

December 1, 2005

Thomas M. Gray, M.S., DABT
Senior Toxicologist
The American Petroleum Institute
Petroleum HPV Testing Group
1220 L. Street, N.W.
Washington, DC 20005

Dear Dr. Gray:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Heavy Fuel Oils Category posted on the ChemRTK HPV Challenge Program Web site on July 2, 2004. I commend The American Petroleum Institute 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, we ask that the Petroleum HPV Testing Group advise the Agency, within 90 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: N. Patel
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission: Heavy Fuel Oils Category

Summary of EPA Comments

The sponsor, The American Petroleum Institute, submitted a test plan and robust summaries to EPA for the Heavy Fuel Oils category dated June 17, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on July 2, 2004. This category contains both finished products (residual fuels) and the primary refinery streams from which they are blended.

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

1. Category Justification. EPA agrees with the rationale for the heavy fuel oils category and subdivision of the refinery streams into seven subcategories reflecting their processing history. However, the health data supporting the category and the subcategory approach are inconclusive.
2. Physicochemical Properties. The submitter needs to provide melting point data for more category members. The submitter also needs to clarify some discrepancies in the boiling point data and show how the vapor pressure, partition coefficient, and water solubility data reflect the substances in the Test Plan; otherwise, the submitter needs to provide data that are more reflective of these substances. The submitter needs to provide certain SMILES notations.
3. Environmental Fate. EPA recommends that the submitter provide additional discussion of the susceptibility to biodegradation of hydrocarbons in specific carbon number ranges.
4. Health Effects. The acute toxicity data are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's proposed *in vitro* gene mutation and chromosomal aberration tests, but reserves judgment on new testing for repeated-dose, reproductive and developmental toxicity endpoints pending submission of all available data.
5. Ecological Effects. The acute toxicity data are adequate for the purposes of the HPV Challenge Program, except that acute toxicity studies are needed in all three aquatic species on the atmospheric residue in order to address the concern for organometals content. EPA also recommends a chronic toxicity study in aquatic invertebrates on the residual fuel oils because of the calculated Log Kow ranges.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Heavy Fuel Oils Category Challenge Submission

Category Definition

The submitter proposes a category that covers two groups: finished residual fuels that are marketed to consumers (CAS Nos. 68476-33-5 and 68553-00-4), and the 30 process streams from which the finished residual fuels are blended. The submitter has subdivided the process streams into seven subcategories based on processing history:

- 1) atmospheric residual: CAS Nos. 64741-45-3, 64742-78-5, 68333-22-2, 68607-30-7, 70592-79-9, and 68476-32-4;
- 2) atmospheric distillate: CAS Nos. 68410-00-4 and 68783-08-4;
- 3) vacuum residual: CAS Nos. 68512-62-9 and 70913-85-8
- 4) vacuum distillate: CAS Nos. 64741-57-7, 64742-59-2, 64742-86-5, 68955-27-1, 70592-76-6, 70592-77-7, and 70592-78-8
- 5) cracked residual: CAS Nos. 64741-62-4, 64741-75-9, 64741-80-6, 68187-58-6, 68478-17-1, and 68783-13-1

6) cracked distillate: CAS Nos. 64741-61-3, 64741-81-7, 68333-26-6, 68333-27-7, and 70955-17-8, and
7) reformer residual: CAS Nos. 64741-67-9 and 68478-13-7.

The category members are composed mainly of hydrocarbons ranging in carbon number from C20 to C50, although some members contain hydrocarbons with carbon numbers as low as C7. The category members are complex mixtures and contain various amounts and types of polycyclic aromatic hydrocarbons; heterocyclic compounds containing sulfur, nitrogen, and oxygen; and organometallic compounds. There is no specific information available on the compositions of the category members, and it is not possible to define their exact compositions because there is so much variability associated with these streams and the compositions vary widely as a function of many factors (e.g., finished market product specifications, materials available at a given refinery at a given time, etc.).

Some data from other HPV Challenge program test plans--Gas Oils, Asphalt, Aromatic Extracts--are used to support the heavy fuel oils category.

Category Justification

EPA agrees with the rationale for grouping the members of the heavy fuel oils category. EPA also agrees with the assumption that the finished residual heavy fuel oil members will have properties that are bounded by the process streams used to blend them, and that it is appropriate to further frame the process streams into seven subcategories.

With regard to developing physicochemical and environmental fate data, the submitter considers the category as a whole and anticipates that these properties will vary as a function of carbon number range and component type (e.g., aromatic, aliphatic). No pattern could be identified for pour point. The boiling points of the category members appear to depend more on the carbon number ranges of the hydrocarbons in the process streams than on the process histories. The other physicochemical and environmental fate properties, such as octanol/water partition coefficient and environmental distribution, have few or no data associated with them, but the submitter anticipates that the properties will depend on a combination of carbon number and molecular type (e.g., aromatic or aliphatic). This pattern is consistent with other petroleum product categories, but provides only limited support for the grouping since no consistent pattern that distinguishes this category from others can be identified.

For the health effect endpoints, while the rationale that the process history of a refinery stream determines its chemical composition appears to hold for some of the process streams (e.g., atmospheric distillate), it does not appear to be consistently true. For example, atmospheric residual contains both high- and low-sulfur members (CAS Nos. 68476-32-4 and 68607-30-7), cracked residual contains streams with predominantly aromatic components and those that appear to be predominantly non-aromatic (CAS Nos. 68187-58-6 and 64741-80-6), and vacuum residual (two members) has one member that has undergone solvent extraction and one member that has not (implying significant overall compositional differences). These and other differences between members within one process history subcategory appear sufficient to cause significant variations in test results. It is therefore unclear from the information in the test plan how toxicity for one member of a subcategory will reasonably represent the toxicities for the other members. At a minimum, additional detailed discussion is needed to support this approach. The acute toxicity and *in vitro* mutagenicity and chromosomal aberrations information appears to be consistent across the subcategories, indicates a generally uniform response across the entire category, and supports the category. The submitted acute toxicity and mutagenicity data do not, however, support the proposed subcategories approach because for most of the subcategories, data for only one subcategory member (or no data at all) were provided for these health effect endpoints, precluding an evaluation of whether test results for one member of a subcategory are representative of other subcategory members or whether a trend of toxicity is established within the subcategory.

For repeated-dose studies, data indicate a range of no-observed-adverse-effect levels (NOAELs) across the subcategories (which supports the subcategory approach), but only one test is available for each of

six subcategories, and no data are available for the other two subcategories. Therefore, no conclusion can be reached about how representative the available repeated-dose studies are for each subcategory, and the data supporting the category or the subcategory approach are inconclusive. For the developmental toxicity endpoint, data across the subcategories indicate significant differences, but no information is available to support consistency of data within each subcategory because only one test is available for each of five subcategories, and no data are available for the other three subcategories. Therefore, the data are inconclusive and cannot be used to support the subcategory approach. No reproductive toxicity data were provided.

Finally, acute fish and invertebrate toxicity data are consistent across the category and support the grouping, but the available algal toxicity data vary considerably.

Collectively, the physiochemical, environmental fate and ecotoxicity data provide limited support for grouping the chemicals into a category and subcategories; however, the health data as submitted are inconclusive for supporting the subcategories approach.

Test Plan

General Comment

It would be helpful to include a matrix of available data for each subcategory and residual fuel oils.

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

Melting point. The data are adequate for the individual chemicals listed. However, the data are not sufficient to address this endpoint for the category. The submitter provided measured pour point data for 8 of the 32 substances in the heavy fuel oils category and intends to use read-across to interpret data gaps. The use of the read-across approach is inappropriate in this case because pour points are not predictable and are too sensitive to impurities. The submitter needs to provide data for more of the representative CAS numbers listed in Figure 1 of the Test Plan, in order to present a more complete picture of this endpoint for these substances.

Boiling point. EPA reserves judgment on the adequacy of the boiling point data, pending clarification by the submitter of the following points:

The submitter provided data for Bunker C Light Fuel Oil, Bunker C (Alaska) Fuel Oil, and Bunker C Fuel Oil. These values are of limited value because the submitter did not relate the compositions of these substances to the category members. The submitter needs to address this issue.

The submitter provided data on boiling point ranges for 26 of the 32 substances in the heavy fuel oils category. However, where the reported value is the distillation range given in the CAS number definition, this may not always represent the boiling point ranges of the substances included under the definition. For example, the definition for CAS No. 64741-62-4 gives a distillation range of >350 °C. Yet data provided by the submitter from commercial brochures or material safety data sheets, give two distillation ranges of 150-600 °C and 202-511 °C that are well outside the boiling point range in the CAS number definition. Without other comparisons of measured data with the defined distillation ranges for substances covered under a given CAS number definition in the robust summary, it is not certain whether the distillation range accurately represents the boiling point ranges of the substances covered under the other subcategories. The submitter needs to address this point.

It appears that the submitter intends to use the data given for 26 of the substances in the category to read across to the six category members that are without data. As the subcategories are based on process history, it is expected that a read-across evaluation for members of a subcategory will be based

on data obtained from a representative substance within the subcategory. Given the differences in the compositions in the heavy fuel oils between subcategories, a read-across approach across subcategories may not be appropriate in all cases. Consequently, the submitter needs to provide additional information and justification for any reading across between subcategories.

Vapor pressure. The data provided are not adequate for the purposes of the HPV Challenge Program for the following reasons:

The submitter provided Reid vapor pressure data for a finished residual fuel oil (CAS No. 68476-33-5), for a refinery process stream, catalytically cracked clarified oil (CAS No. 64741-62-4), and for individual compounds that are stated to be representative of the hydrocarbons and other components of the heavy fuel oils. The submitter states that the data reflect the “varied nature of these substances”. However, the submitter does not correlate the vapor pressures to the composition of the test substances. Furthermore, it is not clear from the submitter’s discussion in the robust summary and the test plan (pages 21-22) how these data are to be used to describe the vapor pressures of the category members. The submitter simply states that because of the complexity in the composition of the heavy fuel oils, the partial pressures of the individual compounds in these substances may be low, but does not provide a quantitative approach for determining the vapor pressures of the heavy fuel oils from the estimated vapor pressures on pages 7-8 of the robust summary. For these reasons and the limited availability of measured vapor pressure data, it can not be determined whether the values provided are representative of the other category members. The submitter needs to clarify how these data are representative of the category members presented in Figure 1 of the Test Plan. Otherwise, the submitter needs to provide data that adequately represent the category.

Partition coefficient. The data provided are not adequate for the purposes of the HPV Challenge Program. The submitter provided measured or estimated partition coefficient data for series of compounds that represent the hydrocarbon components found in heavy fuel oils: *n*-alkanes, *iso*-alkanes, cycloalkanes, olefins, aromatics, quinolines, cyclic carboxylic acids, thiophene, and dibenzothiophenes. The partition coefficients range from 1.7 to 25. The estimated values were derived from EPIWIN (EPA 2000); the submitter did not provide specific structural information on the compounds used in the calculations. In any event, the range of estimated values provided by the submitter is not useful because the data are not correlated with the compositions of the various category members. The submitter needs to clarify how these data represent the category members in Figure 1 of the Test Plan. Otherwise, the submitter needs to provide data that is adequately representative. An HPLC octanol-water protocol might help provide the range of Kow values that are in each mixture.

Water solubility. The data provided are not adequate for the purposes of the HPV Challenge Program. The submitter reported similar measured water solubilities for three finished residual fuel oils in water: No. 6 fuel oil, Bunker C heavy fuel oil and Bunker C light fuel oil. Two other water solubilities for finished residual fuel oils [Bunker C heavy fuel oil, and catalytically cracked clarified oil (CAS No. 64741-62-4)] were given in the robust summary but no descriptions of the test methods were provided. Therefore, the quality of the data could not be evaluated. The water solubilities cannot be correlated to the composition of the test substances, especially to the proportion of one and two-ring aromatics, or specific compositional information for the process streams, so it is uncertain whether the water solubilities given for the finished residual fuel oils will adequately represent the solubilities of the process streams. Therefore, reading across from these data to the other 30 category members is not appropriate. The submitter needs to clarify how these data represent the category members in Figure 1 of the Test Plan. Otherwise, the submitter needs to provide data that adequately represent the category.

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

Photodegradation. The data provided by the submitter for this endpoint are adequate for the purposes of the HPV Challenge Program.

Stability in water. The information provided by the submitter for this endpoint are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitter has provided a technical discussion on the biodegradation of crude oil in water based on a review of information from the literature and commercial sources. In general, the information presented by the submitter provides an adequate overview of the biodegradability of crude oils in water. However, EPA recommends that the submitter provide additional discussion of the susceptibility of hydrocarbons in specific carbon number ranges to biodegradation. Generally, C1-C4 hydrocarbons are biodegraded by select organisms, whereas hydrocarbons with carbon numbers >C22 are typically not available to degrading organisms (ATSDR 1999). This technical discussion should also address the biodegradation of other fractions of significance, if applicable.

Fugacity. The submitter reports a summary of the distributions of 49 model hydrocarbons that were calculated with a Mackay Level I EQC fugacity model. The submitter needs to state in the robust summary that it used a level I fugacity model. The level I distribution data provided are adequate for the endpoint in this case.

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

Acute toxicity. The acute toxicity endpoint is adequately addressed for the purposes of the HPV Challenge Program. The available data are consistent through subcategories and show low, and similar, acute toxicities of the test substances.

Genetic toxicity. EPA agrees with the submitter's proposed testing for the *in vitro* gene mutation (modified Ames test) and chromosomal aberration toxicity endpoints on residual fuel oils and atmospheric residue, atmospheric distillate, cracked distillate and reformer residue subcategories.

Repeated-dose and developmental toxicity. Data are available for both repeated-dose and developmental toxicity endpoints on one category member for five subcategories. Data are also available for repeated-dose toxicity for residual fuel oils. No repeated-dose toxicity data were submitted for the vacuum residues and reformer residues subcategories, and no developmental toxicity data are available for residual fuel oils. The submitter proposed a combined repeated-dose/reproductive/developmental toxicity screening test following OECD TG.422 for the reformer residues subcategory and a combined reproductive/ developmental toxicity screening test following OECD TG 421 for residual fuel oils

From the submitted data it appears that cracked residues is the most toxic subcategory and atmospheric residues the least toxic. Several studies are available for both endpoints for some of the subcategories, but only one robust summary is provided, making it difficult without all available data to conclude that the study is representative and presents the worst case scenarios for the subcategory. The submitter needs to provide summaries for all studies mentioned, and better compositional data on the tested subcategory members, to help reveal the determinants of toxicity. The submitter also needs to explain any decisions to use one study rather than another to represent the toxicity of a category or subcategory. EPA reserves judgment on the need for the proposed testing pending receipt and evaluation of all available data.

Reproductive toxicity. No data were provided for this endpoint. Data on histopathological examination of male reproductive organs and a study to determine potential effects on gonadal function, reproductive

organs and mating behavior in male rats were submitted on atmospheric distillates, vacuum distillates, and cracked residues. According to the SIDS manual, reproductive toxicity is addressed "if existing data on the chemical include a developmental toxicity study and a 90-day repeated-dose study that sufficiently documents that reproductive organs were examined histologically and indicate no effects." The robust summary for a 13-week repeated-dose dermal toxicity study on cracked distillates states that female reproductive organs were examined microscopically, but no specific information is provided. The submitter needs to provide summaries of this information for the reproduction toxicity endpoint. The submitter also needs to provide any information on histopathological examination of reproductive organs from the nonsummarized available repeated-dose toxicity studies.

Ecological Effects (fish, invertebrates, and algae)

The acute toxicity data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program except for the atmospheric residuals subcategory. For the latter, in order to address a concern for the high level of organometals, acute toxicity testing on all three aquatic species needs to be conducted on CAS No. 63741-45-3.

EPA suggests that a chronic toxicity study on aquatic invertebrates be considered on the residual fuel oils (CAS No. 68476-33-5) because the calculated Log Kow values range from 1.7 to 25 for the category members.

Specific Comments on the Robust Summaries

Physicochemical Properties

The submitter needs to incorporate SMILES notations for all EPIWIN calculations where SMILES was used.

Vapor pressure. According to the submitter, the vapor pressure values given on pages 7-8 were calculated using an accepted estimation method (EPIWIN); however, specific information on the structures used to calculate the vapor pressures was not given in the robust summary. EPA was able to derive the same vapor pressures for the majority of the listed compounds using the SMILES notation. However, it appears that in some of the cases the submitter used measured values from the experimental database in EPIWIN. In other cases (n-alkane, C7; isoalkane, C7; olefins, C7; quinoline) the calculated and measured values are very similar. If the submitter has provided measured data for the vapor pressures of the representative compounds, these should be identified in the robust summary.

Human Health Effects

Acute toxicity. The submitter needs to identify the test substances and/or CAS numbers for the studies submitted for vacuum distillates and cracked residues, coker heavy gas oil, sample F-97. It is not clear if the tested substances are category members.

Repeated-dose, genetic, and developmental toxicity. The submitter needs to provide CAS numbers for some of the test materials.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

References

ATSDR.1999. Agency for Toxic Substances and Disease Registry. Toxicological Profile for Total Petroleum Hydrocarbons. p 73-74 (<http://www.atsdr.cdc.gov/toxprofiles/tp123-c5.pdf>).

EPA. 2000. Estimation Program Interface (EPI) Suite, version 3.10. U.S. Environmental Protection Agency, Washington, DC.