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ENVIRONMENTAL HEALTH AND SAFETY DEPARTMENT
ENVIRONMENTAL AND HEALTH SCIENCES LABORATORY
P.O. BOX 1029
PRINCETON, NEW JERSEY 08543-1029
TELEPHONE (609) 737-5520
FAX NO. (609) 737-5572
(609) 737-5580

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CARL R. MACKERER, Ph.D.
MANAGER, ENVIRONMENTAL AND HEALTH
SCIENCES LABORATORY

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Dear Sir:

In May, 1987, Mobil submitted a TSCA Section 8(e) notification on the toxicity of clarified slurry oil (CAS 64741-62-4). Supplemental submissions to this 8(e) have been made on several other refinery streams, to describe the relationship between stream composition and toxicity. This submission consists of interim and final reports from developmental and subchronic dermal toxicity studies done on several streams which have been the subject of earlier submissions and one additional stream which shows limited toxicity and completes the correlation between toxicity and chemical composition.

The following reports are enclosed:

Study #	CAS #	Study Title
50541	64741-62-4	Clarified Slurry Oil Developmental Toxicity Study in Rats
Final Report I- 59-PP		
Study # 50391-B ① - 37-PP		
Study # 60411 ③ - 12-PP		
Study # 61996 ④ - 33-PP		
Study # 627101 ⑤ - 34-PP		
Study # 63244 ⑥ - 28-PP		
Study # 63456 ⑦ - 65-PP		
Study # 63563 ⑧ - 27-PP		
Study # 64002-⑨ - 44-PP		
Study # 64165 ⑩ - 52-PP		
Study # 64165 ⑪ - 27-PP		
Study # 64184-⑫ - 50-PP		
Study # 64283-⑬ - 40-PP		

Seventy percent in utero fetal death occurred at 30 mg/kg/day applied dermally for 20 days. Many other adverse fetal effects including malformations were observed. The NOEL was 4 mg/kg/day.

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50391-B	64741-81-7	<p>Thirteen-Week Dermal Administration of Heavy Coker Gas Oil to Rats: Biophase Report</p> <p>Increased mortality was observed at 125, 500 and 2000 mg/kg/day (10%, 100% and 100% respectively).</p>
60411	64741-62-4	<p>Effectiveness of Daily Removal at Preventing CSO Toxicity During Two-Week Dermal Administration to Rats</p> <p>Toxicity was greatly reduced by removal after either 15 minutes or 2 hours; but signs of toxicity were still observed at 500 mg/kg/day.</p>
61996-1	64741-82-8	<p>Thirteen-Week Dermal Administration of Beaumont Coker Light Gas Oil to Rats: Interim Report</p> <p>Rats treated with 500 or 2000 mg/kg/day were sacrificed moribund. Thymus weight was decreased at 30 and 125 mg/kg/day. No NOEL was found.</p>
62710-1	64741-62-4	<p>Thirteen-Week Dermal Administration of Ferndale Snytower Bottoms to Rats</p> <p>Lethality was observed at 125 mg/kg/day and above. NOEL is less than 8 mg/kg/day.</p>
63244	64741-62-4	<p>Four-Week Dermal Administration of Ferndale Snytower Bottoms to Male Rats: Daily Application and Removal.</p> <p>Removal of the test material within 15 to 30 minutes after dosing reduced toxicity but a 35 to 50% decrease in platelet count and a 40 to 70% decrease in thymus weight still occurred.</p>
63456	68915-97-9	<p>Thirteen-Week Dermal Administration of Heavy Atmospheric Gas Oil to Rats</p> <p>Serum chemistry and hematology parameters were affected at 125 mg/kg/day and above. A severe reduction in hematopoiesis in the bone marrow and focal necrosis and increased areas of hematopoiesis in liver were seen in rats treated with 500 mg/kg/day.</p>

- | | | |
|---------|------------|---|
| 63563 | 64741-62-4 | <p>Oral and Dermal Administration of Clarified Slurry Oil (CSO) to Male C3H Mice.</p> <p>Mice were dosed with 1000 mg/kg/day by both the oral and dermal routes. CSO was more toxic by the dermal route. Severe liver necrosis and decreased thymus weight were observed.</p> |
| 64002-I | 64741-80-6 | <p>Thirteen-Week Dermal Administration of Visbreaker Residue to Rats</p> <p>Minor effects on hematology and clinical chemistry were observed. The NOEL was 250 mg/kg/day.</p> |
| 64165-I | 64741-81-7 | <p>Thirteen-Week Dermal Administration of Joliet Heavy Coker Gas Oil to Rats</p> <p>Testes, epididymus and thymus were decreased in size. The NOEL was 8 mg/kg/day.</p> |
| 64165-M | 64741-81-7 | <p>Reproductive Assessment of Male Rats Exposed Dermally to Joliet Heavy Coker Gas Oil for Thirteen Weeks</p> <p>This report contains additional information on the effects reported for 64165-I.</p> |
| 64184-I | 64741-81-7 | <p>Thirteen-Week Dermal Administration of Torrance Heavy Coker Gas Oil to Rats</p> <p>Platelet count and thymus weight were decreased at 125 mg/kg/day. WBC was increased. The NOEL was 30 mg/kg/day.</p> |
| 64283 | 8002-05-9 | <p>Postnatal Development and Survival Study in Offspring of Rats Exposed Dermally to Belridge Heavy</p> <p>Red vaginal discharge, decreased body weight gain and delayed parturition were seen in the dams. Decreased survival and body weight were seen in the pups.</p> |

Study numbers appended by the letter B or I indicate a biophase or interim report which contains all data currently available. Results of histopathological examination of tissues taken in these studies will be submitted when they become available.

Sincerely,


C. R. Mackeret

Enclosures

CONTAINS NO CBT

CLARIFIED SLURRY OIL
DEVELOPMENTAL TOXICITY STUDY IN RATS

STUDY NO. 50541

FINAL REPORT - AMENDED

VOLUME ONE

M. H. Feuston

MOBIL ENVIRONMENTAL AND HEALTH SCIENCE LABORATORY
P. O. BOX 1029
PRINCETON, NJ 08540

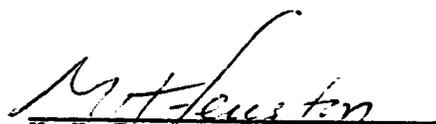
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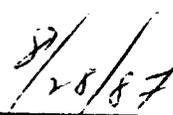
Study Title: Clarified Slurry Oil Developmental Toxicity Study in Rats

Study Number: 50541 Final Report - Amended

ADDITIONAL COMMENT

This report is the amended version of the Final Report. The amendments have been incorporated in the report in an attempt to make the report more easy to read. The amendments to the Final Report have not changed the interpretation of the study results.


M. H. Feuston, Study Director


Date

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EXECUTIVE SUMMARY

Clarified Slurry Oil was administered once daily via dermal application to groups of ten presumed-pregnant rats at doses of 0, 4, 8, 30, 125, and 250 mg/kg/day. All groups were administered the test material on gestation days 0-19.

The following indicators of toxicity were observed at levels as low as 8 mg/kg/day (the lowest dose used in the prior 13-week dermal toxicity study whose results were reported to the EPA/OTS): the effects seemed to be dose-related:

- Maternal:
- o Decreased body weight and food consumption
 - o Increased liver weight (relative)
 - o Vaginal bleeding
 - o Atrophy of the thymus
 - o Abnormal serum chemistry
 - o Decreased litter size

- Fetal:
- o Increased in utero death of the embryo/fetus
(100% at 250 mg/kg/day; 70% even at 30 mg/kg/day)
 - o Decreased body weight/crown-rump length (growth)
 - o Anomalous development (external and internal organs (viscera))

Because evidence of developmental toxicity (anomalies, resorptions, and intrauterine growth retardation) was observed only at dosages which produced some maternal toxicity, additional testing would be necessary to distinguish between direct effects on the embryo or fetus, and those resulting from toxicity to the mother. Based on these data, 4 mg/kg/day represents the NOAEL (No-Observed-Adverse-Effect-Level) for both maternal and developmental toxicity.

SUMMARY

A developmental toxicology study was conducted at Mobil's Environmental and Health Science Laboratory to obtain preliminary data on the influence of Clarified Slurry Oil (CSO) on parameters of reproductive performance during gestation including implantation of the egg, the ability to successfully maintain pregnancy, and viability and development of the embryo/fetus. CSO, the residual hydrocarbon fraction from the Fluidized Catalytic Cracker, was administered once daily via dermal application to groups of ten presumed-pregnant rats at doses of 0, 4, 8, 30, 125, and 250 mg/kg/day. All groups were administered the test material on gestation days 0-19.

Signs of maternal toxicity which were observed in animals exposed to CSO included vaginal bleeding, a decrease in body weight gain, a reduction in food consumption, and aberrant serum chemistry. These effects were observed in some animals exposed to levels as low as 8 mg/kg/day. Increased liver weights (relative to body weight) and atrophy of the thymus were observed at 250 mg/kg/day, but not at 4 mg/kg/day; these results are consistent with those obtained in the 13-week dermal toxicity study (Study No. 20525, 13-week Toxicity Study by Dermal Application of Clarified Slurry Oil) previously reported on the same material.

The number of resorptions was markedly increased and the number of viable fetuses decreased by administration of CSO at dosages of 30 mg/kg/day and above. The mean percentage of resorptions reported was 69.9%, 97.1%, and 100% for dosages of 30, 125, and 250 mg/kg/day, respectively. The mean litter size of the 30 mg/kg/day group was 4.8 fetuses/litter. This was only about

one-third the average size of the control litters (15.4 and 14.3 fetuses/litter). The 125 mg/kg/day group contained only 2 viable fetuses.

Fetuses from pregnant females exposed to CSO at dose levels in excess of 8 mg/kg/day were smaller than fetuses from the control and 4 mg/kg/day groups. Abnormal external development was observed in viable and nonviable fetuses exposed in utero to CSO at 8, 30, and 125 mg/kg/day. Anomalies observed included cleft palate, micrognathia (shortened lower jaw), kinked tail, and edema (excessive amount of fluid in the tissues). One-half of the affected fetuses were not viable at the time of external examination. Abnormal development of fetuses exposed to CSO was also observed at the time of soft tissue (visceral) and skeletal evaluations. Visceral anomalies observed in viable fetuses included enlarged ventricles of the brain, displacement of the esophagus from a left-sided position to a right-sided position, and anomalous development of the heart. A variety of skeletal variations and malformations were observed in CSO-exposed and control fetuses. However, the degree of aberrant development was not as severe as in the CSO-exposed groups.

In conclusion, dermal administration of CSO at very low-dose levels has an adverse effect on parameters of reproductive performance during gestation, and on in utero survival and development of concepti. Because evidence of developmental toxicity was observed only at doses which produce some maternal toxicity, additional testing would be necessary to distinguish between direct effects on the embryo or fetus, and those resulting from toxicity to the mother.

1.0 INTRODUCTION

As part of a larger program to define the toxicologic properties of various refinery streams, Clarified Slurry Oil (CSO), the residual hydrocarbon fraction from the Fluidized Catalytic Cracker, has been tested for hazards it may present in an occupational environment by dermal contact. In addition to causing skin cancer, CSO has been found to cause damage to the liver, bone marrow, and thymus at very low levels of dermal exposure (Report No. MTR-4-2S-86). Since it was not known if CSO would interfere with pregnancy, a developmental toxicology test was conducted at Mobil's Environmental and Health Science Laboratory (MEHSL) in which CSO was applied to the skin of pregnant female rats. This route of exposure was chosen because industrial use of the material can result in repeated human skin contact. The dose levels were chosen based on data obtained in a thirteen-week study previously conducted on the same material (Study No. 20525, 13-Week Toxicity Study by Dermal Application of Clarified Slurry Oil).

This developmental toxicity study was designed to detect, in a relatively short period of time, both reproductive and developmental effects which might be related to exposure to the test material. The assay, which involves exposure of the dams throughout gestation, provides an efficient means to evaluate the effect of CSO on maternal food consumption, body weight gain, and serum parameters, as well as implantation of the egg, and viability and normal development of the embryo/fetus.

2.0 METHODOLOGY

2.1 Experimental Design

Presumed-pregnant rats were distributed among eight experimental groups: remotely-housed dermal control, proximately-housed dermal control, and six CSO-exposed groups (Table 1). At the start of the dosing phase of the study, Groups 1-7 contained ten presumed-pregnant females and Group 8 contained five presumed-pregnant females. Because inhalation of the test material could be a confounding factor in the study, the "Remote" Control animals were not housed in the same animal room as the "Proximate" Control animals and the CSO dermally-treated animals. Additionally, air samples were collected from the animal rooms housing the various control and test animals by a member of Mobil's Inhalation Toxicology Group.

The study was designed initially to include residue analyses of maternal blood, fetuses, and placentae. However, the dams assigned to this group (Group 8, 125 mg/kg/day) resorbed their entire litters, precluding any analyses. The data on these animals are included in some of the computer-generated summary reports but will not be discussed in this Final Report since the results are comparable to the results of Group 5 (Experimental Group, 125 mg/kg/day).

All treatments were performed on each of gestation days 0-19, where designation as gestation day 0 followed detection of a vaginal plug (*in situ* or expelled) and spermatozoa in the vaginal lavage fluid (refer to Section 2.5). Group 7 females were administered 8 mg/kg/day CSO on gestation day 0 and on alternating days thereafter; this dose was designated as "4 mg/kg/day."

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Table 1
Summary of Experimental Design

EXPERIMENTAL GROUPS:

- Group 1 : Remote Dermal Control (0 mg/kg body weight/day)
Group 2 : Proximate Dermal Control (0 mg/kg body weight/day)
Group 3 : CSO Dermal (8 mg/kg body weight/day)
Group 4 : CSO Dermal (30 mg/kg body weight/day)
Group 5 : CSO Dermal (125 mg/kg body weight/day)
Group 6 : CSO Dermal (250 mg/kg body weight/day)
Group 7 : CSO Dermal ("4 mg/kg body weight/day")*

RESIDUE GROUP:

- Group 8 : CSO Dermal (125 mg/kg body weight/day)**

* Dosed at 8 mg/kg/day every other day (on gestation days 0, 2, 4, 6, 8, 10, 12, 14, 16, 18).

** Dams resorbed their entire litters. No residue analyses performed.

All the animals were monitored throughout gestation until sacrifice for 1) changes in appearance, behavior, and excretory function, and 2) signs of ill-health, mortality, or abortion. A prepartum investigation on a variety of fetal and maternal parameters for each of the groups was undertaken to assess the influence of CSO on reproductive performance. The study was initiated on February 19, 1986. The biophase was completed on March 20, 1986, and fetal skeletal and visceral examinations were completed on September 3, 1986 and September 24, 1986, respectively.

2.2 Animal Data

One hundred and two Sprague-Dawley female rats (approximately 9 weeks old) were obtained from Charles River Breeding Laboratories, Kingston, New York. They were acclimated to the test facility for two weeks before the breeding period was initiated. The animals were provided Purina[®] Certified Rodent Chow #5002 (Meal) ad libitum. Drinking water was delivered, ad libitum, by an automatic watering system. In order to minimize water stagnation and bacterial growth, the distribution lines in the animals rooms were scheduled to be flushed daily by a high-pressure flush station. No contaminant was considered to be present in the feed or water at a level sufficient to interfere with this study. Animals were maintained in air-conditioned rooms set to maintain 20-22°C, 40-60% relative humidity, and 12 hour light-dark cycles. Each animal was individually identified by a numbered metal ear tag on gestation day 0.

2.3 Materials to Be Administered

Test Material: Clarified Slurry Oil [CAS 64741-62-4]

Identification: CRU #86001

Density: 1.07 g/ml

Stability: 5 years when stored at room temperature

2.4 Test Material Administration/Control

The test article evaluated in this study is the same as that tested in the 13-week dermal toxicity study which was the subject of Mobil's TSCA Section 8(e) Notice. Although the test article designation (CRU #86001) for the

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developmental toxicity study differs from that (CRU #10298102) for the subchronic dermal toxicity study, the test material for both studies was taken from the same drum. The test material was administered to pregnant females in Groups 3-8 via dermal application on gestation days 0-19. This interval spans the entire period of embryogenesis. Dermal administration was chosen as the route of exposure because industrial use of the material can result in repeated human skin contact.

Since inhalation of the test material could be a confounding factor during the course of the study, air samples were collected from the animal rooms housing the various control and test animals by a member of the Inhalation Toxicology Group. Charcoal sorption tube samples of room air were taken both during and after dermal dosing with CSO. Air was drawn through the sample tubes at approximately 200 ml/min for 60-120 minutes. Samples were then submitted to the Analytical Chemistry Group for quantitative and qualitative analysis by gas chromatography/ mass spectrometry.

2.4.1 Dermal Application

2.4.1.1 CSO Dermal Administration (Groups 3-8)

Presumed-pregnant rats were dosed dermally on the days specified in Section 2.4. CSO was applied once daily to the clipped, intact dorsal skin of the rat at a dose level of 8, 30, 125, or 250 mg/kg body weight/day. Group 7 females were administered 8 mg/kg/day CSO on gestation day 0 and on alternating days thereafter; "4 mg/kg/day" was used as designation for this dose level. In no case were the application sites covered.

CSO was measured using a 10 μ l syringe (calibrated in 0.1 μ l) for Groups 3, 4, and 7, a 50 μ l syringe (calibrated in 1 μ l) for Group 5, or a 100 μ l syringe (calibrated in 1 μ l) for Group 6, and during dispensing was spread evenly on the clipped dorsal skin of the rat using the tip of the syringe. No needle was used. To minimize ingestion of the test material, the rats were fitted with cardboard Elizabethan-style collars. These collars are lined with latex tubing to minimize the development of irritation or lesions. Collars were fitted on the rats on gestation day 0 and replaced as necessary. The rats were clipped on gestation day 0 and once weekly thereafter. The amount of test material to be applied to each animal was calculated using the most recently recorded body weight for each animal, the dose level, and the density of the test material.

2.4.1.2 Dermal Control (Groups 1 and 2)

Presumed-pregnant rats were clipped and collared as above (Section 2.4.1.1). The dorsal skin of each rat was stroked with the tip of a 1 cc syringe, but no test material was applied. Proximate Control animals were housed in the same room as the CSO-exposed animals. Remote Control animals were housed in a different room in order to maintain some control animals known not to have been exposed to the test material.

2.5 Mating Period

During the mating period female rats which had not previously borne pups were placed with male rats in a ratio of 1:1 and observed daily for evidence of having engaged in breeding activity. Each morning during the period of cohabitation, the drop-pan papers under the animal cages were checked for the

presence of expelled vaginal sperm plugs; additionally, each female rat was examined for the presence of in situ vaginal sperm plugs. Vaginal lavage fluid was obtained from each female which exhibited a vaginal plug in situ or on the drop-pan papers, and was examined for the presence of spermatozoa. Females that were positive for sperm plug as well as 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 75 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.

2.6 Assignment to Experimental Group

Presumed-pregnant rats were randomly distributed among one of Groups 1-6 using a computer-generated table of random numbers for a stratified sample of six. This procedure continued until all of the six groups contained ten presumed-pregnant females. Due to the unusual dosing regimens of Groups 7 ("4 mg/kg/day") and 8 (Residue Group, 125 mg/kg/day), ten and five presumed-pregnant females, respectively, were assigned to these groups on the first day of mating on which at least fifteen presumed-pregnant females were obtained.

2.7 Observations During Gestation

2.7.1 Appearance and Clinical Signs (Tables 3A, 3B, and 4)

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

2.7.2 Body Weight and Food Consumption (Tables 5-7)

The body weight of each presumed-pregnant female was measured to the nearest 0.1 gram (Mettler balance, Model PE 3000) on days 0, 3, 6, 10, 13, 16, and 20 of gestation. Similarly, the amount of food consumed by each animal was calculated for gestation day intervals 0-3, 3-6, 6-10, 10-13, 13-16, and 16-20. Stainless-steel feeders, identified individually by female rat number, were weighed on a Mettler balance (Model PE 3000) on the first day and last day of the specified interval. Feeders were weighed before noon. Since rats feed mainly at night, more definite control of the weighing time is unnecessary. If additional food was added to a feeder on an unspecified day, the amount of food added was documented. When a rat spilled nonrecoverable amounts of food, the "consumption data" for that animal were excluded from data calculations for that collection interval.

2.8 Female Necropsy (Tables 8-11)

Each female rat was sacrificed by over-exposure to ether on its 20th day of presumed gestation. The thoracic and abdominal cavities were exposed and all organs were examined grossly for evidence of pathosis. The thymus and liver of animals exposed to 0, 4, and 250 mg/kg/day were removed, trimmed of excess tissue, and weighed to the nearest 0.001 gram on a Sartorius analytical balance. Thymus was fixed in 10% formalin before weighing. The liver and thymus were preserved in 10% formalin. No histopathology has been scheduled for these tissues.

2.8.1 Clinical Chemistry (Table 12)

Blood samples were collected at the time of sacrifice from the aorta of each rat and allowed to clot in a SST Serum Separator Tube (Beckman-Dickinson, Rutnerford NJ). The samples were provided to a member of the Biochemical Toxicology Section for clinical chemistry analyses. A detailed description of the procedures employed for the clinical chemistry analysis is available in the MEHSL Archives (Study No. 50541CA, Serum Chemistry Assays of Blood Samples Collected from Control and Treated Female Sprague-Dawley Rats in a Developmental Toxicity Screen of Clarified Slurry Oil). The quantity or activity of the following serum components were measured:

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

2.8.2 Cesarean Sectioning

2.8.2.1 Uterine/Ovarian Examination (Table 13)

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. Corpora lutea, or "yellow bodies," are ovarian endocrine "structures" which develop at the sites from which eggs are ovulated. The ovaries of nonpregnant females were grossly examined and then discarded. All remarkable findings were recorded. The weight of the intact uterus was measured to the nearest 0.1 gram on a Mettler balance (Model PE 3000) and recorded. The uterine contents of each pregnant rat were exposed, and the number and location of implantations, early and late resorptions, and live and dead fetuses were recorded. An "early resorption" was defined as a reabsorbed dead conceptus in which it was not grossly evident that organogenesis had occurred; a "late resorption" was defined similarly but as one in which it was evident that organogenesis had occurred. A "live fetus" was defined as a fetus which responded to a stimulus, such as touch; a "dead fetus" did not respond to stimuli, nor did it demonstrate the autolysis characteristic of late resorptions. The uterus of each female rat that appeared non-gravid was pressed between two glass slides and examined grossly for evidence of implantation.

2.8.2.2 Fetal Evaluations (Tables 14-19)

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 of a gram on a Mettler balance (Model PE 3000), measured to the nearest millimeter for crown-rump distance, and grossly examined for external anomalies. After gross evaluation, fetuses in each litter were equally distributed between two groups. Approximately one-half of the fetuses in each litter were fixed in Bouin's solution and examined for soft tissue (visceral) anomalies using a modification of the Wilson's technique with sectioning by razor blade. The remaining fetuses in each litter were peeled, eviscerated, fixed in 95% ethanol, macerated in potassium hydroxide, differentially stained for cartilage and bone, cleared in glycerin, and examined for skeletal anomalies.

2.9 Data Analyses and Storage

Raw data were collected, processed, and analyzed by the Grosse Data Acquisition/Reporting System. Maternal biophase data (body weights and food consumption), and cesarean section data, and fetal data (body weights and crown-rump distances) 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. Thymus and liver weights were analyzed by ANOVA followed by Duncan's Multiple Range Test. Differences between control and treated groups were considered statistically significant if the probability of the difference being due to chance was less than 5% ($p < 0.05$).

All raw data and study reports will be stored in the Document Archives of MEHSL. All specimens will be stored in the Tissue Archives of MEHSL.

3.0 RESULTS

Except for the results presented in Section 3.2, only data generated for the pregnant animals will be presented.

3.1 Air Sampling Analyses

Table 2 presents the concentration of CSO detected at the time of sample collection. Over 96% of the vapors collected in the room housing the proximate control and CSO-exposed animals consisted of ortho- or para-xylene. Vapors were present during the dosing procedure in the cubicles housing the CSO-exposed animals, as well as in the cubicles housing the Proximate Control animals. After dosing, vapors were below the limit for detection in the cubicles housing the CSO-exposed animals, but not in the cubicles housing the control animals. Vapors were not detected in the room housing the Remote Control animals.

Table 2

Exposure of Experimental Animals to CSO Vapors

LOCATION* (Room No.)	TIME OF SAMPLE COLLECTION	MEAN CSO CONCENTRATION (mg/cubic meter)
Remote Control (325)	During the day	ND**
High Dose (324)	During dosing	3.7
	After dosing	ND
Proximate Control (324)	During dosing	2.5
	After dosing	0.6

* Room or cubicle from which sample was collected.

** Outside the limit of detection (0.09 mg/cubic meter).

3.2 Observations During Gestation

Incidental and CSO-related observations reported during gestation are presented in Tables 3A and 3B, respectively. Individual observations for each rat during gestation are presented in Appendix 5.1. The red nasal exudate, chromodacryorrhea, and lacrimations that were observed in control and CSO-exposed groups are common in animals that are collared. Also, neck lesions were observed in control and CSO-exposed groups, in spite of the protective soft rubber tubing that lines the inner surface of the cardboard collar. Scratches and/or scabs were observed on the backs of a few of the animals at the time of the first clipping and probably occurred during the mating activity. Alopecia was observed in some of the animals in all of the experimental groups. Due to the low incidences and the lack of dose-related responses, none of the observations listed in Table 3A are considered to be test material related.

Except for two dams exposed to 4 mg/kg/day which exhibited erythema, flaking, and scabs, there were no signs of dermal irritation in dams exposed to CSO. It is possible that discoloration of the skin, which was produced by CSO (the material is brown-black in color) at the site of application at higher dosages, masked observation of the dermal effects. Discoloration of the fur, probably from contact with the test material, was observed in animals exposed to 125 mg/kg/day (2/10) and 250 mg/kg/day (10/10). This was not observed in any of the other groups. Some animals in all of the groups exposed to CSO at dosages of 30 mg/kg/day or greater were cold to touch and/or had decreased stool.

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