

July 25, 2002

Richard Henrich  
Great Lakes Chemical Corporation  
Highway 52 N.W.  
West Lafayette, IN 47996

Dear Mr. Henrich:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Isopropylated Triphenyl Phosphate, posted on the ChemRTK HPV Challenge Program Web site on December 19, 2001. I commend Great Lakes Chemical 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 HPV 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 attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Great Lakes Chemical Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

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 HPV Challenge Program Web site "Submit Technical Questions" 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 [tsc-hotline@epa.gov](mailto:tsc-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

Attachment

cc: W. Sanders  
A. Abramson  
C. Auer  
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:  
Isopropylated Triphenyl Phosphate**

**SUMMARY OF EPA COMMENTS**

The sponsor, Great Lakes Chemical Corporation, submitted a test plan and robust summaries to EPA for Isopropylated Triphenyl Phosphate (CAS No. 68937-41-7) dated November 29, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 19, 2001.

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

1. General. Because isopropylated triphenyl phosphate is a mixture, the submitter needs to fully identify the composition of the test substance in all studies that have been submitted as well as all tests that the submitter plans to conduct.
2. Physicochemical and Environmental Fate Data. EPA agrees with the submitter's proposed testing/modeling for water solubility, photodegradation, stability in water, biodegradation and fugacity.
3. Health Endpoints. (a) EPA disagrees with the submitter that the acute oral toxicity endpoint has been adequately addressed. (b) EPA agrees with the submitter's proposal to test for gene mutations and chromosomal aberrations. (c) EPA agrees with the submitter that reproductive and developmental toxicity testing is necessary to address these endpoints. (d) EPA does not agree with the submitter that the repeated-dose study is adequate and recommends conducting a combined repeated-dose toxicity test with reproductive and developmental screening according to OECD TG 422.
4. Ecotoxicity. EPA reserves judgement on the adequacy of the fish and aquatic invertebrate toxicity endpoints because of missing physical and chemical property data in the robust summaries. EPA agrees with the submitter's proposal to test for toxicity to aquatic plants. .

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

**EPA COMMENTS ON THE ISOPROPYLATED TRIPHENYL PHOSPHATE CHALLENGE SUBMISSION**

**Test Plan**

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

The test plan for these endpoints is adequate for the purposes of the HPV Challenge Program. However, a full characterization of the test substance needs to be provided.

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

The test plan for these endpoints is adequate for the purposes of the HPV Challenge Program.

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

Except for the dermal study, all the acute toxicity studies are inadequate. However, EPA believes that the submitter may be able to enhance the data on the acute oral toxicity endpoint by utilizing the dosing data from the 28-day repeat-dose study to estimate an acceptable LD50. EPA agrees with the submitter's proposal to test for reproductive and developmental toxicity. EPA disagrees with the submitter that the 28-day repeated-dose study is adequate for that endpoint. Rather than repeating a 28-day study, EPA recommends that the submitter use the OECD combined protocol (OECD TG 422) for repeated-dose with developmental and reproductive testing. EPA agrees with the submitter that testing to address the gene mutation and chromosomal aberration endpoints is necessary and will be conducted using OECD in vitro protocols.

*Acute Toxicity.* A dermal rat study (1990) used 3 rather than 5 animals per sex, however, no deaths were seen during the 14-day observation period following the 24-hour occluded exposure to 2000 mg/kg. This study is adequate, but the submitter needs to enhance the robust summary. The acute oral study (1975) claiming an LD50 >20,000 mg/kg is inadequate. Although the males survived, all females, except one, died. Other deficiencies include: one dose was used, no clinical signs or necropsy results were reported,

the substance was not properly identified, and no statistical results were described.

*Repeated-dose Toxicity.* Important information was omitted from the robust summary for the repeated-dose study (1976). Abnormal hematological values were reported for the high dose group and abnormal clinical chemistry measurements were reported for the mid and high dose groups but no quantitative data were supplied and the abnormal parameters were not identified. The sex of the animals that died was not provided. In addition, the only tissues selected for histopathology were the liver and kidneys.

#### Ecological Effects (fish, daphnia, and algal toxicity)

EPA reserves judgment on the adequacy of the fish and aquatic invertebrate toxicity endpoints. The robust summaries are missing necessary data elements (see specific comments on robust summaries). The toxicity data infers that the chemical may have been tested above the aqueous water solubility limit and perhaps the chemical is unstable. The results of the water solubility and stability tests will help explain the submitted ecological test results. All testing for aquatic toxicity endpoints must be done below or at the chemicals' aqueous water solubility limit. EPA agrees with the submitter that testing is necessary in order to assess acute toxicity to aquatic plants. The submitter reported a Log P value of 5.1. Log P values of  $\leq 4.2$  suggest that chronic daphnia testing may be needed. For more information and guidance pertaining to difficult-to-test substances and chemicals with high log P values refer to the OECD Web site at <http://www.oecd.org/ehs/test/monos.htm>.

#### **Specific Comments on the Robust Summaries**

Each summary should clearly identify the test substance by the chemical name and include information on the percent composition of constituents.

#### Health Effects

*Acute Dermal Toxicity.* Information on statistical methods used needs to be provided.

#### Ecotoxicity.

The submitter needs to provide information on water solubility, stability in water, dissolved oxygen (DO), water hardness, and pH.

#### **Followup Activity**

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