

201-14643



NCIC HPV

Sent by: Mary-Beth
Weaver

08/05/2003 12:24 PM

To: NCIC HPV, moran.matthew@epa.gov

cc:

cc:

Subject: Response to EPA Comments - GE Plastics CAS RNs 550-44-7,
41663-84-7, 527-60-6



"John P. Van Miller" <jvanmiller@toxregserv.com> on 08/05/2003 10:49:18 AM

To: oppt.ncic@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA
cc: "Ronald L Joiner (GEP)" <Ronald.Joiner@gepex.ge.com>, Stephen Dimond
<stephen.dimond@gep.ge.com>

Subject: Response to EPA Comments - GE Plastics CAS RNs 550-44-7, 41663-84-7, 527-60-6

Attached please find responses to EPA's comments on the following Test Plans for the HPV Chemical Challenge Program:

- 1) N-Methylphthalimide (PI: CAS RN 550-44-7)
- 2) 4-Nitro-N-Methylphthalimide (4-NPI: CAS RN 41663-84-7)
- 3) 2,4,6-Trimethylphenol (246-TMP: CAS RN 527-60-6)

Thank you.

John P. Van Miller, Ph.D., DABT
Toxicology/Regulatory Services
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PI_CAS 550-44-7_GE Response_August 5 2003.pdf



4-NPI_CAS 41663-84-7_GE Response_August 5 2003.pdf



246-TMP_CAS 527-60-6_GE Response_August 5 2003.pdf

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TOXICOLOGY/REGULATORY SERVICES, INC.

August 5, 2003

Linda Fisher, Acting Administrator
US Environmental Protection Agency
PO Box 1473
Merrifield, VA 22116

Via Electronic Submission

Attention: Chemical Right-to-Know Program, AR-201

Re: Response to Comments on Test Plan for CAS RN 527-60-6

On behalf of General Electric Company – Plastics (GE Plastics; Registration Number 1100342), Toxicology/Regulatory Services (TRS) is submitting responses to the EPA Comments on Test Plans/Robust Summaries for 2,4,6-Trimethylphenol (CAS RN 527-60-6). Please address any further correspondence to:

Dr. Ronald L. Joiner
Manager, Global Toxicology
General Electric Company
One Plastics Avenue
Pittsfield, MA 01201
Phone: 413-448-6323; Fax: 413-448-6590
EMAIL: Ronald.Joiner@GEP.GE.COM

Thank you,

John P. Van Miller, Ph.D., DABT

General Electric Company – Plastics: Response to Comments on the Test Plan for 2,4,6-Trimethylphenol (CAS RN 527-60-6)

Below is a reproduction of the comments submitted to the General Electric Company – Plastics (GE Plastics) Test Plan submission for the above referenced chemical in the HPV Challenge Program. Questions and comments from EPA that require input are formatted in ***Bold/Italic*** font and GE Plastic's response follows each entry. Responses are made to specific comments rather than Summary Comments.

EPA Comments on Chemical RTK HPV Challenge Submission: 2,4,6-Trimethylphenol

Summary of EPA Comments

The sponsor, General Electric Company-Plastics, submitted a test plan and robust summaries to EPA on December 30, 2002 for 2,4,6-Trimethylphenol (CAS No. 527-60-6). 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 Agency agrees with the submitter that adequate data are available for these endpoints for the purposes of the HPV Challenge program. Because the submitter plans to repeat the studies to “ensure accuracy and completeness,” EPA strongly recommends that the new measurements follow OECD guidelines.
2. Environmental Fate. The data provided for photodegradation, stability in water (hydrolysis), and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program. EPA agrees with the submitter's proposal to perform biodegradation testing of this chemical. The submitter needs to address deficiencies in the photodegradation robust summary.
3. Health Effects. Adequate data are available for acute and genetic toxicity endpoints for the purposes of the HPV Challenge Program. EPA agrees with the submitter's proposal to conduct a combined repeated-dose/reproductive/developmental toxicity screening test to address these endpoints. The submitter needs to specify the route of administration of the test substance for this test.
4. Ecological Effects. The fish and algae endpoints have been adequately addressed for the purposes of the HPV Challenge Program. The submitter needs to add SAR estimates or test data on an analogous chemical to support the limited data for the daphnia endpoint.

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

EPA Comments on the 2,4,6-trimethylphenol Challenge Submission

Test Plan

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

The Agency agrees with the submitter that adequate data are available for these endpoints for the purposes of the HPV Challenge program. However, the submitter plans to repeat the studies to “ensure accuracy and completeness.” If the submitter pursues this option, EPA strongly recommends that the measurements follow OECD guidelines.

RESPONSE: All new studies will be conducted in compliance with OECD guidelines and Good Laboratory Practices.

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

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

Biodegradation. EPA agrees with the submitter’s proposed biodegradation testing. The testing should follow OECD TG 301 (ready biodegradation).

RESPONSE: The biodegradation study will be conducted in compliance with OECD Guideline 301B and Good Laboratory Practices.

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

EPA agrees with the submitter’s proposal to conduct a combined repeated-dose/reproductive/developmental toxicity screening test (OECD TG 422) to address these endpoints. The submitter needs to specify the route of administration of the test substance for this test.

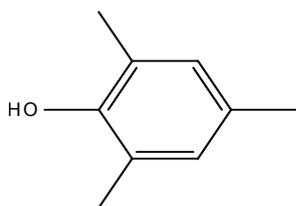
RESPONSE: The route of administration for the OECD 422 study will be oral gavage.

Ecological Effects (fish, invertebrates, and algae).

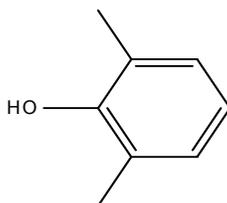
Adequate data are available for the fish and algae endpoints for the purposes of the HPV Challenge Program.

Daphnia. The 24-hour study in daphnia is shorter than the normally required 48 hours for this test. The submitter needs to support the findings of the 24-hour study in daphnia with SAR estimates or measured data on an analogous chemical. Also, the submitter can provide a robust summary for a study by Kuehn et al., 1989, titled “Results of the Harmful Effects of Selected Water Pollutants (Anilines, Phenols, Aliphatic Compounds) to Daphnia Magna.”

RESPONSE: Studies for the closely related 2,6-xyleneol (see structures below) are available. Robust summaries for these studies, as well as for the Kuehn et al. study, will be included in the final submission.



2,4,6-trimethyl phenol



2,6-xyleneol

Specific Comments on the Robust Summaries

Environmental Fate

Photodegradation. In the photodegradation robust summary, the submitter included language not pertinent to this endpoint. The submitter needs to remove the paragraphs related to “Biodegradation potential”, “Estimation of Environmental Distributions”, “Common Features of the Models”, and “Model Results for TMP”. These three last sections are already covered under Section 8.1-Theoretical Distribution (fugacity calculation). The submitter needs to post its photodegradation results in a format similar to that followed under section 7.0, Stability in Water.

Theoretical distribution (fugacity calculation). The submitter needs to post its fugacity results in a format similar to that followed under section 7.0, Stability in Water.

RESPONSE: The Photodegradation Expert Statement and the Theoretical Distribution (fugacity calculation) relate to the ECOSAR/EPIWIN model determinations. The entire text of the Expert Statement was included for each endpoint to ensure clarity of approach to the modeling. In the final submission, we will delete non-critical information for the model Expert Statement to comply with the EPA’s request.

References

Kuehn, R., M. Pattard, K-D. Pernak, and A. Winter. 1989. Results of the Harmful Effects of Selected Water Pollutants (Anilines, Phenols, Aliphatic Compounds) to Daphnia Magna. Water Res. 23(4): 495-500.