

May 8, 2003

Randy Deskin, Ph.D., D.A.B.T.
Director, Toxicology and Product Regulatory
Compliance Department
Cytec Industries, Inc.
5 Garret Mountain Plaza
West Peterson, NJ 07424

Dear Dr. Deskin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for m-Diisopropenylbenzene posted on the ChemRTK HPV Challenge Program Web site on January 16, 2003. I commend Cytec Industries, Inc. 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 Cytec Industries, Inc. 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.

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:
m-Diisopropenylbenzene**

Summary of EPA Comments

The sponsor, Cytec Industries Inc., submitted a test plan and robust summaries to EPA for *m*-diisopropenylbenzene (CAS No. 3748-13-8) dated December 18, 2002. EPA posted the submission on the ChemRTK HPV Challenge web site on January 16, 2002.

EPA has reviewed this submission and reached the following conclusions:

1. Physicochemical Properties. The data provided by the submitter for melting point, boiling point, vapor pressure, and partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide test data for water solubility.
2. Environmental Fate. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.
3. Health Effects. (a) EPA agrees with the submitter's plan to conduct chromosomal aberration testing. (b) The submitter needs to provide additional documentation to support exemption from reproductive toxicity testing on the basis that the chemical is a closed system intermediate. (c) Reduced testing does not apply to the developmental toxicity endpoint. Therefore, the submitter needs to provide developmental toxicity data.
4. Ecological Effects. The data provided for fish, aquatic invertebrates, and green algae are adequate for the purposes of the HPV Challenge Program pending the addition of quantitative structure-activity relationship (QSAR) data to the robust summaries.

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

**EPA Comments on the m-Diisopropenylbenzene
Challenge Submission**

Test Plan

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

The data provided by the submitter for melting point, boiling point, vapor pressure, and octanol/water partition coefficient are adequate for the purposes of the HPV Challenge Program.

Water solubility. The submitter provided a measured water solubility value of 5.6 mg/L at 25° C (Stanek, 2002). This study did not follow GLP or OECD TG 105. This measured value is comparable to an estimated value of 4.633 mg/L at 25° C (WSKOWIN). However, the measured value is not comparable to the experimental value in EPIWIN (Chem Inspect Test Inst., 1992) for a close analog, diisopropylbenzene (CAS # 25321-09-9), which has a water solubility value of 0.072 mg/L at 25 °C. Given the almost 100-fold difference observed between these measured values, the water solubility data appear to be inadequate for this endpoint. The submitter needs to provide measured water solubility data following OECD TG 105.

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

The data provided by the submitter for stability in water, biodegradation and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program.

Photodegradation. The data provided by the submitter for atmospheric oxidation are adequate for the purposes of the HPV Challenge Program. However, EPA recommends that the submitter comment on the potential for this chemical to undergo direct photolysis.

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

Adequate data are available for the acute toxicity, repeated-dose toxicity, and gene mutation endpoints for the purposes of the HPV Challenge Program. The submitter plans to conduct a test for chromosomal aberrations, for which EPA recommends OECD TG 473. The submitter requests an exemption from reproductive and developmental toxicity testing based on EPA's guidelines for chemical intermediates. However, additional documentation is needed to qualify for this exemption, which would apply to reproductive but not developmental toxicity testing.

Reproductive Toxicity. No data were submitted for this endpoint and no testing is proposed, based on the submitter's assertion that m-diisopropenylbenzene is a closed system intermediate.

"Guidance for Testing Closed System Intermediates for the Challenge Program", available at (<http://www.epa.gov/chemrtk/guidocs.htm>), allows for a reduced testing protocol, provided certain criteria are met. The information required to judge a "closed system intermediate" claim must address the following:

- I. Site information
 - A. Number of sites.
 - B. Basis for "closed process" conclusion at each site.
 - 1) Process description.
 - 2) Monitoring data showing no detection.
 - 3) In the absence of monitoring data, the basis for believing that releases do not occur.
 - C. Data on "presence in distributed products."
- II. Information on transport (mode, volume, controls, etc)
- III. A data search showing that the chemical is not present in other end products

EPA does not believe that the information provided by the submitter is sufficient to satisfy the requirements for classification as a closed-system intermediate eligible for reduced testing in the HPV Challenge Program.

The submitter states that m-diisopropenylbenzene is manufactured in an enclosed, continuous process but does not provide a description of the process or a flow diagram. All manufactured m-diisopropenylbenzene is transported in bulk to another facility of the submitter, where approximately 95% (approximately 2.5 million pounds) of the chemical is used in the production of diisocyanate monomer. In addition, approximately 20,000 pounds are transferred in drums to a facility of a different company where it is converted to other chemicals used in optical products. No descriptions of the last two processes or flow diagrams are provided. Approximately 100,000 pounds are transferred in drums for export as a chemical intermediate in the production of fragrances. It is also stated that during transport the chemical is pumped from drums in an open area outside, raising the potential for human or environmental exposures as a result spills or fugitive releases. And lastly, no information is provided on where or how the exported material is handled. More complete descriptions are needed to show that manufacturing and process operations are closed.

As to data on “presence in distributed products,” the submitter states only that the product purification process removes unreacted chemical in the diisocyanate monomer production process and that analytical data on the final product normally show no chemical present at the limit of detection. However, no analytical data are provided and the limit of detection is not stated. Also, no information is provided on the presence of *m*-diisopropenylbenzene in the optical products produced by another company. Data are needed to support the conclusion that *m*-diisopropenylbenzene is not present in distributed products. Moreover, the submitter does not provide any supporting evidence that the chemical is not present in other end products.

Developmental Toxicity. The submitter requests an exemption from testing based on the reduced testing requirements for closed system intermediates. However, this exemption does not apply to developmental toxicity. Therefore, the submitter needs to provide developmental toxicity data, preferably a reproductive/developmental toxicity screening test following OECD TG 421.

Ecological Effects (fish, invertebrates, and algae)

The data submitted for fish, aquatic invertebrate, and algae show much lower toxicity values than are predicted for this chemical. This is consistent with the experimental conditions and an estimated Henry’s Law Constant of 3.48×10^{-3} , indicating that *m*-diisopropenylbenzene volatilizes readily from water. Also, some of the concentrations in the testing range were above the water solubility limit. Rather than repeat the tests, in this case it is reasonable for the sponsor to supplement the robust summaries with QSAR data to better characterize the aquatic toxicity of *m*-diisopropenylbenzene.

Followup Activity

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