574 (A)
	4		16	4	538 (A)
	3		15	3	468 (A)
	2		14	2	472 (A)
FRONT	1		13	1	453 (A)

		LEVEL 3		LEVEL 4	
	CAGE #		CAGE #		CAGE #
BACK	12		24	12	626 (A)
	11		23	11	605 (A)
	10		22	10	588 (A)
	9		21	9	554 (A)
	8	880 (D)	20	8	535 (A)
	7	663 (D)	19	7	531 (A)
	6	600 (D)	18	6	523 (A)
	5	641 (D)	17	5	517 (A)
	4	623 (D)	16	4	497 (A)
	3	608 (D)	15	3	492 (A)
	2	542 (D)	14	2	468 (A)
FRONT	1	451 (D)	13	1	454 (A)

		LEVEL 5		LEVEL 6	
	CAGE #		CAGE #		CAGE #
BACK	1		24	12	24
			23	11	23
			22	10	22
	9		21	9	21
	8	937 (D)	20	8	20
	7	654 (D)	19	7	19
	6	819 (D)	18	6	18
	5	799 (D)	17	5	17
	4	762 (D)	16	4	16
	3	730 (D)	15	3	15
	2	630 (D)	14	2	14
FRONT	1	486 (D)	13	1	459

Virgin

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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