November 9, 2009

Rich Davi
Global Product Stewardship
And Regulatory Affairs Manager
ExxonMobil Chemical Company
1545 Route 22 East
Annandale, New Jersey 08801

Dear Mr. Davi:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Gases, Petroleum, Extractive, C4-6 Isopentene Rich Reaction Products w/Methanol, Ether Fraction, Hydrogenated, Cracked, Isopentene Fraction (C4-6 IRRP Fraction) posted on the ChemRTK HPV Challenge Program Web site on November 12, 2008. I commend ExxonMobil Chemical Company 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 ExxonMobil 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 me 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/*

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: O. Hernandez
R. Lee
J. Willis

**EPA Comments on Chemical RTK HPV Challenge Submission:**
**C4-6 IRRP Fraction**

## Summary of EPA Comments

The sponsor, ExxonMobil Chemical Company, submitted a test plan and robust summaries to EPA for the complex mixture identified as gases, petroleum, extractive, C4-6 isopentene rich reaction products with methanol, ether fraction, hydrogenated, cracked, isopentene fraction (C4-6 IRRP Fraction, CAS No. 108083-44-9) dated September 25, 2008. The submitter provided data for two major constituents: *n*-hexane (CAS No. 110-54-3, 24%) and cyclohexane (CAS No.110-82-7, 21%), and for *n*-heptane (CAS No. 142-82-5) as a proposed analog for the third major constituent, 2,4-dimethylpentane (CAS No. 108-08-7, 35%). EPA posted the submission on the ChemRTK HPV Challenge website on November 12, 2008.

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

1. Analog Justification. EPA agrees with evaluating the mixture in this case by using toxicity information on the three major constituents. The constituents *n*-hexane and cyclohexane are reasonable representatives of the toxicity of approximately 45% of the mixture. However, the submitter's proposal to use *n*-heptane as an analog for 2,4-dimethylpentane is not supported for health effects or biodegradation.

2. Physical Chemical Properties. Available data are adequate for the purposes of the HPV Challenge Program.

3. Environmental Fate. Available data are adequate for the photodegradation, stability in water, and fugacity endpoints for the purposes of the HPV Challenge Program. Biodegradation data are adequate for cyclohexane and hexane. The submitter needs to provide adequate biodegradation data for 2,4-dimethylpentane or on the sponsored mixture.

4. Health Effects. Existing data are inadequate for these endpoints for the purposes of the HPV Challenge Program because there are no health effects data on a major constituent, 2,4-dimethylpentane, and the proposed analog for 2,4-dimethylpentane is not supported. The submitter needs to provide adequate data to characterize the sponsored substance.

5. Ecological Effects. Available data are adequate for acute fish, daphnia, and algal toxicity for the purposes of the HPV Challenge program.

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

## EPA Comments on the C4-6 IRRP Fraction Challenge Submission

### Testing Approach and Analog Justification

The sponsored chemical is a complex mixture of approximately 18 constituents (Test Plan, page 6, Table 1). Most are saturated aliphatics (87%) with about 6% methoxypentanes and furans. The three major constituents (about 80% of the mixture) are *n*-hexane (CAS No. 110-54-3, 24%), 2,4-dimethylpentane (CAS No. 108-08-7, 35%) and cyclohexane (CAS No.110-82-7, 21%). The submitter proposes to use data for these three major constituents to characterize the SIDS endpoints for the mixture.

EPA believes that in this case this approach is reasonable in principle. However, the sponsor proposes a different chemical (*n*-heptane, CAS No. 142-82-5) as an analog for *n*-hexane for the biodegradation endpoint and for 2,4-dimethylpentane for biodegradation and all of the aquatic toxicity and human health endpoints. *n*-Heptane is a very minor constituent of the sponsored substance at only 0.1%, while 2,4-dimethylpentane is the highest-concentration constituent of the mixture. Under the submitter's proposed approach, the submitted information for the three representative constituents *n*-hexane, cyclohexane, and

*n*-heptane (as an analog for hexane and 2,4-dimethylpentane) would reflect about 80% of the mixture for most endpoints.

For biodegradation, EPA considers *n*-heptane to adequately represent *n*-hexane but not 2,4-dimethylpentane (see discussion under Test Plan, below).

For health effects, there is no discussion in the Test Plan to justify of the use of the linear molecule heptane as an analog for the branched 2,4-dimethylpentane. Given the likely differences in metabolism products and their relevance to potential toxicity, and the lack of a technical discussion on the appropriateness of the use of *n*-heptane as an analog for 2,4-dimethylpentane, EPA considers the justification for the use of these analog data inadequate for the purposes of the HPV Challenge Program. Thus, EPA believes that the test plan for health effects reflects only about 45% of the mixture composition.

For ecological effects, the submitter's approach using *n*-heptane data to characterize 2,4-dimethylpentane is reasonable.

Lesser constituents. Benzene (CAS No. 71-43-2) has been assessed in the OECD HPV program and the information can be accessed at the following link: http://cs3-hq.oecd.org/scripts/hpv/. TAME (CAS No. 994-05-8) has been assessed in the OECD HPV program and the information can be accessed at the following link: http://ecb.jrc.ec.europa.eu/esis/.

**Test Plan**

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

The submitted data are adequate for these endpoints for the purposes of the HPV Challenge Program. The submitter provided no data for the mixture but summarized data for the three major constituents. EPA recommends that the submitter report the range of values available for all individual constituents in addition to the individual values for representative chemicals.

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

Existing data are adequate for photodegradation, stability in water, and fugacity for the purposes of the HPV Challenge Program.

*Biodegradation*. The submitter provided OECD 301F test data for cyclohexane and *n*-heptane, the latter intended to read across to both *n*-hexane and 2,4-dimethylpentane (heptane and "heptanes" are both listed as constituents of the mixture at levels of 0.1% and 3.1%, respectively).

EPA considers *n*-heptane to adequately represent *n*-hexane, as they are both linear and only differ by a single carbon. However, 2,4-dimethylpentane is branched at both ends and is not expected to degrade as rapidly as the linear alkanes. The submitter needs to provide ready biodegradation data for 2,4-dimethylpentane or on the sponsored mixture in accordance with OECD TG 301.

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

The test plan proposes that data presented for three principal constituents of the sponsored chemical mixture satisfy the human health SIDS endpoints. EPA accepts this approach but disagrees with the proposed use of *n*-heptane data to characterize the constituent 2,4-dimethylpentane (as discussed above).

With each representative constituent evaluated independently for data adequacy, existing data are adequate for all human health endpoints for *n*-hexane and cyclohexane (as representative constituents

for C4-6 IRRP Fraction) for the purposes of the HPV Challenge Program. Data are inadequate to characterize the constituent 2,4-dimethylpentane. The submitter needs to submit adequate data for the latter or reconsider its approach to characterizing the sponsored substance.

Ecological Effects (fish, invertebrates, and algae)

Submitted data are adequate for these end points for the purposes of the HPV Challenge Program.

**Specific Comments on the Robust Summaries**

Health Effects

*Genetic Toxicity (Gene Mutations)*. *Cyclohexane.* Missing from the summary of a study in *Salmonella typhimurium* (p. 29/41) is information on the use and response of positive controls.

*Genetic Toxicity (Chromosomal Aberrations)*. *n-Hexane.* In the cytogenetics assay on page 23/36, the summary mentions a separate mouse study that should be presented in full robust summary format as a separate entry.

*Reproductive/Developmental Toxicity*. *n-Hexane.* There are no reproductive toxicity data presented in the robust summaries. The positive findings in the study designed to evaluate the male reproductive system (misplaced in the developmental toxicity section of the robust summaries – p. 28/36) more appropriately belong in the reproductive section which currently has no entries. Also, testicular weight changes were measured and reported in the 13-week inhalation repeated-dose study (p. 22/36); the sponsor needs to state whether the female reproductive system was evaluated in this repeated-dose study.

**Followup Activity**

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