

May 22, 2003

David Brandwene
Senior Toxicologist
Akzo Nobel Functional Chemicals, Inc.
5 Livingstone Avenue
Dobbs Ferry, NY 10522-3407

Dear Dr. Brandwene:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2,2',2",2'''-(1-ethanediyldinitrilo)tetrakisacetonitrile posted on the ChemRTK HPV Challenge Program Web site on January 24, 2003. I commend Akzo Nobel Functional Chemicals, 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 Akzo Nobel Functional Chemicals, 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 Heffer, 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: A. Abramson
W. Penberthy
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:
2,2',2'',2'''-(1-Ethanediyldinitrilo)tetrakisacetonitrile**

Summary of EPA Comments

The sponsor, Akzo Nobel Functional Chemicals LLC, submitted a test plan and robust summaries to EPA for 2,2',2'',2'''-(1-ethanediyldinitrilo)tetrakisacetonitrile (also called ethylenediaminetetraacetonitrile or EDTN, CAS No. 5766-67-6) dated December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 24, 2003. Information is also included for an analog, propylenediaminetetraacetonitrile (PDTN, CAS No. 110057-45-9).

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

1. Physicochemical Properties and Environmental Fate. The submitter needs to provide measured vapor pressure and water solubility data.
2. Health Effects. EPA believes that information provided by the submitter is not sufficient to meet the criteria for claiming EDTN as a closed-system intermediate. EPA agrees with the submitter's plan to conduct a developmental toxicity study and recommends that a combined reproduction/developmental toxicity screening test be carried out instead of the proposed developmental toxicity study.
3. Ecological Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.

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

EPA Comments on the 2,2',2'',2'''-(1-Ethanediyldinitrilo)tetrakisacetonitrile Challenge Submission

Test Plan

General Comment.

The submitter provides adequate support and justification for the use of data on PDTN as an analog to EDTN.

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

Adequate data are available for melting point, boiling point, and partition coefficient. The submitter needs to provide measured data for vapor pressure and water solubility.

Vapor Pressure. The estimated vapor pressure for EDTN is approximately five orders of magnitude lower than the measured data for the analog PDTN. Given that the molecular weight for EDTN is lower than PDTN, the resulting vapor pressure would be expected to be higher, not significantly lower. Comparison of the measured and estimated vapor pressures for PDTN indicate that the estimated value does not reliably reflect the vapor pressure of this type of chemical. Thus, the submitter needs to provide measured data.

Water Solubility. The estimated water solubility for EDTN is approximately three orders of magnitude higher than for PDTN. While the water solubility for EDTN would be expected to be slightly higher, the estimate may significantly overstate the water solubility of EDTN. Comparison of the measured and

estimated water solubilities for PDTN indicate that the estimated value does not reliably reflect the water solubility of this type of chemical substance. Because reliable data are necessary for the estimation techniques, e.g., fugacity, the submitter needs to provide measured water solubility data.

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

Adequate data are available for these endpoints, either from EDTN or the analog PDTN. As noted above, measured data are needed for vapor pressure and water solubility and thus the fugacity calculation should be updated when measured data become available.

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

Adequate data are available for acute, repeated-dose, and genetic toxicity endpoints for the purposes of the HPV Challenge Program. The submitter plans to conduct a test for developmental toxicity, for which EPA recommends OECD TG 421 (reproduction/developmental toxicity screening test) instead of the proposed OECD TG 414 protocol. The submitter requests an exemption from reproductive toxicity testing based on EPA's guidelines for closed-system intermediates.

Reproductive Toxicity. No data were submitted for this endpoint and no testing is proposed, based on the submitter's assertion that EDTN is a closed-system intermediate. As discussed below, EPA does not believe the closed-system intermediate criteria have been met. However, if the submitter conducts the recommended OECD TG 421 instead of OECD TG 414, the reproductive toxicity endpoint would then be addressed.

The Guidance for Testing Closed System Intermediates for the Challenge Program <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 believes that the information provided by the submitter is not sufficient to satisfy the requirements for classification as a closed-system intermediate. Repeated exposure is likely to occur when bags of the chemical are emptied into a reactor used to produce another chemical substance. In addition, repeated exposure may occur while putting the chemical into bags at the site of manufacture or in transport of empty bags to the site of manufacture for re-use; no information on these activities is provided in the test plan.

I. Site information

- A. Number of sites.

The test plan states that EDTN is manufactured at a U.S. facility and transported to three other sites, two of which are outside the U.S. The Chemical Economics Handbook (SRI, 2000) identifies four sites owned by other firms that produce ethylenediaminetetraacetic acid (EDTA), the product manufactured from this chemical intermediate. However, EDTA can be produced directly from simpler

chemicals without isolating the chemical which is the subject of this test plan; it is not known if the other sites isolate the chemical. The sole use EPA found for EDTN is the manufacture of EDTA.

B. Basis for “closed process” conclusion at each site.

1) Process description.

No information is provided in the test plan on the manufacture or isolation of the chemical. However, the objectionable nature of chemicals used to produce this intermediate make it highly likely that closed systems are used.

The chemical is transported in woven polypropylene bags. No information is provided to substantiate that the bags are filled in a manner that precludes potential exposure to the chemical substance.

At the site where EDTN is reacted, the bags are opened and emptied into a reactor. Although workers wear protective equipment, the transfer is not done in closed systems.

Empty bags are returned to the manufacturing site for reuse. No information is provided to demonstrate that exposure of persons handling the sacks does not occur.

2) Monitoring data showing no detection.

Wastewater from production of EDTN is disposed by injection into a deep well at the manufacturing facility. According to the test plan, waste from the reactor contains approximately 0.03% of EDTN.

C. Data on “presence in distributed products.”

According to the test plan, measurement of residual EDTN in the product EDTA have not been made. The test plan states that it is extremely unlikely that EDTN will be found in EDTA.

II. Information on transport (mode, volume, controls, etc)

According to the test plan, EDTN is transported in woven polypropylene bags. At the site where the chemical is reacted, the bags are stored in a warehouse.

III. A data search showing that the chemical is not present in other end products.

No supporting evidence is provided.

Developmental Toxicity. EPA agrees with the submitter’s plan to conduct a test for developmental toxicity. However, EPA recommends the submitter conduct a combined reproduction/developmental toxicity screening test (OECD TG 421) instead of the proposed developmental toxicity study (OECD TG 414).

Ecological Effects (fish, invertebrates, and algae).

Adequate existing data are available for these endpoints.

Specific Comments on the Robust Summaries

Generic comments.

The submitter needs to identify the purity of the test substance. When data for PDTN are used to address an EDTN endpoint, the substance entry should be stated as “other test substance; analog PDTN” to clearly indicate the use of PDTN as an analog.

Followup Activity

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