

June 5, 2003

Dr. Ronald Joiner
Manager, Global Toxicology
General Electric Company-Plastics
One Plastic Avenue
Pittsfield, MA 01201

Dear Dr. Joiner:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 4-Nitro-N-Methylphthalimide posted on the ChemRTK HPV Challenge Program Web site on January 30, 2003. I commend the General Electric Company-Plastics 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 General Electric Company-Plastics 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: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: 4-Nitro-N-Methylphthalimide

Summary of EPA Comments

The sponsor, General Electric Company-Plastics (GE Plastics), submitted a test plan and robust summaries to EPA for 4-Nitro-N-Methylphthalimide (4-NPI) (CAS No. 41663-84-7) dated December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 30, 2003.

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

1. Physicochemical Properties. The data provided by the submitter for melting point, boiling point, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's proposal to determine vapor pressure.
2. Environmental Fate. The data provided by the submitter for stability in water (hydrolysis) are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's test plan for photodegradation, transport and distribution, and biodegradation.
3. Health Effects. The submitter proposed testing for the reproduction toxicity endpoint. Because there is an adequate developmental toxicity study, EPA believes that the reproduction toxicity endpoint may be addressed if the submitter provides information on histopathologic evaluation of the reproductive organs for both sexes from the submitted 13-week repeated-dose oral toxicity test.
4. Ecological Effects. The studies for fish, invertebrates, and algae endpoints are inadequate. Testing is needed to address these endpoints.

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

EPA Comments on the 4-nitro-n-methylphthalimide Challenge Submission

General

EPA has evaluated this submission as if the chemical were not used as a closed system intermediate. However, the use pattern described in the submission "...a site-limited intermediate made at a single location in the U.S....used as a reactive intermediate to make high molecular weight polyetherimide polymer" indicates that the submitter may have the option to submit as a site limited intermediate if supporting information is provided. The Guidance for Testing Closed System Intermediates for the Challenge Program allows for a reduced testing protocol provided certain criteria are met (refer to <http://www.epa.gov/chemrtk/closed9.htm>).

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, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program. There are some discrepancies in the test plan and in the robust summaries regarding partition coefficient and water solubility that need to be corrected.

Vapor pressure. The submitter indicates in the test plan that testing is needed for the vapor pressure endpoint. EPA agrees. To satisfy this endpoint, the submitter needs to provide vapor pressure data following OECD TG 104.

Partition coefficient and water solubility. In the test plan (page 4) the submitter states that GLP-compliant OECD methods were used to determine the $\log K_{ow}$ and water solubility for 4-NPI; however, in the robust summaries the submitter states that measurements using OECD TGs 105 and 107 were not possible due to significant hydrolysis of 4-NPI during the course of testing. The submitter provided a calculated $\log K_{ow}$ and water solubility for 4-NPI. The test plan (page 4) needs to be modified to reflect the data in the robust summaries for these endpoints.

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

Adequate data are available for stability in water (hydrolysis) for the purposes of the HPV Challenge Program. The submitter indicates in the test plan that testing is needed for the photodegradation, transport and distribution, and biodegradation endpoints. EPA agrees with the test plan for these endpoints.

Biodegradation. To address the biodegradation endpoint, the submitter needs to provide measured ready biodegradation data following OECD TG 301. Considering that this chemical undergoes rapid hydrolysis, the submitter needs to provide biodegradation data on the hydrolyzed product.

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

Adequate data are available for the acute, repeated-dose, genetic, and developmental toxicity endpoints for the purposes of the HPV Challenge Program.

Reproduction Toxicity. No data were submitted. The submitter proposed testing for this endpoint; however, this testing may not be needed if the submitter provides information on histopathologic evaluation of the reproductive organs for both sexes from the submitted 13-week repeated-dose oral toxicity test. Such information along with the adequate developmental toxicity study will address the reproduction toxicity endpoint for the purposes of the HPV Challenge Program. If testing is needed, the submitter should use OECD TG 421 (combined reproductive/developmental screening test).

Ecological Effects (fish, invertebrates, and algae).

The submitted studies for fish, invertebrates, and algae are inadequate because the maximum nominal concentrations tested (15.06 mg/L) were well below the water solubilities for the sponsored substance (360 mg/L) or its hydrolysis product (1000 mg/L). Since the half life of 4-NPI is 6.4 hours at pH 7, EPA suggests the testing be conducted on the hydrolyzed product (4-NPI-H) on all three species using mean measured concentrations.

Specific Comments on the Robust Summaries

Health Effects.

Repeated-Dose Toxicity. The submitter needs to provide histopathological data of the reproductive organs, if available, for the robust summary of the submitted 13-week gavage study in rats.

Followup Activity

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

