

August 14, 2000

Lorraine E. Twerdok, Ph.D., DABT  
Manager, Health Sciences  
American Petroleum Institute  
1220 L. Street, N.W.  
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 Petroleum Cokes, CAS Nos. 64741-79-3 and 64743-05-1, submitted April 7, 2000. I commend the American Petroleum Institute for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website 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 attached Comments on the Chemical RTK website within the next few days. As noted in the comments, we ask that API advise the Agency, within 60 days of the posting on the Chemical RTK website, how it intends to pursue its activities on these chemicals. Please respond either by email ([oppt.ncic@epa.gov](mailto:oppt.ncic@epa.gov), [hpv.crtk@epa.gov](mailto:hpv.crtk@epa.gov), or [chem.rtk@epa.gov](mailto:chem.rtk@epa.gov)) or by regular mail to:

Carol Browner, Administrator  
US Environmental Protection Agency  
P.O. Box 1473  
Merrifield, VA 22116  
Attention: Chemical Right-to-Know Program

EPA will post your response on the Chemical RTK website.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button 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](mailto:tsca-hotline@epa.gov).

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

Sincerely,

*/s/*

Oscar Hernandez, Director  
Risk Assessment Division

Attachment

cc: W. Sanders  
C. Auer  
N. Patel  
A. Abramson

## **EPA Comments on Chemical RTK Challenge Submission: Petroleum Cokes**

### **SUMMARY OF EPA COMMENTS**

The sponsor, the American Petroleum Institute Petroleum HPV Testing Group, submitted a Test Plan and Robust Summaries to EPA. EPA posted the submission on the ChemRTK website on April 21, 2000. The proposed information-gathering plan is for two substances, petroleum (green) coke (CAS No. 64741-79-3 ) and calcined coke (CAS No. 64743-05-1), considered by the sponsor to constitute a petroleum cokes category.

EPA has reviewed this submission and found that, in general, the test plan and robust summaries were well-organized and easy to follow. The Agency has reached the following conclusions:

1. The submission supports the proposed analogy between the two substances on the basis of substance composition and existing data.
2. EPA agrees with the proposed Test Plan for physicochemical properties, environmental fate, and health effects.
3. EPA suggests the following changes to the environmental effects Test Plan: conduct a chronic toxicity test in daphnid with green coke (CAS # 64741-79-3) in lieu of the proposed acute toxicity tests in daphnids and algae, in order to optimize bioavailability of the leachable constituents.
4. EPA agrees with the plan to conduct earthworm and terrestrial plant studies.
5. As a general matter, EPA prefers to apply the term "category" to groups of three or more chemicals. Such groups provide a range of endpoint data for similar chemicals that may allow one to identify trends and then use those trends to estimate missing data. On the other hand, extrapolation of data from one of a pair of chemicals to the other, or analog assessment, requires a close and well-supported (not merely hypothetical) relationship between the two chemicals for each endpoint in question. For more on these topics see "Guidance for Development of Chemical Categories in the HPV Challenge Program" and "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program", at [www.epa.gov/opptintr/chemrtk/guidocs.htm](http://www.epa.gov/opptintr/chemrtk/guidocs.htm).

EPA is asking the Sponsor to advise the Agency within 60 days how it intends to pursue activities on the chemicals in its submission.

### **EPA COMMENTS ON THE PETROLEUM COKES CHALLENGE SUBMISSION**

EPA's comments are organized as follows: General; Substance Definition; Test Substance Justification; Test Plan; Specific Comments on Robust Summaries.

#### **General**

EPA views the inclusion of a Plain Language Summary as helpful. The Test Plan in general is very inclusive and thorough.

#### **Substance Definition**

The definition is clearly presented and complete, with appropriate care and attention to the substance descriptions, including those for various physical forms of the materials.

### **Test Substance Justification**

The submission presents a case for considering two petroleum coke substances as a “category” (although EPA prefers to reserve the term “category” for groups of three or more chemicals, which provide a range of endpoint data for similar chemicals that may allow one to identify trends and estimate missing data from the trends). EPA believes the presentation adequately supports this proposal. It discusses the similarities and differences between the two substances, including relative hydrocarbon and metal levels, and shows the relevance of existing data on the subject and related materials.

### **Test Plan**

#### Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

EPA concurs that testing and modeling of physicochemical endpoints need not be conducted for green or calcined petroleum coke because the properties (mixtures, mostly carbon, amorphous with no unique structure) of these substances preclude developing meaningful data.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution). For the same reasons noted above under Chemistry, EPA concurs that these substances are not amenable to environmental fate testing/modeling.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity). EPA agrees with the proposed plan not to conduct acute toxicity tests; to conduct a reproductive/developmental toxicity test on green coke and extrapolate the results to calcined coke; and to apply the existing genetic toxicity data on green coke to calcined coke. Although EPA understands that the basis for choosing to test green coke is its residual hydrocarbon content, the Agency is also interested in the potential effects of the metal constituents in coke. From the information in the submission plus the analysis of the test substance used in the two-year studies (IRDC 1985 as cited in the submission), EPA assumes that the type and amount of metals in green and calcined coke are similar.

Environmental Effects. The sponsor proposes to conduct acute toxicity tests with green coke in algae and daphnids, and terrestrial toxicity tests with green coke in earthworms and terrestrial plants. EPA agrees with the plan to conduct the terrestrial toxicity tests, on the grounds that one use of petroleum coke involves application to soils. EPA has the following comments on the aquatic toxicity test plan:

(1) EPA suggests that the sponsor conduct a chronic toxicity test in daphnids (OECD Guideline 211) and not perform acute toxicity tests in daphnids or algae. Testing must address the potential for hydrocarbons and metals in green coke to leach into water. Acute toxicity testing in this case is not likely to be informative, since such leaching may be too slow to result in effects during 96 hours. A 21-day daphnid chronic test allows a longer time for non-carbon constituents to enter the water column and become bioavailable.

(2) The sponsor suggests that fish acute testing is unnecessary for these substances, generalizing that daphnids are more sensitive than fish to environmental chemicals. EPA's position is that when acute testing is necessary, complete base-level testing (fish, invertebrates, aquatic plants) is required for SIDS-level reviews. Existing toxicity data for particular types of chemicals may make it possible to omit one or more test species on a case-by-case basis. However, EPA is not arguing for fish acute testing of petroleum coke, because the Agency is suggesting that the sponsor conduct a chronic daphnid test instead of acute tests.

## **Specific Comments on Robust Summaries**

The only robust summaries submitted described health effects studies. EPA evaluated each acute, repeat dose, and genotoxicity robust summary and determined that all were adequate summaries for the purposes of the U.S. HPV Challenge Program. The robust summaries for carcinogenicity and “human experience”, while not among the required SIDS endpoints, were reviewed for their relevance to the test plan.

**Acute Toxicity.** The “robust summary” for acute inhalation toxicity reported on page 6 of the Petroleum Coke robust summary submission does not summarize a study *per se*, but refers to three different “repeat-dose” studies to show that high levels (daily doses for 6 hours via inhalation of up to 30.7 mg/m<sup>3</sup> in rats/monkeys for two years and 50 mg/m<sup>3</sup> in rats for five days) did not result in any treatment-related mortalities.

*Brief Summary of Five-Day Study:* This study was reported on pages 9-10 of the robust summary package. Rats were exposed (nose-only) to high levels of coke (50 mg/m<sup>3</sup>) for 6 hours/day for five days and then followed for 63 days (serial sacrificing at 7, 28, and 63 days). Important results related to acute toxicity: lung inflammation (green coke more severe than calcined coke) and no mortalities.

*Brief Summary of the Two-Year Studies:* Specific comments on this study are presented in the repeat-dose toxicity discussion below. For the acute toxicity endpoint, it is important to recognize that both rats and monkeys were exposed to daily doses of up to 30.7 mg/m<sup>3</sup> for two years without any treatment-related mortalities.

On the basis of the information provided, EPA agrees with the sponsor that no acute toxicity test for either petroleum coke is needed.

**Repeat Dose Toxicity.** The robust summaries for repeat dose inhalation toxicity reported on pages 6-8 and 11-12 of the Petroleum Coke robust summary submission summarize a two year inhalation study conducted with Sprague-Dawley rats and monkeys (*Macaca fascicularis*), respectively, both under whole-body exposure conditions with daily exposures for 6 hours/d, 5 days/wk at coke levels of 0, 10.2 and 30.7 mg/m<sup>3</sup>.

*Results in Rats:* Expected lung effects (inflammatory response) likely due to dust overload were observed. No changes were noted with respect to clinical condition, growth rates, ophthalmological findings or serum biochemistry. EPA agrees that the statistically significant findings relative to the segmented neutrophils and lymphocytes are inconsistent and “probably indicative of mild inflammatory reaction.” However, an important result not presented in the robust summary was the significant non-neoplastic (metaplasia, sclerosis, and in females keratin cysts) changes in the lungs at the high dose level.

*Results in Monkeys:* Expected lung effects (inflammatory response) likely due to dust overload were observed. No changes noted with respect to clinical condition, growth rates, ophthalmological findings, serum biochemistry, or hematological parameters.

There is no plan to further test either green or calcined coke for repeat dose toxicity effects, and EPA agrees that the 2-year studies adequately address this SIDS endpoint.

**Genotoxicity Studies.** Seven (four *in vitro* and three *in vivo*) different robust summaries were submitted, and all used green coke as the test substance (pages 12-18 of the robust summary package). All are adequate summaries and EPA has the following comments:

*Basis for dose selection.* It would be helpful if the basis for the doses used in all assays was described.

*Cytogenetic assay (summary on page 16).* The target tissue from which the samples were taken should be noted.

*Cytogenetic assay (summary on page 17).* The basis for the claim of misreading slides should be indicated (slides mislabeled, mistakenly read, etc.).

EPA agrees that the genotoxicity data from green coke are expected to apply to calcined coke.

**Followup Activity**

EPA requests that the Sponsor advise the Agency within 60 days how it intends to pursue activities on the chemicals in its submission.