

April 17, 2003

Edwin L. Mongan, III
Manager, Environmental Stewardship
E.I. du Pont de Nemours & Company
Safety, Health & Environmental Excellence Center
1007 Market Street
DuPont 6062
Wilmington, DE 19898

Dear Mr. Mongan:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Mononitrile Category posted on the ChemRTK HPV Challenge Program Web site on December 20, 2002. I commend E.I. du Pont de Nemours & 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 E.I. du Pont de Nemours & 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.

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: Mononitrile Category

Summary of EPA Comments

The sponsor, E. I. du Pont de Nemours & Company, Inc., submitted a test plan and robust summaries to EPA for the Mononitrile Category dated December 3, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 20, 2003. The category consists of 2-methyl-3-butenitrile (CAS No. 16529-56-9); 2-pentenenitrile, cis and trans isomers (CAS No. 13284-42-9); 3-pentenenitrile, cis and trans isomers (CAS No. 4635-87-4); and 4-pentenenitrile (CAS No. 592-51-8).

EPA has reviewed this submission and reached the following conclusions:

1. Category Justification. The structural similarity among category members and submitted data indicate that the proposed category is reasonable for most physicochemical and environmental fate properties and for health effects. The submitter needs to provide additional data to show that the category grouping can be supported for aquatic toxicity.
2. Physicochemical Properties and Environmental Fate. Available data are adequate for all endpoints except vapor pressure and stability in water.
3. Health Effects. Data are adequate for all endpoints except for reproductive and developmental toxicity. EPA agrees with the submitter that testing of 2-pentenenitrile according to OECD TG 422 will adequately address the reproduction/developmental toxicity endpoints.
4. Ecological Effects. The acute toxicity data on fish, invertebrates, and algae are inadequate because of various study design deficiencies. EPA recommends that a full set of acute toxicity tests be performed using 2-pentenenitrile and 3-pentenenitrile.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Mononitrile Category Challenge Submission

Category Definition

The mononitrile category comprises four straight- and branched-chain five-carbon alkene nitriles.

The category definition is adequate.

Category Justification

According to the submitter, the nitrile group and limited chain length of each category member suggest that the four isomers should have similar physicochemical, environmental, and toxicological properties. The measured and estimated values provided generally support this conclusion except for hydrolysis rate and aquatic toxicity. The two allylic nitriles may be susceptible to nucleophilic substitution and therefore to hydrolysis, so that the category may not apply to the stability in water endpoint. In the case of aquatic toxicity, EPA considers allylic and vinylic cyanides to be separate structure types that cannot be evaluated according to a simple narcosis model, and are thus not directly comparable with each other or with the simpler 4-pentenenitrile.

Test Plan

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

EPA agrees that available data are adequate for melting point, boiling point, water solubility, and octanol/water partition coefficient. Testing is needed for vapor pressure.

Melting Point. The submitter provided only estimated data for this endpoint. According to OECD TG102, measured data are not necessary if a chemical's melting point is $<0^{\circ}\text{C}$. EPA identified an analogue, 1-pentanenitrile (CAS No. 110-59-8), with a melting point of -96°C , which suggests that the estimated data are adequate. However, the submitter needs to add a rationale of this nature, with appropriate analogue data, to the test plan and robust summaries.

Vapor Pressure. The submitter provided only estimated vapor pressure values that, according to OECD guidelines, are adequate only if they are $<10^{-5}$ Pa. Since all of the values are above this threshold, the submitter needs to conduct vapor pressure studies on 2-methyl-3-butenenitrile, 4-pentenenitrile, and either 2-pentenenitrile or 3-pentenenitrile.

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

EPA agrees that available data are adequate for biodegradation and fugacity.

Photodegradation. Indirect photolysis data are adequate, but the submitter needs to add the information to Table 3 of the test plan.

Stability in Water. In the robust summary section for this endpoint, the submitter provided estimated data for volatility from surface water, which does not address the endpoint. Furthermore, because the allyl nitriles, 2-methyl-3-butenenitrile and 3-pentenenitrile, may be more susceptible to hydrolysis than the other category members, hydrolysis studies need to be conducted on these two compounds. When the data become available, the submitter needs to add the information to Table 3 of the test plan.

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

EPA agrees with the submitter's approach to these endpoints.

Genetic Toxicity. EPA agrees with the submitter's plan to test 2-pentenenitrile for chromosomal aberrations following OECD Guideline 473 to address this endpoint and extrapolate the results to other category members.

Reproductive/Developmental Toxicity. The submitter has indicated that it will conduct a combined reproductive and developmental toxicity testing of 2-pentenenitrile "using the OECD TG 422." EPA agrees that the OECD TG 422 screen, which also addresses the repeated-dose endpoint, is the appropriate test because then all three interrelated systemic toxicity endpoints will be tested by the same route of administration (oral) with no increase in the number of animals.

Ecological Effects (fish, invertebrates, and algae).

Fish, Invertebrates, and Algae. Acute toxicity test data on 2-methyl-3-butenenitrile, 2-pentenenitrile, and 3-pentenenitrile are inadequate because nominal concentrations were used for volatile chemicals that require closed test systems and measured concentrations. Furthermore, as stated under Category Justification, EPA considers that the allylic and vinylic cyanides cannot be evaluated according to a simple narcosis model or likened to each other or to 4-pentenenitrile. EPA therefore recommends that the full set of acute toxicity tests be performed with 2-pentenenitrile and 3-pentenenitrile according to OECD Guidelines 201-203. The test results for 3-pentenenitrile can be extrapolated to 2-methyl-3-butenenitrile.

The ECOSAR estimates for 4-pentenenitrile are acceptable provided they are supported by measured data on a satisfactory (non-vinyl, non-allyl) unsaturated or saturated analog.

Specific Comments on the Robust Summaries

Environmental Fate

Photodegradation. The submitter needs to provide a robust summary of the AOPWIN model results, including input parameters and a discussion as to whether mononitriles absorb sunlight at >290 nm.

Fugacity. The submitter needs to provide a robust summary of fugacity modeling results, including input parameters.

Health Effects

Genetic Toxicity. Robust summaries of bacterial mutagenicity assays on 2-methyl-3-butenitrile, 2-pentenenitrile, and 3-pentenenitrile omitted the cytotoxic concentrations.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.