

May 8, 2003

Peter Schlom  
National Starch and Chemical Company  
10 Funderne Avenue  
Bridgewater, NJ 08807

Dear Mr. Schlom:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2-Propenamide, N-(1,1,3,3-Tetramethylbutyl)- posted on the ChemRTK HPV Challenge Program Web site on January 17, 2003. I commend National Starch and 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 National Starch and Chemical Company 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 "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](mailto: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: C. Auer  
A. Abramson  
W. Penberthy  
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:  
N-(1,1,3,3-Tetramethylbutyl)-2-propenamide**

**Summary of EPA Comments**

The sponsor, ICI Americas, Inc., submitted a test plan and robust summaries to EPA for N-(1,1,3,3-tetramethylbutyl)-2-propenamide (CAS No. 4223-03-4) dated December 18, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 17, 2003.

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

1. Physicochemical Properties. EPA agrees with the submitter's proposed testing for melting point, boiling point, vapor pressure, partition coefficient, and water solubility.
2. Environmental Fate. The photodegradation data provided by the submitter are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's approach to stability in water (hydrolysis), biodegradation, and transport and distribution (fugacity).
3. Health Effects. EPA agrees that data are needed for the acute, repeated-dose, and reproductive toxicity endpoints. EPA reserves judgement on the adequacy of the submitted *in vivo* mouse micronucleus assay, pending additional information. In addition, the submitter needs to address deficiencies in the robust summaries.
4. Ecological Effects. EPA agrees with the submitter's proposal to conduct fish, aquatic invertebrate, and algal testing following OECD guidelines.

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

**EPA Comments on the  
N-(1,1,3,3-Tetramethylbutyl)-2-propenamide Challenge Submission**

**Test Plan**

General.

The submitter needs to correct the CAS number reported on page 4.

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

EPA agrees with the submitter's proposed testing for melting point, boiling point, vapor pressure, partition coefficient, and water solubility.

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

The photodegradation data provided by the submitter are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's plan to test for stability in water and biodegradation and to estimate fugacity.

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

toxicity).

EPA agrees with the submitter's proposal to conduct testing for the acute, repeated-dose, and reproductive toxicity endpoints and recommends that the submitter follow OECD TG 425 for the acute toxicity test and consider using the *in vitro* cytotoxicity protocol to estimate the starting dose. Although the submitter states that no fertility testing is proposed pending the results of planned testing (Section 2.4.6), OECD TG 422 satisfies the endpoint for reproduction/fertility. As an alternative to conducting an acute toxicity test, the submitter should consider using the dose range-finding data for the recommended OECD TG 422 test to address this endpoint.

The test plan does not specifically address the developmental toxicity endpoint. This omission needs to be corrected. However, the recommended OECD TG 422 will address this endpoint.

The submitter needs to address deficiencies in the robust summaries.

*Genetic Toxicity.* Adequate data are available for the gene mutation endpoint for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of the submitted OECD TG 474, *in vivo* mouse micronucleus assay, pending receipt of the following additional information: 1) criteria for dose selection; 2) a more detailed robust study summary.

The submitter also needs to change "*in vitro*" to "*in vivo*" for the mouse micronucleus assay in Table 2.

Ecological Effects (fish, invertebrates, and algae).

All aquatic toxicity testing should be conducted using mean measured concentrations and analytical monitoring. In the case of algal toxicity, both growth rate and biomass endpoints should be reported.

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

#### General.

The submitter needs to provide Section 1. of the IUCLID Data Set or state that the test substance is "as prescribed by Section 1.1 - 1.4 of the **Test Plan**".

#### Health Effects.

*Genetic Toxicity.* Although the studies were conducted following OECD guidelines and complied with GLP, many details are missing in the robust summaries for bacterial mutations such as the purity of the test material, the number of replicates per concentration, the number of colonies per concentration that were counted, and the criteria for positive results. The summary for the *in vivo* mouse micronucleus assay also omits details such as the purity of the test material, the age and weight of the animals at the start of the test, number of animals per concentration, the duration of exposure, details of how the study was conducted (e.g., rationale for dose level selection, test substance preparation and administration, description of treatment and sampling schedules), signs of toxicity, number of cells examined, and the criteria for determining whether the results are positive, negative, or equivocal. Such details are essential for assessing the adequacy of the underlying data. The submitter is encouraged to review the guidance on developing robust summaries (available at: <http://www.epa.gov/chemrtk/robsumgd.htm> ) and consider revising the robust summaries.

### **Followup Activity**

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