

Aug. 25, 2005

Lorraine E. Twerdok, Ph.D., DABT
Manager, Health Science
American Petroleum Institute
Petroleum HPV Testing Group
1220 L. Street, NW
Washington, DC 20005

Dear Dr. Twerdok:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Kerosene/Jet Fuel Category posted on the ChemRTK HPV Challenge Program Web site on March 3, 2004. I commend the API Petroleum HPV Testing Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, EPA is commenting only on the six fuel streams. If the Petroleum HPV Testing Group wishes to maintain the 14-member category, more detailed information on the eight solvents will need to be incorporated into the test plan and the final category analysis. We ask also that the Testing Group advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: M. E. Weber
N. Patel
J. Willis

**EPA Comments on Chemical RTK HPV Challenge Submission:
Kerosenes/Jet Fuel Category**

Summary of EPA Comments

The sponsor, The American Petroleum Institute's Petroleum HPV Testing Group, submitted a test plan and robust summaries to EPA for the Kerosenes/Jet Fuel category on December 30, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 3, 2004. The category includes 14 kerosene-range refinery streams.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Definition. EPA is commenting only on the six fuel streams addressed in detail in the test plan.
2. Category Justification. With the exclusion of distillates (petroleum), steam-cracked petroleum distillates, C5-C18 fraction, the category of six fuel streams is reasonable.
3. Physicochemical Properties and Environmental Fate. The submitted data for these endpoints are adequate for the purposes of the HPV Challenge Program. However, the submitter needs to clarify the reporting of the biodegradation results.
4. Health Effects. Data are adequate for the acute toxicity, repeated-dose toxicity, chromosomal aberration, and developmental toxicity endpoints for the purposes of the HPV Challenge Program. EPA reserves judgement on the data submitted for gene mutation and reproductive toxicity pending receipt of additional information. The submitter needs to address deficiencies in the robust summaries.
5. Ecological Effects. The acute toxicity data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program. EPA suggests that a study of chronic toxicity to aquatic invertebrates be considered for the category member hydrodesulfurized kerosene.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Kerosenes/Jet Fuel Category Challenge Submission

General

EPA recommends that the submitter remove distillates (petroleum), steam-cracked petroleum distillates, C5-C18 fraction ("the C5-C18 fraction"), CAS No. 68477-58-7, from the proposed category, or provide additional data to support its inclusion.

Inclusion of a matrix of available data and test substances/category member(s) would help assess data adequacy.

Category Definition

Category Members. The submitter defines the category as 14 kerosene-range refinery streams, known generically as "kerosene." Six of these streams are primarily used as fuels and the remaining eight as solvents. The streams are complex mixtures of paraffinic, isoparaffinic, naphthenic (cycloparaffinic), and aromatic (mainly alkylbenzene) hydrocarbons ranging in carbon number from C₅ to C₂₅ (mainly C₉ to C₁₆).

Olefins constitute less than 5% of the mixtures, by volume, and polycyclic aromatic hydrocarbon (3-7 fused rings) content is typically very low.

Only the six fuel streams are addressed in detail in the test plan. The submitter states that the eight solvent streams are sponsored by the International Hydrocarbon Solvents Consortium or the ACC Olefins Panel's Low Benzene Naphtha Group. EPA has only identified two of the eight that have been included in submissions to the HPV Challenge Program to date: CAS No. 64742-47-8 in the Fuel Oils Category, <http://www.epa.gov/chemrtk/fueloils/c13435tc.htm>, and CAS No. 64741-98-6, Low benzene naphthas category, <http://www.epa.gov/chemrtk/lowbenze/c13437tc.htm>.

Because of the lack of attention in the test plan to the eight solvent streams and how their data will be related to data on the other substances, EPA is commenting only on the six fuel streams. If the submitter wishes to maintain the 14-member category, more detailed information on the eight solvents will need to be incorporated into the test plan and the final category analysis, including any data reported by the other sponsors.

The six fuel streams are described as follows:

CAS Number	Stream Name	Description (carbon number; boiling pt.; composition)
8008-20-6	Kerosene (petroleum)	C9-C16; boiling point range ca. 150 °C to 290°C; 79-82% saturated, 1.3-2.5% olefinic, and 15.5-19.6% aromatic hydrocarbons
64742-14-9	Acid treated light distillate, light	C9-C16; boiling point range ca. 150 °C to 290°C; 76.19% saturated, 2.29% olefinic and 21.52% aromatic hydrocarbons
64742-31-0	Chemically neutralized light distillates (petroleum)	C9-C16; boiling point range ca. 150 °C to 290 °C; 78.95% saturated, 7.15% olefinic, and 13.9% aromatic hydrocarbons
64742-81-0	Hydrodesulfurized kerosene (petroleum)	C9-C16; boiling point range ca. 150 °C to 290°C; 77.2-82% saturated, 1.0-1.66% olefinic, and 18-21.4% aromatic hydrocarbons
64742-96-7	Heavy aliphatic solvent	C11-C16; boiling point range ca. 190 °C to 290°C; 99.16% saturated, and <1.0-13% aromatic hydrocarbons
68477-58-7	Distillates (petroleum), steam-cracked petroleum distillates, C5-18 fraction	

Supporting Substances. Jet fuels (e.g., Jet A, JP-8, etc.) are referenced in the submission because they are composed almost entirely of two sponsored category members, straight run kerosene (CAS No. 8008-20-6) or hydrodesulfurized kerosene (CAS No. 64742-81-0), and provide supporting data for the category. Information on sweetened kerosene (petroleum) (CAS No. 91770-14-9), hydrocracked heavy aromatic solvent naphtha (petroleum) (CAS No. 101316-80-7), Nigerian diesel fuel (CAS No. 68334-30-5), and other kerosenes/jet fuels is also included to characterize the category.

Category Justification

The submitter's category rationale is based on a similarity in compositions of the refinery streams. The submitter expects the similarities in the compositions of the streams to result in similar physicochemical, environmental fate, and toxicological properties. In general, the data provided by the submitter support the grouping of the category members with carbon number ranges of C9-C16, and the measured data and estimated values appear to show a similarity in the properties of these compounds. However, Test Plan Table 1, which reports compositional data, omits data for the C5-C18 fraction without explanation. Similarly, Appendix A provides the boiling ranges for all but the C5-C18 fraction. The C5-C8 substances in the C5-C18 fraction stream are expected to have physicochemical and environmental properties that differ from the components of the other fuel streams whose carbon numbers range from C9 to C16. For example, for the ecotoxicity endpoints, the C5 to C8 hydrocarbons will be more water-soluble than those of the other members and therefore of greater potential concern.

Therefore, unless the submitter can provide data to support the claim that the C5-C18 stream resembles the other category members in composition, properties and toxicity characteristics, the category is reasonable only with the deletion of the C5-C18 fraction.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for these endpoints for streams with carbon number ranges of C9-C16 are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water, and fugacity are adequate for streams with carbon number ranges of C9-C16 for the purposes of the HPV Challenge Program.

Biodegradation. The data provided by the submitter are adequate for streams with carbon number ranges of C9-C16 for the purposes of the HPV Challenge Program. However, the submitter reported ready biodegradation data for two fuel mixtures, with results expressed as a percentage of the theoretical oxygen demand (ThOD). In order to calculate ThOD for complex mixtures such as these, it is necessary to know the components of the mixture and their percentages of the total. It is also necessary to account for nearly all the mixture in order to have a ThOD value that can be used to express test results as % ThOD. In principle this can be done, but can be quite difficult or even impossible for very complex mixtures. The submitter needs to verify that ThOD was used and not the chemical oxygen demand (COD), which is often used as a surrogate for ThOD when mixtures are tested.

Health Effects (acute toxicity, repeated dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The data submitted for acute toxicity, repeated-dose toxicity, chromosomal aberrations, and developmental toxicity endpoints for streams with carbon number ranges of C9-C16 are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the data submitted for the gene mutation and reproductive toxicity endpoints pending receipt of additional information. The submitter needs to address deficiencies in the robust summaries.

Repeated-dose toxicity. A 28-day dermal study on straight run kerosene, API sample 83-09 in rabbits provides microscopic findings in testes at the high dose level (2000 mg/kg/day) and treatment-related organ weight changes in the mid- (1000 mg/kg/day) and high-dose male and female groups. However, a 13-week dermal study on hydrodesulfurized kerosene in rats failed to yield any treatment-related

toxicological effects at the highest dose tested (494 mg/kg/day), nor did a 28-day inhalation study in rats that was tested at single concentration of 24 mg/m³.

The 104-week dermal carcinogenicity study in mice is not adequate to address the repeated-dose toxicity endpoint owing to the use of only one sex and the absence of examination of parameters stipulated by OECD guidelines (e.g., hematology, clinical chemistry, and a complete histopathology).

Terse summaries were provided for dermal studies in rabbits (28-day) and in mice (13-week). EPA believes that on a weight-of-evidence basis these studies and those discussed above adequately address the repeated-dose toxicity endpoint. The submitter needs to upgrade the two non-robust summaries.

Genetic toxicity (gene mutations). EPA reserves judgement on this endpoint. (1) The submitter needs to identify which studies, if any, were conducted using closed systems, or what guideline modifications, if any, were employed to address the potential volatility of test substances. (2) Several robust summaries provided for the Ames test are given a Klimisch code of "3" with the statement "the standard Ames Assay is an unsuitable test system for insoluble petroleum products" (p. 57). However, additional detailed robust summaries for modified Ames and mouse lymphoma assays are designated a with Klimisch code of "1." The submitter needs to explain why this statement applies in some cases and not others. Finally, the submitter needs to address deficiencies in the robust summaries (see Specific Comments on the Robust Summaries).

Reproductive toxicity. A dermal OECD TG 421 study in rats using hydrodesulfurized kerosene was submitted for the endpoint. However, the study failed to induce significant toxicity or reach the limit dose required by the OECD guidelines at the maximum dose tested (494 mg/kg/day). The submitter needs to provide the rationale for selecting the dose levels and indicate whether there were any reproductive effects seen at the dose levels above 494 mg/kg/day from the preliminary two-week range finding study.

The data from rodent dominant lethal assays on Jet Fuel A and deodorized kerosene would not be adequate to satisfy the requirements for the reproductive toxicity endpoint. The study on Jet Fuel A did not show dose-/treatment-related effects at the highest concentration tested, and the fertility index in the negative control group was unusually low during the first week of mating. The summary for the study on deodorized kerosene provided insufficient details for an independent evaluation of data adequacy.

Ecological Effects (fish, invertebrates, and algae)

Data submitted for hydrodesulfurized kerosene are adequate to satisfy all acute ecological effects endpoints for streams with carbon number ranges of C9-C16. EPA suggests that a study of chronic toxicity to aquatic invertebrates be considered on hydrodesulfurized kerosene because the calculated Log Kow ranges of 3.3 -8.2 for the sponsored substances suggest a potential for chronic effects.

The reason for including ecotoxicological test data for sweetened kerosene (CAS No. 91770-14-9) and hydrocracked heavy aromatic solvent naphtha (CAS No. 101316-80-7) is unclear.

Specific Comments on the Robust Summaries

Human Health Effects

Genetic toxicity (gene mutations). Missing study details include whether the tests were conducted in closed systems, the test guidelines used, test material CAS numbers, response to positive controls, the number of replicates/concentration, the number of colonies per concentration counted, statistical methods used, culture conditions and the criteria for evaluating results.

Genetic toxicity (chromosomal aberrations). In the robust summaries for *in vivo* cytogenetics tests and *in vivo* SCE assays, missing study details include the guideline used, test material CAS numbers, positive

control use/response and criteria for evaluating the result.

In a robust summary for an *in vitro* sister chromatid exchange (SCE) assay in Chinese Hamster Ovary (CHO) cells on hydrodesulfurized kerosene (ref. #24), the submitter needs to address the following apparent reporting discrepancies: (1) in the absence of exogenous activation, the group mean SCEs/cell value for the positive control triethylenemelamine (TEM) was reported as 2.76, which is lower than the value of 9.20 reported for solvent controls; and (2) in assays both with and without metabolic activation, flask mean SCEs/cell were 3- to 4-fold greater for positive controls than for solvent or untreated controls, but the positive control values were not reported to be statistically significantly different from those for solvent or untreated controls despite no evidence of overlap of standard deviations from the mean.

Developmental toxicity. The submitter needs to provide the identity and composition of the test material for the developmental toxicity study in rats via whole-body inhalation (ref. #7).

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.