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November 15, 1993

U.S. Environmental Protection Agency
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Attn: TSCA Document Receipts (TS-790)
ET G-99
401 "M" Street, S.W.
Washington, DC 20460

RE: TSCA Section 8(e)
Notification on Di-isopropyl
ether, CAS 108-20-3

Dear Sir:

The _____ has investigated the developmental effects of di-isopropyl ether in rats. A statistically significant increase in rudimentary 14th ribs at vapor concentrations of 14.6 and 29.3 mg/l was observed. Maternal toxicity, possibly secondary to the stress of an inhalation exposure, was also observed at these dose levels. We do not believe that this result demonstrates a significant risk to human health, but the data are being submitted because of uncertainty in interpreting EPA criteria for reporting results of reproductive health studies. The report for this study is enclosed.

Confidentiality is being claimed for the company name and names of company employees. All pages containing this information have been stamped confidential. Two copies of this notification are being submitted; confidential information has been excised from one copy and circled on the other. The substantiation for the confidentiality claim is attached.

Sincerely,

Enclosures

This report is being made in compliance with Section 8(e) of the Toxic Substances Control Act (15 U.S.C. 2607), pursuant to our understanding of the Statement of Interpretation and Enforcement Policy (43 Fed. Reg. 11110 et. seq.). It has been compiled based on information available within the time period given. The corporation and individual signator also reserve the right to supplement any or all of the data contained herein and to revise or amend any conclusion drawn therefrom.

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SUBSTANTIATION OF CONFIDENTIALITY CLAIM

Confidentiality is being claimed for the submitter's identity and the names of company scientists which appear in the submission.

1. This confidentiality claim is being made on the submitter's behalf.
2. No time limit is specified for this claim since we cannot assign a time at which the material being reported will no longer be of commercial interest to the submitter.
3. The information contained in this submission has not been previously submitted to any governmental agency.
4. The information is kept in an Archive and other company confidential files to which access is restricted to authorized personnel.
5. No one outside _____ has access to the information involved in this confidentiality claim.
6. The information for which confidentiality is being claimed does not appear in any advertising or promotional material, material safety data sheet, technical data sheet, professional or trade publication, or any other media available to the public or to our competitors.
7. To our knowledge, no confidentiality determinations have been made by the EPA, other Federal agency, or court in connection with this information.
8. These claims are being made in order to retain maximum utility of the information for the corporation which incurred the costs of the study being reported.
9. The test article discussed in this submission is not patented.
10. The substance covered by this submission has been commercially available from other manufacturers for many years.
 - a. Our competitors are aware that it is on the market.
 - b. In the past this material has been burned for fuel and added to gasoline. We are not aware of current uses.
11. Reverse engineering is not an issue in this confidentiality claim since the structure of the test article is being disclosed.
12. Disclosure of this information would not reveal confidential processes or concentrations of substances in a mixture. The information is unrelated to the effects of the substances on human health or the environment.
13. The CAS number is provided in the submission cover letter.
14. The subject of this notification and the information being claimed confidential are not subject to FIFRA regulation or reporting.

REPORT RELEASE

TO LIAISON:

STUDY NUMBER: 64721

CRU NUMBERS: 91510, 91642

SAMPLE NAMES: Di-Isopropyl Ether (DIPE)

STUDY TITLE: Developmental Toxicity Study in Rats Exposed via Inhalation to Di-Isopropyl Ether (DIPE) Vapors

REQUESTING DIVISION: _____

RESULTS:

Presumed-pregnant rats were exposed to Di-Isopropyl Ether (DIPE) vapors for six hours daily during gestation days 6-15. The mean vapor concentrations at the three dose levels were measured to be 1.9, 14.0, and 30.8 mg/L with DIPE representing approximately 95, 92, and 92% of the total vapor concentration, respectively. Two additional groups served as controls; one untreated control and one inhalation sham control. All remaining animals were killed on gestation day 20.

Exposure to DIPE vapors resulted in slight maternal and developmental toxicity at the mid and high dose concentrations. Evidence of maternal toxicity consisted of clinical signs of 'anesthetic effects' in several high dose females, a significant reduction in body weight gain, and a significant decrease in food consumption. A dose-related increase ($p < 0.01$ at the mid and high dose concentrations) in the incidence of rudimentary 14th ribs was the only indicator of adverse fetal developmental effects. There was no apparent toxicity, either maternal or fetal, at the lowest exposure level.

Study Director

10-19-93

Date

Supervisor

10-18-93

Date

Manager, Mammalian/Genetic Toxicology

11/4/93

Date

Manager

11/7/93

Date

DISTRIBUTION: Archives/original All signatories

Study 64721-Final Report

Study Personnel

Developmental Toxicology Group Supervisor:

Inhalation Toxicology Group Supervisor:

Study Director:

Study Participants - technical:

Study Participants - animal care:

(supervisor)

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Study No. 64721CA - Serum Chemistry Data for a Developmental Toxicity Study in Rats
Exposed Via Inhalation to Di-Isopropyl Ether (DIPE) Vapors
Study Biochemist

EXECUTIVE SUMMARY

Presumed-pregnant rats were exposed to Di-Isopropyl Ether (DIPE) vapors for six hours daily during gestation days 6-15. The mean vapor concentrations at the three dose levels were measured to be 1.9, 14.0, and 30.8 mg/L with DIPE representing approximately 95, 92, and 92% of the total vapor concentration, respectively. Two additional groups served as controls; one untreated control and one inhalation sham control. All remaining animals were killed on gestation day 20.

Exposure to DIPE vapors resulted in slight maternal and developmental toxicity at the mid and high dose concentrations. Evidence of maternal toxicity consisted of clinical signs of 'anesthetic effects' in several high dose females, a significant reduction in body weight gain, and a significant decrease in food consumption. A dose-related increase ($p < 0.01$ at the mid and high dose concentrations) in the incidence of rudimentary 14th ribs was the only indicator of adverse fetal developmental effects. There was no apparent toxicity, either maternal or fetal, at the lowest exposure level.

SUMMARY

An inhalation/developmental toxicity study was conducted at

to obtain data on the effects of Di-Isopropyl Ether (DIPE) on parameters of reproductive performance during gestation and the viability and development of the embryo/fetus. DIPE was administered during gestation days 6-15 for six hours per day via pulmonary exposure to presumed-pregnant rats at mean concentrations of 1.9, 14.0, and 30.8 mg/L. Two additional groups served as controls; one untreated control and one inhalation sham control. All remaining animals were killed on gestation day 20.

Exposure to DIPE vapors resulted in signs of slight anesthesia, a significant reduction in body weight gain, and a significant decrease in food consumption at 14.0 and 30.8 mg/L. Maternal serum chemistry values were not affected by DIPE vapor exposure. No adverse effects were observed for fetal parameters at the time of cesarean section (viability, body weight, external development) or subsequent fetal visceral examination. Fetal skeletal examination revealed a statistically significant ($p < 0.01$) increase in the incidence of rudimentary ribs at 14.0 and 30.8 mg/L.

Based on the data generated, exposure to DIPE vapors during gestation results in both maternal and developmental toxicity at 14.0 mg/L and above.

1.0 INTRODUCTION

A developmental toxicity study was conducted at in which presumed-pregnant animals were exposed to DIPE vapors via inhalation. This route of administration was chosen because of the potential for vaporization of DIPE during production, handling, and use as a gasoline additive. The dose levels chosen were the same as those used in the 13-week inhalation study that was being run concurrently (Study No. 64661). The primary objective of this study was to evaluate the effects of DIPE vapors on female rats during gestation (body weight gain, food consumption, serum chemistry parameters) and to determine if *in utero* exposure to the material adversely affects fetal viability and development.

2.0 METHODOLOGY

2.1 Experimental Design

Presumed-pregnant rats were distributed into five groups: two control groups (untreated and sham) and three groups exposed to DIPE at approximate concentrations of 1.9, 14.0, and 30.8 mg/L, respectively (see Section 2.6.1 for additional details on DIPE concentrations). Animals in

Group 1 (Untreated Control) received no treatments. Animals in Groups 2-4 were exposed (either sham or test material) for six hours on each of gestation days 6-15. At the start of the dosing phase of the study, each group contained 22 presumed-pregnant females.

All the animals were monitored throughout the study until sacrifice for 1) changes in appearance, behavior, and excretory function, and 2) signs of ill-health, mortality, abortion and/or dystocia. A prepartum investigation on a variety of maternal and fetal parameters for Groups 1-5 was undertaken to assess the influence of DIPE vapors on reproductive performance and development of offspring. The inclusive dates for specific study activities were as follows:

Acclimation Period:	October 1-14, 1991
Mating Period:	October 14-25, 1991
Gestation Period:	October 15 -November 14, 1991
Cesarean Section:	November 4-14, 1991
Skeletal Examinations:	March 24 -September 17, 1993
Visceral Examinations:	March 10, 1992 -July 6, 1993

2.2 *Animal Data*

One hundred thirty female Sprague-Dawley rats [VAF/Plus CrI:CD(SD)BR; approximately 9 weeks old] were obtained from Charles River Breeding Laboratories, Kingston, New York. The male rats used as breeders were already in-house and had been received on July 15, 1991, from the same Charles River facility. The females were acclimated to the test facility for two weeks before the breeding period was initiated. Each female was individually identified by a numbered metal ear tag on gestation day 0. With the exception of exposure periods (at which time no food or water was available to females in Groups 2-4), tap water and Purina Certified Rodent Chow #5002 were provided *ad libitum* during the course of the study.

When not in exposure chambers, animals were housed in air-conditioned rooms set to maintain 68-72°F, 40-60% relative humidity, and 12-hour light-dark cycles. The average temperature throughout the study ranged from 69-71°F in the animal rooms with no significant deviations (on several days, the temperature reached 73°F). The temperature inside the inhalation chambers averaged 73°F ± 2°. The average humidity in the animal rooms ranged from 37-65%, with the humidity dropping occasionally into the low 30's. Humidity in the inhalation chambers was higher and averaged 60±9, 61±7, 66±7, and 51±8% in chambers 1-4, respectively. This large deviation in humidity is not unexpected since the chambers are sealed during the exposure period and then opened during the nonexposure periods. During the weekend of October 26, 1991, the lights were on in each animal room for an extra hour until the timers could be reset to accommodate the change from Daylight Savings Time to Eastern

Standard Time. None of the above deviations from set temperature, humidity, or lighting adversely effected study results.

2.3 Mating Period

During the mating period (2 weeks, excluding Saturday and Sunday nights when pairs were not cohabited), female rats which had not previously borne pups were placed with male rats in a ratio of 1:1. Each morning during the periods of cohabitation, females were monitored for the presence of vaginal or tray plugs. If either was present, a vaginal lavage sample was obtained and examined for the presence of spermatozoa. Females that were positive for spermatozoa were considered to be at day 0 of presumed gestation and were placed in individual housing units. The cohabitation period was continued until 110 presumed-pregnant female rats were obtained. Female rats which showed no evidence of breeding activity, and the male rats used for breeding, were returned to the general rat population in the facility.

2.4 Assignment to Experimental Groups

On day 0 of gestation, presumed-pregnant female rats were distributed to one of Groups 1-5 using a computer-generated table of random numbers for a stratified sample size of 5. This procedure was continued until each group contained 22 presumed-pregnant females.

2.5 Material Administered

Test Material: Di-Isopropyl Ether (DIPE)

Identification: CRU# 91510 Used 10-21-91 through 11-1-91

CRU# 91642 Used 11-2-91 through 11-9-91

Both CRU samples were received from the same lot of DIPE which was being stored at the laboratory. Shipments were made to as more material was needed.

Expiration Date: 05-01-92 when refrigerated.

2.6 Test Material Administration

2.6.1 DIPE Vapor Administration (Groups 3 -5)

Presumed-pregnant females in Groups 3-5 were exposed to DIPE vapors for 6 hours daily on each of gestation days 6-15. They were singly housed in the inhalation chambers throughout this period and did not receive food or water during exposures. All exposures were performed by members of the Inhalation Toxicology group. In general, neat DIPE was vaporized via heat generated from hot water (~115°F), mixed with air, and carried to the inhalation chambers. The air stream carrying the DIPE was divided and diluted as needed to supply the varying concentrations to each of the three DIPE chambers. Analysis of samples taken from the three chambers indicated that the mean total vapor concentrations were 1.9, 14.0, and 30.8 mg/L.

DIPE represented approximately 95, 92, and 92%, respectively of those total vapors (see Table 1). A more detailed description of vapor generation and exposure conditions can be found in the Support Data book for this study in a memo to the study file which was prepared by the Study Inhalation Toxicologist.

TABLE 1

Summary of Exposure Data

GROUP	TARGET CONCENTRATION (mg DIPE/L)	ACTUAL DIPE CONCENTRATION (mg DIPE/L)*	TOTAL VAPOR CONCENTRATION (mg vapor/L)*
1	---	---	---
2	0.0	0.0	0.0
3	3.1	1.8	1.9
4	14.6	12.9	14.0
5	29.3	28.2	30.8

* As measured by gas chromatography.

2.6.2 Untreated and Sham Control (Groups 1 and 2)

Females in the Inhalation Sham Control group were also housed in the inhalation chambers throughout gestation days 6-15. These animals were treated in an identical manner to those in the DIPE-exposed groups except that no DIPE vapors were administered. The Untreated Control animals were housed in a separate room in standard stainless-steel cages with wire bottoms and fronts. Food and water were available to the untreated females at all times and no treatments (sham or otherwise) were performed.

2.7 Observations During the Gestation Period

2.7.1 Appearance and Clinical Signs

Each presumed-pregnant female was observed at least once daily throughout gestation until sacrifice for signs of pathosis, abortion, premature delivery, and/or death. All unusual findings were noted.

2.7.2 Body Weight and Food Consumption Measurements

The body weight of each presumed-pregnant female was measured to the nearest 0.1 gram on gestation days 0, 6, 13, 16, and 20. A measured amount of food was provided for each female on gestation day 0; food consumption per female was measured to the nearest 0.1 gram on each of gestation days 6, 13, 16, and 20.

2.8 Female Necropsy

Each female rat was sacrificed by over-exposure to diethyl ether on its 20th day of presumed gestation. A blood sample for clinical chemistry analysis was obtained from ten pregnant females per group via the abdominal aorta. The thoracic and abdominal cavities of each female were exposed and the organs examined grossly for evidence of pathosis. No maternal tissues (other than the blood samples) were saved.

2.8.1 Serum Chemistry Analyses

The blood samples collected at the time of sacrifice were allowed to clot in an SST Serum Separator Tube (Beckman-Dickinson, Rutherford, NJ). The samples were then given to a member of the Biochemical Toxicology Section for serum chemistry analyses. A more detailed description of the procedures employed for the serum chemistry analysis are available in the

Archives [Study 64721CA, Serum Chemistry Data for a Developmental Toxicity Study in Rats Exposed Via Inhalation to Di-Isopropyl Ether (DIPE) Vapors]. The quantity or activity of the following serum components was measured:

Alanine Aminotransferase (ALT)	Glucose
Albumin	Lactate Dehydrogenase (LDH)
Albumin/Globulin Ratio	Phosphorus, Inorganic
Alkaline Phosphatase (ALP)	Potassium
Aspartate Aminotransferase (AST)	Sodium
Bilirubin, Total	Sorbitol Dehydrogenase (SDH)
Calcium	Total Protein
Chloride	Triglycerides
Cholesterol	Urea Nitrogen
Creatinine	Uric Acid
Globulin	

2.8.2 Uterine/Ovarian Examination

The ovaries and uterus of each rat were excised and examined grossly. The number of corpora lutea per ovary of each pregnant female was counted and recorded; the ovaries were then discarded. The ovaries of nonpregnant females were grossly examined and then discarded. All remarkable findings were recorded. The weight of each intact gravid uterus was measured to the nearest 0.1 gram and recorded. The uterine contents were then exposed and the number and location of all implantations (early/late resorptions and live/dead fetuses) were recorded. The uterus of each female rat that appeared non-gravid was pressed between two glass slides and examined grossly to confirm that no implantation sites were present.

2.8.3 *Fetal Evaluations*

Each live fetus was stripped of its surrounding extra-embryonic membranes, and its umbilical cord was clamped flush with the abdominal wall. The cord was then severed distal to the clamp. Each fetus was gendered, weighed to the nearest 0.1 gram, and grossly examined for external anomalies. The following definitions and terminology were used in describing fetal findings [1]:

Malformation: A permanent structural deviation which generally is incompatible with, or severely detrimental to, normal postnatal survival or development. Additionally, absence of a structure which should have been present, as well as deviations in tail development, are also classified as malformations.

Variation: A variation is a divergence beyond the usual range of structural constitution. It has an indeterminate effect on health and generally has no effect on survival.

Incidental: An incidental finding is generally an accidental event, e.g., accidentally, tip of tail was cut off.

After gross evaluation, fetuses in each litter were equally distributed into two groups, and preparation began for either soft tissue or skeletal evaluations. Fetuses assigned to the soft tissue analysis group were fixed in Bouin's solution. Visceral examination was performed using a modification of the Wilson technique of free-hand sectioning by razor blade; only fetuses in Groups 1, 2, and 5 were examined for soft tissue anomalies. Fetuses assigned to the skeletal analysis group were eviscerated, fixed in 95% ethanol, macerated with potassium hydroxide, and stained for bone. Fetuses from Groups 1-5 (17, 14, 15, 15, and 15 litters, respectively), were examined for skeletal anomalies; not all litters could be read in those groups since the specimens in one of the staining boxes dissolved during the maceration process. The specific litters affected are listed in the 'memos' section of the Support Data book for this study.

2.9 *Data Analyses and Storage*

Data were collected, processed, and analyzed using the Reproduction module of the Grosse Data Acquisition/Reporting System. Maternal biophase data, cesarean section data, and fetal data were evaluated statistically by analysis of variance (ANOVA) followed by group comparisons using Fisher's Exact or Dunnett's test. Fetal skeletal and visceral data were recorded by hand and subsequently entered into the Grosse System. The data were evaluated statistically by ANOVA followed by group comparisons using Fisher's Exact test. Differences between control and treated groups were considered to be statistically significant if the probability of the difference being due to chance was less than 5% ($p < 0.05$).

Serum chemistry data were collected using the Grosse Clinpath System. The data were evaluated statistically by analysis of variance followed by group comparisons using Tukey's Multiple Comparison test. Observed statistically significant differences ($p < 0.05$) were reported only if a linear relationship (>99% confidence level, Pearson's correlation coefficient) was established.

The study Support Data book, Gestation and Cesarean Section Direct Data Printout books, Visceral Examination book, Skeletal Examination book, Grosse System printouts of all individual animal data, clinical chemistry data with associated records, and all released reports will be maintained in the Document Archives of . Fetal visceral and skeletal tissues will be stored in the Tissue Archives of

3.0 RESULTS

With the exception of clinical observations and necropsy findings, only data generated for pregnant animals will be discussed. Similarly, summary tables which calculate means and standard deviations will include only the data for pregnant animals. As stated above in Section 2.9, Grosse System printouts of individual animal data can be found in the document archives and are not included in this report.

3.1 *Clinical Observations*

Clinical observations during gestation are presented in Table 2. Those observations not related to DIPE exposure are chromodacryorrhea, lesions on neck, swollen and red snout, red nasal exudate, respiratory distress, and soft stool. Chromodacryorrhea and red nasal exudate are common findings in rats that are under stress. Since they are seen with regularity in control animals and animals that are not on study, these findings are not considered to be a direct effect of DIPE exposure. The cause of the soft stool noted in several females is unknown, however, since it occurred in both untreated and sham control animals, this finding is not considered to be related to test material exposure.

The lesion on the neck of one female and the swollen snouts of two other females apparently resulted from the animals being caught in the stainless steel springs used to hold the food jars in place within each cage. The isolated occurrence of respiratory distress was caused by severe facial and nasal injury resulting from a female's efforts to free herself when her incisors got caught in the wire mesh siding of her cage. Once dislodged by the technical staff, she was considered moribund and immediately killed.

Lacrimation, weakness/unsteadiness, and salivation were noted in several DIPE-exposed females at the highest dose level. Lacrimation was also seen in two females from the mid-dose

group. The signs were observed during, or immediately following, exposure periods and are considered to be a direct result of exposure to DIPE. The animals returned to normal appearance shortly after cessation of each daily exposure. An accurate determination of the total incidence of these findings during each exposure could not be made for all animals. These "symptoms" of exposure generally occurred during the exposure and only animals at the front of each inhalation chamber are clearly visible; animals positioned in the middle or rear of the chamber could not be observed.

3.2 *Body Weights and Food Consumption*

Mean body weights, mean body weight changes, and mean net body weight changes are presented in Tables 3-5, respectively. In general, there were significant decreases ($p < 0.01$) in body weight gain for all chambered females during the time that they were housed in the inhalation chambers (Table 4; Days 6 to 16; Groups 2-5). The significant reduction in weight gain for the sham control group (Group 2) indicates that being housed in the chambers may have been stressful for the animals. Even so, there does appear to be a dose response for reduced body weight gain among the DIPE-exposed groups; only at the highest concentration was the mean weight gain significantly less ($p < 0.01$) than that of the sham control group. The mean net body weight gains presented in Table 5 reflect a similar pattern. All chambered groups were adversely affected ($p < 0.05$) when compared to the untreated control and a dose response is apparent among the groups exposed to DIPE vapors. There was no statistically significant difference between the mean net body weight gain of any DIPE-exposed group and the sham control group.

Mean food consumption values (grams/animal/day) are presented in Table 6. Except for Group 3 (low dose DIPE), decreased food consumption corresponded to the decreased body weight gains seen in the chambered groups. However, unlike the body weight gains, the means for food consumption for both Groups 4 and 5 (mid and high dose DIPE) were significantly different ($p < 0.01$) from that of the sham control group; indicating a DIPE-related response. When presented in terms of food consumption relative to body weight (grams/kg/day; Table 7), only Groups 4 and 5 consumed significantly ($p < 0.01$) less food during the exposure period than the control groups.

3.3 *Observations at Cesarean Section*

3.3.1 *Necropsy Findings*

No treatment related effects were noted at the time of macroscopic examination.

3.3.2 *Serum Chemistry Analyses*

There were no significant effects on the serum chemistry of female rats exposed to DIPE vapors.

3.3.3 *Reproductive and Developmental Evaluations*

A summary of the reproductive data is presented in Table 8. Reproductive parameters were unaffected by DIPE exposure. The one female mortality recorded was discussed previously in Section 3.1 and was not related to treatment.

Mean fetal body weights, a parameter of body growth and development, were comparable among all experimental groups (Table 9). Similarly, there were no DIPE related findings at the time of fetal external observations (Table 10).

Fetal visceral examinations revealed no treatment related findings (Table 11). Although there were several incidences of malformation occurring in the untreated control fetuses, there were no malformations observed in those fetuses exposed to DIPE. Fetal skeletal examinations (Table 12) indicate that fetuses from dams exposed to 14.0 and 30.8 mg/L had an increased incidence ($p < 0.01$) of rudimentary 14th ribs. There was also an increase in the incidence of sternbrae which were incompletely ossified among the fetuses in the high dose group, however, there is no dose-related response and the finding is not considered to be related to DIPE exposure.

4.0 DISCUSSION AND CONCLUSIONS

Exposure of pregnant rats to DIPE vapors at concentrations of 14.0, and 30.8 mg/L resulted in both maternal and developmental toxicity. The signs of toxicity noted in the high dose group females during exposure (lacrimation, unsteadiness, salivation) were not unexpected. As an ether, it is not surprising that DIPE would produce, to some degree, a physiological response consistent with that class of anesthetics [2,3]. All chambered females also exhibited signs of stress including decreased body weight gain and food consumption, however these responses appeared to be more severe as DIPE vapor concentration increased. At both 14.0 and 30.8 mg/L these effects were significantly different from both the untreated and sham control groups (the reduced body weight gain of females exposed to 14.0 mg/L was not statistically different from the sham control, but is considered to be biologically significant).

The increased incidence of rudimentary 14th ribs in fetuses exposed to DIPE appears to be indicative of developmental toxicity. No other adverse developmental effects were noted. Whether or not the adverse skeletal effect is related to the stress of the dams or directly attributable to DIPE exposure is uncertain. The role of maternal stress in the development of rudimentary ribs has been investigated. It has been shown that maternal stress may influence the occurrence of rudimentary ribs in CD-1 mice [4] and that maternal stress may induce transient changes in the sensitive border between thoracic and lumbar vertebrae of fetuses (i.e., the occurrence of rudimentary ribs which disappear as the pups mature)[5]. However, it

has also been suggested that the occurrence of rudimentary ribs may be evidence of the teratogenic potential of a material if administered at higher doses [6]. In the present study, it should be noted that *all* chambered females exhibited signs of stress, but only in the mid and high dose DIPE groups was there an increase in rudimentary ribs.

In conclusion, exposure to DIPE vapors during gestation days 6-15 resulted in slight maternal toxicity at 14.0 and 30.8 mg/L. Fetal developmental toxicity in the form of rudimentary ribs was also present at these same dose levels. There were no adverse maternal or fetal effects related to DIPE exposure at the 1.9 mg/L concentration.

5.0 SIGNATURES FOR REPORT APPROVAL

_____	10-19-93	_____	10-18-93
	Date		Date :
Study Director		Supervisor	
_____	11/4/93	_____	11/7/93
	Date		Date
Manager, Mammalian/Genetic Toxicology		Manager,	

TABLE 2
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION
 64721

	DAY OF GESTATION																						
	GROUP#	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	TOTAL
# OF FEMALES EXAMINED	1	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22
	2	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22
	3	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22
	4	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22
	5	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22	22
LESIONS ON NECK	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EARTAG REPLACED	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SNOUT SWOLLEN AND RED	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NOSE																							
RED NASAL EXUDATE	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORAL-BUCCAL																							
SALIVATION	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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TABLE 3
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
MEAN MATERNAL BODY WEIGHTS DURING GESTATION - grams 64721

DAY	DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
		1	2	2	3	3	4	4	5		
DAY 0	MEAN	251.3	242.1	259.3	244.6	254.7					
	S.D.	24.6	23.3	26.7	20.8	25.0					
	N	22	20	21	22	22					
DAY 6	MEAN	284.0	276.2	292.9	278.8	289.9					
	S.D.	25.0	23.4	28.3	21.0	28.8					
	N	22	20	21	22	22					
DAY 13	MEAN	324.0	303.5	325.2	298.4a	302.2a					
	S.D.	29.0	25.6	33.3	21.0	26.0					
	N	22	20	21	21	22					
DAY 16	MEAN	352.9	325.7a	350.5c	320.1b	322.9b					
	S.D.	29.8	28.1	36.8	25.9	30.5					
	N	22	20	21	21	22					
DAY 20	MEAN	420.6	399.4	424.1	391.5a	402.9					
	S.D.	32.9	37.0	41.7	32.8	29.6					
	N	22	20	21	21	22					

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

TABLE 4
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 MEAN MATERNAL BODY WEIGHT CHANGE DURING GESTATION - grams

64721

DAYS	DOSAGE GROUP	UNTREAT. CONTROL	SHAM CONTROL	3.1 MG/			14.6 MG/			29.3 MG/		
				1	2	L	3	L	4	L	5	
DAYS 0 TO 6	MEAN	33	34	34	34	34	34	34	34	34	35	
	S.D.	12	5	9	9	9	9	9	9	9	7	
	N	22	20	21	21	22	22	22	22	22	22	
DAYS 6 TO 13	MEAN	40	27b	32a	32a	20b	20b	20b	20b	20b	12bd	
	S.D.	11	6	9	9	9	9	9	9	9	11	
	N	22	20	21	21	21	21	21	21	21	22	
DAYS 13 TO 16	MEAN	29	22a	25	25	22a	22a	22a	22a	22a	21b	
	S.D.	6	6	8	8	7	7	7	7	7	12	
	N	22	20	21	21	21	21	21	21	21	22	
DAYS 6 TO 16	MEAN	69	50b	58b	58b	42b	42b	42b	42b	42b	33bd	
	S.D.	11	9	14	14	9	9	9	9	9	13	
	N	22	20	21	21	21	21	21	21	21	22	
DAYS 16 TO 20	MEAN	68	74	74	74	71	71	71	71	71	80b	
	S.D.	8	11	12	12	11	11	11	11	11	10	
	N	22	20	21	21	21	21	21	21	21	22	
DAYS 0 TO 20	MEAN	169	157	165	165	147b	147b	147b	147b	147b	148b	
	S.D.	20	21	22	22	18	18	18	18	18	13	
	N	22	20	21	21	21	21	21	21	21	22	

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a - P<0.05, b - P<0.01; GROUP 2: c - P<0.05, d - P<0.01.

TABLE 5
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF UTERINE AND NET BODY WEIGHTS (grams) 64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
	1	2	1	2	3	4	4	5	5	5
GRAVID UTERUS	MEAN	84.9	86.0	89.7	81.6	83.9				
	S.D.	11.5	9.7	10.8	15.1	9.4				
	N	22	20	21	21	22				
CARCASS	MEAN	335.6	313.4	334.4	309.8a	319.0				
	S.D.	31.6	31.5	36.8	24.8	27.1				
	N	22	20	21	21	22				
NET WEIGHT CHANGE FROM DAY 6	MEAN	51.7	37.3b	41.5a	31.9b	29.0b				
	S.D.	13.8	11.3	13.3	11.5	8.1				
	N	22	20	21	21	22				

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

CARCASS WEIGHT - TERMINAL BODY WEIGHT MINUS UTERINE WEIGHT
 NET WEIGHT CHANGE FROM DAY 6 - CARCASS WEIGHT MINUS DAY 6 BODY WEIGHT

TABLE 6
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
MEAN MATERNAL FOOD CONSUMPTION DURING GESTATION -- SUMMARY

DAYS	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1	2	3	4	5	6	7	8	9	10
Females Pregnant	22	20	21	22	22					
MATERNAL FOOD CONSUMPTION -- grams/ANIMAL/DAY										
DAYS 0 TO 6										
MEAN	22.2	22.0	22.6	22.2	22.2					
S.D.	3.0	2.2	2.6	2.3	2.3					
N	22	20	21	22	22					
DAYS 6 TO 13										
MEAN	26.4	24.2a	25.8	21.5bd	19.8bd					
S.D.	3.1	2.3	2.5	1.8	1.9					
N	22	20	21	20	22					
DAYS 13 TO 16										
MEAN	28.3	25.6a	27.4	24.2b	23.0bc					
S.D.	3.5	2.3	3.3	2.5	2.1					
N	22	19	20	20	21					
DAYS 16 TO 20										
MEAN	30.7	28.6	30.1	28.9	30.3					
S.D.	3.1	3.5	3.6	3.1	2.2					
N	22	20	20	21	21					

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

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TABLE 7
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 MEAN MATERNAL FOOD CONSUMPTION DURING GESTATION -- SUMMARY

DAYS	N	UNTREAT. CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
		1	2	3	4	5	5		
Females Pregnant	22	20	21	22	22				
MATERNAL FOOD CONSUMPTION -- grams/KG/DAY									
DAYS 0 TO 6	6	88.8	91.5	87.5	90.9	90.9			
S.D.		10.6	9.2	8.2	9.5	8.6			
N		22	20	21	22	21			
DAYS 6 TO 13	13	92.8	88.0	88.4	77.7bd	68.5bd			
S.D.		6.5	6.8	5.4	8.4	6.7			
N		22	20	21	20	22			
DAYS 13 TO 16	16	87.2	84.4	84.0	81.3a	76.1bd			
S.D.		7.7	5.2	4.4	7.4	7.0			
N		22	19	20	20	21			
DAYS 16 TO 20	20	87.0	87.6	85.7	90.4	94.3bd			
S.D.		6.2	6.7	5.4	6.7	8.2			
N		22	20	20	21	21			

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

TABLE 8
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIFE) VAPORS
SUMMARY OF REPRODUCTION DATA

64721

DOSAGE	UNTREAT.		SHAM CONTROL		3.1 MG/		14.6 MG/		29.3 MG/	
	CONTROL	1	2	2	L	L	L	L	L	L
GROUP					3	4	4	5	5	5
Females Mated	N	22	22	22	22	22	22	22	22	22
Pregnant	N	22	20	20	21	22	22	22	22	22
Aborted	‡	100	91	91	95	100	100	100	100	100
Premature Births	N	0	0	0	0	0	0	0	0	0
Dams with Viable Fetuses	N	0	0	0	0	0	0	0	0	0
Dams with all Resorptions	N	22	20	20	21	21	21	21	22	22
Female Mortality	N	0	0	0	0	0	0	0	0	0
	‡	0.0	0.0	0.0	0.0	0.0	4.5	1	0	0.0
Corpora Lutea	N	384	345	345	371	361	361	361	388	388
	MEAN	17.5	17.3	17.3	17.7	17.2	17.2	17.2	17.6	17.6
	S.D.	1.5	1.5	1.5	2.1	2.1	2.4	2.4	2.1	2.1
Implantation Sites	N	365	334	334	352	328	328	328	367	367
	MEAN	16.6	16.7	16.7	16.8	15.6	15.6	15.6	16.7	16.7
	S.D.	2.2	1.7	1.7	2.1	2.7	2.7	2.7	1.7	1.7
Preimplantation Loss	‡	4.7	3.1	3.1	4.9	8.9	8.9	8.9	5.1	5.1
	S.D.	12.2	6.8	6.8	7.5	12.4	12.4	12.4	5.4	5.4
Viable Fetuses	N	336	309	309	334	312	312	312	345	345
	MEAN	15.3	15.4	15.4	15.9	14.9	14.9	14.9	15.7	15.7
	S.D.	2.1	1.7	1.7	1.9	2.7	2.7	2.7	1.8	1.8
Viable Male Fetuses	N	156	158	158	172	163	163	163	174	174
	‡	46	51	51	51	52	52	52	50	50
Viable Female Fetuses	N	180	151	151	162	149	149	149	171	171
	‡	54	49	49	49	48	48	48	50	50
Dead Fetuses	N	0	0	0	0	0	0	0	0	0
Resorptions	N	29	25	25	18	16	16	16	22	22
	MEAN	1.3	1.3	1.3	0.9	0.8	0.8	0.8	1.0	1.0
	S.D.	1.3	1.0	1.0	0.9	0.8	0.8	0.8	1.0	1.0
	MEAN ‡	7.6	7.4	7.4	4.9	5.0	5.0	5.0	5.9	5.9
	S.D.	7.1	6.1	6.1	5.2	5.6	5.6	5.6	6.1	6.1
Dams with Resorptions	N	16	14	14	12	12	12	12	13	13
	‡	73	70	70	57	57	57	57	59	59

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

TABLE 9
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL MEANS
 64721

FETAL WEIGHTS	UNITS: GRAMS	MEAN	S.D.	N	DOSAGE GROUP											
					UNTREAT. CONTROL 1	SHAM CONTROL 2	3.1 MG/L 3	14.6 MG/L 4	29.3 MG/L 5							
of all Viable Fetuses		3.7	0.3	22	3.7	0.3	20	3.8	0.2	21	3.7	0.3	21	3.6	0.2	22
of Male Fetuses		3.8	0.3	22	3.8	0.3	20	3.8	0.3	21	3.8	0.3	21	3.7	0.2	22
of Female Fetuses		3.6	0.2	22	3.7	0.3	20	3.7	0.3	21	3.6	0.2	21	3.5	0.2	22

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a - P<0.05, b - P<0.01; GROUP 2: c - P<0.05, d - P<0.01.

TABLE 10
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL GROSS OBSERVATIONS

64721

DOSAGE	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1	2	1	2	3	4	5	4	5	
Litters Evaluated	22	20	21	21	21	21	21	21	21	21
Fetuses Evaluated	336	309	334	334	334	312	312	312	345	345
Live	336	309	334	334	334	312	312	312	345	345
Dead	0	0	0	0	0	0	0	0	0	0
---GENERAL										
Fetal Incidence	0	0	0	0	0	0	0	0	0	0
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
V HEMATOMA										
Fetal Incidence	0	0	0	0	0	0	0	0	0	1
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
TOTAL FETAL GROSS OBSERVATIONS										
Fetal Incidence	0	0	0	0	0	0	0	0	0	1
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.										
M-MALFORMATION V-VARIATION A-ANOMALY										

TABLE 11
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SOFT TISSUE OBSERVATIONS

64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1	2	3	4	5	6	7	8	9	10
Litters Evaluated	22	20	0	0	0	22	0	0	0	0
Fetuses Evaluated	162	150	0	0	0	167	0	0	0	167
Live	162	150	0	0	0	167	0	0	0	167
Dead	0	0	0	0	0	0	0	0	0	0
---GROSS EXAM										
Fetal Incidence	1	0	0	0	0	0	0	0	0	0
	0.6	0.0				0.0				0.0
Litter Incidence	1	0	0	0	0	0	0	0	0	0
	4.5	0.0				0.0				0.0
M SITUS INVERSUS										
Fetal Incidence	1	0	0	0	0	0	0	0	0	0
	0.6	0.0				0.0				0.0
Litter Incidence	1	0	0	0	0	0	0	0	0	0
	4.5	0.0				0.0				0.0
---EYES										
Fetal Incidence	1	0	0	0	0	0	0	0	0	0
	0.6	0.0				0.0				0.0
Litter Incidence	1	0	0	0	0	0	0	0	0	0
	4.5	0.0				0.0				0.0
M MICROPTHALMIA										
Fetal Incidence	1	0	0	0	0	0	0	0	0	0
	0.6	0.0				0.0				0.0
Litter Incidence	1	0	0	0	0	0	0	0	0	0
	4.5	0.0				0.0				0.0
---HEART										
Fetal Incidence	1	1	1	1	1	0	0	0	0	0
	0.6	0.7	0.7	0.7	0.7	0.0	0.0	0.0	0.0	0.0
Litter Incidence	1	1	1	1	1	0	0	0	0	0
	4.5	5.0	5.0	5.0	5.0	0.0	0.0	0.0	0.0	0.0

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M-MALFORMATION V-VARIATION A-ANOMALY

TABLE 11
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
SUMMARY OF FETAL SOFT TISSUE OBSERVATIONS

64721

DOSAGE	GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
		1	22	2	20	3	0	4	0	5	5
Litters Evaluated	N		22		20		0		0		0
Fetuses Evaluated	N		162		150		0		0		22
Live	N		162		150		0		0		167
Dead	N		0		0		0		0		167
M DOUBLE AORTIC ARCH Fetal Incidence	N	1		0							0
	‡	0.6		0.0							0.0
Litter Incidence	N	1		0							0.0
	‡	4.5		0.0							0.0
M LEVOCARDIA Fetal Incidence	N	0		1							0
	‡	0.0		0.7							0.0
Litter Incidence	N	0		1							0
	‡	0.0		5.0							0.0
---KIDNEY Fetal Incidence	N	3		0							2
	‡	1.9		0.0							1.2
Litter Incidence	N	2		0							1
	‡	9.1		0.0							4.5
V DILATATION OF RENAL PELVIS Fetal Incidence	N	3		0							2
	‡	1.9		0.0							1.2
Litter Incidence	N	2		0							1
	‡	9.1		0.0							4.5
---BLADDER Fetal Incidence	N	0		1							0
	‡	0.0		0.7							0.0
Litter Incidence	N	0		1							0
	‡	0.0		5.0							0.0

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a - P<0.05, b - P<0.01; GROUP 2: c - P<0.05, d - P<0.01.
M-MALFORMATION V-VARIATION A-ANOMALY

TABLE 11
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SOFT TISSUE OBSERVATIONS 64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
	1	2	3	4	5	6	7	8	9	10
Litters Evaluated	N 22	20	0	0	0	22				
Fetuses Evaluated	N 162	150	0	0	0	167				
Live	N 162	150	0	0	0	167				
Dead	N 0	0	0	0	0	0				
V BLADDER ENLARGED										
Fetal Incidence	N 0	1	0	0	0	0				
	% 0.0	0.7				0.0				
Litter Incidence	N 0	1	0	0	0	0				
	% 0.0	5.0				0.0				
---URETERS										
Fetal Incidence	N 11	6	0	0	0	6				
	% 6.8	4.0				3.6				
Litter Incidence	N 7	5	0	0	0	5				
	% 32	25				23				
V DISTENDED URETER(S)										
Fetal Incidence	N 11	6	0	0	0	6				
	% 6.8	4.0				3.6				
Litter Incidence	N 7	5	0	0	0	5				
	% 32	25				23				
---GONADS										
Fetal Incidence	N 1	5	0	0	0	0 ^c				
	% 0.6	3.3				0.0				
Litter Incidence	N 1	4	0	0	0	0 ^c				
	% 4.5	20				0.0				
M ECTOPIC TESTES										
Fetal Incidence	N 0	5 ^a	0	0	0	0 ^c				
	% 0.0	3.3				0.0				
Litter Incidence	N 0	4 ^a	0	0	0	0 ^c				
	% 0.0	20				0.0				

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M-MALFORMATION V-VARIATION A=ANOMALY

TABLE 11
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SOFT TISSUE OBSERVATIONS

64721

DOSAGE	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1	2	3	4	5	6	7	8	9	10
Litters Evaluated	22	20	0	0	0	0	0	0	0	0
Fetuses Evaluated	162	150	0	0	0	0	0	0	0	0
Live	162	150	0	0	0	0	0	0	0	0
Dead	0	0	0	0	0	0	0	0	0	0
M TESTES REDUCED IN SIZE										
Fetal Incidence	1	0	0	0	0	0	0	0	0	0
Litter Incidence	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Litter Incidence										
Litter Incidence	1	0	0	0	0	0	0	0	0	0
TOTAL FETAL SOFT TISSUE OBSERVATIONS										
Fetal Incidence	14	12	6	6	6	6	6	6	6	6
Litter Incidence	8.6	8.0	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6
Litter Incidence										
Litter Incidence	9	8	5	5	5	5	5	5	5	5
Litter Incidence										
Litter Incidence	41	40	23	23	23	23	23	23	23	23

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M-MALFORMATION V-VARIATION A-ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS 64721

	DOSAGE		SHAM CONTROL		3.1 MG/		14.6 MG/		29.3 MG/	
	UNTREAT. CONTROL	GROUP	1	2	L	L	L	L	L	L
Litters Evaluated	17	N	17	14	15	15	15	15	15	15
Fetuses Evaluated	132	N	132	115	121	115	115	115	120	120
Live	132	N	132	115	121	115	115	115	120	120
Dead	0	N	0	0	0	0	0	0	0	0
----SKULL										
Fetal Incidence	20	N	20	22	16	14	7ad	14	14	12
	15	‡	15	19	13	13	6.1	12	12	12
Litter Incidence	8	N	8	9	6	6	6	8	8	8
	47	‡	47	64	40	40	40	53	53	53
V INTERPARIETAL INCOMPLETELY OSSIFIED										
Fetal Incidence	12	N	12	2a	12c	3	6	6	6	6
	9.1	‡	9.1	1.7	9.9	2.6	5.0	5.0	5.0	5.0
Litter Incidence	7	N	7	2	5	2	3	3	3	3
	41	‡	41	14	33	13	20	20	20	20
V SUPRAOCCIPITAL INCOMPLETELY OSSIFIED										
Fetal Incidence	14	N	14	17	12	5c	13	13	13	13
	11	‡	11	15	9.9	4.3	11	11	11	11
Litter Incidence	7	N	7	9	4	5	7	7	7	7
	41	‡	41	64	27	33	47	47	47	47
V MAXILLA INCOMPLETELY OSSIFIED										
Fetal Incidence	1	N	1	1	2	0	3	3	3	3
	0.8	‡	0.8	0.9	1.7	0.0	2.5	2.5	2.5	2.5
Litter Incidence	1	N	1	1	2	0	2	2	2	2
	5.9	‡	5.9	7.1	13	0.0	13	13	13	13
V MALAR INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	10	N	10	10	8	3	4	4	4	4
	7.6	‡	7.6	8.7	6.6	2.6	3.3	3.3	3.3	3.3
Litter Incidence	4	N	4	6	3	3	2	2	2	2
	24	‡	24	43	20	20	13	13	13	13

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

DOSAGE	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/		14.6 MG/		29.3 MG/	
	GROUP	1	2	L	L	L	L	L	L	L
Litters Evaluated	N	17	14	15	15	15	15	15	15	15
Fetuses Evaluated	N	132	115	121	121	115	115	120	120	120
Live	N	132	115	121	121	115	115	120	120	120
Dead	N	0	0	0	0	0	0	0	0	0
V SQUAMOSAL INCOMPLETELY OSSIFIED										
Fetal Incidence	N	12	8	7	7	3	3	6	6	6
	‡	9.1	7.0	5.8	5.8	2.6	2.6	5.0	5.0	5.0
Litter Incidence	N	6	4	3	3	3	3	3	3	3
	‡	35	29	20	20	20	20	20	20	20
V PARIETAL INCOMPLETELY OSSIFIED										
Fetal Incidence	N	4	3	6	6	2	2	6	6	6
	‡	3.0	2.6	5.0	5.0	1.7	1.7	5.0	5.0	5.0
Litter Incidence	N	4	3	3	3	1	1	4	4	4
	‡	24	21	20	20	6.7	6.7	27	27	27
V FRONTAL INCOMPLETELY OSSIFIED										
Fetal Incidence	N	0	0	1	1	0	0	0	0	0
	‡	0.0	0.0	0.8	0.8	0.0	0.0	0.0	0.0	0.0
Litter Incidence	N	0	0	1	1	0	0	0	0	0
	‡	0.0	0.0	6.7	6.7	0.0	0.0	0.0	0.0	0.0
---CERVICAL VERT.										
Fetal Incidence	N	0	2	0	0	2	2	1	1	1
	‡	0.0	1.7	0.0	0.0	1.7	1.7	0.8	0.8	0.8
Litter Incidence	N	0	2	0	0	2	2	1	1	1
	‡	0.0	14	0.0	0.0	13	13	6.7	6.7	6.7
V CERVICAL VERTEBRAE INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	N	0	2	0	0	1	1	1	1	1
	‡	0.0	1.7	0.0	0.0	0.9	0.9	0.8	0.8	0.8
Litter Incidence	N	0	2	0	0	1	1	1	1	1
	‡	0.0	14	0.0	0.0	6.7	6.7	6.7	6.7	6.7

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

	DOSAGE GROUP		UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
	1	2	1	2	1	2	3	4	3	4	5	5
Litters Evaluated	17	14	17	14	15	15	15	15	15	15	15	15
Fetuses Evaluated	132	115	132	115	121	121	121	115	115	120	120	120
Live	132	115	132	115	121	121	121	115	115	120	120	120
Dead	0	0	0	0	0	0	0	0	0	0	0	0
M CERVICAL RIB												
Fetal Incidence	0	0	0	0	0	0	0	1	0.9	0	0	0.0
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.0
Litter Incidence	0	0	0	0	0	0	0	1	6.7	0	0	0.0

---THORACIC VERT.												
Fetal Incidence	7	4	7	4	4	4	4	8	7.0	9	9	7.5
Litter Incidence	5.3	3.5	5.3	3.5	3.3	3.3	3.3	7.0	7.0	7.5	7.5	7.5
Litter Incidence	5	3	5	3	4	4	4	8	8	6	6	6
Litter Incidence	29	21	29	21	27	27	27	53	53	40	40	40
V THORACIC CENTRA INCOMPLETELY OSSIFIED/UNOSSIFIED												
Fetal Incidence	7	3	7	3	4	4	4	8	7.0	7	7	5.8
Litter Incidence	5.3	2.6	5.3	2.6	3.3	3.3	3.3	7.0	7.0	5.8	5.8	5.8
Litter Incidence	5	2	5	2	4	4	4	8	8	4	4	4
Litter Incidence	29	14	29	14	27	27	27	53	53	27	27	27
M THORACIC CENTRA MISSHAPEN												
Fetal Incidence	0	0	0	0	0	0	0	0	0	1	1	0.8
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.8	0.8
Litter Incidence	0	0	0	0	0	0	0	0	0	1	1	6.7
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.7	6.7	6.7
M THORACIC VERTEBRAE FUSED												
Fetal Incidence	0	0	0	0	0	0	0	0	0	1	1	0.8
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.8	0.8
Litter Incidence	0	0	0	0	0	0	0	0	0	1	1	6.7
Litter Incidence	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.7	6.7	6.7

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1	2	3	4	5	6	7	8	9	10
Litters Evaluated	17	14	15	15	15					
Fetuses Evaluated	132	115	121	115	115					
Live	132	115	121	115	115					
Dead	0	0	0	0	0					
M THORACIC TRANSVERSE PROCESS SHORTENED										
Fetal Incidence	0	1	0	0	0					
	0.0	0.9	0.0	0.0	0.0					
Litter Incidence	0	1	0	0	0					
	0.0	7.1	0.0	0.0	0.0					
M THORACIC CENTRA REDUCED IN SIZE										
Fetal Incidence	0	1	0	0	0					
	0.0	0.9	0.0	0.0	0.0					
Litter Incidence	0	1	0	0	0					
	0.0	7.1	0.0	0.0	0.0					
M THORACIC VERTEBRAE INCOMPLETE										
Fetal Incidence	0	1	0	0	0					
	0.0	0.9	0.0	0.0	0.0					
Litter Incidence	0	1	0	0	0					
	0.0	7.1	0.0	0.0	0.0					
M THORACIC CENTRA MISALIGNED										
Fetal Incidence	0	1	0	0	0					
	0.0	0.9	0.0	0.0	0.0					
Litter Incidence	0	1	0	0	0					
	0.0	7.1	0.0	0.0	0.0					
---LUMBAR VERT.										
Fetal Incidence	1	0	0	0	0					
	0.8	0.0	0.0	0.0	0.0					
Litter Incidence	1	0	0	0	0					
	5.9	0.0	0.0	0.0	0.0					

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a - P<0.05, b - P<0.01; GROUP 2: c - P<0.05, d - P<0.01.
M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS 64721

DOSAGE	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
	1	2	3	4	5					
Litters Evaluated	17	14	15	15	15					
Fetuses Evaluated	132	115	121	115	120					
Live	132	115	121	115	120					
Dead	0	0	0	0	0					
V LUMBAR CENTRA INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	1	0	0	0	0					
§	0.8	0.0	0.0	0.0	0.0					
Litter Incidence	1	0	0	0	0					
§	5.9	0.0	0.0	0.0	0.0					
---SACRAL VERT.										
Fetal Incidence	13	16	15	5c	6c					
§	9.8	14	12	4.3	5.0					
Litter Incidence	7	9	9	4	6					
§	41	64	60	27	40					
V SACRAL TRANSVERSE PROCESS INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	13	16	15	5c	6c					
§	9.8	14	12	4.3	5.0					
Litter Incidence	7	9	9	4	6					
§	41	64	60	27	40					
V SACRAL CENTRA INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	0	0	0	1	1					
§	0.0	0.0	0.0	0.9	0.8					
Litter Incidence	0	0	0	1	1					
§	0.0	0.0	0.0	6.7	6.7					
---CAUDAL VERT.										
Fetal Incidence	26	32	36	11ad	12ad					
§	20	28	30	9.6	10					
Litter Incidence	8	10	13a	7	8					
§	47	71	87	47	53					

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/L		14.6 MG/L		29.3 MG/L	
	1		2		L	L	L	L	L	L
Litters Evaluated	N	17	14		15		15		15	
Fetuses Evaluated	N	132	115		121		115		120	
Live	N	132	115		121		115		120	
Dead	N	0	0		0		0		0	
V CAUDAL TRANSVERSE PROCESS INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	N	25	32		36		11ad		12d	
	%	19	28		30		9.6		10	
Litter Incidence	N	8	10		13a		7		8	
	%	47	71		87		47		53	
V CAUDAL CENTRA INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	N	1	1		0		1		1	
	%	0.8	0.9		0.0		0.9		0.8	
Litter Incidence	N	1	1		0		1		1	
	%	5.9	7.1		0.0		6.7		6.7	
---STERNBRAE										
Fetal Incidence	N	96	91		82		69ad		102a	
	%	73	79		68		60		85	
Litter Incidence	N	17	14		14		15		15	
	%	100	100		93		100		100	
V STERNBRAE INCOMPLETELY OSSIFIED/UNOSSIFIED										
Fetal Incidence	N	93	84		77		67c		96	
	%	70	73		64		58		80	
Litter Incidence	N	17	14		14		15		15	
	%	100	100		93		100		100	
V STERNBRAE INCOMPLETELY OSSIFIED/UNOSSIFIED (>2)										
Fetal Incidence	N	3	7		5		2		6	
	%	2.3	6.1		4.1		1.7		5.0	
Litter Incidence	N	3	5		4		2		4	
	%	18	36		27		13		27	

SIGNIFICANT DIFFERENCE BETWEEN GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
M-MALFORMATION VARIATION A=ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

	DOSAGE		UNTREAT.		SHAM		3.1 MG/		14.6 MG/		29.3 MG/	
	GROUP	CONTROL	1	2	L	3	L	4	L	5		
Litters Evaluated	N	17		14	15		15	15		15		15
Fetuses Evaluated	N	132		115	121		115	115		120		120
Live	N	132		115	121		115	115		120		120
Dead	N	0		0	0		0	0		0		0

---RIBS												
Fetal Incidence	N	5	6	10	10		20bd	33bd		33bd		33bd
	‡	3.8	5.2	8.3	8.3		17	28		28		28
Litter Incidence	N	5	3	7	7		7	13bd		13bd		13bd
	‡	29	21	47	47		47	87		87		87
V 14TH RIB RUDIMENTARY/SHORT/EXTRA												
Fetal Incidence	N	4	4	6	6		20bd	33bd		33bd		33bd
	‡	3.0	3.5	5.0	5.0		17	28		28		28
Litter Incidence	N	4	1	4	4		7c	13bd		13bd		13bd
	‡	24	7.1	27	27		47	87		87		87
V 13TH RIB RUDIMENTARY/SHORT												
Fetal Incidence	N	0	1	4	4		0	0		0		0
	‡	0.0	0.9	3.3	3.3		0.0	0.0		0.0		0.0
Litter Incidence	N	0	1	3	3		0	0		0		0
	‡	0.0	7.1	20	20		0.0	0.0		0.0		0.0
M NUMBER OF RIBS < 13												
Fetal Incidence	N	0	1	0	0		0	0		0		0
	‡	0.0	0.9	0.0	0.0		0.0	0.0		0.0		0.0
Litter Incidence	N	0	1	0	0		0	0		0		0
	‡	0.0	7.1	0.0	0.0		0.0	0.0		0.0		0.0
V RIBS WAVY												
Fetal Incidence	N	1	0	0	0		0	0		0		0
	‡	0.8	0.0	0.0	0.0		0.0	0.0		0.0		0.0
Litter Incidence	N	1	0	0	0		0	0		0		0
	‡	5.9	0.0	0.0	0.0		0.0	0.0		0.0		0.0

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.

M=MALFORMATION V=VARIATION A=ANOMALY

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS
 64721

DOSAGE GROUP	UNTREAT. CONTROL		SHAM CONTROL		3.1 MG/ L		14.6 MG/ L		29.3 MG/ L	
	1	2	3	4	5	6	7	8	9	10
Litters Evaluated	17	14	15	15	15	15	15	15	15	15
Fetuses Evaluated	132	115	121	115	120	115	120	115	120	120
Live	132	115	121	115	120	115	120	115	120	120
Dead	0	0	0	0	0	0	0	0	0	0
---METACARPALS										
Fetal Incidence	0	2	0	1	1	0.0	0.9	1	1	0.8
Litter Incidence	0	1.7	0.0	0.9	0.9	0.0	0.9	1	1	0.8
V METACARPALS: NUMBER OF OSSIFICATIONS < 3-4										
Fetal Incidence	0	2	0	1	1	0.0	0.9	1	1	0.8
Litter Incidence	0	1.7	0.0	0.9	0.9	0.0	0.9	1	1	0.8
---METATARSALS										
Fetal Incidence	0	1	0	1	1	0.0	0.9	1	1	0.8
Litter Incidence	0	0.9	0.0	0.9	0.9	0.0	0.9	1	1	0.8
V METATARSALS: NUMBER OF OSSIFICATIONS < 4										
Fetal Incidence	0	1	0	1	1	0.0	0.9	1	1	0.8
Litter Incidence	0	0.9	0.0	0.9	0.9	0.0	0.9	1	1	0.8
---PELVIS										
Fetal Incidence	1	6	1	1	1	0.8	0.9	1	1	0.8
Litter Incidence	0.8	5.2	0.8	0.9	0.9	0.8	0.9	1	1	0.8
SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01. M=MALFORMATION V=VARIATION A=ANOMALY										

TABLE 12
 DEVELOPMENTAL TOXICITY STUDY IN RATS EXPOSED VIA INHALATION TO DI-ISOPROPYL ETHER (DIPE) VAPORS
 SUMMARY OF FETAL SKELETAL OBSERVATIONS

64721

	DOSAGE		SHAM CONTROL	3.1 MG/		14.6 MG/		29.3 MG/	
	GROUP	UNTREAT. CONTROL		L	L	L	L	L	L
Litters Evaluated	N	17	14	15	15	15	15	15	15
Fetuses Evaluated	N	132	115	121	115	120	115	120	120
Live	N	132	115	121	115	120	115	120	120
Dead	N	0	0	0	0	0	0	0	0
V PUBIS INCOMPLETELY OSSIFIED/UNOSSIFIED									
Fetal Incidence	N	1	5	1	1	1	1	1	1
	‡	0.8	4.3	0.8	0.9	0.8	0.9	0.8	0.8
Litter Incidence	N	1	3	1	1	1	1	1	1
	‡	5.9	21	6.7	6.7	6.7	6.7	6.7	6.7
V ISCHIUM INCOMPLETELY OSSIFIED/UNOSSIFIED									
Fetal Incidence	N	0	4a	0	1	1	1	1	1
	‡	0.0	3.5	0.0	0.9	0.9	0.9	0.8	0.8
Litter Incidence	N	0	3	0	1	1	1	1	1
	‡	0.0	21	0.0	6.7	6.7	6.7	6.7	6.7
TOTAL FETAL SKELETAL OBSERVATIONS									
Fetal Incidence	N	103	95	93	85	85	85	110bc	92
	‡	78	83	77	74	74	74	92	92
Litter Incidence	N	17	14	15	15	15	15	15	15
	‡	100	100	100	100	100	100	100	100

SIGNIFICANTLY DIFFERENT FROM GROUP 1: a = P<0.05, b = P<0.01; GROUP 2: c = P<0.05, d = P<0.01.
 M-MALFORMATION V-VARIATION A-ANOMALY

6.0 REFERENCES

1. Environmental Protection Agency (1986) Proposed guidelines for the health assessment of suspect developmental toxicants. Federal Register 51 (185) p. 34028-34040.
2. Machle, W., E.W. Scott, J. Treon (1939). The Physiological Response to Isopropyl Ether and to a Mixture of Isopropyl Ether and Gasoline. *Journal of Industrial Hygiene and Toxicology* 21:72-96.
3. Kirwin, C.J., and E.E. Sandmeyer (1981). Ethers. In *Patty's Industrial Hygiene and Toxicology*, Edited by G.D. Clayton and F.E. Clayton, pp. 2491-2513. John Wiley & Sons, New York.
4. Beyer, P.E. and Chernoff, N. (1986). The Induction of Supernumerary Ribs in Rodents: Role of the Maternal Stress. *Teratogenesis, Carcinogenesis, and Mutagenesis* 6:419-429.
5. Kimmel, C.A. and Wilson, J.G. (1973). Skeletal Deviations in Rats: Malformations or Variations? *Teratology* 8:309-316.
6. Wickramaratne, G.A. (1988). The Post-natal Fate of Supernumerary Ribs in Rat Teratogenicity Studies. *Journal of Applied Toxicology* 8:91-94.

CECATS DATA:

Submission # BEHQ: 1173-12765 (5) SEQ A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Confidential

SUB. DATE: 11/15/93

OTS DATE: 11/15/93

CSRAD DATE: 12/14/93

CHEMICAL NAME:

CASE#

108-20-3

CECATS TRIAGE TRACKING DBASE ENTRY FORM

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0630 REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/UNDERWAY
- 0403 NOTIFICATION OF WORKERS/OTHERS
- 0404 LABEL/MSDS CHANGES
- 0405 PROCESS/HANDLING CHANGES
- 0406 APP/USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

INFORMATION TYPE:

P F C

- 0201 ONCO (HUMAN)
- 0202 ONCO (ANIMAL)
- 0203 CELI. TRANS (IN VITRO)
- 0204 MUTA (IN VITRO)
- 0205 MUTA (IN VIVO)
- 0206 REPRO/TERATO (HUMAN)
- 0207 REPRO/TERATO (ANIMAL)
- 0208 NEURO (HUMAN)
- 0209 NEURO (ANIMAL)
- 0210 ACUTE TOX. (HUMAN)
- 0211 CHR. TOX. (HUMAN)
- 0212 ACUTE TOX. (ANIMAL)
- 0213 SUB ACUTE TOX (ANIMAL)
- 0214 SUB CHRONIC TOX (ANIMAL)
- 0215 CHRONIC TOX (ANIMAL)

- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04

INFORMATION TYPE:

- 0216 EPI/CLIN
- 0217 HUMAN EXPOS (PROD CONTAM)
- 0218 HUMAN EXPOS (ACCIDENTAL)
- 0219 HUMAN EXPOS (MONITORING)
- 0220 ECOVAQUA TOX
- 0221 ENV. OCC/REL/FATE
- 0222 EMER INCI OF ENV CONTAM
- 0223 RESPONSE REQUEST DELAY
- 0224 PROD/COMP/CHEM ID
- 0225 REPORTING RATIONALE
- 0226 CONFIDENTIAL
- 0227 ALLERG (HUMAN)
- 0228 ALLERG (ANIMAL)
- 0239 METAB/PHARMACO (ANIMAL)
- 0240 METAB/PHARMACO (HUMAN)

P F C

- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04

INFORMATION TYPE:

- 0241 IMMUNO (ANIMAL)
- 0242 IMMUNO (HUMAN)
- 0243 CHEM/PHYS PROP
- 0244 CLASTO (IN VITRO)
- 0245 CLASTO (ANIMAL)
- 0246 CLAS ID (HUMAN)
- 0247 DNA DAM/REPAIR
- 0248 PROD/USE/PROC
- 0251 MSDS
- 0299 OTHER

P F C

- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04
- 01 02 04

TRIAGE DATA: NON-CBI INVENTORY

YES (CONTINUE)

NO (DROP)

DETERMINE

ONGOING REVIEW

YES (DROP/REFER)

NO (CONTINUE)

REFER:

SPECIES

RAT

TOXICOLOGICAL CONCERN:

LOW L/M - metabolic study toxic at
14 mg/L
 MED
 HIGH

USE:

PRODUCTION:

COMMENTS: Non-CBI