

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA  
**DISTILLATES OF MINERAL OIL**

Chemical Code # 401, Tolerance #: 149  
SB 950 #  
Original date: 12/18/01

I. DATA GAP STATUS

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

---

Toxicology one-liners are attached.

All record numbers through 117330 were examined.

\*\* indicates an acceptable study.

**Bold face** indicates a possible adverse effect.

File name: t011218

Original by: M. Silva, 12/18/01

## II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

### COMBINED, MOUSE

**149 - 018 117312** “Twenty-Four Month Dermal Carcinogenesis/Chronic Toxicity Screening Bioassay of Refinery Streams in C<sub>3</sub>H/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 C<sub>3</sub>H/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).

### CHRONIC TOXICITY, RAT

#### Subchronic Study:

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)

### CHRONIC TOXICITY, DOG

No study submitted.

### ONCOGENICITY, RAT

No study submitted.

### ONCOGENICITY, MOUSE

**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.

**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 C<sub>3</sub>H/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. **GO-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 which distill at the temperatures of these products. Possible adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 12/5/00).

#### REPRODUCTION, RAT

No study submitted.

#### TERATOLOGY, RAT

No study submitted.

#### TERATOLOGY, RABBIT

No study submitted.

## GENE MUTATION

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).

**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 ug/plate & 2-aminoanthracene, 2 ug/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 ul/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 mm<sup>3</sup> 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).

## CHROMOSOME EFFECTS

No study submitted.

## DNA DAMAGE

No study submitted.

#### MISCELLANEOUS STUDIES

149 - 015 117302 "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 LD<sub>50</sub> was calculated to be greater than 5000 mg/kg. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 11/9/00).