

December 23, 2003

Ms. Gail M. Garvin
Global Environment 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 Crude 2-chloro-4-trifluoromethyl-3-acetoxydiphenyl ether posted on the ChemRTK HPV Challenge Program Web site on August 22, 2003. I commend Dow AgroSciences LLC 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 Dow AgroSciences LLC 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:
Crude 2-Chloro-4-Trifluoromethyl-3'-Acetoxydiphenyl Ether (RH-35,201 Crude)**

Summary of EPA Comments

The sponsor, Dow AgroSciences LLC, submitted a test plan and robust summaries to EPA for crude 2-chloro-4-trifluoromethyl-3'-acetoxydiphenyl ether (RH-35,201 crude), CAS No. 50594-77-9, dated May 22, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on August 22, 2003.

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

1. Physicochemical Properties. The submitter needs to provide measured vapor pressure data and provide melting and boiling point data on a purer grade of the chemical.
2. Environmental Fate. EPA recommends that the submitter use a level III model when running its fugacity model.
3. Health Effects. Adequate data are available for all endpoints except for gene mutation. EPA reserves judgement on the adequacy of the data submitted for gene mutation pending receipt of additional information. In addition, the submitter needs to address deficiencies in the robust summaries.
3. Ecological Effects. Adequate data are available for all ecological endpoints.

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

EPA Comments on the Crude 2-chloro-4-trifluoromethyl-3'-acetoxydiphenyl Ether (Rh-35,201 Crude) Challenge Submission

Test Plan

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

The data provided by the submitter for water solubility are adequate for the purposes of the HPV Challenge Program. The submitter needs to add vapor pressure and water solubility to its list of physicochemical properties on page 4 of the test plan.

Melting Point. The submitter measured the melting point of the crude material (47.3-53.1% pure) according to OECD TG 102. Because this material is so impure, the data are not accurate for the active ingredient. The submitter did not explain why the impure material was used. A purer grade of material (94.5% pure) was available for use as an HPLC standard in the water solubility and partition coefficient tests. A melting point measured for this purer material is needed.

Boiling Point. The submitter measured the boiling point of the crude material (47.3-53.1% pure) according to OECD TG 103. Because this material is so impure, it is impossible to determine if the data are accurate for the active ingredient. The submitter did not explain why the impure material was used. A purer grade of material (94.5% pure) was available for use as an HPLC standard in the water solubility and partition coefficient tests. A boiling point measured for this purer material is needed.

Vapor pressure. The submitter did not provide any information on vapor pressure. The submitter needs to provide measured vapor pressure data following OECD guidelines.

Partition Coefficient. The partition coefficient was measured for the crude material (47.3-53.1% pure) according to OECD Guideline 107 (the shake-flask method). As the active ingredient was not detected in the water phase, the partition coefficient could not be calculated (the HPLC method, OECD Test Guideline 117, would be a better choice than the shake-flask method for a material of such low water solubility, and is less sensitive to impurities). As the log K_{ow} can be estimated using KOWWIN, an estimated value is acceptable. The Agency obtained an estimated log K_{ow} value of 4.41. The submitter needs to supply an estimated log K_{ow} and corresponding robust summary.

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

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

Fugacity. The submitter proposes to evaluate fugacity using level I fugacity modeling. Although EPA had previously recommended the use of level I, this model is somewhat limited. EPA now recommends the level III model, which provides a more rigorous level of analysis. EPA believes that values based on a level III fugacity model are more realistic and useful for estimating a chemical's fate in the environment. The submitter should use measured physicochemical data as inputs to the model. Estimated or calculated values introduce uncertainties that then become magnified in modeling applications.

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

Adequate data are available for all endpoints except gene mutation for the purposes of the HPV Challenge Program. The submitter also needs to address deficiencies in the robust summaries.

Repeated-dose and developmental toxicity. The submitter needs to provide a separate robust summary for each of these endpoints from the combined repeated-dose/reproductive/developmental toxicity screening test results.

Genetic toxicity (gene mutations). EPA reserves judgement on the adequacy of the data submitted for gene mutations because the documentation (ames4.bmp) for results of the third Ames test (The Dow Chemical Company, 1977) is missing. Additional genetic toxicity data are available in the TSCATS database (files 423703 and 423705).

Ecological Effects (fish, invertebrates, and algae)

Ecological data submitted for fish, daphnia, and green algae are adequate. However, the sponsor needs to add missing data elements to the robust study summaries.

Specific Comments on the Robust Summaries

Health Effects

Genetic toxicity. The omitted information in the robust summary for an Ames test conducted in 1977 includes whether the concentrations were based on 100% active ingredient and the results document.

Reproductive toxicity. Missing information for the robust summary for a combined repeated-dose and reproductive/developmental toxicity screening assay in rats includes the magnitude of the decrease in

parental body weight and the basis for selecting a parental NOAEL of 500 ppm. From the data provided, the NOAEL appears to be 1,500 ppm.

Ecological Effects

Fish. Missing study details include the number of fish per concentration and the results of daily measurements and/or ranges for temperature, pH, and dissolved oxygen.

Invertebrates. Missing study details include temperature, pH, and dissolved oxygen concentrations, which were reportedly measured at 0 and 48 hours.

Algae. The summary needs to state clearly whether test concentrations were nominal or measured. Missing study details include the values for illumination, temperature, and cell concentrations (all recorded daily), and pH (recorded at 0 and 96 hours).

Followup Activity

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