June 24, 2004

Anne P. LeHuray, Ph.D.
Technical Contact
The American Chemistry Council
Rubber and Plastic Additives Panel
1300 Wilson Boulevard
Arlington, VA 22209

Dear Dr. LeHuray:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for (1H-Isoindole 1,3-(2H)-dione, 2-(cyclohexylthio) posted on the ChemRTK HPV Challenge Program Web site on January 27, 2004. I commend The American Chemistry Council Rubber and Plastic Additives Panel 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 Panel 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 Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. 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: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
2-(Cyclohexylthio)-1H-isoindole-1,3-(2H)-dione,

Summary of EPA Comments

The sponsor, the American Chemistry Council Rubber and Plastic Additives Panel, submitted a test plan and robust summaries to EPA for 2-(cyclohexylthio)-1H-isoindole-1,3-(2H)-dione (N-(cyclohexylthio)-phthalimide, CTP; CAS No. 17796-82-6), dated December 18, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 27, 2004.

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

1. Physicochemical Properties. The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The submitter needs to provide ready biodegradation data for this chemical. The submitter also needs to take into account and indicate how hydrolysis affects the biodegradation of this chemical.

3. Health Effects. Adequate data are available for all health endpoints for the purposes of the HPV Challenge Program. The submitter needs to address some deficiencies in the robust summaries.

4. Ecological Effects. Adequate data are available for all ecological effects endpoints for the purposes of the HPV Challenge Program. However, the submitter needs to provide data elements missing from several robust summaries.

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

EPA Comments on the 2-(Cyclohexylthio)-1h-isoindole-1,3-(2h)-dione Challenge Submission

Test Plan

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

The data provided by the submitter for these endpoints 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 the purposes of the HPV Challenge Program.

Biodegradation. The available data are not adequate. The submitted semi-continuous activated sludge test using adapted inoculum does not measure ready biodegradability. In order to evaluate this endpoint, the submitter needs to generate ready biodegradation data for this chemical following OECD TG 301. The submitter also needs to take into account and indicate how hydrolysis may affect the biodegradation of this chemical.

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

The submitted data are adequate for all health effects endpoints for the purposes of the HPV Challenge Program. The submitter needs to address some deficiencies in the robust summaries.

Ecological Effects (fish, invertebrates, and algae)

The submitted data are adequate for all ecological effects endpoints for the purposes of the HPV Challenge Program.

Specific Comments on the Robust Summaries

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

Acute toxicity. For the acute oral toxicity study in rats exposed to >96% CTP, the 95% confidence limits of 7380 - 9100 mg/kg far exceed the administered doses (1580 - 3160 mg/kg) and appear to have been copied from the following summary for rats exposed to 25% CTP. In addition to correcting this error it would be prudent to verify all the information in these two summaries.

Genetic toxicity. The number of replicates needs to be stated in the robust summary for the mouse lymphoma forward mutation assay.

Reproductive toxicity. The robust summary for the one-generation reproductive toxicity assay in rats is missing information, including the group size for F0 females, the ratio of males and females at mating, the organs that were weighed, and the magnitude of the reduction in body weights in high-dose F0 females and F1 males and females.

Ecological Effects

The submitter needs to provide the amount of solvent/carrier concentration used in each test where a carrier was reported as part of the test methodology.

Followup Activity

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