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201-14028



2005 SEP 13 AM 9:04
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September 1, 2005

Oscar Hernandez, Director – OPPT Risk Assessment Division
Environmental Protection Agency

Chemical Right-to-Know – HPV Challenge Program

Thank you for the comments provided on the HPV Test Plan and Robust Summaries for Crude 2-chloro-4-trifluoromethyl-3'-acetoxydiphenyl Ether (Rh-35,201 Crude) (CAS 50594-77-9). Provided below is the response of Dow AgroSciences (DAS) to the Agency's comments. As requested and referenced in our comments, we have updated the relevant robust summaries. The revised IUCLID document is included as an attachment in this email.

DAS Response to EPA Conclusions (noted in *italics*):

1. Physicochemical Properties. 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

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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. 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.

Response: The sponsors appreciate the Agency's confirmation that the data for the water solubility is adequate. Due to the limited availability of the pure material, physical properties were estimated using crude material. In the updated robust summary, the physical properties have been calculated for the pure material. While we understand that OECD test guidelines are required for product registration, we maintain that the measured values for these parameters, as conducted in 1967 prior to the publication of OECD guidelines, using scientifically valid methods, are adequate to fulfill data requirements for the purposes of the HPV program.

2. Environmental Fate. 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.

Response: The sponsors appreciate the Agency's confirmation that the data for photodegradation, stability in water and biodegradation are adequate. The sponsors agree with the agency's recommendations for using the Level III model where the nature of the chemical renders the analysis viable. Unfortunately, Level III analysis would not be scientifically valid in the case of this chemical.

3. Health Effects. 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 judgment 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).

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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.

Response: The sponsors appreciate the confirmation that most of the health effect data is adequate to meet most of the HPV requirements. However, the sponsor does not see the necessity or value in breaking the current/updated robust summary into two documents. The missing Ames Test will be attached to this response.

4. Ecological Effects. 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.

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).

Response: The robust summaries for all studies have been revised to provide additional information on exposure conditions and test concentrations. The sponsors maintain that, although the sand shrimp is not the usual species upon which aquatic toxicity testing is conducted, it satisfies the requirements for SIDS-level endpoint testing.

We do appreciate the time that you spent in review of our Robust Summaries and Test Plan. We hope that you find that the further information provided in our response above and in the updated robust summaries adequately addressed the issues that were identified.

Regards,

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