August 26, 2003

Gail M. Garvin
Global Environmental Health and Safety Specialist
Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268

Dear Ms. Garvin:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 2,3,4,5,6-Pentachloropyridine posted on the ChemRTK HPV Challenge Program Web site on April 25, 2003. I commend Dow AgroSciences, LLC 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 Dow AgroSciences 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 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,

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:
2,3,4,5,6-Pentachloropyridine

Summary of EPA Comments

The sponsor, Dow AgroSciences, LLC, submitted a test plan and robust summaries to EPA for 2,3,4,5,6-pentachloropyridine (CAS No. 2176-62-7) dated April 16, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on April 25, 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, and partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured vapor pressure and water solubility data following OECD guidelines.

2. Environmental Fate. 1) The data provided by the submitter for photodegradation are adequate for the purposes of the HPV Challenge Program. 2) The submitter needs to provide a technical discussion in the stability in water robust summary. 3) The biodegradation data provided by the submitter are inadequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data. 4) EPA recommends using the Level III EQC model to estimate distribution in the environment.

3. Health Effects. EPA agrees with the submitter's test plan, except that EPA recommends the submitter conduct a combined reproductive and developmental toxicity screening study instead of the proposed developmental toxicity study.

4. Ecological Effects. EPA reserves judgement on the adequacy of submitted fish studies pending submission of missing critical data elements. EPA recommends that the submitter conduct toxicity testing for daphnia in addition to the proposed algal test because the data submitted for aquatic invertebrates are inadequate to address this endpoint.

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

EPA Comments on the 2,3,4,5,6-pentachloropyridine Challenge Submission

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, and partition coefficient are adequate for the purposes of the HPV Challenge Program.

Vapor pressure. The submitter provided a vapor pressure of 0.014 mm Hg at 25 °C from Gehring et al. (1967) and stated that this is a measured value. The value in Gehring was extrapolated to 25 °C from one value (vapor pressure = 1 mm Hg at 94 °C). According to EPA guidelines, calculations showing a value less than $1x10^{-5}$ Pa ($8x10^{-8}$ mm Hg) at 25 °C may be acceptable in lieu of measuring vapor pressure. However, the estimated value is greater than $8x10^{-8}$ mm Hg at 25 °C and the extrapolated value is based on limited data that are questionable and inadequate. The submitter needs to provide measured vapor pressure data following OECD guidelines.

Water solubility. The submitter provided a "measured" water solubility of 8.5 mg/L at 25 °C in the robust summary without the test method. The reference given for this water solubility value cites regression equations for the estimation of water solubility (Lyman et al. 1982). The data provided by the submitter

are inadequate for this endpoint, since only estimated values are available. The submitter needs to provide measured water solubility data following OECD guidelines.

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

The data provided by the submitter for photodegradation are adequate for the purposes of the HPV Challenge Program.

Stability in water (hydrolysis). While EPA agrees that pentachloropyridine does not contain any functional groups that are susceptible to hydrolysis, the submitter still needs to provide a brief technical discussion in the robust summary as stated in the test plan.

Biodegradation. The submitter provided only scanty data in the robust summary section 3.6 BOD5, COD, or BOD5/COD Ratio; however, the summary lacked information such as type of biodegradation (aerobic or anaerobic), source and concentration of inoculum, contact time, percent degradation, etc. The data provided by the submitter are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data for this chemical following OECD Guideline 301.

Transport and distribution (fugacity). No robust summary is provided for this endpoint. The submitter stated in the test plan that a Level I EQC model will be used to estimate the distribution of pentachloropyridine in the environment and that EPIWIN v3.02 will be used to estimate the properties needed to run the Level I EQC model. EPA now recommends the use of EQC level III, which provides a more rigorous level of analysis. Values based on a Level III fugacity model are more realistic and useful for estimating a chemical's fate in the environment. Results and input data need to be in robust summary format.

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

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

Genetic Toxicity. EPA agrees with the submitter that a gene mutations test and an *in vitro* cytogenetics test should be conducted to address this endpoint. The tests should be conducted following OECD guidelines.

Reproduction Toxicity. EPA recommends that the submitter conduct a combined reproductive and developmental toxicity screening test following OECD Test Guideline 421, rather than OECD Guideline 414, because reproductive effects have been observed in a 90-day repeated-dose study.

Developmental Toxicity. The developmental toxicity endpoint will be adequately addressed by the EPA-recommended combined reproduction/developmental toxicity screening study following OECD Test Guideline 421.

Ecological Effects (fish, invertebrates, and algae)

Fish. The fish data submitted were lacking too many study details to determine the adequacy of the data; therefore, EPA reserves judgement on the fish endpoint pending submission of missing study details.

Invertebrates. EPA recommends that the testing in invertebrates be conducted because the data submitted for aquatic invertebrates are inadequate to address this endpoint. The submitted sand shrimp study was conducted without using analytical monitoring and no test type was reported.

Algae. EPA agrees with the submitter's proposed testing on algae.

Testing for both aquatic invertebrates and algae should be conducted using measured concentrations.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The first oral study should not be given a reliability code of 1 because the number of animals per dose was limited.

Repeated-Dose Toxicity. The submitter needs to explain the statement “complete necropsy examination” in the 90-day study. If histopathological analysis was conducted, then the submitter should list the organs that were examined.

Ecological Effects

Fish. For the 96-hour test with *Pimephales promelas*, the submitter needs to provide the following information: pH, dissolved oxygen, DO, water hardness, and water temperature; age of the testing organisms at test initiation; replicate numbers; test concentrations; test conditions; statistical analyses used; 95% confidence intervals; control mortality; and measurement analyses.

Followup Activity

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