

November 17, 2005

Clyde Livingston  
Chemical Regulatory Compliance  
Monsanto Company  
800 North Lindbergh Blvd.  
St. Louis, MO 63167

Dear Mr. Livingston:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Glyphosate Intermediate, posted on the ChemRTK HPV Challenge Program Web site on November 2, 2004. I commend Monsanto Company 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 Monsanto 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](mailto:oppt.ncic@epa.gov) and [chem.rtk@epa.gov](mailto:chem.rtk@epa.gov).

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. 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](mailto: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: N. Patel  
J. Willis

## **EPA Comments on Chemical RTK HPV Challenge Submission: Glyphosate Intermediate**

### **Summary of EPA Comments**

The sponsor, Monsanto Company, submitted a test plan and robust summaries to EPA for N-(carboxymethyl)-N-(phosphonomethyl)glycine (Glyphosate Intermediate, GI, CAS No. 5994-61-6) dated December 8, 2003. EPA posted the submission on the ChemRTK HPV Challenge Website on November 2, 2004.

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

1. Physicochemical Properties. The submitter needs to add information to the robust summaries.
2. Environmental Fate. The submitter needs to provide measured ready biodegradation data and fugacity Level III modeling data and additional information on indirect photodegradation.
3. Health Effects. The submitted data for the acute, repeated-dose, reproductive and developmental toxicity endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the gene mutation endpoint pending submission of critical information in the robust summary. In addition, the submitter needs to either provide analog chromosomal aberration data or conduct an *in vitro* study to address this endpoint. The submitter needs to address deficiencies in the robust summaries.
4. Ecological Effects. The submitted data are adequate for all endpoints 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 Glyphosate Intermediate Challenge Submission**

#### **General**

The test plan proposes glyphosate as an analog for addressing the endpoints for GI. If glyphosate data are used to address health effects endpoints, the submitter needs to support the approach with information on similarities between GI data and glyphosate data and provide the corresponding robust summaries.

#### **Test Plan**

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

The data provided by the submitter for the melting point, vapor pressure, partition coefficient and water solubility endpoints are adequate for the purposes of the HPV Challenge Program.

*Boiling point*. The submitter stated in the robust summary that GI is "not distillable" but did not provide any additional information. The melting point robust summary states that GI decomposes when heated above 200 °C. The submitter needs to add this information to the boiling point robust summary.

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

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

*Photodegradation.* While the submitted data are adequate, the submitter needs to add the GI atmospheric oxidation data to the robust summary and test plan.

*Biodegradation.* The submitted data were developed using acclimated cultures and thus are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data on GI following OECD TG 301, using un-acclimated or non-adapted cultures.

*Fugacity.* The submitter needs to provide Level III modeling data in order to assess the distribution of GI in the environment.

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

The submitted data for the acute, repeated-dose, reproductive and developmental toxicity endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the gene mutation endpoint pending addition of critical information to the robust summary. In addition, the submitter needs to provide data for the chromosomal aberration endpoint. EPA recommends the use of analog data or *in vitro* testing on the sponsored substance according to OECD TG 473. The submitter needs to address deficiencies in robust summaries.

*Repeated-Dose Toxicity.* Although the 28-day repeated-dose dermal toxicity data are adequate to address this endpoint, EPA suggests that the submitter provide a robust summary of the 13-week inhalation toxicity/reproduction study, focusing on systemic effects and histopathological findings in addition to the reproductive organs because of potential inhalation or oral occupational exposure during GI manufacture.

*Genetic Toxicity (gene mutations).* The main deficiency in the submitted negative microbial mutagenicity assay (Ames test) is that it was conducted at concentrations ranging from 0.1 to 500 ug/plate with no evidence of cytotoxicity at the highest concentration and no justification for selecting these concentrations. The OECD guidelines recommend a highest concentration for this test of 5000 ug/plate. EPA reserves judgement on the adequacy of data for this endpoint pending submission of adequate justification for the low dose used in the study. If this information is not available, the submitter needs to either provide adequate analog data or conduct a study according to OECD TG 471.

*Genetic Toxicity (chromosomal aberrations).* No data were submitted to address this endpoint. The submitter needs to either provide analog data or conduct *in vitro* testing according to OECD TG 473 to address this endpoint.

### Ecological Effects (fish, invertebrates, and algae)

The submitted data are adequate for all endpoints for the purposes of the HPV Challenge Program.

### **Specific Comments on the Robust Summaries**

#### Physicochemical Properties

*Melting Point.* The robust summary lacks the description of the method used.

*Water Solubility.* The robust summary lacks a detailed description of the method used and is missing critical information such as whether and how key experimental parameters such as pH and buffering capacity were controlled.

## Health Effects

*Repeated-Dose Toxicity.* The repeated-dose dermal toxicity summary did not specify the study guideline used, a list of organs and tissues that were examined microscopically, adequate characterization of dermal lesions and whether or not any blood parameters were evaluated (hematology and clinical chemistry).

*Genetic Toxicity.* The submitted negative microbial mutagenicity assay (Ames) lacks information on control response, effects by concentration, criteria for a positive response, and statistical methods used.

*Reproductive Toxicity.* The submitter needs to provide the following information in the robust summary for the inhalation reproductive toxicity study, if available: information on the rat strain, test substance purity, aerosol particle size, female reproductive organs examined microscopically (if any), incidence of effects by sex and by treatment/mating regimen, statistical methods used, and statistical significance.

*Developmental Toxicity.* The submitter needs to provide the following information in the robust summary for the developmental toxicity study: the guideline followed, statistical methods used, results of statistical analysis, and details on the observed maternal toxicity.

## **Followup Activity**

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