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TSCA section 8E

Submitting Organization MOBIL OIL CORP

Project

Request Title
LETTER FROM MOBIL OIL CORPORATION TO USEPA SUBMITTING SUPPLEMENTAL INFORMATION CONCERNING ENCLOSED STUDIES ON CRUDE OILS AND HEAVY ATMOSPHERIC GAS OIL WITH ATTACHMENTS

Chemical Category
CRUDE OILS

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Mobil Oil Corporation

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Dear Sir:

In November, 1985, 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 contains results of testing done on two crude oils and heavy atmospheric gas oil. We believe that the toxicity seen in these tests is caused by the same chemical components responsible for the toxicity of other refinery streams.

Reports for the following studies are being submitted at this time:

1
49
50
42
48
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51

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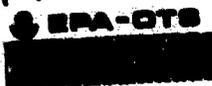
Study #	CAS #	Study Title
63836	8002-05-9	Developmental Toxicity Study in Rats Exposed Dermal to Lost Hills Light
63848	8002-05-9	Developmental Toxicity Study in Rats Exposed Dermal to Belridge Heavy
64282	8002-05-9	Postnatal Development and Survival Study in Offspring of Rats Exposed Dermal to Lost Hills Light
63834-I	8002-05-9	Thirteen-Week Dermal Administration of Lost Hills Light to Rats. (Interim Report)
63846-I	8002-05-9	Thirteen-Week Dermal Administration of Belridge Heavy to Rats. (Interim Report)
64146	68915-97-9	Developmental Toxicity Study in Rats Exposed Dermal to Heavy Atmospheric Gas Oil.

The interim reports for the thirteen week studies contain all data currently available. Results of histopathological examination of tissues taken in these studies will be submitted when they become available.

89910000331

C.R. Mackerer
C. R. Mackerer

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FINAL REPORT

DEVELOPMENTAL TOXICITY STUDY IN RATS
EXPOSED DERMALLY TO LOST HILLS LIGHT

STUDY NO. 38836

MCDI. ENVIRONMENTAL AND HEALTH SCIENCE LABORATORY
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* Volume Two will be retained by the Archives of MENSIL and will not be distributed with this Final Report.

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7.0 Reports (Archived Individually)

**Study No. 63836I - Developmental Toxicity Study in Rats Exposed
Dermally to Lost Hills Light
S.L. Kerstetter, Study Director**

**Study No. 63836P - Developmental Toxicity Study in Rats Exposed
Dermally to Lost Hills Light, Pathology Section
G.E. Cox, Study Pathologist**

**Study No. 63836CA - Serum Chemistry Data for a Developmental
Toxicity Study of Lost Hills Light in the
Sprague-Dawley Rat
J.J. Yang, Study Biochemist**

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EXPOSURE SUMMARY

Loft Hills Light was dermally applied to presumed-pregnant rats during gestation days 0-19. Prenatal Developmental Toxicity group animals were dosed at 0, 125, 500, or 2000 mg/kg/day; Postnatal Developmental Toxicity group animals were dosed at 0 or 2000 mg/kg/day.

MATERNAL TOXICITY: NOAEL - 125 MG/KG/DAY

Loft Hills Light exposure was maternally toxic at doses of 500 and 2000 mg/kg/day. Signs of toxicity included a statistically significant reduction in net maternal body weight gain and food consumption, decrease in thymus weight, and increase in liver weight. Aberrant serum chemistry parameters were also observed.

DEVELOPMENTAL TOXICITY: NOAEL - 500 MG/KG/DAY

Developmental toxicity was observed at the 2000 mg/kg/day dose level and included increased in utero death, decreased fetal weights, and skeletal (increased incidence of incompletely ossified skeletal structures) and visceral (right-side esophagus) anomalies.

POSTNATAL TOXICITY: NOAEL - NOT ACHIEVED

Postnatal evaluation revealed a significant increase in the number of stillborn pups and a decrease in pup survival for the 2000 mg/kg/day group. The liveborn in this treated group weighed significantly less than control pups on postpartum days 0 and 4.

SUMMARY

Lost Hills Light was applied once daily via dermal application to presumed-pregnant rats at doses of 0, 125, 500, or 2000 mg/kg/day. All Prenatal and Postnatal Developmental Toxicity group animals were dosed on gestation days 0-19. Prenatal Developmental Toxicity group animals were sacrificed on gestation day 20. Postnatal Developmental Toxicity group animals, as well as their offspring, were sacrificed on postpartum day 4.

A significant decrease in net maternal body weight gain and food consumption, a decrease in thymus weight, an increase in liver weight, and aberrant serum chemistry parameters were noted in females exposed to Lost Hills Light at doses of 500 and 2000 mg/kg/day. A significant increase in absorptions and a corresponding decrease in litter size were observed for the 2000 mg/kg/day Prenatal group. Fetuses from this group weighed significantly less than control fetuses and had a greater incidence of incompletely ossified skeletal structures (nasal bones, vertebrae), findings indicative of growth retardation. Visceral anomalies were limited and included right-sided esophagus seen in two fetuses from the high dose group. Although not statistically significant, this malformation has been observed previously in fetuses exposed to refinery streams.

Postnatal assessment revealed a significant increase in the number of stillborn pups and a decrease in pup survival for the 2000 mg/kg/day Postnatal group. The liveborn in this group weighed significantly less than control pups on postpartum days 0 and 4.

In summary, dermal application of Lost Hills Light resulted in maternal toxicity at doses of 500 and 2000 mg/kg/day and developmental toxicity at 2000 mg/kg/day. Neonatal growth and survival were adversely affected in pups exposed in utero at 2000 mg/kg/day.

1.0 INTRODUCTION

A developmental toxicology study was conducted at Mobil's Environmental and Health Science Laboratory (MEHSL) in which Lost Hills Light, a crude oil from California, was applied to the skin of pregnant rats. The dermal route of exposure was chosen since the transport and refining of this crude oil can result in repeated human skin contact. The primary objectives of this study were to evaluate the effects of Lost Hills Light on female rats during gestation (food consumption, body weight gain, viability and development of the offspring, and serum chemistry parameters) and to determine if in utero exposure to Lost Hills Light adversely affects postnatal survival of neonates. Selection of dose levels was based on the results of a subchronic range finding study using this material (Study No. 63883).

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 effects on maternal food consumption and body weight gain, implantation of the egg, viability and normal development of the embryo/fetus, and postnatal survival of neonates. The study was also designed to include maternal serum chemistry analyses. This assay provides additional information which may assist in interpretation of study results.

2.0 METHODOLOGY

2.1 Experimental Design

Presumed-pregnant rats were distributed into two groups: Prenatal and Postnatal Developmental Toxicity groups. The Prenatal Developmental

Toxicity group ("Prenatal" group) was divided further into four groups (Groups 1-4) with graded doses ranging from 0 (control) - 2000 mg/kg/day. The Postnatal Developmental Toxicity group ("Postnatal" group) was divided into two groups (Groups 5 and 6) with doses of 0 and 2000 mg/kg/day. Prenatal and Postnatal group animals were administered the test material throughout gestation (days 0-19). The dosing regimen is summarized in Table 1. At the start of the dosing phase of the study, the Prenatal and Postnatal groups contained twelve presumed-pregnant females per group.

TABLE 1
Summary of Experimental Design

GROUP	DOSE LEVEL (mg/kg/day)	ROUTE	DAYS OF ADMINISTRATION*
Prenatal Groups:			
Group 1	0	Sham Control	0-19
Group 2	125	Dermal	0-19
Group 3	500	Dermal	0-19
Group 4	2000	Dermal	0-19
Postnatal Groups:			
Group 5	0	Sham Control	0-19
Group 6	2000	Dermal	0-19

* Designation as gestation day 0 followed detection of a vaginal plug (in situ or expelled) and spermatozoa in the vaginal lavage fluid.

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 fetal and maternal parameters for Groups 1-4 was undertaken to assess the influence of Lost Hills Light on reproductive performance and development of offspring. Also, a postpartum investigation on a limited

number of maternal and neonatal parameters for Groups 5 and 6 was performed to assess the influence of Lost Hills Light on parturition and postnatal survival of neonates. The inclusive dates for specific study activities were as follows:

Acclimation Period:	February 20, 1990 - March 5, 1990
Mating Period:	March 5 - 15, 1990
Gestation Period:	March 6 - April 9, 1990
Cesarean Section:	March 26 - 29, 1990
Postpartum Period:	March 31 - April 10, 1990
Skeletal Examination:	April 17 - June 11, 1990
Visceral Examination:	October 5, 1990 - January 18, 1991

2.2 Animal Data

One hundred four Sprague-Dawley female rats [VAF/Plus CrI:CD(SD)BR; approximately 9 weeks old] were obtained from Charles River Breeding Laboratories, Kingston, New York. The animals were virus-free at the time of arrival and were acclimated to the test facility for two weeks before the breeding period was initiated. Tap water and Purina Certified Rodent Chow #5002 (meal) were provided ad libitum during the course of the study. Animals were housed 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 Material Administered

Test Material: Lost Hills Light (Bakersfield, CA)
Identification: CPU #89645
Density: 0.90 g/ml
Expiration Date: 11-01-94

2.4 Test Material Application/Control

2.4.1 Lost Hills Light Dermal Application (Groups 2-4, 6)

The test material was applied to pregnant females in Prenatal groups

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2-4 and Postnatal group 6 via dermal application on gestation days 0-19. This interval spans the entire period of embryogenesis. Animals were clipped and collared on gestation day 0 and then clipped once weekly thereafter; collars were replaced as necessary. The amount of test material to be applied to each animal was calculated using the most recently recorded body weight for that animal, the dose level, and the density of the test material. Lost Hills Light was applied once daily to the clipped, intact, nonoccluded, dorsal surface of the rat at a dose level of 125, 500, or 2000 mg/kg body weight/day. Lost Hills Light was measured using a 50 μ l syringe (calibrated in 1.0 μ l) for Group 2, a 500 μ l syringe (calibrated in 10.0 μ l) for Group 3, and a 1.00 ml syringe (calibrated in 0.01 ml) for Groups 4 and 6. During dispensing, the test material was spread evenly on the dorsal skin of the rat using the tip of the syringe. No needle was used.

2.4.2 Sham Control (Groups 1 and 5)

Presumed-pregnant rats were clipped and collared as above (Section 2.4.1). The dorsal skin of each rat was stroked with the tip of a 1.00 ml syringe, but no test material was applied.

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

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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 72 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 Groups

Presumed-pregnant female rats were distributed to one of Prenatal groups 1-4 using a computer-generated table of random numbers for a stratified sample size of four. Similarly, presumed-pregnant rats were distributed to one of Postnatal groups 5-6 using a computer-generated table of random numbers for a stratified sample size of two. These procedures were continued until each group contained twelve presumed-pregnant females.

2.7 Observations During the Gestation/Postpartum Period

2.7.1 Appearance and Clinical Signs

Each presumed-pregnant female was observed at least once a day throughout gestation until sacrifice for signs of pathosis, abortion, premature delivery, dystocia and/or death. Dams and their litters were observed on postpartum days 0 through 4 for signs of pathosis and/or death. On postpartum day 0, pups were examined for external malformations and variations. Pups were observed daily for the presence of milk in their stomachs; absence of milk was recorded. All unusual findings were noted.

2.7.2 Body Weights and Food Consumption

2.7.2.1 Prenatal Groups

The body weight of each Prenatal group female was measured to the nearest

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0.1 gram on days 2, 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 the first 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. When a rat spilled nonrecoverable amounts of food, the "consumption data" for that animal were excluded from data calculations for that collection interval.

2.7.2.2 Postnatal Groups

Body weights and food consumption measurements were performed on the days described in Section 2.7.2.1. Also, the body weights of Postnatal group animals were measured on postpartum days 0 and 4, and recorded. Food consumption measurements were not made during the postpartum period. The body weights of the offspring were measured according to gender for each individual litter on postpartum days 0 and 4, and recorded.

2.8 Female Necropsy

2.8.1 Prenatal Groups

Each female rat was sacrificed by over-exposure to diethyl ether on its 20th day of presumed gestation. The abdominal cavity was exposed and the reproductive organs were examined grossly for evidence of pathosis. Following removal of the uterus and ovaries, the carcass was given to the Pathology group for thymus and liver weights, and macroscopic examination of the remaining organs. Thymus and liver weights were measured to the nearest 0.001 gram, and recorded by a member of the Pathology group. Only the livers of pregnant females were preserved in 10% neutral buffered formalin.

2.8.1.1 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 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 and recorded. The uterine contents of each pregnant rat were 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, examined grossly for evidence of implantation, and then discarded. The uteri and ovaries of pregnant females were discarded following data collection.

2.8.1.2 Serum Chemistry

Blood samples were collected at the time of sacrifice from the aorta of each rat and allowed to clot. The samples were given to a member of the Biochemical Toxicology group for analyses. A summary report describing the results is available in the MEHSL Archives (Study No. 65236CA). 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	Potassium
Aspartate Aminotransferase (AST)	Sodium
Bilirubin, Total	Sorbitol Dehydrogenase (SDH)
Calcium	Total Protein
Chloride	Triglycerides
Cholesterol	Urea Nitrogen
Creatinine	Uric Acid
Globulin	

2.8.1.3 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 of a gram, and grossly examined for external anomalies. The following definitions and terminology were used in describing fetal findings [1]:

- Anomaly:** Any deviation (malformation or variation) from "normal."
- 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. Groups 1, 3, and 4 were examined for anomalies using a modification of Wilson's technique of sectioning by razor blade. Fetuses assigned to the skeletal analysis group were differentially stained for cartilage and bone; all Prenatal groups were examined.

2.8.2 Postnatal Groups

Females with surviving offspring were sacrificed by over-exposure to diethyl ether on postpartum day 4; females with no surviving pups were

sacrificed on the day the last pup in the litter died. The abdominal cavity of each adult female was exposed and the reproductive organs were examined grossly for evidence of pathosis. The uterus was excised, examined for the total number of implantations, and then discarded. Following uterine examination, the carcass was given to the Pathology group for thymus and liver weights, and macroscopic examination of the remaining organs. Thymus and liver weights were measured to the nearest 0.001 gram, and recorded by a member of the Pathology group. Only the livers of pregnant females were preserved in 10% neutral buffered formalin. All pups were sacrificed by over-exposure to diethyl ether on postpartum day 4; no tissues were saved.

2.9 Data Analyses

Prenatal group 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 visceral and skeletal data were recorded by hand and subsequently entered into the Grosse system. The data were statistically evaluated by ANOVA followed by group comparisons using Fisher's Exact test.

Postnatal group data generated during gestation were collected, processed, and analyzed as described above for the Prenatal groups. However, the data were filed in the system under Study No. 63836R. Data generated during the postnatal phase were recorded by hand and late-entered into the Grosse system under Study No. 63836R. Implantation sites per litter, live pups per litter, and pup weight per litter were hand calculated.

Thymus and liver weights were collected, processed, and analyzed using the Pathology module of the Grosse system. The data were filed in the system

under Study No. 63836 and 63836R for Prenatal and Postnatal groups, respectively, and were statistically evaluated using Tukey's test.

Serum chemistry data were collected and processed using the Clinpath module of the Grosse system and analyzed by ANOVA followed by group comparisons using Tukey's test. For all statistical analyses, 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% ($p < 0.05$).

3.0 RESULTS

3.1 Clinical Observations

Incidental and Lost Hills Light-related observations reported during gestation are presented in Tables 2A and 2B for Prenatal and Postnatal groups, respectively. Observations for both Prenatal and Postnatal groups were similar. The red nasal exudate and chromodacryorrhea noted in control and treated groups are common in animals that are collared and/or stressed. Scratches were observed on the backs of several of the animals at the time of the first clipping and probably occurred during mating activity. A few females developed neck lesions, in spite of the protective soft rubber tubing that lines the inner surface of the cardboard collar.

The red vaginal discharge observed in the 2000 mg/kg/day groups was considered to be test material related. This finding is usually indicative of some degree of litter resorption and this appears to be the case in the present study. One female in the 125 mg/kg/day group also exhibited red vaginal discharge. This is not considered to be treatment related since 1) she only had one resorption, 2) this finding has been seen in control females at this facility, and 3) it is an isolated occurrence in the 125

mg/kg/day group. One high-dose Prenatal female was pale in color. Slight skin irritation, which was limited to erythema and scabs, was observed in only a few of the treated animals. It was uncertain whether the irritation was caused by the test material or, more likely, animal-induced (via scratching or biting). Generally, due to the restrictive nature of the collars, access to the test site and ingestion of the material are minimized. However, the material used in this study could not be confined to the dorsal surface of the animals due to its tendency to spread following application. Consequently, the animals were covered with the material and, in an attempt to groom themselves, scratched and nipped the borders and surrounding areas of the test site. In view of this, ingestion of the material was probable.

3.2 Body Weights and Food Consumption

Mean body weights and body weight changes during gestation are presented in Tables 3(A and B) and 4(A and B), respectively. Uterine and net body weights of Prenatal group animals are presented in Table 5. Animals exposed to Lost Hills Light at levels of 500 and 2000 mg/kg/day gained significantly less weight overall (days 0-20) than the control animals (Tables 4A and 4B). Net body weight gain was also significantly reduced at these dose levels for the Prenatal group animals (Table 5). No statistically significant differences were observed between control and treated animals during the postpartum period (Table 6).

Mean daily food consumption values during gestation of the Prenatal and Postnatal group females are presented in Tables 7A and 7B, respectively. The 500 and 2000 mg/kg/day groups consumed significantly less food during early to mid gestation but had food consumption values similar to control values during the latter part of gestation.

3.3 Observations at Cesarean Section

3.3.1 Necropsy Findings

An increase in the number of females in the 2000 mg/kg/day group with a small thymus was noted during macroscopic examination. Absolute and relative thymus weights were significantly reduced at this dose level (Table 8). A reduction in thymus weight was also apparent at the 500 mg/kg/day dose level, however, the effect was not statistically significant. An increase in absolute liver weight (Table 8) was noted at the 500 and 2000 mg/kg/day dose levels, with relative liver weights being significantly increased at these levels.

3.3.2 Serum Chemistry Analyses

Adverse effects on serum components were noted at the 500 and 2000 mg/kg/day dose levels (Table 9). Aberrant serum chemistry values were obtained for AST, ALT, alkaline phosphatase, cholesterol, triglycerides, total bilirubin, A/G ratio, inorganic phosphorus, and SDH. With the exception of the A/G ratio, all of the aforementioned components showed a linear relationship (>99% confidence level, Pearson's correlation coefficient) between dose and serum level. When compared to historical serum reference values and with the exception of AST and ALT, the dose-reponse curve for each component at the 2000 mg/kg/day dose level fell outside the normal range as defined by the 10th and 90th percentiles of the historical data.

3.3.3 Reproductive Evaluations

A significant increase in mean number/percent resorptions and a corresponding decrease in litter size was observed at the 2000 mg/kg/day dose level (Table 10).

3.3.4 Fetal Evaluations

Mean fetal body weights, a parameter of body growth and development, were significantly decreased at a level of 2000 mg/kg/day (Table 11). No effects attributable to the test material were observed at the time of fetal external examination. Fetal skeletal examination revealed an increase in incomplete ossification of various skeletal structures which included nasal bones and vertebrae (Table 12). This increase was significant at the 2000 mg/kg/day dose level. At the time of visceral examination, two incidences of right-sided esophagus were observed in the 2000 mg/kg/day group, a malformation seen only in fetuses exposed to refinery streams (Table 13).

3.4 Observations During the Postpartum Period

Observations reported during lactation are presented in Table 14. The skin irritation noted during lactation for the 2000 mg/kg/day group was most likely due to the animals' grooming rather than the test material itself since none of these females had skin irritation at the end of the exposure period. Due to the "sticky" nature of the material, it could not be removed by wiping. An attempt was made to shave these animals to remove as much of the "contaminated" hair as possible. However, the material persisted on the animals during lactation and these females were observed to have groomed themselves relatively more than the control animals.

3.4.1 Necropsy Findings

No test material related findings were noted during macroscopic examination for the Postnatal group animals. Similarly, thymus and liver weights were not adversely affected.

3.4.2 Litter Data

Natural delivery data and litter data from Postnatal group animals are

summarized in Table 15. One female in the control group was noted as having dystocia and was sacrificed moribund on gestation day 24. Her right uterine horn was convoluted, making delivery impossible. Her data are excluded from Table 15. Three females in the 2000 mg/kg/day group had no viable offspring; their litters were totally resorbed. Two additional females in this group had their entire litters (2 pups/litter) die by postpartum day 3. A significant increase in the number of stillborn pups was noted for the 2000 mg/kg/day group. Additionally, liveborn pups in this group weighed significantly less on days 0 and 4 compared to the control pups.

Although the duration of gestation was not significantly affected, there was a tendency for most of the treated females to deliver in the afternoon of gestation day 22 or on the morning of gestation day 23. The majority of females in the control group delivered on the morning of gestation day 22. The biological significance of this "delayed delivery", if any, for the treated group is uncertain.

4.0 DISCUSSION AND CONCLUSIONS

Daily application of Lost Hills Light on the skin of pregnant rats during gestation was shown to be maternally toxic at 500 and 2000 mg/kg/day and developmentally toxic at 2000 mg/kg/day. Maternal effects included a reduction in net maternal body weight gain and food consumption, a decrease in thymus weight (Prenatal), and an increase in liver weight (Prenatal). Red vaginal discharge was noted in females in the 2000 mg/kg/day Pre- and Postnatal groups. The discharge was probably due to increased in utero death at this dose level.

Of the serum chemistry parameters that were adversely affected, triglycerides and A/G ratio may be a result of the large number of resorptions observed in the 2000 mg/kg/day group. It has been found that

pregnant animals which resorb a large percentage of their litter have serum values similar to those of nonpregnant animals [2]. Cholesterol, aspartate aminotransferase (AST), alkaline phosphatase, alanine aminotransferase (ALT), and sorbitol dehydrogenase (SDH) levels were increased at a dose of 2000 mg/kg/day. These results may strongly suggest hepatic damage given the elevation of two liver-specific enzymes (ALT, SDH) in addition to the increase in liver weight noted for the high dose group. An increase in liver weight was also seen in the subchronic study on this material (Study No. 63834). Other serum effects in the present study included elevated phosphorus levels noted for the 2000 mg/kg/day group and a dose-dependent decrease in bilirubin.

Lost Hills Light exposure resulted in adverse developmental effects at the 2000 mg/kg/day dose level. Fetal body weights were significantly lower at this level. Fetuses from the high dose group had a greater incidence of incompletely ossified skeletal structures (nasal bones, vertebrae). These variations, in conjunction with body weight depression, may be indicative of some degree of growth retardation. Right-sided esophagus, a visceral malformation, was noted in two fetuses in the high dose group. Although the incidence was not statistically significant, this finding has been observed in developmental toxicity studies on refinery streams [3, 4, 5, 6, 7, 8, 9] and is considered to be of biological significance.

Adverse effects were also noted during the postnatal phase of this study. Pup body weights were significantly lower at the 2000 mg/kg/day dose level. Pups from the treated group weighed less at the beginning (day 0) and end (day 4) of the postpartum period. A significant increase in the number of stillborn pups was noted for the treated group. Additionally, pup mortality was higher for the treated group (11%) than for the control group (1%). The results indicate that Lost Hills Light produced an adverse effect on

parturition, pup growth, and pup survival. A more extensive postnatal study is currently being conducted (Study No. 64282) to more clearly define the effects of Lost Hill Light on postnatal survival and development.

The adverse effects noted in this study were not unexpected. Toxicologic evaluation of refinery streams, complex mixtures of hydrocarbons which result from the processing of crude oil, also reveal comparable toxicity. This study has shown that dermal application of Lost Hills Light resulted in maternal toxicity at 500 and 2000 mg/kg/day and developmental toxicity at 2000 mg/kg/day. Similarly, neonatal growth and survival were adversely affected following in utero exposure to the test material.

[It should be noted that due to the dispersing nature of the material and the high dose at which it was applied (2000 mg/kg/day), the material could not be confined to the dorsal surface of the animals. Although measures were taken to minimize ingestion of the material, oral ingestion cannot be precluded.]

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