

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION

MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
MINERAL OIL - **SOLVENTS**

Chemical Code # 000401, Tolerance # 00149, SB 950 # 754
Original date: 7/19/01

I. DATA GAP STATUS

Chronic rat:	Data gap, no study on file
Chronic dog:	Data gap, no study on file
Oncogenicity, rat:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, inadequate study, possible adverse effect indicated
Reproduction, rat:	Data gap, no study on file
Teratology, rat:	Data gap, inadequate study, possible adverse effect indicated
Teratology, rabbit:	Data gap, no study on file
Gene mutation:	Data gap, inadequate study, possible adverse effect indicated
Chromosomal aberration:	Data gap, inadequate study, no adverse effect indicated
DNA damage:	No data gap, no adverse effect.
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

File name: T010719

Original: Kishiyama & Silva, 7/19/01

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study submitted

CHRONIC TOXICITY, RAT

Subchronic Study:

149 - 024 117141 A14-Day Subchronic Inhalation Toxicity in Rats," (Whitman, F.T.; Exxon Biomedical Sciences, Inc., Toxicology Laboratory, East Millstone, NJ; Project #: 209918; 1/9/91). MRD-87-099 was administered as a liquid droplet aerosol to Crl:CD BR (Sprague-Dawley) VAF/Plus rats (5/sex/dose) at 0, 50, 500 and 1500 mg/m³ (actual: 0, 55, 511 and 1507 mg/m³) for 10 days (6 hours/day). Body weight and food consumption was statistically significantly decreased in both sexes at the high dose. Incidence of rales (1st week of exposure only) was increased, primarily at ≥ 500 mg/m³. Increased incidence of exfoliation, alopecia, and scabs was observed at 1500 mg/m³. Liver weights were increased for females at 1500 mg/m³. Platelet and WBC counts were increased 145% and 222%, respectively, for males at 1500 ppm. WBC counts were increased 168% in females at 1500 mg/m³. Blood and clinical chemistry effects were observed in both sexes, primarily at ≥ 500 mg/m³. **Possible adverse effects: male and female in all dosed groups were affected with increased amounts of alveolar macrophage accumulations in their lungs, which in some cases, associated with interstitial pneumonitis;** NOEL < 50 mg/m³. Lung/trachea weights were increased for males at 1500 mg/m³ and for females at ≥ 500 mg/m³. Males at 1500 mg/m³ showed anterior nasal turbinate focal infiltrations of neutrophilic inflammatory cells. UNACCEPTABLE (not performed according to FIFRA Guidelines). These data are supplemental. (Kishiyama & Silva, 11/6/00).

No FIFRA Guideline chronic rat study submitted.

CHRONIC TOXICITY, DOG

No study submitted

ONCOGENICITY, RAT

No study submitted

ONCOGENICITY, MOUSE

149-025 117142 A Dermal Carcinogenesis Assay in C3H/HeNCr 1 BR Mice,@ (Federici, T.M. Exxon Biomedical Sciences, Inc., Toxicology Laboratory, Project Number #: 288011; 12/14/90). MRD-86-880 (neat) and at 25% and 50% dilutions (SN101 or toluene vehicles) and MRD-87-008 (neat) were applied dermally to the clipped backs of C3H/HeNCr1BR male mice (50/group) twice per week in 37.5 μ l for 24 months. Results showed body weights at 25% and 50% MRD-86-800 in Solvent S100N, 25% in toluene (MRD-85-722), toluene alone and benzo[a]pyrene were statistically significantly (but only marginally: 3.5 to 5.4%) decreased compared to (solvent MRD-87-017) control. Dermal irritation was the most noted in-life observation. **Possible adverse effect: Squamous cell neoplasms of the skin for 8% and 10% of animals treated with test articles 100% MRD-86-880 and 100% MRD-87-008, respectively.** UNACCEPTABLE (no females tested,

no rationale for dose selection, too few dose levels, no untreated control, no food consumption data, no hematology, and no GLP sign-off). The data are supplemental. (Kishiyama & Silva, 11/2/00).

REPRODUCTION, RAT

No study submitted

TERATOLOGY, RAT

149 - 020 117321 “Developmental Toxicity of EDS Recycle Solvent and Fuel Oil,” (McKee, R.H., Pasternak, S.J. and Traul, K. A.; Published in: *Toxicology*, 46 (1987) 205-215). Two coal-derived liquids recycle solvent (boiling range 200-427 °C) and an experimental industrial fuel oil (boiling range 204-538 °C), were administered by gavage, each at 0 (5 ml/kg white oil), 0.1, 0.5 and 1.0 g/kg to mated female Sprague-Dawley rats (25/dose with 50 females in the control group) daily during gestation days (gd) 6-19. Rats were sacrificed on gd 20 and the uterine contents were removed and examined. Test materials were produced by direct coal liquefaction and contained substantial amounts of material boiling above 370 °C (including PAHs). Recycle solvent induced significant bodyweight decreases in dams at 1.0 mg/kg and fuel oil induced decreases at ≥ 0.5 g/kg. Uterine weights in both groups were significantly decreased and resorptions were significantly increased at ≥ 0.5 g/kg. Maternal NOEL = 0.1g/kg (both treatments). Number of fetuses (due to resorptions), crown-rump lengths and fetal body weights were significantly decreased from both treatments at ≥ 0.5 g/kg. Developmental NOEL (both treatments) = 0.1 g/kg. The limited number of high dose fetuses precluded a rigorous analysis of malformations. Possible adverse effect indicated: Developmental delays from both treatments. These data are supplemental. (Kishiyama & Silva, 12/22/00).

TERATOLOGY, RABBIT

No study submitted

GENE MUTATION

149 - 027 117145 “Microbial Mutagenesis in *Salmonella* Mammalian Microsome Plate Incorporation Assay,” (Przygoda, R.T.; Exxon Biomedical Sciences, Inc., Toxicology Laboratory, East Millstone, NJ; Project #: 209925; 3/18/88). MRD-87-099 was evaluated for mutagenic potential at 1000, 5000, 10000, 25000, and 50000 $\mu\text{g}/\text{plate}$ using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 with and without Aroclor-induced rat liver activation, in triplicate, single trial. Background lawn was slightly reduced for tester strains TA98 (-S9) and TA1537 (5x S9). MRD-87-099 did not significantly increase the number of revertant colonies relative to the negative control. UNACCEPTABLE (copies of tables are not complete, inadequate description of test material, and no GLP sign-off). Possibly upgradeable. No adverse effect indicated. Supplemental data. (Kishiyama & Silva, 5/4/01).

149 - 027 117146 “Microbial Mutagenesis in *Salmonella* Mammalian Microsome Plate Incorporation Assay Test Material MRD-87-100,” (Przygoda, R.T.; Exxon Biomedical Sciences, Inc., East Millstone, NJ; Toxicology Laboratory, Project #: 210025; 4/4/88). MRD-87-100 was evaluated for mutagenic potential at 1000, 5000, 10000, 25000 and 50000 $\mu\text{g}/\text{plate}$ using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 with and without Aroclor-induced rat liver activation, in triplicate plates, single trial. Background appeared slightly reduced for tester strain TA1538 (- S9). MRD-87-100 did not significantly increase the number of revertant colonies relative to the negative control. Not acceptable, but possibly upgradeable with submission of missing

data (copy of tables are not complete, inadequate description of test material, and no GLP sign-off). No adverse effect indicated. (Kishiyama & Silva, 5/4/01).

149 - 020 117326 "Estimation of the Mutagenicity of Hydrocarbon Fractions Utilizing the Bacterial Assay Procedure with Mammalian Tissue Metabolic Activation," (No author indicated. Hine Incorporated, Health and Environmental Sciences Department, HESD Publication No.: 26-60103, Report No. 6, 1978). VM & P Naphtha, Stoddard Solvent, Rubber Solvent, 140 Flash Aliphatic Solvent, Mixed Xylenes, 60 Solvent, 70 Solvent, 50 Thinner, Deodorized Kerosene, 80 Thinner and High Solvency Naphtha were diluted 1:10 in DMSO (plus metabolic activation) then evaluated for mutagenic potential using *Salmonella typhimurium* strains TA98 and TA100. The positive control was 2-diacetylaminofluorene. The test material was spotted on plates of bacteria. No increase in the number of revertant colonies were observed after treatment with test compounds. The positive controls functioned as expected. NOT ACCEPTABLE. Not upgradeable (major deficiencies). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 1/4/01).

CHROMOSOME EFFECTS

149 - 021 117332 "Mutagenicity Study of Thirteen Petroleum Fractions," (Hine Laboratories, San Francisco, CA; Project #: U-150-14 (EA-1); Report #4, 1973). VM and P naphtha, stoddard solvent, rubber solvent, mixed xylenes, 60 solvent, 70 solvent, 140 aliphatic solvent, 80 thinner, 50 thinner, deodorized kerosene, high aromatic solvent, 40 thinner and toluene concentrate, at 1.0 ml/kg, were injected subcutaneously into 10 Swiss-Webster white male mice/dose and intraperitoneally into 10 Long-Evans male rats/dose. Positive controls were triethylenephosphoramidate for mice and triethylenemelamine for rats. The treated males (mice & rats) were mated with untreated females (of respective species). Male mice were housed with 3 females for one week for a total of 8 weeks. Male rats were mated with 2 females per week for ten weeks. Mutagenic index was not increased with the petroleum fractions tested in this study and there were no other treatment-related effects. Positive controls were functional. UNACCEPTABLE. (major deficiencies). These data are supplemental. (Kishiyama & Silva, 5/2/01).

DNA DAMAGE

**149 - 027 117147 "MRD-87-099: *In Vivo* Mammalian Bone Marrow Micronucleus Assay," (Przygoda, R.T.; Exxon Biomedical Sciences, Inc., East Millstone, NJ; Toxicology Laboratory, Project #: 209930; 5/20/88). MRD-87-099 was administered intraperitoneally (single dose) to CD-1 mice (5/sex/dose/sacrifice time) at 1.0, 2.5 and 5.0 g/kg and evaluated for DNA damaging potential. Mice were sacrificed and bone marrow was collected at 24, 48 and 72 hours after dosing. The statistically significant increase in micronucleated polychromatic erythrocytes for males treated with 5 grams MRD-87-099 and sacrificed at 48 hours. was reported as not biologically significant because the mean value (1.6) was within the historical control range (0 - 4/1000 PCE). NOEL > 5000 g/kg (Micronuclei were not induced with MRD-87-099 treatment.) Acceptable. No adverse effect. (Kishiyama & Silva, 5/4/01).

**149 - 027 117149 MRD-87-100: *In Vivo* Mammalian Bone Marrow Micronucleus Assay ,@ (Przygoda, R.T.; Exxon Biomedical Sciences, Inc., Toxicology Laboratory, East Millstone, NJ; Project #: 210030; 5/20/88). MRD-87-100 was administered in a single intraperitoneal treatment to CD-1 mice (5/sex/dose) at 1.0, 2.5, and 5.0 g/kg and was evaluated for mutagenic potential. Mice were sacrificed and bone marrow was collected at 24, 48, and 72 hours after dosing. No significant increase in micronucleus formation or overt toxicity was observed in the report. Acceptable. No adverse effect. (Kishiyama & Silva, 5/14/01).

NEUROTOXICITY

Not required at this time.

OTHER STUDIES

149 - 020 117323 "Assessment of the Potential Reproductive and Subchronic Toxicity of EDS Coal Liquids in Sprague-Dawley Rats," (McKee, R.H., Plutnick, R.T., Traul, K.A.; Published in: Toxicology, 46: 267-280, (1987). Recycle solvent and fuel oil (recycle solvent /vacuum gas oil 70/30) were administered via gavage (5 times/week for 13 weeks) to Sprague-Dawley rats (54 females & 18 males) at 0.02, 0.1 and 0.5 g/kg/day. White oil control was given at 5 ml/kg (90 females & 36 males). Test animals were mated after the 13-week dosing period and were evaluated for reproductive effects. Following the 13th week of treatment, 18 females were removed from each dosing group for subchronic toxicity study. Each male was housed with 2 females from the corresponding dosage group for 10 consecutive nights, or until mating was confirmed. Mated females were maintained without additional dosing through the gestation and lactation periods to postpartum day 21. Reproduction results: There was no evidence of reproductive toxicity. Subchronic results (14 days after last dosing): There was a slight decrease in hemoglobin and hematocrit in high dose recycle solvent group. Liver weight increased and brain weight, erythrocyte counts, hemoglobin and hematocrit levels were slightly reduced in females for fuel oil at 0.5 g/kg/day. Hemoglobin was decreased and serum cholesterol was increased for males at 0.5 g/kg/day fuel oil. These data are supplemental. No adverse effect. (Kishiyama & Silva, 1/3/01).