April 29, 2005

Marcia Hardy, D.V.M., Ph.D.
Technical Contact
Albemarle Corporation
451 Florida Street
Baton Rouge, LA 70801

Dear Dr. Hardy:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2,2'-(1,2-ethanediyl)bis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione, posted on the ChemRTK HPV Challenge Program Web site on March 9, 2004. I commend Albemarle Corporation 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 Albemarle 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
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-1H-Isoindole-1,3(2H)-dione)

Summary of EPA Comments

The sponsor, Albemarle Corporation, submitted a test plan and robust summaries to EPA for 2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione (ethylenebis(tetrabromophthalimide); EBTBP, CAS No. 32588-76-4), dated December 15, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 9, 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 data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

3. Health Effects. The data provided by the submitter for the acute toxicity, mutagenicity, repeated-dose, reproductive and developmental toxicity endpoints are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide data or conduct testing for chromosomal aberrations. The submitter needs to address deficiencies in the robust summaries.

4. Ecological Effects. Although the data provided by the submitter are not adequate for the purposes of the HPV Challenge Program, testing is not needed because of the chemical's high octanol-water partition coefficient value and low water solubility.

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

EPA Comments on the 2,2'-(1,2-Ethanediyl)bis(4,5,6,7-tetrabromo-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. EPA recommends that the submitter include the physicochemical data in table 1 of the test plan.

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

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

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

The data provided by the submitter for the acute toxicity, gene mutation, and repeated-dose, reproductive and developmental toxicity endpoints are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide data on chromosomal aberrations and address deficiencies in the robust summaries.

Repeated-Dose Toxicity. The 28-day repeated-dose study was conducted in males only. Although the terminal organ weight and histopathology data were not collected for all the animals in the 90-day repeated-dose study and the data collected aren't as extensive as outlined in OECD TG 408, the lack of toxicity to observed organ systems at 1000 mg/kg suggests that little new information would be gleaned from further testing. Therefore, the data are deemed adequate for the repeated-dose toxicity endpoint for the purposes of the HPV Challenge Program.

Genetic Toxicity (chromosomal aberrations). No data were submitted and no testing was proposed. Testing is needed for this endpoint according to OECD TG 473.

Reproductive Toxicity. No data were submitted and no testing was proposed. Although the robust summary for the 90-day repeated-dose toxicity study does not indicate that the reproductive organs were weighed, the reproductive organs were examined histopathologically without evidence of toxicity. Also, there was no evidence of toxicity in the testes in the 28-day repeated-dose study and no evidence of maternal or fetal toxicity in the developmental toxicity study. Considering the weight of evidence for the absence of mammalian toxicity, no further testing is needed at this time for the purposes of the HPV Challenge Program.

Ecological Effects (fish, invertebrates, and algae)

The submitter provided no adequate studies to address the ecological endpoints. However, given the EPIWIN-predicted low water solubility value of 3.029×10^{-9} mg/L and the high log K_{ow} value of 9.8, EPA agrees with the submitter's proposal not to conduct further ecotoxicity testing.

Fish. The robust summary for the single test conducted in orange-red killifish *(Oryzias latipes)* was inadequate to satisfy the acute toxicity to fish endpoint because the study duration was 48 hours rather than the OECD TG 203-stipulated 96 hours, and study details were insufficient.

Specific Comments on the Robust Summaries

The submitter needs to assign reliability codes to its robust summaries.

Health Effects

The submitter needs to report the purity of the test substance used in all health studies in the robust summaries. The submitter needs to flag key studies in the robust summaries and assign reliability codes (for guidance, visit: http://www.epa.gov/chemrtk/datadfin.htm) to the data presented.

Acute Toxicity. The robust summary for the acute oral toxicity study should include information on clinical findings at necropsy. Histopathological findings, if any, should also be included.

Genetic Toxicity (*gene mutations*). The data for all studies should be presented, preferably in tabulated form, showing the mean number of revertants/plate with standard deviations, any cytotoxicity observed, and the number of replicates used. Solvent and positive controls need to be identified as well as the means of metabolic activation.

Reproductive Toxicity. A robust summary based on the information in the repeated-dose and developmental toxicity studies needs to be prepared for this endpoint. It should specify the reproductive organs examined and the results of these evaluations, as well as any other methods and results used to assess reproductive outcomes.

Followup Activity

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