

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA (all Mineral Oil DPN #'s)

Chemical	Chemical Code	Tolerance Number	SB950 Number
MINERAL OIL	401	149	754
PETROLEUM HYDROCARBONS	473	50444	789
PETROLEUM OIL (Unclassified),	765	50392	297
ISOPARAFFINIC HYDROCARBONS	1641	50667	713
PETROLEUM DISTILLATES (refined)	763	50427	476
PETROLEUM DISTILLATES	2106	50792	788

Original date: 12/14/01

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, inadequate study
Chronic toxicity, dog:	Data gap, inadequate study
Oncogenicity, rat:	Data gap, inadequate study, possible adverse effect indicated
Oncogenicity, mouse:	Data gap, inadequate study, possible adverse effect indicated
Reproduction, rat:	Data gap, no studies submitted
Teratology, rat:	Data gap, inadequate study, no adverse effect
Teratology, rabbit:	Data gap, no studies submitted
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, acceptable study, no adverse effect
DNA damage:	Data gap, no studies submitted
Neurotoxicity:	Data gap, inadequate study, no adverse effect

Toxicology one-liners are attached.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T011214

Original: Kishiyama & Silva, 12/14/01

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

The one-liners/summaries are arranged by study types (Chronic Toxicity, Rat; Chronic Toxicity, Dog; Chronic Toxicity, Mice: Oncogenicity, Mouse; Reproduction, Rat; Teratology, Rat: Teratology, Rabbit; Gene Mutation; Chromosome; DNA and Miscellaneous) and tolerance/DPN number (149, 50067, 50444, 50792, 50427, 50392).

Note: Mineral oil studies filed under D00149 were further categorized into test article groups with similar characteristics. This further separation is to indicate some test materials were different but generally identified as mineral oil. The inclusion of studies into selected categories (paraffinic, petroleum hydrocarbons, jet fuel, kerosene, solvent, distillates and unclassified) were based on limited information and some may be appropriate for more than one category, due to the involvement of more than one kind of test article in the same study.

CHRONIC TOXICITY, RAT

Petroleum Hydrocarbon (naphthalene based):

149 - 017 117308 "Inhalation Toxicology of Oil Mists (I. Chronic Effects of White Mineral Oil)," (Wagner, WM.D., Wright, P.G., Stokinger, H.E.; U.S. Dept. of Health, Education & Welfare, Public Health Service; Industrial Hygiene Journal, March-April, 1964, pages 158-168). Petroleum base "light" mineral-oil aerosol mist (naphthalene-base saturated hydrocarbons; molecular weight = 350-410; 25-30 carbons) at 5 (current TLV) and 100 mg/m³ used to treat mongrel dogs, Dutch rabbits, Holtzman-Sprague-Dawley rats, Golden-Syrian hamsters and CF #1 and CAF₁/Jax mice (6 hours/day, 5 days/week; 12-26 months) in a full-body inhalation study. All animals were males. NOEL = 5 mg/m³ for all species & strains (At 100 mg/m³, an increase in basic and magnesium-activated phosphatase activities in blood serum and lung of dogs and rats occurred. Histopathology showed a significant increase in pulmonary alveolar and hilar lymph node oil deposition and/or lipid granuloma formation after 12 months of exposure in dogs and rats at 100 mg/m³.) No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 2/6/01).

Paraffinic

(Subchronic)

149 - 023 117136 "A Three Month Oral Toxicity Study of MRD-77-6, MRD-77-7, MRD-77-8, and MRD-77-9 in Rats," (Rinehart, W.E.; Bio/dynamics Inc., Project #: 77-1755; 9/1/77). MRD-77-6, MRD-77-7, MRD-77-8 and MRD-77-9 (paraffinic white oils) were fed in diet to Long-Evans rats (20/sex/dose) at 0, 300 and 1500 ppm for three months. Total leukocytes was increased significantly (148% and 140%) with MRD-77-7 (1500 ppm) and MRD-77-6 (300 ppm); and slightly increased (107 - 132%) with MRD-77-8 and MRD-77-9. NOEL > 1500 ppm (No toxicologically relevant effects from any compound to either sex.) UNACCEPTABLE (Report contains no information on the stability and characterization of test articles, no analysis of dosing material, no animal age or rationale for dose selection [two dose/test article], no GLP or QA sign-off and no MTD). (Kishiyama & Silva, 11/2/00).

Solvent (paraffinic: based on other studies using test articles with the MRD prefix)

(Subchronic)

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 mg/m³. 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: males and females in all dosed groups were affected with increased amounts of alveolar macrophage accumulations in their lungs, which in some cases, were 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).

Deodorized kerosene

(Subchronic)

149 - 016 117305 "Four Week Subchronic Inhalation Toxicity Study in Rats," (Ulrich, C.E.; International Research and Development Corporation, Mattawan, MI; IRDC Study 418-027; 6/28/86. API #81-07, API #81-09, and API #81-10 each at a nominal concentration of 25 mg/m³ were administered via whole body inhalation exposure 6 hours/day, 5 days/week for 4 weeks to 20 Charles River CD[®] rats/sex/group. Treatment related effects were: increased leukocytes (29 & 31%) and lymphocytes (21 & 32%) for API #81-10 treated males and females. An increased incidence in subacute inflammation of the respiratory mucosa occurred with the API #81-09 treatment. UNACCEPTABLE (not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 5/18/01).

Petroleum Hydrocarbon

149 - 017 117306 "Evaluation of 90-Day Inhalation Toxicity of Petroleum and Oil Shale Diesel Fuel Marine (DFM)," (Gaworski, C.L., MacEwen, J.D., Vernot, E.H., Haun, C.C., Leahy, H.F., Hall, A.; Air Force Aerospace Medical Research Laboratory, AAMRL-TR-85-074, NMRI 85-57; 12/85). Petroleum (P-DFM) and Oil Shale Diesel Fuel Marine (SO-DFM) were administered continuously by inhalation at 50 and 300 mg/m³ to Beagle dogs (whole body, 3/sex/dose), CDF (Fischer 344)/Crl/BR rats (150/sex/dose) and female C57BL/6 mice (150/dose) for 90 days. All dogs were terminated (90 days), while only 1/3 rodents were terminated. A post-dosing observation period was extended to 19 months (interim kill; 1/3 rodents) and 24 months (sacrifice remainder). NOEL Dogs: SO-DFM & P-DFM = 50 mg/m³ (BUN increased with SO-DFM at ≥ 50 mg/m³. Absolute liver weights increased with P-DFM at 300 mg/m³. Hepatocytic vacuolization occurred with P-DFM at 300 mg/m³.) NOEL Mice: SO-DFM < 50 mg/m³ & P-DFM = 50 mg/m³ (Survival reduced at ≥ 50 mg/m³ SO-DFM. Increased pulmonary inflammation with SO-DFM and liver inflammation with P-DFM at 300 mg/m³. Hepatocellular degeneration with SO-DFM at ≥ 50 mg/m³. Post-exposure with SO-DFM, showed increased bone marrow hyperplasia at ≥ 50 mg/m³.) NOEL (Rats) for SO-DFM & P-DFM < 50 mg/m³ (Body weight gain was reduced (both sexes ≥ 50 mg/m³) with P-DFM and with SO-DFM (males: 300 mg/m³). Both sexes sacrificed after 90-days dosing (P-DFM) had increased nasal mucosal inflammation (P-DFM 300 mg/m³). Males sacrificed after 90-days (P- or SO-DFM) had increased kidney hyaline degeneration. Renal tubular epithelial necrosis occurred in males at 300 mg/m³ (P- or SO-DFM). Inflammation of renal cortical interstitium was increased in males (300 mg/m³ SO-DFM). Kidney lesions were increased, post-exposure, in males treated for 90 days (both treatments ≥ 50 mg/m³). Kidney adenomas (male: P-DFM, 50 mg/m³ & SO-DFM 300 mg/m³), mammary gland fibroadenomas (males & females: SO-DFM & female: P-DFM, 300 mg/m³), pituitary carcinomas (male: SO-DFM & female: SO-DFM, ≥ 50 mg/m³ & P-DFM, 300 mg/m³), thyroid follicular cell

tumors (female: SO-DMF ≥ 50 mg/m³) and thyroid C-cell tumors (male: P-DFM ≥ 50 mg/m³ & female: 300 mg/m³; female: SO-DFM ≥ 50 mg/m³) were higher than controls). Not acceptable or upgradeable (major deficiencies).. Possible adverse effect indicated. (Kishiyama & Silva, 1/30/01).

Distillate/refined

(Acute)

149 - 015 117302 A Acute Oral Toxicity Study with 7552 Sample 6025-F-51205 (White Oil) in Albino Rats,” Harrison, W.A.; Industrial Bio-Test Laboratories Inc., IBT #: 601-05633; 10/16/74; Note: This study not listed in IBT Tracking System Report). Mineral oil (6025-F-51205, purity not stated) was administered by gavage to Sprague-Dawley rats (5/sex/dose) as a single dose at 5000 mg/kg (undiluted). Treated animals displayed hypoactivity and ruffled fur after one hour and oily fur was observed around the urinary area after 5 hours. After two days, the animals appeared normal. There were no other treatment-related effects reported over 14 days. NOTE: The acute oral LD₅₀ was calculated to be greater than 5000 mg/kg. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 11/9/00).

Refined Petroleum hydrocarbon (paraffinic, naphthanic):

(Subacute)

149 - 015 117301 A90-Day Subacute Oral Toxicity Study with Code 7552, sample 6025-F-51205 (White Oil) in Albino Rats,” (Morrow, L.; Industrial Bio-Test Laboratories Inc., IBT #: 621-05634; 2/6/75; NOTE: This study was not listed in the IBT tracking system.) Mineral oil (6025-F-51205, purity not stated) was fed in diet to Charles River albino rats (15/sex/dose) at 0 and 10000 ppm for 90 days. Reduced liver (11%) and heart (8%) weight were reported as normal variation for a random population of rats. No other treatment related effects reported. UNACCEPTABLE (insufficient information). Not upgradeable. No adverse effect. (Kishiyama & Silva, 11/9/00)

149 – 015 117297, 117298, 117299, 117300 “API Mineral Oil Review,” (API White Oil Workgroup: Hulse, M., Klan, M.J., Noreyko, J.M., Reitman, F.A., Skisak, C.M., Smith, J.H., Tietze, P.G., Vernot, E.H.; Health and Environmental Sciences Department, American Petroleum Institute, 1/92). Record #: 117297 is the API Mineral Oil Review and contains primarily a toxicology profile of mineral oils. Record #'s: 117298 – 117300 are appendices to the main review. “Food Additives: A More Sensitive and Selective Ultraviolet Absorption Criterion for Mineral Oil,” (Haenni, E.O., Frank, J.L., Jr., Howard, J.W., Leibel, R.L.; Division of Food, Food and Drug Administration, Washington, DC; Published in: Journal of the Association of Official Agricultural Chemists, 45(1):59 – 64, 1962) is Appendix 4 (117298). This volume contains issues dealing with the regulation of mineral oils. “Toxicological Overview of Hyperphagocytic Granuloma Associated With Medicinal White Oil and Related Materials,” (Hernandez, L.E.; Shell Oil Company; Health, Safety and Environment – Toxicology; 12/20/89) is Appendix 5 (117299) of the review. This volume contains the results of a dietary study in which rats were fed medicinal white oil in their diets for 90 days. Microgranulomatous changes were found in the liver, spleen and mesenteric lymph nodes. In addition, the report contains a discussion of granulomatous changes and a comparison of effects in different species, including rat, dog, mouse, goat, rabbit, hamster, gerbil, chicken, goat and squirrel monkey. White mineral oil, petrolatum and petroleum wax were among the oils tested. “Liquid Mineral Hydrocarbons in Food: Review of Current Issues, Exxon Corporation’s Toxicological Data and Consideration of Potential Human Health Effects,” (Freeman, J.J., Biles, R.W., Cragin, D.W., McKee, R.H., Nikiforov, A.I., Smith, J.H.; Exxon Biomedical Sciences, Inc., East Millstone, NJ and Exxon Chemical International, Inc., Kraainem, Belgium, 10/5/89; Report #: MR.18DO.89) is Appendix 6 (117300) of the review. It is a technical report containing a toxicology profile of liquid mineral hydrocarbons from petroleum. The report also discussed the potential hazard of these oils as direct or

indirect food additives. No worksheets on any of the above record numbers was made. M. Silva, 7/18/01.

CHRONIC TOXICITY, DOG

Petroleum Hydrocarbon

149 - 017 117308 "Inhalation Toxicology of Oil Mists (I. Chronic Effects of White Mineral Oil)," (Wagner, WM.D., Wright, P.G., Stokinger, H.E.; U.S. Dept. of Health, Education & Welfare, Public Health Service; Industrial Hygiene Journal, March-April, 1964, pages 158-168). Petroleum base "light" mineral-oil aerosol mist (naphthalene-base saturated hydrocarbons; molecular weight = 350-410; 25-30 carbons) at 5 (current TLV) and 100 mg/m³ used to treat mongrel dogs, Dutch rabbits, Holtzman-Sprague-Dawley rats, Golden-Syrian hamsters and CF #1 and CAF₁/Jax mice (6 hours/day, 5 days/week; 12-26 months) in a full-body inhalation study. All animals were males. NOEL = 5 mg/m³ for all species & strains (At 100 mg/m³, an increase in basic and magnesium-activated phosphatase activities in blood serum and lung of dogs and rats occurred. Histopathology showed a significant increase in pulmonary alveolar and hilar lymph node oil deposition and/or lipid granuloma formation after 12 months of exposure in dogs and rats at 100 mg/m³.) No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 2/6/01).

Paraffinic

(Subchronic)

149 - 024 117139 "A Three Month Oral Toxicity Study of MRD-77-6, MRD-77-7, MRD-77-8, and MRD-77-9 in Dogs," (Rinehart, W.E.; Bio/dynamics Inc., Project No. 77-1756; 9/1/77). MRD-77-6, MRD-77-7, MRD-77-8, and MRD-77-9 were fed in diet to Beagle dogs (4/sex/dose) at 0, 300 and 1500 ppm for three months. Increased frequency of soft stools, mucoidal and mucohemorrhagic fecal discharge and emesis was reported. Slight decrease in testes and increase in liver weight for males and reduced ovary weight for females were reported. UNACCEPTABLE (Report contains no information on the stability and characterization of test articles, no analyses of dosing materials and rationale for dose selection; only two doses/test article were used, no tabulated data on physical observations were presented, the actual health of the dogs is unknown during the study and no GLP or QA sign-off was included). Not upgradeable. (Kishiyama & Silva, 11/3/00).

Petroleum Hydrocarbon

149 - 017 117306 "Evaluation of 90-Day Inhalation Toxicity of Petroleum and Oil Shale Diesel Fuel Marine (DFM)," (Gaworski, C.L., MacEwen, J.D., Vernot, E.H., Haun, C.C., Leahy, H.F., Hall, A.; Air Force Aerospace Medical Research Laboratory, AAMRL-TR-85-074, NMRI 85-57; 12/85). Petroleum (P-DFM) and Oil Shale Diesel Fuel Marine (SO-DFM) were administered continuously by inhalation at 50 and 300 mg/m³ to Beagle dogs (whole body, 3/sex/dose), CDF (Fischer 344)/Crl/BR rats (150/sex/dose) and female C57BL/6 mice (150/dose) for 90 days. All dogs were terminated (90 days), while only 1/3 rodents were terminated. A post-dosing observation period was extended to 19 months (interim kill; 1/3 rodents) and 24 months (sacrifice remainder). NOEL Dogs: SO-DFM & P-DFM = 50 mg/m³ (BUN increased with SO-DFM at ≥ 50 mg/m³. Absolute liver weights increased with P-DFM at 300 mg/m³. Hepatocytic vacuolization occurred with P-DFM at 300 mg/m³.) NOEL Mice: SO-DFM < 50 mg/m³ & P-DFM = 50 mg/m³ (Survival reduced at ≥ 50 mg/m³ SO-DFM. Increased pulmonary inflammation with SO-DFM and liver inflammation with P-DFM at 300 mg/m³. Hepatocellular degeneration with SO-DFM at ≥ 50 mg/m³. Post-exposure with SO-DFM, showed increased bone marrow hyperplasia at ≥ 50 mg/m³.) NOEL (Rats) for SO-DFM & P-DFM < 50 mg/m³ (Body weight gain was reduced (both sexes ≥ 50 mg/m³) with P-DFM and with SO-DFM (males: 300 mg/m³). Both sexes sacrificed after 90-days dosing (P-DFM) had increased nasal mucosal inflammation (P-DFM 300 mg/m³). Males sacrificed after 90-days (P- or SO-DFM) had increased kidney hyaline degeneration. Renal tubular epithelial necrosis occurred in males at 300 mg/m³ (P- or SO-DFM). Inflammation of renal cortical interstitium was increased in males (300 mg/m³ SO-DFM). Kidney lesions were increased, post-exposure, in males treated for 90 days (both treatments ≥ 50 mg/m³). Kidney adenomas (male: P-DFM, 50 mg/m³ & SO-DFM 300 mg/m³), mammary gland fibroadenomas (males & females: SO-DFM & female: P-DFM, 300 mg/m³), pituitary

carcinomas (male: SO-DFM & female: SO-DFM, ≥ 50 mg/m³ & P-DFM, 300 mg/m³), thyroid follicular cell tumors (female: SO-DMF ≥ 50 mg/m³) and thyroid C-cell tumors (male: P-DFM ≥ 50 mg/m³ & female: 300 mg/m³; female: SO-DFM ≥ 50 mg/m³) were higher than controls). Not acceptable or upgradeable (major deficiencies).. Possible adverse effect indicated. (Kishiyama & Silva, 1/30/01).

CHRONIC TOXICITY, MICE

Petroleum Hydrocarbon

(Subchronic)

See 149 - 017 117306 (above, Chronic dog).

ONCOGENICITY, RAT

Paraffinic

149 - 017 117309 “Experiments to Create Cancer with Liquid Paraffin, Yellow Petrolatum and Wool Fat,” (Schmähl, D., Reiter, A.; Published in: *Arz. Forsch.*, 3:403-406;1953). Liquid paraffin was injected in 2.5 ml once subcutaneously and i.p. in a total dose of 9 ml/rat, divided over 15 individual injections in 40 weeks to BDI, BDIII and W rats (30 rats; strain not specified for each test). Another group was fed liquid paraffin (2% of diet) for 500 days (30 rats). Yellow vaseline was administered as 3 ml i.p. (8 rats) or 1 ml subcutaneously (26 rats). Wool fat was administered 1 ml i.p. + 1ml subcutaneously at the same time (18 rats), once only. Male rats, after i.p. liquid paraffin injection, developed 3 malignant spindle-cell sarcomas (2 testicular & 1 abdominal) and 1 malignant myo-sarcoma. All rats had extensive abdominal growths and warts after i.p. liquid paraffin-injection. There were massive adhesions and spleen, liver or kidneys were surrounded by stiff, fatty membranes, accompanied by a yellow trans-sudation was in the abdomen. Paraffin inclusions occurred in liver and lymph glands. The report considered that liquid paraffin could not be considered “inactive.” Vaseline induced 1 osteo-sarcoma near the i.p. injection site at day 658 (related to treatment) and a 2nd rat developed solid, whitish knots (spindle-cell granulation). Vaseline was in the subcutis as spherical cysts or in the abdominal cavity and was non-irritating. Wool fat induced heavy ascites a few hours after injection (5 rats died). The remaining rats had “heavy overgrowths” in the abdominal cavity, with chronic local irritating effects. Possible adverse effect: tumors from liquid paraffin and vaseline. These data are supplemental. (Kishiyama & Silva, 2/6/01).

ONCOGENICITY, MOUSE

Jet Fuel:

149 – 017 117310 “Tumorigenic evaluation of Jet Fuels JP-TS and JP-7, Following Vapor Inhalation Exposure,” (Kinhead, E.R., Gaworski, C.L., Flemming, C.D., Harris, R., Witt, W., Davis, H., Schmidt, R.; Maintech Environmental Technology, Inc., Dayton, OH, University of California, Irvine, USAF School of Aerospace Medicine, Brooks Air Force Base, TX; Supported by DOD Contract #: F33615-90-C-0532; Published in *The Toxicologist*, #1390, 12(1):355, 1992). JP-TS and JP-7 are middle-distillate jet fuels that were vaporized to produce a chamber atmosphere similar to those encountered in field conditions. Fischer 344 rats and C57BL/6 mice were exposed for 1 year to 200 and 1000 mg JP-TS/m³ or 150 and 750 mg JP-1/m³ for 6 hours/day (5 days/week; 6/sex/dose/species). Histopathology was renal lesions in male rats (consistent with other light hydrocarbon inhalation studies). Renal neoplasms were increased in male rats during a 1 year observation period following the 1 year exposure. No treatment-related degenerative changes or increased incidence in tumors were observed in mice. Possible adverse effect indicated in male rats. Summary only; not a FIFRA Guideline study (no worksheet). M. Silva, 7/18/01.

Unclassified

149 – 010 115552 “Dermal Oncogenicity Studies of MH-982, MH-983, MH-1147, MH-1148, MH-1173, MH-1174, MH-1175, MH-1255 and MH-1256 in Male C3H/HeJ Mice,” (DePass, L.R., Homan, E.R., McLain, D.E.; Joint Operation: Mellon Institute/Union Carbide Corporation (Bushy Run Center); Report #: 46-509; 10/29/84). MH-983, MH-1147, MH-1148, MH-1173, MH-1174, MH-1175, MH-1255 and MH-1256 were applied (25 ul each, neat) to clipped backs of C3H/HeJ male mice (50/dose). MH-982 was the positive control substance and was applied as a 5% w/w dilution in MH-983. Applications were 3 times/week (except holidays) beginning at age 49 to 63 days, until death or until all survivors had developed tumors. **Possible adverse effect indicated:** There was an increased incidence in skin tumors with MH-982 (positive control), MH-1174, MH-1175 and MH-1256 treatments. Mortality rate increased with MH-982, MH 1174, MH-1175 and MH-1256. All but MH-983 and MH1174 were also skin irritants. Not acceptable. These data are supplemental. Kishiyama & Silva, 5/29/01.

Distillates(Paraffinic and naphthenic oil base)

149 - 013 116794 “Lifetime Dermal Carcinogenesis Bioassay of Selected Petroleum Streams in CD Mice,” (Cerven, D.R.; MB Research Laboratories, Spinnerston, PA; Project #: MB 85-7684; 1/15/88). R&M #85-01 to #85-10 (petroleum refining streams) were applied dermally to CR CD1 mice (25/sex/compound; control = R&M #85-12 = USP white oil), 3 times/week for 2 years. Positive control (Benzo(a)pyrene, 0.15% w/v in toluene) had 100% mortality prior to 12 months of treatment. R&M #85-01 and 02 had 90% mortality prior to 18 months. R&M 85 - 01, 02, 03, 04, 05, 08, 09 and 10 significantly increased ($p < 0.05$) the incidence of non-neoplastic lesions compared to the negative control (Group 12) as follows: Groups 1, 2, 3, 4, 5, 8, 9 & 10 had hyperkeratosis and acanthosis of the epidermis (at the test site only). Also, necrosis and/or ulceration of the epidermis and alopecia accompanied the changes in groups 1, 2, 3 & 5. The dermis of Groups 1, 2, 3, 4, 5, 8, 9 & 10 showed increased fibrosis of the interstitium. Group 4 dermal fibrosis was accompanied by an increase in chronic lymphocytic inflammation of the interstitium. Hair follicles (test site only) in mice from Groups 1, 2, 5, 8 & 9 were affected with alopecia and acanthosis of the epithelium. Sebaceous glands of the skin (test site) of mice in Groups 1, 2, 5, 7, 8 & 9 had ectasis of the excretory ducts. **Possible adverse effect indicated.** UNACCEPTABLE (major variance and insufficient information) and not upgradeable. These data are supplemental. (Kishiyama & Silva, 10/23/00).

50427 - 009 115416: This is the same study as 149 - 013 116794, but with less information.

Distillates (kerosene, naphthenic, aromatics, paraffinic)

149 - 018 117312 “Twenty-Four Month Dermal Carcinogenesis/Chronic Toxicity Screening Bioassay of Refinery Streams in C₃H/HeJ Mice,” (Dennis, M.W.; Primate Research Institute, PRI Study #: AP-190r; October 1989). Eleven petroleum refinery streams API #'s 84-01, #84-02, 83-06, 83-07, 83-08, 83-09, 83-11, 83-12, 83-16, 83-18, and #83-19) were applied dermally (2x/week) to C₃H/HeJ male mice (50/group) at 50 µl (undiluted), for 24 months. Dermatotoxic effects were observed for all test materials. **Carcinogenic effect was ranked strong (API #84-01, API #83-07, API #83-16, and benzo(a)pyrene), moderate (API #83-08 and API #83-09) and weak (API #84-02, API #83-11, API #83-12 and API #83-18).** API #83-06, 83-19 and toluene were comparable to the control. UNACCEPTABLE. Major deficiencies. Not upgradeable. (Kishiyama & Silva, 10/31/00).

Distillate

149 – 020 117316 “Dermal Carcinogenic Activity of Petroleum-Derived Middle Distillate Fuels,” (Biles, R.W., McKee, R.H., Lewis, S.C., Scala, R.A., DePass, L.R.; Bushy Run Research Center; Published in: *Toxicology*, 53:301 – 314 (1988)). The following compounds, origins and boiling ranges: virgin heating oil blending base (US 287-585 °F), lightly refined paraffinic oil (US, 490-610 °F), commercial #2 heating oil from different sources (Middle East/Carribbean Pool, 383-705 °F; US, 331-678 °F; Middle East , 419-676 °F; Western Canadian, 322-644 °F; Western Canadian/Venezuelan,

313-666 °F, Western Canadian/Tar Sands, 323-667 °F), Virgin heating oil blending base (sample 1) + catalytically cracked middle distillate (US 287-700 °F) and light catalytic cycle oil (US 640 °F) were applied in 25 µl aliquots to the clipped dorsal surface of male C3H/HeJ mice (40-50/group, 5/cage) 3 times/week for the lifetime of the mice or until all animals in the group developed carcinomas. Highly refined mineral oil was the negative control. The study was conducted over a 4-year period. Animals were examined daily for dermal tumors and all mice received full necropsy at termination or death. The report states that carcinogenic potential of petroleum-derived materials is related to PAH content and that liquids that boil below PAH distillation range (700 °F) “would not be carcinogenic”. Earlier studies supporting this conclusion were of short duration but recent studies with repeated application of petroleum-derived materials (middle distillate fuels 350-700 °F) produced tumors in mouse skin. The current study tested tumorigenic potential of a series of middle distillates, which varied with respect to boiling range, composition and source of blending stocks. Results with most samples showed low tumor yields (significantly increased over control), with long median latencies (by Weibull distribution function). Parameters examined did not affect tumorigenicity, as there were no apparent differences among treatment groups. Tumorigenic activity was not associated with PAH content and therefore was not PAH-dependent. There were also non-neoplastic dermal changes (hyperplasia) which may indicated preneoplasia. Possible adverse effect indicated. These data are supplemental. M. Silva, 12/6/00.

Distillate

149 - 020 117317 “Evaluation of Dermal Carcinogenic Potential of Tar Sands Bitumen-Derived Liquids,” (McKee, R.H., Stubblefield, W.A., Lewis, S.C., Scala, R.A., Simon, G.S., DePass, L.R.; Published in: Fundamental and Applied Toxicology, 7:228-235 (1986), Exxon Corporation, East Millstone, NJ). Tar sands (80% sand, 10% water, 10% hydrocarbons), bitumen (hydrocarbons derived from tar sands), untreated naphtha (boiling range: 50-250 °C), crude gas oil (> 250 °C) and 3 thermally and catalytically cracked liquids derived from crude gas oil (boiling range: light, 149-316°C, heavy > 316 °C, blended 2:1 heavy/light gas oils >316 °C) were applied dermally (shaved backs) to C₃H/HeJ male mice (50/group, 5/cage) 3 times/week in 25 µl aliquots throughout the life-time. Negative control was highly refined white oil. Results showed the tar sands (0 tumors), bitumen (1 malignant & 1 benign tumor) and untreated naphtha (1 malignant tumor) produced few total epidermal tumors. Crude oil (11M, 2B), light (11M, 4B), heavy (46M, 2B) and gas blend (47M) produced numerous tumors. **Reduced survival correlated with rapid development of tumors (squamous cell carcinomas) in mice treated with heavy and blended gas oils. Carcinogenic potential was moderate for light gas and crude oil.** Supplemental study. (Kishiyama & Silva, 12/7/00).

Petroleum Hydrocarbon (unrefined and hydrotreated lubricating oils)

149 - 020 117318 “The Dermal Carcinogenic Potential of Unrefined and Hydrotreated Lubricating Oils,” (McKee, R.H., Daughtrey, W.C., Freeman, J.J., Federici, T.M., Phillips, R.D., Plutnick, R.T.; Journal of Applied Toxicology, 9(4):265-270 (1989), Exxon Biomedical Sciences, Inc., East Millstone, NJ). Several samples of naphthenic distillates (unrefined light, 549-810 °F, viscosity at 40°C= 16.3; hydrotreated light, 546-819 °F, viscosity at 40°C = 16; hydrotreated light, 533-830 °F, viscosity at 40°C = 15.7; unrefined heavy, 649-909 °F, viscosity at 40°C = 62.2; hydrotreated heavy, 607-892 °F, viscosity at 40°C = 45.9; hydrotreated heavy 608-905 °F, viscosity at 40°C = 45.4; unrefined heavy 794-1058, viscosity at 40°C = 484.7; hydrotreated heavy, 743-1047 °F, viscosity at 40°C. = 272.1, hydrotreated heavy, 732-1050 °F, viscosity at 40°C. = 255.4) were applied dermally to male C3H mice (40/group) twice weekly at 37.5 µl aliquots undiluted for up to 24 months to test potential for dermal carcinogenicity. Hydrotreated oils (reduced in polycyclic aromatic hydrocarbons) of all viscosities did not induce tumors or affect survival. Possible adverse effect indicated. **Epidermal tumors were induced with all unrefined distillates (heavy & light) of all specific activities.** These data are supplemental. (Kishiyama & Silva, 12/7/00).

Solvent (paraffinic: based on other studies using test articles with MRD prefix)

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 µl 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).

Paraffinic

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 µl 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).

Paraffinic (also naphthenic)

149 - 017 117311 "The Carcinogenicity of New and Used Lubricants," (Agee, J., Barkley, W., LaDow, K., Rapien, I., Spalding, S., Stemmer, K.L., Suskind, R.R., Trosset, R.P.; Kettering Laboratory, University of Cincinnati, Cincinnati, OH; API Project #: PS-36; 7/83). Composite motor oil, 5 paraffinic base stocks (viscosities = 64, 133, 331, 485 & 990 SUS) and 2 naphthenic base stocks (viscosities of 83 & 2008 SUS) each at 50 mg doses were applied dermally to interscapular skin of male C3H/HeJ mice (50/group) twice/week for 104 weeks. The number of animals with moderate epilation, together with crusty skin, was increased when treated with formulations containing toluene. Moderate epilation of the skin was observed on 4, 22, 24, 32, 36, 40, and 94% of animals treated with Used Composite Motor Oil, Paraffinic Oil 64 SUS, Paraffinic Oil 485 SUS, Paraffinic Oil 331 SUS, Paraffinic Oil 990 SUS, Paraffinic Oil 133 SUS and Napthenic Oil 83 SUS, respectively. Skin irritation was not observed on animals in the control (no treatment), Napthenic Oil 2008 SUS and New Composite Motor Oil groups. **The number of mice with tumors and skin irritation increased and the latent period for tumors decreased with used composite motor oil treatment.** Not acceptable or upgradeable (major deficiencies). These data are supplemental. (Kishiyama & Silva, 2/7/01).

Distillates

149 - 018 117312 "Twenty-Four Month Dermal Carcinogenesis/Chronic Toxicity Screening Bioassay of Refinery Streams in C₃H/HeJ Mice," (Dennis, M.W.; Primate Research Institute, PRI Study #: AP-190r; October 1989). Eleven petroleum refinery streams API #'s 84-01, #84-02, 83-06, 83-07, 83-08, 83-09, 83-11, 83-12, 83-16, 83-18, and #83-19) were applied dermally (2x/week) to C₃H/HeJ male mice (50/group) at 50 µl (undiluted), for 24 months. Dermatotoxic effects were observed for all test materials. **Carcinogenic effect was ranked strong (API #84-01, API #83-07, API #83-16, and benzo(a)pyrene), moderate (API #83-08 and API #83-09) and weak (API #84-02, API #83-11,**

API #83-12 and API #83-18). API #83-06, 83-19 and toluene were comparable to the control. UNACCEPTABLE. Major deficiencies. Not upgradeable. (Kishiyama & Silva, 10/31/00).

Kerosene

149 - 019 117313 “Lifetime Dermal Carcinogenesis/Chronic Toxicity Screening Bioassay of Refinery Streams in C₃H/HeJ Mice,” - Final Report: Lifetime Carcinogenicity Evaluation (weeks 1-142). Dennis, M.W.; Primate Research Institute, PRI Study No: AP-135r; 1/30/89. Twelve petroleum refinery streams (API #81-03, API #81-07 to 10, API #81-13 to 15, API #81-24, API #83-01 to 03) were evaluated for carcinogenic activity. Compounds were administered dermally, undiluted (50 µl), twice/week for the lifetime of fifty C₃H/HeJ male mice/group. Dermatotoxic effects were reported for all test materials. **Possible adverse effect: Refinery streams were ranked as “strong”: API #81-15; “intermediate”: API #81-07, API #81-09, API #81-10, API #83-02; API #83-03 or “weak”: API #81-03, API #83-01 in carcinogenic effect.** Not acceptable and not upgradeable. There were major deficiencies and the study was not performed according to FIFRA Guidelines. (Kishiyama & Silva, 11/7/00).

REPRODUCTION, RAT

Solvent

(Subchronic)

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).

TERATOLOGY, RAT

Jet Fuel

149 - 020 117320 “Inhalation/Teratology Study in Rats: Jet Fuel A (Final Report),” (Beliles, R.P.; Litton Bionetics, Inc., Kensington, MD; LBI Project #: 21035-01; 5/79). Jet Fuel A was administered to CRL:COBS CD (SD) BR mated female rats (15-20/dose) in airborne concentrations of 0, 102.5 and 394.7 ppm for 6 hours/day during gestation days 6 through 15. Eye irritation or infection occurred for 10%, 35% and 100% of animals in the control, low and high dose groups, respectively. Maternal NOEL = 102.5 ppm Developmental NOEL > 400 ppm (There were no treatment-related effects at any dose.) UNACCEPTABLE (no dose selection rationale, too few dose levels, no individual maternal data, numerous deficiencies). Not upgradeable. No adverse effect indicated. (Kishiyama & Silva, 12/11/00).

Kerosene

149 - 020 117322 "A Teratology Study in Rats (Kerosene)," (Beliles, R.P.; Litton Bionetics, Inc., LBI Project No. 20698-10; 3/79). Kerosene was administered in air (as a vapor) to mated CRL:COBS CD (SD) BR rats (20/dose) at 0, 106.4 and 364.0 ppm (6 hours/day) during gestation days (gd) 6 through 15. Maternal NOEL >364.0 ppm. Developmental NOEL > 364.0 ppm. There were no treatment-related effects (maternal or fetal) at any dose. This study is not acceptable and not upgradeable, due to lack of an MTD, as well as numerous deficiencies (no dose selection rationale reported; should be 3 test levels, no individual maternal data). No adverse effects indicated, however there was no MTD. These data are supplemental. (Kishiyama & Silva, 12/27/00).

TERATOLOGY, RABBIT

No study submitted

GENE MUTATION**Paraffinic**

149 - 014 116795 "Mutagenicity Evaluation of Extract of 925981-1 in the Microbial Reverse Mutation Assay by Preincubation Method," (Jagannath, D.R.; Hazleton Biotechnologies Company, Kensington, MD; Project #: HBC 20988; 5/86). A DMSO extract of 925981-1 was evaluated for mutagenicity at 0 (DMSO), 7, 15, 20, 30, 40, 50 and 100 µl/plate with Aroclor-induced hamster liver metabolic activation (S9 Mix), using *Salmonella typhimurium* strain TA 98. Bacteria were incubated with the test material for 20 minutes before adding agar and plating in triplicate. Tested only with activation. No increase in the number of revertants occurred with 925981-1 treatments. UNACCEPTABLE (Not a FIFRA Guideline study). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 5/25/01).

149 - 014 116797 "Mutagenicity Test on an Extract of 917700-5 in the Ames *Salmonella*/Microsome Reverse Mutation Assay by the Preincubation Method," (Jagannath, D.R.; Hazleton Laboratories America, Inc., Kensington, MD; Project #: HLA 9826-0-401E; 5/8/87). A DMSO extract of 917700-5 was evaluated for mutagenicity at 7, 15, 20, 30, 40, 50, and 100 µl/plate with Aroclor 1254-induced male hamster liver metabolic activation (S9 Mix), using *Salmonella typhimurium* strain TA 98. Bacteria were incubated with the test material for 20 minutes before adding agar and plating in triplicate. Tested only with activation. There was no increase in the number of revertants with the extract of 917700-5 treatments. UNACCEPTABLE (not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 5/25/01).

Solvent

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 µg/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).

Solvent

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 µg/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).

Distillate

149 - 020 117325 “Estimation of the Dermal Carcinogenicity Activity of Petroleum Fractions Using A Modified Ames Assay,” (Blackburn, G.R., Dietch, R.A., Schreiner, C.A., Mehlman, M.A., Mackerer C.R.; *Cell Biology and Toxicology*, 1(1): 67-80, 1984). The ***Salmonella* mutagenesis assay** was modified to improve sensitivity in determining mutagenic activity of 13 petroleum-derived refined distillates (corn oil = control) with TA98. The oils have similar densities, so dosing was based on extract volume (added directly to pre-incubation tubes) not weight (positive controls: Benzo(a)pyrene, 5 µg/plate & 2-aminoanthracene, 2 µg/plate). Aroclor-induced rat and hamster liver S9 activities were compared (no S9, 1x & 8x rat S9, 1x, 8x & 8x + 2x NADP hamster S9) for species variation or activity (tested with chemically neutralized hydrotreated heavy naphthenic distillate, 10 µl/plate). Results showed DMSO-extracted oils produced solutions that more easily interacted with strain TA98. Increases in S-9 up to 8x increased assay sensitivity, due to increased activating enzyme levels. The 13 oils were ranked for mutagenic activity (Table 6). Data from a previously performed **dermal carcinogenicity study**, using C3H-HeJ male mice (50/dose, 2x/week) and the same oil samples used in the mutagenicity study were examined to compare dermal carcinogenicity rankings with mutagenicity for each test compound. All compounds had been used for dermal treatment at 25 or 50 mg undiluted (except mix of heavy catalytic cracked distillate & catalytic cracked clarified oil—diluted 50% into toluene to ameliorate toxicity). Control groups were 50 mg of toluene (solvent) or 50 mg of 0.05% B(a)P in toluene (positive). Dosing was for 80 weeks, or until a papilloma > 1 mm³ occurred. Carcinogenicity results were ranked (Table 2). Relative mutagenicity and dermal carcinogenicity potency rankings of the test compounds correlated (r = 0.97). Not acceptable and not upgradeable. These data are supplemental. Possible adverse effects indicated. (Kishiyama & Silva, 1/25/01).

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).

Jet Fuel A (also shale oil)

149 - 020 117327 “Mutagenicity Evaluation of Six Petroleum Substances in an *In Vivo/In Vitro* Urine Assay,” (Jagannath, D.R.; Litton Bionetics, LBI Project #: 20988; 11/ 82). Urine was collected from

male Sprague-Dawley rats, previously gavaged with Mineral Oil U.S.P., Jet Fuel A, Shale Oil RO-1, API-PS-8-76D5 or API-PS-8-76C5 at 5 ml/kg or API-PS-8-76C6 at 2.5 g/kg. The urine concentrates in DMSO were added at 25, 50, 100, 150, 200 and 300 µl/plate, then evaluated for mutagenic potential using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537. **Shale Oil RO-1 treatment was associated with an increase in the number of TA98 revertant colonies.** UNACCEPTABLE (major deficiencies). Not upgradeable. These data are supplemental. (Kishiyama & Silva, 1/24/01).

Paraffinic

149-020 117328A “*In Vivo and In Vitro* Mutagenicity Studies Paraffinic Oil 78-9 70 SUS/100°F,” (Hoberman, A.M.; Hazleton, Laboratories Inc., Project Numbers: 596-111, 596-112 & 596-113; 6/19/82). 70 Second Paraffinic Oil (AP #78-9) at concentrations of 40000, 45000, 80000, 160000 and 240000 µg/plate (+/- S9) was assessed for mutagenicity by use of *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 by plate incorporation and 20-minute preincubation assays with triplicate plates per concentration in a single trial. No evidence of mutagenicity with 78-9-70 was observed under study conditions. However, test article insolubility and inability to demonstrate toxicity hindered a full evaluation for mutagenic potential using this system. UNACCEPTABLE. These data are supplemental. (Kishiyama & Silva, 1/22/01).

149 - 020 117328B “*In Vivo and In Vitro* Mutagenicity Studies Paraffinic Oil 78-9 70 SUS/100°F”; Part B: Mouse Lymphoma Forward Mutational Assay,” (Hoberman, A.M., Hazleton Laboratories Inc., Project #'s: 596-111, 596-112 & 596-113; 6/19/82). 70 Second Paraffinic Oil (78-9 70) at concentrations ranging from 8,670 to 121, 380 µg/ml (+/- S9 Mix) was used on L5178Y mouse lymphoma cells. **Some 78-9-70 (+S9 Mix) had two-fold increases (non-dose related) in the frequency of mutation.** The results are equivocal; however, because the culture media was saturated with 78-9 70 at all doses. This makes the observed increases (without dose-response) uninterpretable. Not acceptable and not upgradeable (inadequate dose selections, plus missing information) These data are supplemental. (Kishiyama & Silva, 1/24/01).

149 - 021 117329 “Polynuclear Aromatic Analyses and Modified Ames Test on Base Lube Stocks,” (Deitch, R., Mobil Oil Corporation Toxicology Division, Study #'s: 61312, 61322, 61332, 61342, and 61352; 9/89). Second Paraffinic Base Stocks 800, 550, 350, 150 and 70 were tested with *Salmonella typhimurium* strain TA98 at 50, 40, 30, 20, 10, 7 and 5 µl with metabolic activation from hamster liver, using 8x the usual concentration. No evidence of mutagenicity reported. UNACCEPTABLE (no rationale for dose selection, statistical analyses, analysis of dosing material, GLP and QA sign-off, treatments without metabolic activation; only one *Salmonella typhimurium* strain and some data not legible). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 5/2/01).

Distillate, refined

149 - 021 117330 “Predicting Carcinogenicity of Petroleum Distillation Fractions Using A Modified *Salmonella* Mutagenicity Assay,” (Blackburn, G.R., Deitch, R.A., Schriener, C.A., Mackerer, C.R.; Published in: Cell Biology and Toxicology, 2(1):63-84, 1986). The Ames *Salmonella*/microsomal activation mutagenesis assay was modified (using TA98) to improve the sensitivity of testing complex mixtures derived from refining and processing of petroleum. The oil samples (distillation point range: 120-1070°F; 22 different fractions tested) were dissolved in Cyclohexane and extracted with DMSO to produce an aqueous solution that readily interacts with the tester bacteria. S-9 from hamsters, along with NADP (4 - 8 mM) were used for the S-9 Mix with a 20 minute preincubation step before plating. The results (according to the authors) were similar to those produced in previous animal bioassays. Therefore, this modified assay method is useful for detecting potential carcinogenic activity of refinery

streams and blends containing components boiling over 500°F. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 5/2/01).

Jet Fuel

**** 149 - 022 117335A** “*In Vitro* and *In Vivo* Mutagenicity Studies Jet Fuel A,” (Kapp, R.W. Jr.; Hazleton Laboratories America, Inc., Vienna, VA; Project #: 596-106; 8/13/79). Jet Fuel A (100% pure) was used on L5178Y mouse lymphoma cells at concentrations of 0, 100, 200, 400, 800, 1200, 1600, 2000 and 24000 µg/ml without S9 and at 0, 25, 50, 75, 100, 125, 150, 175 and 200 µg/ml with S9 (3 plates/dose) in a 4 hour exposure, followed by 2 days of cell expression. Single trial. **Mutation frequency was increased (2.3 to 5.4x) with Jet Fuel A at 100, 125, 150 and 175 µg/ml with metabolic activation (+S9).** ACCEPTABLE. (Kishiyama & Silva, 4/11/01).

** 149 - 022 117335B “*In Vitro* and *In Vivo* Mutagenicity Studies Jet Fuel A,” (Kapp, R.W. Jr.; Hazleton Laboratories America, Inc., Vienna, VA; Project #: 596-104; 8/13/79). Jet Fuel A (100% pure) was used with *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 in a plate incorporation mutagenicity assay at 0, 244.6, 733.7, 2201.2, 6603.7, 19811 and 39622 µg/plate (+S9) and at 0, 252.9, 758.7, 2276, 6828, 20484 and 40968 µg/plate (no S9). A repeat trial was performed at 0, 249.6, 748.7, 2246.1, 6738.3 and 20215 µg/plate (no S9). Jet Fuel A doses of approximately 20,000 and 40,000 µg/plate were not toxic to *S. typhimurium* but exceeded the limits of solubility. The number of revertants did not significantly increase with Jet Fuel A either with or without metabolic activation, when compared with negative controls. ACCEPTABLE. No adverse effect. (Kishiyama & Silva, 4/11/01).

Kerosene

149-022 117338A “Mutagenicity Evaluation of Hydrodesulfurized Kerosene (API #81-07) [in the Mouse Lymphoma Forward Mutation],” (Cifone, M.A.; Litton Bionetics, Inc., Kensington, MD; Project PS-4-LBI (503-1); API Medical Research Publication: 32-30240; 12/4/84). API# 81-07 technical (100% pure) at 0, 6.25, 12.5, 25.0 and 37.5 nl (no S9) and at 0, 3.91, 7.81, 15.6, 31.3 and 62.5 nl/ml (+ S9) was evaluated for mutagenicity using mouse lymphoma cells in a single trial, with single or duplicate culture. There were no treatment-related effects either with or without S9 at any dose. This study is not acceptable and is not upgradeable (single trial). The data are supplemental. (Kishiyama & Silva, 4/24/01).

149-022 117339A “Mutagenicity Evaluation of Kerosene,” (Brusick, D.J.; Litton Bionetics, Inc., LBI Project #: 2697; 3/77). Kerosene was tested at 0, 0.001-5.0 µl/plate and 0.625% - 5% (rat liver in suspension assay) using *Salmonella typhimurium* strains (TA1535, TA1537, TA1538, TA98, TA100) and *Saccharomyces cerevisiae* (D4) by plate overlay and suspension methods. Mouse lymphoma cells were exposed to 0.008 - 0.130 µl/ml and 0.004 - 0.065 µl/ml (+S9, mouse liver) to evaluate mutagenicity. No mutagenic activity was observed with kerosene in the three tests. Not acceptable and not upgradeable. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 4/25/01).

Kerosene, Hydrodesulfurized

149-022 117339B “Mutagenicity Evaluation of Kerosene” (Brusick, D.J.; Litton Bionetics, Inc., Kensington, MD; LBI Project No. 2697; 3/77). Kerosene administered *via* a single I.P. injection at 0, 0.04, 0.13 and 0.40 ml/rat (males) in an acute study and once daily for 5 days at 0, 0.02, 0.06 and 0.18 ml/rat (male) in a subchronic study. Sacrifice was scheduled for 5 males/group at 6, 24 and 48 hours (acute study) and at 6 hours after the final injection (subchronic study). Structural chromosome aberrations did not increase significantly relative to the control (acetone) for all treatments (including the positive control, which was nonfunctional). UNACCEPTABLE. Not upgradeable (Fifty suitable

metaphases were not located for many of the animals). There were insufficient data to determine a possible adverse effect. These data are supplemental. (Kishiyama & Silva, 4/26/01).

Kerosene

149 - 022 117340 “L5178Y TK+/- Mouse Lymphoma Mutagenesis Assay of API 83-09,” (Rogers-Back, A.; Microbiological Associates, Inc., Study No. T2460.701; 10/10/85). API 83-09 at 0.01 to 0.21 µl/ml (no S9) and at 0.0067 to 0.21 µl/ml (+S9 [rat liver]) was evaluated for mutagenicity (1-3 replicates/dose) using mouse lymphoma cells (L5178Y TK+/-). **Mutation frequency was significantly increased as follows:** No S9 = 2 - 13 times (0.056 & 0.042 µl/ml), 3 - 8 times (0.021 - 0.067 µl/ml) and 2 times (0.032 µl/ml) in Tests #1, 2 and 4 respectively; +S9 = 3.5 times (0.21 µl/ml) in Test #2. UNACCEPTABLE (no individual data, copy of report is not of good quality). (Kishiyama & Silva, 4/27/01).

CHROMOSOME EFFECTS

Solvent

**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 AMRD-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).

Solvents (also thinners, kerosene)

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).

Paraffinic

149 - 020 117328C “*In Vivo and In Vitro* Mutagenicity Studies Paraffinic Oil 78-9 70 SUS/100°F,” (Hoberman, A.M., Hazleton Laboratories America, Inc.; Project #'s: 596-111, 596-112 & 596-113; 6/19/82). 70 Second Paraffinic Oil (AP #78-9-70) was administered for 5 consecutive days to Sprague-Dawley rats (5/sex/dose) at 0 (corn oil), 500, 1000 and 2000 mg/kg, using bone marrow cells (femurs) to evaluate potential for induction of chromosomal aberrations. Animals were sacrificed on the day following the final dose. Fifty metaphases per animal were scored. No treatment related effects were observed. This study is not currently acceptable, but is possibly upgradeable upon submission of a QA statement, page 37, rationale for dose selection and analysis of dosing material. No adverse effects. (Kishiyama & Silva, 1/24/01)

Petroleum Hydrocarbon

149 – 020 117324 “The Genotoxic and Carcinogenic Potential of Engine Oils and Highly Refined Lubricating Oils,” (McKee, S.C., Przygoda, R.T.; Exxon Biomedical Sciences, Inc., East Millstone, NJ). Three *in vitro* assays were compared (*Salmonella* and the mouse lymphoma, Syrian hamster embryo (SHE) morphologic transformation assays) to the dermal carcinogenicity of a series of petroleum-derived materials including engine oils and highly refined lubricating oils. One sample of the unused gasoline engine oil was not active in an epidermal carcinogenesis bioassay. This material was also not mutagenic to *Salmonella* and did not transform SHE cells. Primary components of engine oils are highly refined lubricating oil base stocks. The highly purified fractions tested were not dermal carcinogens, nor were they mutagenic or transforming. Conversely, other materials, including unrefined vacuum distillates and solvent extracts of these distillates were both carcinogenic and genotoxic. Thus, results in all *in vitro* and *in vivo* assays correlated. These data are supplemental (no worksheet) and was an abstract only (no data were presented). M. Silva, 7/17/01.

Kerosene, straight run

**149 - 021 117333 “The Acute *In Vivo* Cytogenetics Assay in Male and Female Rats of API Sample 83-09,” (Putman, D.L.; Microbiological Associates, Inc., Bethesda, MD; Testing Facility Number: MA Study No. T2460.105001; 5/13/85). API-83-09 was administered to Sprague-Dawley rats (5/sex/dose/time point) as a single IP injection at 0.3, 1.0 and 3.0 gm/kg. Triethylenemelamine was the positive control at 24 hours and was functional. Bone marrow cells, arrested in metaphase, were collected at 6, 24, and 48 hours after treatment. API 83-09 treatments did not significantly increase the number of cells with aberrations or the number of aberrations per cell in this study. ACCEPTABLE No adverse effect. (Kishiyama & Silva, 5/4/01).

Jet Fuel

** 149 - 022 117335B “*In Vitro and In Vivo* Mutagenicity Studies Jet Fuel A,” (Kapp, R.W. Jr.; Hazleton Laboratories America, Inc., Vienna, VA; Project #: 596-104; 8/13/79). Jet Fuel A (100% pure) was used with *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 in a plate incorporation mutagenicity assay at 0, 244.6, 733.7, 2201.2, 6603.7, 19811 and 39622 µg/plate (+S9) and at 0, 252.9, 758.7, 2276, 6828, 20484 and 40968 µg/plate (no S9). A repeat trial was performed at 0, 249.6, 748.7, 2246.1, 6738.3 and 20215 µg/plate (no S9). Jet Fuel A doses of approximately 20,000 and 40,000 µg/plate were not toxic to *S. typhimurium* but exceeded the limits of solubility. The number of revertants did not significantly increase with Jet Fuel A either with or without metabolic activation, when compared with negative controls. ACCEPTABLE. No adverse effect. (Kishiyama & Silva, 4/11/01).

Kerosene , treater and deoderized (also distillates and jet fuel).

**149 - 022 117337 “Sister Chromatid Exchange Assay in Chinese Hamster Ovary (CHO) Cell with API 81-07 Hydrodesulfurized Kerosene,” (Putman, D.L.; Microbiological Associates, Inc.; Laboratory

Study #: T5337.334006; 10/88). API -81-07 (purity not provided) was used on Chinese hamster ovary cells (CHO) at 0, 0.007, 0.013, 0.025 and 0.05 µl/ml (no S9) and at 0, 0.05, 0.1, 0.2 and 0.4 µl/ml (+S9) for induction of sister chromatid exchange (SCE). There was no significant treatment-related increase in SCEs. Positive controls behaved as expected. ACCEPTABLE. No adverse effect. (Kishiyama & Silva, 4/12/01)

Kerosene, Hydrodesulfurized

149-022 117338A “Mutagenicity Evaluation of Hydrodesulfurized Kerosene (API #81-07) [in the Mouse Lymphoma Forward Mutation],” (Cifone, M.A.; Litton Bionetics, Inc., Kensington, MD; Project PS-4-LBI (503-1); API Medical Research Publication: 32-30240; 12/4/84). API# 81-07 technical (100% pure) at 0, 6.25, 12.5, 25.0 and 37.5 nl (no S9) and at 0, 3.91, 7.81, 15.6, 31.3 and 62.5 nl/ml (+ S9) was evaluated for mutagenicity using mouse lymphoma cells in a single trial, with single or duplicate culture. There were no treatment-related effects either with or without S9 at any dose. This study is not acceptable and is not upgradeable (single trial). The data are supplemental. (Kishiyama & Silva, 4/24/01).

** 149-022 117338B “Mutagenicity Evaluation of Hydrodesulfurized Kerosene (API #81-07) [in the Rat Bone Marrow Cytogenetic Assay],” (Cimino, M.C.; Litton Bionetics, Inc., Kensington, MD; Project PS-4-LBI (503-1); LBI Project #: 22162 & 20989; 11/84). API# 81-07 (purity not designated) was administered via a single intraperitoneal injection to Sprague-Dawley rats (5/sex/dose/sacrifice time + 5/sex supplementary group at high dose) at 0, 0.3, 1.0 or 3.0 g/kg/day (6, 24 & 48 hour sacrifice) to evaluate induction of structural aberrations in bone marrow cells (50 metaphases/animal; 500 cells counted/animal for mitotic index). High dose animals had mortality, nervous depression and were febrile to the touch. The positive control (TEM) was the only group reported with a significant increase of structural chromosome aberrations. No adverse effect. ACCEPTABLE. (Kishiyama & Silva, 4/13/01).

Jet Fuel

149 - 022 117341 “Mutagenicity Evaluation of Jet Fuel A in the Mouse Dominant Lethal Assay,” (Brusick, D.J., Nguyen, T.D.; Litton Bionetics, Inc., Kensington, MD; LBI Project No: 21141-03; 12/80). Jet Fuel A, was administered to male CD-1 mice (12/dose, 6 hours/day; 5 days/week) via whole body inhalation (vapor) at 0, 100 and 400 ppm for 8 consecutive weeks (40 days total). Virgin, unexposed female mice were mated (48/dose, 2 week intervals) to the treated males soon after the final test article treatment. Dosing occurred during the entire spermatogenesis period. Jet Fuel A did not adversely affect fertility, implantation or resorptions in this study. The number of implants was reduced and resorptions increased with the positive control (TEM). Not acceptable, not upgradeable. (If the number of pregnant females is too low, then it is difficult to assess genetic damage to sperm. In this type of assay, large numbers of pregnant females are needed to assess genetic damage.) These data are supplemental. (Kishiyama & Silva, 4/30/01).

Kerosene, Hydrodesulfurized

149 - 022 117342 “*In Vivo* Sister Chromatid Exchange Assay with API 81-07 Hydrodesulfurized Kerosene,” (Putman, D.L.; Microbiological Associates, Inc., Bethesda, MD; Lab. Study No. T5337.130002; 9/26/88). API 81-07 was administered to B6C3F1 mice (5/sex/dose) in a single IP injection at 400, 2000 or 4000 mg/kg. Bone marrow from the femurs was collected 24-26 hours after treatment. Body weight was slightly reduced for high dose males and females and mid dose males. **Adverse effect: SCE/metaphase in males was statistically significantly increased at all three concentrations (400, 2000, 4000 mg/kg) of API 81-07 tested.** The SCE/cell in females, although higher than control was not statistically significant. UNACCEPTABLE (dosing material analysis to

confirm concentration and stability was not reported; no individual data). Possible adverse effect indicated. Possibly upgradeable. (Kishiyama & Silva, 4/30/01).

DNA DAMAGE

No study submitted

NEUROTOXICITY

Jet Fuel, Petroleum and shale derived

149 - 022 117343 “Neurobehavioral Toxicology of Petroleum- and Shale-Derived Jet Propulsion Fuel No. 5 (JP5),” (Bogo, V., Young, R.W., Hill, T.A., Cartledge, R.M., Nold, J., Parker, G.A.; Published in: Advances in Modern Environmental Toxicology Vol. VI; Chapter 2, 1984; Armed Forces Radiobiology Research Institute and Naval Medical Research Institute, Bethesda, MD). **Inhalation Study:** P-JP5 and SJP5 were administered via inhalation to adult male Sprague-Dawley rats at 1000 and 1600 mg/m³, respectively (6 hrs/day, 5 days/week for 6 weeks). **Gavage Study:** Rats received a single gavage treatment at 24 mg/kg. **Results:** **Inhalation Study:** water consumption increased from Day 8 through 30 with PJP5 and SJP5 treatment. **Gavage Study:** Body weight and food and water consumption were decreased 2-3 days after dosing and the activity of rats increased between 2.5 and 6 hours after dosing with PJP5 and SJP5. No reported neurotoxicity was observed under study conditions. UNACCEPTABLE (too few dose levels, no females, no positive control, no analysis of dosing material, no individual data). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 5/1/01).

MISCELLANEOUS STUDIES

Chronic Studies:

Petroleum Hydrocarbon

149 - 017 117307 “Effects of Prolonged Inhalation of Oil Fogs on Experimental Animals,” (Lushbaugh, C.C., Green, J.W., Redemann, C.E.; Published in: Archives of Industrial Hygiene, 1:237-247, 1950). Automobile (Penn Oil 7, SAE #10) and diesel engine (SGF #1 oil) lubricating oils were administered via inhalation as atomized (fog) particles at 132 and 63 µg/l air, respectively. Particle radii averaged 0.58 micron and 0.45 microns for #10 and #1, respectively. Exposure times to induction of lung irritation and/or pulmonary infection (lipid pneumonia) were 100 and 343 days (mice: CF1 & A), 1 year (rat & rabbit) and 100 days (monkey). Mice, rats and rabbits were unaffected and the occurrence of pulmonary tumors in a highly susceptible “A” mouse strain was not increased with treatment. There was little oil accumulation in lungs of the animals. Retained oil quickly transferred to pulmonary connective tissues and lymph nodes. Auto oil was not as toxic as diesel oil and neither caused lipid pneumonia in animals living in atmospheres of 63-132 µg/l air, since the low pulmonary retention enabled phagocytes to effectively engulf and remove it. **Possible adverse effect indicated in monkeys: Monkeys had greater oil accumulation (lungs) compared to other species tested. Both oils caused fur thinning/baldness over half the body after 100 days. Decreased food consumption, marked wasting and death were attributed to hyperplastic gastritis. Monkeys also had an increase in infectious pneumonia and interstitial inflammation, relative to controls.** These data are supplemental. (Kishiyama & Silva, 2/5/01).

Oncogenicity:

Paraffinic

149-020 117314 “The Carcinogenic Initiating and Promoting Properties of Lightly Refined Paraffinic Oil,” (McKee, R.H., Plutnick, R.T., Przygoda, R.T.; Fundamental and Applied Toxicology, **12**:748-756 (1989)). Dermal carcinogenic potential of petroleum-derived liquids is related to polycyclic aromatic hydrocarbon (PAH) content (distill at > 700 °F). Saturated and aromatic fractions of lightly refined paraffinic oil (LRPO: kerosene, diesel fuel, heating oil), or “middle-distillates,” (boil at 490-610 °F) have very low concentrations of PAH's and were considered non-carcinogenic. In this study, LRPO and subfractions were tested at 0 (DMSO), 10, 50, 100, 500, 1000, 2000, 5000 and 10000 µg/plate (+/- S9 Mix & +/- Tween 80 solubilization) with *Salmonella typhimurium* strain TA-98. *In vivo* **Initiation:** Groups of 30 CD-1 male mice were treated dermally with DMBA at 10 or 50 µg in 25 µl acetone (1 dose), 150 µl LRPO (divided into saturated and aromatic fractions) or acetone (6x at 25 µl each over 2 weeks); and **Promotion:** TPA (2.5 µg in 25 µl acetone) or LRPO or acetone (25 µl) three times weekly. Mice evaluated for initiating potential were treated 352 days and for promotion, 193 days. There was no *in vitro*-induction of gene mutation with LRPO or subfractions. Therefore, the tumorigenicity of LRPO was not due to low levels of PAHs or to an interaction between initiating and promoting constituents. **DMBA/LRPO treated mice had a total of 11 tumors, with a 17% incidence (5/30 mice) which may indicate weak promoter activity.** None of the mice receiving DMBA alone developed tumors. Skin irritation as acanthosis (moderate-severe focal for 10/30 mice/group) and subepidermal inflammatory infiltrate (all LRPO treated mice) may have been responsible for the promotion effects. Supplemental data. (Kishiyama & Silva, 12/4/00).

Distillates

149 - 020 117315 “Evaluation of the Dermal Carcinogenic Potential of Liquids Produced from the Cold Lake Heavy Oil Deposits of Northeast Alberta,” (McKee, R.H., S.C. Lewis; Canadian Journal of Physiology and Pharmacology; **65**:1793 - 1797 (1987)). Raw Bitumen (75% w/v suspension in toluene), Hycracking product (boils at 102-498 °C) and Go-Fining product (undiluted; boils at 259-519 °C) were applied dermally in 25 µl aliquots to the shaved backs of male C₃H/HeJ mice (50/group) 3 times/week until the mice died spontaneously, or until grossly diagnosed squamous cell carcinomas occurred (mice then sacrificed for humane reasons). Highly refined white oil was negative control. All mice were examined daily for appearance of dermal tumors and all received complete necropsies. **G0-Fining treatment decreased survival significantly and increased the incidence of tumors (papillomas progressing to malignancy) to 86% (median latency = 46 weeks). Crude Bitumen induced tumors in 26% of mice (median latency = 2 years).** Hycracking product showed no evidence of epidermal carcinogenicity. The report indicated that the results were predictable, based on previous dermal carcinogenic activity of products that distill at the temperatures of these products. Possible adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 12/5/00).

Distillate (heating oil and diesel fuel)

149 – 020 117316 “Dermal Carcinogenic Activity of Petroleum-Derived Middle Distillate Fuels,” (Biles, R.W., McKee, R.H., Lewis, S.C., Scala, R.A., DePass, L.R.; Bushy Run Research Center; Published in: Toxicology, **53**:301 – 314 (1988)). The following compounds, origins and boiling ranges: virgin heating oil blending base (US 287-585 °F), lightly refined paraffinic oil (US 490-610 °F), commercial #2 heating oil from different sources (Middle East/Carribbean Pool 383-705 °F; US 331-678 °F; Middle East 419-676 °F; Western Canadian 322-644 °F; Western Canadian/Venezuelan 313-666 °F, Western Canadian/Tar Sands 373-667 °F), Virgin heating oil blending base (sample 1) + catalytically cracked middle distillate (US 287-700 °F) and light catalytic cycle oil (US 640 °F) were applied in 25 µl aliquots to the clipped dorsal surface of male C₃H/HeJ mice (40-50/group, 5/cage) 3 times/week for the lifetime of the mice or until all animals in the group developed carcinomas. Highly

refined mineral oil was the negative control. The study was conducted over a 4-year period. . Animals were examined daily for dermal tumors and all mice received full necropsy at termination or death. The report states that carcinogenic potential of petroleum-derived materials is related to PAH content and that liquids that boil below PAH distillation range (700 °F) “would not be carcinogenic”. Earlier studies supporting this conclusion were of short duration but recent studies with repeated application of petroleum-derived materials (middle distillate fuels 350-700 °F) produced tumors in mouse skin. The current study tested tumorigenic potential of a series of middle distillates, which varied with respect to boiling range, composition and source of blending stocks. Results with most samples showed low tumor yields (significantly increased over control), with long median latencies (by Weibull distribution function). Parameters examined did not affect tumorigenicity, as there were no apparent differences among treatment groups. Tumorigenic activity was not associated with PAH content and therefore was not PAH-dependent. There were also non-neoplastic dermal changes (hyperplasia) which may indicated preneoplasia. Possible adverse effect indicated. These data are supplemental. M. Silva, 12/6/00.

Petroleum Hydrocarbon (Distilled Petroleum Oil - bitumen)

149 - 020 117317 “Evaluation of Dermal Carcinogenic Potential of Tar Sands Bitumen-Derived Liquids,” (McKee, R.H., Stubblefield, W.A., Lewis, S.C., Scala, R.A., Simon, G.S., DePass, L.R.; Published in: Fundamental and Applied Toxicology, 7:228-235 (1986), Exxon Corporation, East Millstone, NJ). Tar sands (80% sand, 10% water, 10% hydrocarbons), bitumen (hydrocarbons derived from tar sands), untreated naphtha (boiling range: 50-250 °C), crude gas oil (> 250 °C) and 3 thermally and catalytically cracked liquids derived from crude gas oil (boiling range: light, 149-316°C, heavy > 316 °C, blended 2:1 heavy/light gas oils >316 °C) were applied dermally (shaved backs) to C₃H/HeJ male mice (50/group, 5/cage) 3 times/week in 25 µl aliquots throughout the life-time. Negative control was highly refined white oil. Results showed the tar sands (0 tumors), bitumen (1 malignant & 1 benign tumor) and untreated naphtha (1 malignant tumor) produced few total epidermal tumors. Crude oil (11M, 2B), light (11M, 4B), heavy (46M, 2B) and gas blend (47M) produced numerous tumors. **Reduced survival correlated with rapid development of tumors (squamous cell carcinomas) in mice treated with heavy and blended gas oils. Carcinogenic potential was moderate for light gas and crude oil.** Supplemental study. (Kishiyama & Silva, 12/7/00).

Petroleum Hydrocarbon (naphthenic distillates, unrefined, hydrotreated)

149 - 020 117318 “The Dermal Carcinogenic Potential of Unrefined and Hydrotreated Lubricating Oils,” (McKee, R.H., Daughtrey, W.C., Freeman, J.J., Federici, T.M., Phillips, R.D., Plutnick, R.T.; Journal of Applied Toxicology, 9(4):265-270 (1989), Exxon Biomedical Sciences, Inc., East Millstone, NJ). Several samples of naphthenic distillates (unrefined light, 549-810 °F, viscosity @ 40°C= 16.3; hydrotreated light 546-819 °F, viscosity @ 40°C = 16; hydrotreated light, 533-830 °F, viscosity @ 40°C = 15.7; unrefined heavy 649-909 °F, viscosity @ 40°C= 62.2; hydrotreated heavy 607-892 °F, viscosity @ 40°C = 45.9; hydrotreated heavy 608-905 °F, viscosity @ 40°C = 45.4; unrefined heavy 794-1058, viscosity @ 40°C = 484.7; hydrotreated heavy 743-1047 °F, viscosity @ 40°C. = 272.1, hydrotreated heavy 732-1050 °F, viscosity @ 40°C. = 255.4) were applied dermally to male C3H mice (40/group) twice weekly at 37.5 µl aliquots undiluted for up to 24 months to test potential for dermal carcinogenicity. Hydrotreated oils (reduced in polycyclic aromatic hydrocarbons) of all viscosities did not induce tumors or affect survival. Possible adverse effect indicated. **Epidermal tumors were induced with all unrefined distillates (heavy & light) of all specific activities.** These data are supplemental. (Kishiyama & Silva, 12/7/00).

Developmental (Teratology):**Solvent (also fuel oil)**

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 mg/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).

Mutagenicity:**Paraffinic (also distillates, solvent refined oils, crankcase oils)**

149 - 021 117331 “Adaptation of the *Salmonella*/Mammalian Microsome Test to the Determination of the Mutagenic Properties of Mineral Oils,” (Hermann, M., Chaude, O., Weill, N., Bedouelle, H., Hofnung, M.; Published in: Mutation Research, 77 (1980) 327 – 339). *Salmonella typhimurium* strain TA 98, "S9 was used in the plate incorporation assay. Two techniques to determine potential mutagenicity of mineral oils have been developed by using benzo[a]pyrene dissolved in white oil as a synthetic reference oil. The dispersal of the compound in aqueous medium with Tween 80 is a simpler and a more generally accepted technique, compared to the extraction of polynuclear aromatic hydrocarbons with DMSO. These new techniques make possible the study of potential mutagenicity for various extracts of mineral oil. Mutagenicity was observed with used crankcase oil and petroleum distillates but to a lesser extent with solvent-refined oils. Results correlated with PAH content but not BP content of oils. Supplemental data. (Kishiyama & Silva, 5/2/01).

Acute Oral Toxicity:**Kerosene**

149 – 016 117304 “Petroleum Hydrocarbon Toxicity Studies: XI. Animal and Human Response to Vapors of Deodorized Kerosene,” (Carpenter, C.P., Geary, Jr., D.L., Myers, R.C., Nachreiner, D.J., Sullivan, L. J., King, J.M.; Carnegie-Mellon Institute of Research, Carnegie-Mellon University, Pittsburgh, PA; 12/22/75; Published in: Toxicology and Applied Pharmacology, 36:443-456, 1976). **Acute Study:** Deodorized Kerosene (composed of paraffins, naphthenes, aromatics; boiling point temperature range: 406 – 522 °F) was administered by inhalation (air saturated at 25 °C) to 6 male albino rats for 8 hours, during which time the rats appeared normal. There were no effects on weight gain during the 14 day post-dosing observation period, nor were there effects at autopsy. Six rats were exposed at 0, 6.9, 7.0, 7.4 and 9.6 mg/liter (avg/day for 4 days) for 6 hr/day. After exposure, the extremities of the rats were red, but coordination was normal (sluggish after 3 hours). One day after termination of treatment, rat skin was dry and flakes formed. This effect continued for 4 days and 1/6 rats had hair loss. After 14 days, body weight was normal for rats of that age. No increase in osmotic-erythrocyte fragility was observed among 6 rats treated at 5.9 mg/L for 6 hours (compared to

controls). Mixed breed cats (4 males) were exposed by aerosol inhalation (6.4 mg/L) for 6 hours. No treatment-related effects were observed during treatment or at autopsy after 14 days. Six mice, treated with the highest attainable vapor concentration, were not affected. They were then treated with an aerosol of Deodorized Kerosene at 6.9 mg/L (6900 mg/m³) for upper respiratory irritation. The respiratory rates of the mice were not depressed 50% or more from control values. Neither saturated vapor generated at room temperature nor the above aerosol were irritating to the upper respiratory tracts of mice. **Subacute Inhalation Toxicity:** Rats (25 males/dose) and Beagle dogs (4 males/dose) received repeated daily inhalation exposure (6 hours/day, 5 days/week) to 0, 0.02, 0.048 and 0.10 mg/liter (equivalent to 2.9, 6.9 and 14 ppm) for 3, 8 and 13 weeks. Rats were sacrificed for histopathology after 16 and 40-day intervals as well as 13 weeks (dogs and rats). Results showed no treatment-related effects in any of the monitored criteria (hematology, blood chemistry, body weight, histopathology when inhaled for 67 and 68 days by rats and dogs, respectively). **Human Sensory Response:** Odor threshold was measured with 6 volunteers (age 23-49) exposed at 0.01, 0.001, 0.00, and 0.1 mg/L for 10 seconds Day 1, and 0.1, 0.01, 0.00 and 0.001 mg/L on day 2. The odor threshold was between 0.0002 and 0.002 mg/L. Six volunteers (age 20-63) inhaled a mean measured vapor:air concentration of 0.14 mg/L (20 ppm) for 15 min. There was no discomfort or irritation reported during or following the inhalation period. The volunteers judged Vapor:air concentration of 0.14 mg/L (20 ppm) of Deodorized Kerosene as acceptable for an 8 hour work day. These data are supplemental. M. Silva, 5/17/01.

Chemical	Chemical Code	Tolerance Number	SB950 Number
MINERAL OIL (Solvent, Kerosene, Jet Fuel, Paraffin base)	401	149	754
PETROLEUM HYDROCARBONS	473	50444	789
PETROLEUM OIL (Unclassified),	765	50392	297
ISOPARAFFINIC HYDROCARBONS	1641	50667	713
PETROLEUM DISTILLATES (refined),	763	50427	476
PETROLEUM DISTILLATES	2106	50792	788

TOXICITY, RAT

50392 - 029 117096 "Five-Day Repeated Dose Dermal Toxicity Study in Rats of Light Neutral Oil," (Zellers, J.E., Meckley, D.R.; Gulf Life Sciences Center, Laboratory Project ID#: 1184, 4/12/84). Light Neutral Oil, applied dermally at 0 (Heavy Paraffin Oil), 1.0 (diluted, 42.5% w/v). 1.0 (undiluted) and 2.0 (undiluted) g/kg to Fischer 344 rats (5/sex/dose) for 5 days. Volumes were 2.36, 2.36, 1.18, 2.36 ml/kg, control through high dose. The method of application was not described. Food consumption decrease was dose related and most apparent (reduced 8.3%) for the high dose group. No skin effects were reported. UNACCEPTABLE (Not a FIFRA Guideline study: major variances and insufficient information). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 6/6/01).

50392 - 029 117099 "Five-Day Repeated Dose Inhalation Toxicity Study in Rats of Neutral Light Oil," (Goode, J.W., Patrick, D.L.; Gulf Life Sciences Center, Pittsburgh, PA; Laboratory Project ID: 1185, 7/2/84). Neutral Light Oil technical was used via whole-body inhalation on Fischer 344 rats (5/sex/dose) at 0, 0.5, 1.5 and 3.0 g/m³ (analytic concentrations of 0.54, 1.7, or 2.97 g/m³) for five 6-hour/day exposure periods. NOEL = 0.50 g/m³ (2 females at 3 g/m³ died (days 2 & 4) on study (considered treatment related). Body weights were lower (12%) on study day 5 for females at 3 g/m³. Most treated rats had discolored hair. Both sexes at ≥ 1.5 g/m³ appeared unkempt (porphyrin eyes, perianal, nasal discharge, red material around the mouth & nose). Lung tissues from 3 rats (1 male, 3 g/m³ & 2 females, 1.5 g/m³) had significant signs of lung irritation.) Not acceptable or upgradeable

(not a FIFRA Guideline study; major variances and insufficient information). These data are supplemental. Possible adverse effects indicated (increased mortality, respiratory distress) (Kishiyama & Silva, 6/13/01).

50392 - 030 117100 "Four-Week Repeated Dose Inhalation Toxicity Study in Rats of Light Neutral Oil", (Goode, J. W., Patrick, D.L.; Chevron Environmental Health Center, Inc., Richmond, CA; Laboratory Project ID: 1187, 11/16/84). Light Neutral Oil was used on Fischer 344 rats (10/sex/dose), exposed by inhalation at 0, 0.5, 0.75 or 1.5 g/m³ for a total of 20 exposures (6-hour/day) over 28 days. NOEL < 0.5 g/m³ (Body weights were statistically significantly decreased in males at = 0.75 g/m³. The highest daily incidence of test material on fur, dry red material around mouth and/or nose, clear nasal discharge, and ocular porphyrin and discharge was observed at 1.5 g/m³, but found at all doses. Increased circulating white blood cells with a relative increase in neutrophils were observed in males at = 0.5 g/m³ and in females at 1.5 g/m³. Absolute and relative spleen weights were increased in females at 1.5 g/m³. The absolute and relative liver weights were increased in females at = 0.5 g/m³. Absolute and relative lung weights were increased in both sexes at = 0.5 g/m³. Light neutral oil at all dosages caused hyperplasia of alveolar macrophages in the lung of all test animals. Granulomatous pneumonitis was present in both sexes at 1.5 g/m³ and in 4 females at 0.75 g/m³. Granulomatous hepatitis in the liver occurred in females at 1.5 g/m³. Mononuclear inflammation to nasal turbinates was observed in both sexes at 1.5 g/m³. Not acceptable (Not a FIFRA Guideline study; major variances and insufficient information). No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 6/14/01).

50392 - 030 117101 "Nine-Day Repeated Dose Inhalation Toxicity Study in Rats -Orchard Spray 70," (Gordon, T., Steele, F.; Gulf Life Sciences Center, Pittsburgh, PA; Laboratory ID #: 82-064; 9/15/83). Fischer 344 rats (5/sex/dose) were exposed via inhalation to Orchard Spray 70 at 0, 1 and 1.5 g/m³ for 6 hours/day, 5 days/week (9 days, 5 days/week). **NOEL** <0.5 g/m³ (One female death at 1.5 g/m³ was considered to be treatment-related. Initial, but transient weight decreases occurred in females at 1.5 g/m³. Changes in the lungs consisted of congestion, edema, with hypertrophy and hyperplasia of alveolar macrophages at 1.5 g/m³. Clinical changes occurred in both sexes at = 0.5 g/m³ and included closed eyes, ocular porphyrin, and nasal discharge. Possible adverse effects indicated: severe lung damage, death. **UNACCEPTABLE** (Not a FIFRA Guideline study; major variances). (Kishiyama & Silva, 7/2/01).

TOXICITY, MOUSE

Range-finding study:

50392 - 029 117165 "Four-Week Repeated Dose Dermal Toxicity Range-finding Study in Mice of Light Neutral Oil", (Zellers, J.E., Meckley, D.R.; Gulf Life Sciences Center, Houston, TX; Laboratory Project ID #: 1188R, 8/2/84). Light Neutral Oil diluted (42.5% [w/v]) or undiluted was applied dermally at a daily dose of 50 ul to each C3H/HeNCrIBR mouse (15/sex/dose) 3x per week for four weeks (12 doses). Undiluted heavy paraffin oil at the same dosage volume served as the control group. Food consumption decrease was dose related (reduced 8.3%) for the undiluted treatment. There were no other treatment effects reported. This is not a FIFRA Guideline study. These data are supplemental. (Kishiyama & Silva, 6/6/01).

TOXICITY, RABBIT

50392 - 029 117097 "Two-Week Repeated Dose Toxicity Study in Rabbits Using Gulf Orchard Spray 70", (Zellers, J.E., Crutchfield, D.T.; Gulf Life Sciences Center, Houston, TX; Laboratory Project ID #: 82-046, 6/15/83). Gulf Orchard Spray 70 at 0 (corn oil), 1 (43.1% w/v in corn oil) and 2 g/kg (86.18% w/v undiluted) was applied dermally (with occlusion; 6-hours/day, 5 days/week; 2-weeks - 10 treatments) to New Zealand White rabbits (3/sex/dose at 0 & 1 g/kg and 6/sex at 2 g/kg). Skin was unabraded. Half the rabbits/sex at 2 g/kg were sacrificed 24 hours after the last treatment. The remaining half at 2 g/kg was observed for an additional 2 weeks (recovery) prior to sacrifice. NOEL < 1.0 g/kg (occasional erythema and edema at 1.0 g/kg, more frequent erythema and/or edema and desquamation at 2.0 g/kg occurred. Incidence of acanthosis and hyperkeratosis increased (especially females at 2 g/kg). Acanthosis was observed in 1 control and 3 females at 2 g/kg. Hyperkeratosis was observed in the same control and all 6 females at 2 g/kg. The severity of acanthosis and hyperkeratosis was considered moderate, except for the minimal to slight hyperkeratosis in 3 females at 2 g/kg. After 2 weeks of recovery, edema and erythema were no longer visible; however, desquamation persisted (1/3 males and 2/3 females). Possible adverse effect indicated (persistent dermal effects after the 2-week recovery period.) UNACCEPTABLE. (Not a FIFRA Guideline study: major variances; insufficient data). These data are supplemental. (Kishiyama & Silva, 6/7/01).

50392 - 029 117098, "Two-Week Repeated Dose Toxicity Study in Rabbits Using 100 Paraffine Oil", (Zellers, J.E., Whaley, C.J.; Gulf Life Sciences Center, Pittsburgh, PA; Laboratory Project ID 82-039, 11/15/83). 100 Paraffin Oil, at 0 (corn oil), 1 (diluted/44.3%) and 2 (undiluted) g/kg was applied to unabraded skin, with occlusion (6-hours/day, 5 days/week, 2-weeks) to New Zealand White rabbits (3/sex/dose) with 3/sex for a 2 week recovery period at 2 g/kg. Dosing volume was 2.258 ml/kg for all groups. NOEL < 1 g/kg. Edema, erythema and desquamation showed a dose-related increase in both sexes. A microscopic examination was performed on the skin of 3 control and 6 high dose animal/sex and the incidence of acanthosis and hyperkeratosis was significantly greater at 2 g/kg (100%). After the 2-week recovery period, erythema and edema were greatly reduced in both sexes.) Not acceptable or upgradeable (Not a FIFRA Guideline study.). No adverse effect indicated. (Kishiyama & Silva, 6/11/01).

ONCOGENICITY, MOUSE

50392 - 011 43985 "Dermal Oncogenicity Studies of MH-982, MH-983, MH-1147, MH-1148, MH-1173, MH-1174, MH-1175, MH-1255 and MH-1256 in Male C3H/HeJ Mice." (Bushy Run Research Center, 10/29/84, Study 79-150) Nine samples were tested, all described as liquids with no further characterization. Registered test article was MH-1255. 50 male mice per group; 25 ul undiluted was applied per mouse to the skin three times per week on Monday, Wednesday and Friday with MH-983 designated as the negative control and MH-982 as the positive control. **Possible adverse effect indicated:** Four of nine samples tested increased tumor formation and decreased the time-to-tumor and mean survival (positives were MH-982, MH-1174, MH-1175 and MH-1256. Registered test article, MH-1255, was **not** one of these four positives); unacceptable (Study was designed as a dermal treatment oncogenicity screening study only: no females included, limited tissues for histopathology, no individual data, no rationale for dose, no indication of percent of body surface involved in application. **The other 8 test products need to be identified.**) Not upgradeable. J. Gee, 12/9/87.

NOTE: Study was negative for the registered product, but positive for 4 of 9 samples tested in the series. The report does not identify the other chemicals, which could be analogs of the registered product. Representative species of generically related petroleum products are expected to be tested on

behalf of respective groups to fill data gaps. For this reason, the four positive chemicals are presumed to be representative petroleum products, and a "possible adverse effect" is indicated.

GENE MUTATION

50392 - 001 017076 "Salmonella/Mammalian Microsome Mutagenicity (Ames Test) with Chevron Aromatic Oil." (Standard Oil, 10/12/82). Aromatic oil, coded CAO-CWO #1, 55565-2; tested with Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100 at 0, 0.01, 0.03, 0.1, 0.3 and 1.0 mg/plate as a suspension in DMSO; with and without rat liver activation; triplicate plates, single trial - data presented as the mean \pm standard deviation; unacceptable (single trial, no individual plate counts, no justification for amounts of test material used, test article not adequately described.) Gee, 7/25/85

50392 - 030 117103, "*Salmonella*/Mammalian Microsome Mutagenicity Test (Ames Test) with Four Samples of Hydrocracked Lube Oil Stocks (Pilot Plant)," (Parker, J.A.; Chevron Environmental Health Center, Inc., Richmond, CA; Laboratory Project ID SOCAL 1827, 6/12/81). Hydrocracked Lube oil stocks PE-2-1 (neutral oil 20), PE-2-2 (neutral oil 40), PE-2-3 (neutral oil 110) and PE-2-4 (Bright Stock 32) were used on *Salmonella typhimurium* strain TA100 at 0 (DMSO), 0.01, 0.10, 1.0, 5.0 and 10.0 mg/plate (+/-S9 Mix) to assay mutagenic potential with and without Aroclor 1254 induced male rat liver activation, in triplicate. Exposure time was for 3 days at 37°C. The number of revertant colonies increased slightly (<2x) with **PE-2-4 at 5 and 10 mg/plate** in the presence of S9 Mix at 5 and 10 mg/plate. UNACCEPTABLE and not upgradeable (Not a FIFRA Guideline study. Numerous deficiencies). These data are supplemental. (Kishiyama & Silva, 7/10/01).

50392 - 028 114996 (Summary of 117103)

50392 - 030 117105 "CHO/HGPRT Test Using Orchard Spray 70," (Goode, J.W., Papciak, R.J.; Gulf Life Sciences Center, Pittsburgh, PA; Laboratory Project ID: 82-073, 9/24/83). Orchard Spray 70 at 0 (F127), 4, 32, 256, 512, 1024 and 2048 μ g/ml was evaluated for forward mutations at the HGPRT locus in CHO-K1 Chinese Hamster ovary (CHO) cells with and without Aroclor 1254-induced rat liver activation. After a 5 hour exposure and 8-day expression time, there were no significant changes in mutants/10⁶ clonable cells or in cell survival at > 256 μ g/ml. Not acceptable or upgradeable (No toxicity was observed, therefore it is not possible to evaluate mutagenic potential at the doses used). (Kishiyama & Silva, 7/11/01).

50392 - 030 117106 "The Potential of Four Hydrocracked Lube Oil Stocks and Three RPM Lube Oil Stocks to Mutate Histidine-Deficient Strains of *Salmonella typhimurium*," (Wong, Z.A.; Chevron Environmental Health Center Inc., Richmond, CA; Laboratory Project ID: SOCAL 1753, 12/5/80). Hydrocracked Lube Oil Stocks: DG 2486 Neutral Oil 20 (100), DG 2487 Neutral Oil 40 (200), DG 2488 Neutral Oil 110 (500), DG 2489 Bright Stock 32 (150); RPM Lube Oil Stocks: BO 1350 Chevron Neutral Oil 24 (125), BO 1351 Chevron Neutral Oil 80 (400), BO 1352 Bright Stock 35 (185) were assayed at 0 (DMSO), 0.1, 1.0, or 10 mg/plate and using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 with and without S9. Exposure time was 2-3 days. **Possible adverse effect indicated: DG 2489 Bright Stock 32, DG 2488 Neutral Oil 110 and BO 1350 Chevron Neutral Oil 24 were reported as weakly mutagenic with TA100 and complete liver S9.** Unacceptable (Not a FIFRA Guideline study). (Kishiyama & Silva, 7/11/01).

50392 - 028 114993 (Summary of 117106)

CHROMOSOME EFFECTS

50392 - 030 117102 "Range-Finding Test for the Micronucleus Test: Gulf 100 Paraffine Oil Administered by Gavage for 2 Days," (Harnois, M.C.; Gulf Life Sciences Center; Laboratory Project

ID: 82-026, 11/9/82). Gulf 100 Paraffine oil was administered to CrI:CD-1 (ICR) BR Swiss mice (3/sex/dose) by gavage at 0 (corn oil), 98, 451, 823, 4224 or 8335 mg/kg for 2 days. All mice were terminated 24 hours after the last dose. One femur was removed and the bone marrow was examined. The high dose of 8335 mg/kg did not significantly effect the ratio of polychromatic to normochromatic erythrocytes nor indicate cytotoxicity. **NOEL** >8335 mg/kg (No significant treatment-related effects occurred at any dose. Unacceptable (Not a FIFRA Guideline study.) Data are supplemental. (Kishiyama & Silva, 7/9/01).

50392 - 030 117107 "Micronucleus Test in Mouse Bone Marrow: Gulf 100 Paraffine Oil Administered by Dermal Application for 2 Days," (Harnois, M.C., Kahn, S.H.; Gulf Life Sciences Center, Laboratory Project ID: 82-072, 3/25/83). Gulf 100 Paraffine Oil was administered dermally at 0 (corn oil), 625, 1250, 2500 or 5000 mg/kg (limit test) to CrI:CD[®]-1 (ICR) BR Swiss mice (10/sex/dose) for 2 days. The animals were sacrificed and bone marrow smears were prepared on days 3 and 4, except rats treated with cyclophosphamide (positive control, applied by ip injection) were sacrificed only on day 3. Slides were stained on the day following preparation. No test article related effects reported. UNACCEPTABLE (Insufficient information). (Kishiyama & Silva, 7/12/01).

50392 - 030 117108 "Micronucleus Test in Mouse Bone Marrow: Orchard Spray 70," (Harnois, M.C., Kahn, S.H.; Gulf Life Sciences Center, Pittsburgh, PA; Laboratory Project ID: 82-052, 2/21/83). Orchard Spray 70 was administered by gavage at 0 (corn oil), 1643, 4105, 8218 or 16817 mg/kg to CrI:CD[®]-1 (ICR) BR Swiss mice (3/sex/group) for 2 days. The number of micronucleated polychromatic erythrocytes was not significantly increased with Orchard Spray 70 treatments. Not acceptable or upgradeable (no analysis of dosing solution; more protocol information was necessary). (Kishiyama & Silva, 7/12/01).

50392 - 030 117109 "Range-Finding Test for the Micronucleus Test: Orchard Spray 70 Administered by Gavage for Two Days," (Harnois, M.C.; Gulf Life Sciences Center, Laboratory Project ID: 82-012, 9/29/82). Orchard Spray 70 was administered by oral gavage at 0 (corn oil), 4, 18, 39, 200 or 400 mg/kg to CrI:CD[®]-1 (ICR) BR Swiss mice (3/sex/dose) for 2 days. There were no treatment-related effects reported for this study. A positive control was not performed. Not acceptable or upgradeable (Not a FIFRA Guideline study: no MTD, too few animals/sex/group, no positive control, only 1 sampling time, no analysis of dosing solution, micronuclei were not scored.) (Kishiyama & Silva, 7/13/01).

Chemical	Chemical Code	Tolerance Number	SB950 #'s
MINERAL OIL (Solvent, Kerosene, Jet Fuel, Paraffin base)	401	149	754
PETROLEUM HYDROCARBONS	473	50444	789
PETROLEUM OIL (Unclassified),	765	50392	297
ISOPARAFFINIC HYDROCARBONS	1641	50667	713
PETROLEUM DISTILLATES (refined),	763	50427	476
PETROLEUM DISTILLATES	2106	50792	788

TOXICITY, MOUSE

50427 - 009 115417 "18-Month Skin Painting Study with R-911-10, R-911-11, R-911-12, R-911-13, R-911-14, R-911-15, and R-911-16 in Female Swiss White Mice," (Vondruska, J.F., Jenkins, D.H.; Industrial Bio-Test Laboratories Inc., Northbrook, Illinois; IBT #: J7675; 6/24/71) [Status of IBT study is unknown]. Test compounds were administered dermally (3 times/week for 18 months) to the shaven backs of female Swiss white mice (100/dose). **The incidence of dermal squamous cell**

carcinomas was increased with R-911-10 (positive control) and R-911-11 treatments, compared with controls. UNACCEPTABLE (Not a FIFRA Guideline study; insufficient information due to major variances). (Kishiyama & Silva, 6/5/01).

50427 - 009 115417 same study as 149 - 012 116793

ONCOGENICITY, MICE

50427 - 009 115417 “18-Month Skin Painting Study with R-911-10, R-911-11, R-911-12, R-911-13, R-911-14, R-911-15, and R-911-16 in Female Swiss White Mice,” (Vondruska, J.F., Jenkins, D.H.; Industrial Bio-Test Laboratories Inc., Northbrook, Illinois; IBT #: J7675; 6/24/71) [Status of IBT study is unknown]. Test compounds were administered dermally (3 times/week for 18 months) to the shaven backs of female Swiss white mice (100/dose). **The incidence of dermal squamous cell carcinomas was increased with R-911-10 (positive control) and R-911-11 treatments, compared with controls.** UNACCEPTABLE (Not a FIFRA Guideline study; insufficient information due to major variances). (Kishiyama & Silva, 6/5/01).

GENE MUTATION

Mineral Oil: Petroleum Oil (Paraffinic)

50427 - 020 117324 “The Genotoxic and Carcinogenic Potential of Engine Oils and Highly Refined Lubricating Oils,” (McKee, R.H., Przygoda, R.T.; Published in: Environmental Mutagen Society Abstracts, page 72, 1987). The present studies compared the results of several *in vitro* assay procedures (*Salmonella*, mouse lymphoma, syrian hamster embryo (SHE) morphologic transformation assays) to the dermal carcinogenic activity of a series of petroleum-derived materials including engine oils and highly refined lubricating oils. A sample of unused gasoline engine oil was not active in an epidermal carcinogenesis bioassay. This material was not mutagenic in *Salmonella* and did not transform SHE cells. The main constituents of engine oils are highly refined lubricating oil base stocks. Data obtained with these materials are relevant in understanding the toxicity of engine oils. It was found that highly refined lubricating oils were not dermally carcinogenic; nor were they mutagenic or transforming. In contrast, certain other materials, including unrefined vacuum distillates and solvent extracts of these distillates were both carcinogenic and genotoxic. The results in the 3 *in vitro* assays paralleled the *in vivo* carcinogenesis data for all materials tested. Abstract only (no worksheet). These data are supplemental. M. Silva 1/26/01.

50427 - 020 117324 same as 149 - 014 116795.

Distillate

50427 - 009 115419 “Mutagenicity Test on an Emulsion of 917843-1 in the Ames *Salmonella*/Microsome Reverse Mutation Assay by the Preincubation Method,” (Jagannath, D.R.; Hazleton Laboratories America, Kensington, MD; HLA Study #: 8985-1-401E, 5/13/88). 917843-1 (emulsion in 10% Pluronic F68 vehicle) was evaluated for mutagenicity at 0, 15, 30, 40, 60, 80, 100 and 200 µl per plate with hamster liver metabolic activation (S9), using *Salmonella typhimurium* strain TA98 with 20 minute preincubation before adding agar. There were no significant increases in revertant colonies with 917843-1 (+S9) treatments. UNACCEPTABLE (Not a FIFRA Guideline study; major variances and insufficient information). These data are supplemental. (Kishiyama & Silva, 6/5/01).

Distillate/paraffinic oil

50427 - 009 115430 “Mouse Lymphoma Forward Mutation Assay Spray Oil—Gene Mutation Data,” (West, J.; Hazleton Laboratories America, Inc., Kensington, MD; Project #: 596-112; 7/25/90). Paraffinic Oil 78-9-70 (assumed 100%) was evaluated for mutagenicity at 8670, 17340, 34680, 52020, 69630, 86700, 104040 and 121380 µg/ml (with or without S9 Mix), using mouse lymphoma cells. Mutation frequencies with S9 were increased (not dose-related) slightly over twofold with Paraffinic Oil 78-9-70, however, these increases were equivocal. No toxicity reported. UNACCEPTABLE (Not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 6/4/01).

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PETROLEUM OIL (Unclassified),	765	50392	297
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PETROLEUM DISTILLATES	2106	50792	788

TOXICITY, MOUSE**Hydrocarbon**Chronic/Oncogenicity Study:

50444 - 003 052436 “Toxicology and Carcinogenesis Studies of Marine Diesel Fuel and JP-5 Navy Fuel in B6C3F₁ Mice,” (Litton Bionetics, Inc.; National Toxicology Program Technical Report Series #: 310; NIH Publication #: 86-2566; 9/86). JP-5 navy and marine diesel fuels were administered to B6C3F₁ mice (50/sex/dose) as daily (5d/week) dermal treatments for 103 weeks at 0 (acetone), 250 and 500 mg/kg. Systemic NOEL < 250 mg/kg (Both treatments increased the death rate of mice. Marine diesel and JP-5 navy fuel treatments decreased bodyweights at 500 mg/kg. At 250 mg/kg, both fuels induced decreased bodyweights. Both fuels at both doses increased the incidence of skin irritation (ulcers & chronic dermatitis) at the treatment site. Splenic hematopoiesis, plasmacytosis of the axillary lymph node at ≥ 250 mg/kg and amyloidosis (many organs) at 500 mg/kg in females were due to severe dermatitis and skin ulceration. Liver hematopoiesis (females, 500 mg/kg) and urinary bladder inflammatory infiltrates at 500 mg/kg in both sexes, were observed. JP-5 Navy Fuel increased the incidence of amyloid (kidney, adrenal cortex, spleen, and multiple organs) in males at 500 mg/kg and in females (spleen, kidney, multiple organs) at 500 mg/kg due to severe dermatitis and skin ulceration. Granulocytic hyperplasia of bone marrow in males at 500 mg/kg and hyperplasia of axillary lymph nodes in females at 500 mg/kg were observed.) Oncogenicity NOEL < 250 mg/kg (**Possible adverse effect indicated:** Marine diesel fuel at ≥ 250 mg/kg increased the incidence in squamous cell carcinomas at the treatment site as well as hepatocellular adenoma and carcinoma in males. No evidence of carcinogenicity with JP-5 navy fuel treatments. UNACCEPTABLE (Not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 5/31/01).

Subchronic Studies:

50444 - 003 052433 “A Fourteen Day Dermal Administration Study of Marine Diesel Fuel and JP-5 Navy Fuel in B6C3F₁ Mice,” (Litton Bionetics, Inc.; National Toxicology Program Technical Report Series #: 310; NIH Publication #: 86-2566; 9/86). Marine diesel (MDF) and JP-5 Navy fuel was dermally administered for 14 days to B6C3F₁ mice (5/sex/dose). MDF treatment was 0 (95% ethanol), 2000, 4000, 8000, 20000 or 40000 (the neat chemical) mg/kg and JP-5 Navy fuel treatment was 0 (95% ethanol), 5000, 10000, 20000, 30000 or 40000 mg/kg. Mortality was 100% for all mice at ≥ 20000 mg/kg MDF. Mortality was 100% for JP-5 Navy fuel at ≥ 30000 mg/kg in females and at

40000 mg/kg in males. Acanthosis, hyperkeratosis and dermal inflammation occurred at the treatment site for all dosed groups. UNACCEPTABLE (supplemental data; no worksheet). (Kishiyama & Silva, 12/7/01)

50444 - 003 052435 “A 13-Week Dermal Administration Study of Marine Diesel Fuel and JP-5 Navy Fuel in B6C3F₁ Mice,” (Litton Bionetics, Inc.; National Toxicology Program Technical Report Series #: 310; NIH Publication #: 86-2566; 9/86). Marine diesel (DMF) and JP-5 Navy fuel was dermally administered for 13 weeks to B6C3F₁ mice (10/sex/dose). DMF was used at 0 (acetone), 250, 500, 1000, 2000 or 4000 (applied neat) mg/kg and JP-5 Navy fuel was used at 0 (acetone), 500, 1000, 2000, 4000 or 8000 (applied neat) mg/kg. Mortality was 0% for males and 50% for female at 4000 mg/kg DMF. Mortality was 50% for males and 0% for females at 8000 mg/kg JP-5 Navy fuel, but was 40% and 50% at 2000 and 4000 mg/kg, respectively with JP-5 navy fuel treatment. Male body weights were decreased 8-13% at 500 to 4000 mg/kg DMF and were decreased 4-7% at 2000 to 8000 mg/kg JP-5 navy fuel. Active dermatitis at the treatment site was reported at 4000 mg/kg DMF and at all concentrations of JP-5 navy fuel. Possible adverse effect indicated: **The incidence of splenic extramedullary hematopoiesis and liver karyomegaly increased with JP-5 navy fuel at \geq 1000 mg/kg.** Not acceptable (Not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 12/7/01).

50444 - 003 052433 “Single Dermal administration Study of Marine Diesel Fuel in B6C3F₁ Mice,” (Litton Bionetics, Inc; National Toxicology Program Technical Report Series #: 310; NIH Publication #: 86-2566; 9/86). Marine diesel fuel was administered 1 time dermally to B6C3F₁ mice (5/sex/dose) at 5,000, 10,000, 20,000, 30,000 or 40,000 (the neat chemical) mg/kg. No reported treatment related effects occurred. UNACCEPTABLE (supplementary data). (Kishiyama & Silva, 12/7/01)

GENE MUTATION

Hydrocarbon

50444 - 003 052436 “Mutagenicity of Marine Diesel and JP-5 Navy Fuel in *Salmonella typhimurium*,” (National Toxicology Program, National Toxicology Program: TR 310; Research Triangle Park, Raleigh, NC; 9/86). Marine diesel fuel was evaluated for mutagenicity at concentrations ranging from 3 to 3333 μ g/plate (+ & - hamster and rat S9) using *Salmonella typhimurium* strains TA100, TA1535, TA1537 and TA98 and with JP-5 navy fuel (+/- S9) at 10 to 10000 μ g/plate using strains TA100, TA1535, TA97 and TA98. Cells were preincubated 20 minutes before plating in agar. There were two trials with triplicate plates. No evidence of mutagenicity was observed. This was not a FIFRA Guideline study. These data are supplemental. UNACCEPTABLE (no positive controls and insufficient information). (Kishiyama & Silva, 5/31/01).

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PETROLEUM DISTILLATES	2106	50792	788

GENE MUTATION

Paraffinic

50667 - 001 037857 "In vitro Microbiological Mutagenicity Studies of Phillips Petroleum Company Hydrocarbons Propellants and Aerosols." (Stanford Research Institute, 5/13/77) Tested propellants

A-17, A-31, A-108 and F plus aerosols D and E (See letter dated October 11, 1985 for components of A-31 and A-108 in 50667-001); tested with Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100 with and without rat liver activation for 8 and 48 hours at 1 to 50% of the atmosphere above the plates in a dessicator; tested twice on separate days; methylene chloride as the positive control was not effective in TA1537 or TA1538; no increase in reversion rate reported; cytotoxicity by decrease of spontaneous reversion rate with aerosol D, aerosol E and propellant F at higher concentrations; UNACCEPTABLE (no description of propellants A-17 and F and aerosols D and E; no individual plate counts or number of plates per trial; positive control was not effective in two strains). Gee, 10/28/87.

Paraffinic

50667 - 001 037858 "Salmonella typhimurium Mammalian Microsome Plate Incorporation Assay - Soltrol 130 - Final Report." (Hazleton, 8/13/82). Isoparaffinic hydrocarbons (Soltrol 130), C10-C13 isoparaffins, "assumed 100%"; tested with strains TA 1535, TA1537, TA98 and TA 100 with and without rat liver activation, single trial with triplicate plates; 0, 41.2, 123.5, 370.4, 1111.1, 3333.3 or 10000 ug/plate; no increase in reversion rate reported; UNACCEPTABLE - single trial with no demonstration of cytotoxicity at highest concentration and no analysis of test article to demonstrate exposure of Salmonella. JGee, 10/28/87.

Paraffinic

50667 - 001 037859 "Mouse Lymphoma Forward Mutation Assay - Soltrol 130 - Final Report." (Hazleton, 8/2/82) Isoparaffinic hydrocarbons (Soltrol 130), C10-C13 isoparaffins, "assumed 100%"; tested with rat liver activation at 0, 83, 118, 168, 240 343, 490, 700 or 1000 ug/ml (1000 stated to limit of solubility) and without activation at 0, 8.3, 11.8, 16.8, 24.0, 34.3, 49, 70, or 100 mg/ml; generalized protocol indicates a 4 hour incubation with test material; no increase in mutation frequency reported; UNACCEPTABLE (single trial, inadequate report - single page plus one table of summary data which contains only "total survival" in percent and "mutation frequency"; no individual plate counts, not total colony counts, no data for growth by days; only generalized protocol not specified for this study - the full report with raw data should be submitted.) JGee, 10/28/87.

CHROMOSOME EFFECTS

Paraffinic

50667 - 001 037860 "In vitro sister Chromatid Exchange in Chinese Hamster Ovary Cells - Soltrol 130 - Final Report." (Hazleton, 1/13/83) Isoparaffinic hydrocarbons, Soltrol 130, "assumed 100%"; tested in Chinese hamster ovary cells with and without rat liver activation at 0, 0.5, 1.7, 5.0, 17 or 50 mg/ml based on growth inhibition (no data): two hour exposure; scored 50 metaphases per concentration for sister chromatid exchanges; no increase in incidence reported; UNACCEPTABLE (only generalized protocol with a single page specific for this study and one table of summary data - need full report with cytotoxicity data to justify concentrations used. Explanation for including cyclohexane in the table when the solvent was stated to be DMSO.) JGee,10/28/87.

Chemical	Chemical Code	Tolerance Number	SB950 Number
MINERAL OIL (Solvent, Kerosene, Jet Fuel, Paraffin base)	401	149	754
PETROLEUM HYDROCARBONS	473	50444	789
PETROLEUM OIL (Unclassified),	765	50392	297
ISOPARAFFINIC HYDROCARBONS	1641	50667	713
PETROLEUM DISTILLATES (refined),	763	50427	476
PETROLEUM DISTILLATES	2106	50792	788

GENE MUTATION

Distillate

50792 - 003 067197 "*Salmonella*/Mammalian Microsome Mutagenicity Test (Ames Test) with Four Lube Oil Stocks," (Chevron Environmental Health Center, 7/24/81). Lube Oil Stocks (coded PE-2-2, Neutral Oil 20) were tested with *Salmonella typhimurium* TA100 with and without metabolic activation at 0 (vehicle = 0.1 ml DMSO), 0.01, 0.1, 1.0, 5.0 and 10 mg/plate (triplicate plates). No mutagenic effects were observed at any dose level with TA100 (with or without metabolic activation). Positive controls functioned as expected. NOT ACCEPTABLE (only one tester strain used). Not upgradeable. M. Silva, 9/19/88.

** 50792 003 067198 "Ames Test: Pre-incubation Assay of Light Mineral Oil, " (Gulf Life Sciences Center, 3/26/84). Light neutral oil (composition unspecified), was used on *Salmonella typhimurium* tester strains TA97, TA98, TA100, TA1537 and TA 1535 at 0 (vehicle = Pluronic F127--50% w/w in ethanol), 5.0, 10.0, 20.0 and 40.0 mg/plate with and without S-9 activation (triplicate plates). **Possible adverse effect** (an increase in mutagenicity was observed with TA98 +S-9 at \geq 20 mg/plate). No mutagenic effects were observed with other strains with or without activation at any dose level. Positive controls functioned as expected. ACCEPTABLE. M. Silva, 9/20/88.

** 50792 003 067199 "The Potential of Lube Oil Stocks to Mutate Histidine-deficient strains of *Salmonella typhimurium*, " (Chevron Environmental Health Center, Inc., 12/5/80). DG 2486 Neutral Oil 20 (100) was used on *Salmonella typhimurium* strains TA98, TA100, TA1535 & TA1537 at 0 (vehicle = DMSO), 0.1, 1.0 and 10.0 mg/plate with and without activation (duplicate plates). No increase in mutagenicity was observed at any dose with any of the tester strains. The positive controls functioned as expected. ACCEPTABLE. M. Silva, 9/20/88.

SUMMARY : Although study 067198 showed a weak mutagenic response with TA98, it is doubtful that petroleum distillates are point mutagens, based on the overwhelming negative response in the other two tests . In fact, the test material was taken to 40 mg/plate and only a weak mutagenic response was observed (twice background). Therefore, petroleum distillates, refined should not be considered to be a point or time-shift mutagen in the Ames test.

50792 – 007 113392 “Determination of Mutagenic Activity of 62-840 towards *Salmonella typhimurium* TA98 Using Modified Ames Assay,” (Chopra, C.; Bio-Mutatech, Inc., Woodbridge, Ontario, Canada; Project #: 00096; 9/18/86). *Salmonella typhimurium* strain TA98 was used in a mutagenicity assay with 62-840 (petroleum oil) at 0, 10, 20, 30, 40, 60, 80 and 100% (v/v) both with and without metabolic activation (hamster liver S9) for 48 hours (37°C). Strain TA98 was reported to be sensitive to UV light. There were no treatment-related gene mutation effects at any dose. It was not possible to adequately evaluate the mutagenic potential of 62-840, since there were no toxicity studies and only 1 *S. typhimurium* strain was used. Not acceptable and not upgradeable. There were insufficient data to determine the possibility of an adverse effect. M. Silva, 12/13/01

50792 – 004 088471 “Chronic Inhalation Toxicity of a Complex Mineral Oil Mist Atmosphere and Pathology of Repeated Oil Mist Inhalation,” (Kwon, B.K., Waritz, R.S., Stula, E.F.; Hazleton Laboratories, TRW Life Science Center, Falls Church, VA; 5/9/90). Mineral oil (#50 + finish adjuvants, such as bacteriostats, surfactants and minor proprietary ingredients) at 0, 5.5 mg/m³ + 1001 ppm acetone and 105.8 mg/m³ + 972 ppm acetone was administered by inhalation (5 days/week) to ChRCD rats (both sexes, 1 & 2 years), male Beagle dogs (2 years), ChRCD & CAF/JAX male mice (1 year) and gerbil (both sexes, 1 year). There was an increased alkaline phosphatase activity in lungs of male rats after 2 years of exposure. Relative lung weights (lung/bw) in both sexes of rat at 1 year and in males rats at 2 years (60% increase at 105.8 mg/m³). Histopathology in rat lungs at 1 and 2 years

occurred at 105.8 mg/m³ (lung oil granulomas, alveolar epithelial metaplasia to cuboidal cells). Dogs after 1 year developed lung oil granulomas. Lesions in the dogs and rats were less than 5% of the lung mass. Rats that were given a 10-month recovery period contained a slightly reduced amount of oil mist lesions. Gerbils and mice at 100 mg/m³ for up to 1 year did not develop lung oil granulomas. Possible adverse effect indicated: Rats and dogs developed lung oil lesions (granulomas) at 100 mg/m³. These data are supplemental. (Kishiyama and Silva, 12/11/01)