

April 30, 2004

Rod Gerwe, Ph.D.
President, PCA Services, Inc.
PCA Services, Inc.
2704 Trail Wood Drive
Durham, N.C. 27705

Dear Dr. Gerwe:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Alkyl Nitriles Category posted on the ChemRTK HPV Challenge Program Web site on December 19, 2003. I commend Eastman Chemical Company and Solutia, Inc. for their 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 Eastman Chemical Company and Solutia, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

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: Alkyl Nitriles Category

Summary of EPA Comments

The sponsors, Eastman Kodak Company and Solutia, Inc., submitted a test plan and robust summaries to EPA for the Alkyl Nitriles Category dated November 25, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 19, 2003. The category consists of three sponsored compounds, propionitrile (CAS No. 107-12-0), butyronitrile (CAS No. 109-74-0) and isobutyronitrile (CAS No. 78-82-0).

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

1. Category Justification. The category justification is reasonable.
2. Physicochemical Properties and Environmental Fate. Adequate data are available for the alkyl nitriles category for the purposes of the HPV Challenge Program.
3. Health Effects. Adequate data are available for all three members of the category for the acute, genetic, and developmental toxicity endpoints and for propionitrile for the repeated-dose and reproductive toxicity endpoints for the purposes of the HPV Challenge Program. EPA agrees with the submitters' plan to use a category approach to address data gaps for butyronitrile and isobutyronitrile for the repeated-dose and reproductive toxicity endpoints.
4. Ecological Effects. Measured data along with predicted values are adequate for the alkyl nitriles category for the purposes of the HPV Challenge Program. The submitters need to address minor deficiencies in the test plan and robust summaries.

EPA requests that the submitters advise the Agency within 60 days of any modifications to their submission.

EPA Comments on the Alkyl Nitriles Category Challenge Submission

Category Definition

The submitters proposed a category to cover three nitriles that fall within a small carbon number range (C3-C4). These compounds are proprionitrile (CAS No. 107-12-0) and two isomers of butanenitrile, butyronitrile (CAS No. 109-74-0) and isobutyronitrile (CAS No. 78-82-0).

Category Justification

The three aliphatic nitriles that comprise the alkyl nitriles category are structurally similar, consisting of a common functional group (nitrile) and a 2- or 3-carbon alkyl group. The submitters propose that these compounds will have similar physicochemical, environmental, and toxicological properties. More specifically, it is expected that the nitrile function will be the predominant determinant of the toxicity of these compounds. With some minor differences, the physicochemical, environmental fate and toxicological properties of these compounds are similar according to data provided by the submitters.

The values provided by the submitters demonstrate very similar physicochemical properties of the three compounds. These similarities translate into very similar distributions in the environment. Hydrolysis of the three compounds is expected to be negligible at environmental pHs. There are some differences in

the rates at which these compounds degrade in air and in biodegradation rates. The estimated half-lives given for the compounds in reactions with hydroxyl radicals in air range from 15.2 days for isobutyronitrile to 55.2 days for propionitrile. Biodegradation rates of the three alkyl nitriles as measured in BOD5 testing suggest that the compounds are not readily biodegradable. However, the data from BOD20 testing of the butyronitrile isomers and a 14-day MITI test of isobutyronitrile suggest that the butyronitrile isomers may be readily biodegradable in a standard 28-day OECD TG 301C method assay. From the structural similarity of propionitrile and butyronitrile, propionitrile may also be expected to be readily biodegradable using the same OECD test guideline protocol. Therefore, the data submitted for the physicochemical and environmental fate endpoints generally support the category.

Data submitted for the acute fish, invertebrate and algae ecotoxicity endpoints and for the acute mammalian toxicity, genetic toxicity, and developmental toxicity endpoints show similarities among the three compounds with respect to toxic effects and effect levels. The submitters also include data to show that the mode of action for the mammalian toxicities of the alkyl nitriles is cyanide intoxication. Therefore, sufficient information has been presented to support the submitters' justification for the category.

Test Plan

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

The data provided for these endpoints are adequate for the purposes of the HPV Challenge Program.

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

The data provided for these endpoints are adequate for the purposes of the HPV Challenge Program.

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

Adequate data are available for all three members of the category for acute, genetic, and developmental toxicity endpoints and for propionitrile for repeated-dose and reproductive toxicity endpoints for the purposes of the HPV Challenge Program. Given the toxicological similarities among the three chemicals, EPA agrees with the submitters' plan to use a category approach to address data gaps for butyronitrile and isobutyronitrile for the repeated-dose and reproductive toxicity endpoints.

Genetic toxicity. Two robust summaries for mammalian cell gene mutation assay in cultured L5178Y mouse lymphoma cells exposed to propionitrile provided sufficient information to evaluate the studies. However, the submitters need to explain the positive results (both genotoxic and cytotoxic) of one of the studies (ref. # 28) that was conducted at much lower concentrations without exogenous metabolic activation.

Reproductive toxicity. Adequate data are available for propionitrile; however, as functional testing was not conducted by mating treated animals of both sexes, the submitter needs to explicitly describe the results for reproductive histopathology (and testicular weights) from the 14-week repeated-dose study in the robust summaries.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees with the submitters that measured data along with predicted values are adequate for the alkyl nitriles category for the fish, invertebrate, and algae endpoints for the purposes of the HPV Challenge Program. The submitters need to address minor deficiencies in the test plan and robust summaries.

Invertebrates. The test plan (p.10) and robust summary (p.18) for the 48-hour study of propionitrile in *Daphnia magna* report a 48-hour EC50 value of 250 mg/l; however, according to the robust summary, the value corresponded to an LC50 since mortality was the endpoint evaluated. Further, the test plan describes this as “The 96-hour EC50 value...” for this test, whereas the robust summary indicates that the study was conducted for 48 hours. The submitters need to address this discrepancy.

Specific Comments on the Robust Summaries

Ecological Effects

Invertebrates. In the acute toxicity test with propionitrile, the “Result” section of the robust summary (p.18) noted “Three fish exposed to ...”. The word “fish” should be replaced by “daphnids.”

The robust summary of the acute toxicity study with isobutyronitrile does not include an explanation for the loss of test substance. The submitters need to provide this information.

Followup Activity

EPA requests that the submitters advise the Agency within 60 days of any modifications to their submission.