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June 10, 2008

Stephen Johnson, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for S,S',S''-tributyl phosphorotrithioite

Dear Administrator Johnson:

The following comments on Bayer CropScience's test plan for S,S',S''-tributyl phosphorotrithioite (Merphos, CAS No. 150-50-5) are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

This test plan for Merphos uses existing data from acute oral and dermal toxicity studies, repeat dose studies, and rabbit skin and eye irritation tests. While existing data on Merphos is lacking for reproductive toxicity, developmental toxicity, and genotoxicity, the sponsor offers data from the pesticide Tribufos (S,S',S''-tributyl phosphorotrithioate, CAS No. 78-48-8) to fulfill the Screening Information Data Set (SIDS) endpoints requested by the High Production Volume (HPV) Challenge Program. The primary justification for the use of Tribufos as an appropriate analog is the fact that the chemicals differ only by a carbonyl group. Merphos is an intermediate in the production of the pesticide Tribufos. In its comments on the test plan, the EPA has called the sponsor's justification for using Tribufos as an analog into question.

To address EPA's concerns, Bayer CropScience could include data from additional analogs to enhance the weight-of-evidence approach using resources such as the OECD (Q)SAR Toolbox, freely available at www.oecd.org/env/existing_chemicals/qsar. Another in silico tool which Bayer CropScience could use is the ECOSAR program, available at www.epa.gov/oppt/newchems/tools/21ecosar.htm. Modeling both Merphos and Tribufos using ECOSAR would address aquatic invertebrate and plant endpoints for which Merphos data is lacking as well as potentially strengthen the justification for using Tribufos, assuming similar toxicity values are predicted by the program. Bayer CropScience could also further emphasize the similarity of Merphos and Tribufos where data for both exist. For example, the two chemicals demonstrate similar acute and repeat dose toxicity (with regard to LD50 and clinical symptoms and pathology), as well as skin and eye irritation. In fact, Merphos appears to be less

toxic than Tribufos based on data from acute oral and aquatic toxicity tests, possibly due to the reactive potential of the carbonyl group. Thus, the use of Tribufos as an analog is likely to lead to a conservative assessment of Merphos toxicity. A final suggestion to the sponsor for boosting support for the use of Tribufos, would be inclusion of data demonstrating rapid conversion of Merphos to Tribufos in the environment (via oxidation).

Another issue raised on the EPA's response to the test plan is the lack of hydrolysis data for Merphos. As a general rule, physico-chemical and environmental fate data should be available prior to making decisions on additional animal tests because Merphos may rapidly hydrolyze to well-characterized products thereby precluding further testing. Given that some participants have used existing data on hydrolysis products of the HPV chemicals to eliminate animal tests (for an example, see Triisopropylborate, <http://www.epa.gov/chemrtk/triprobtc/c14841tc.htm>), Bayer CropScience should first conduct the necessary hydrolysis study.

In summary, Bayer CropScience should complete characterization of the physical chemical properties of Merphos. Also, the sponsor could bolster the analog justification for Tribufos using the suggestions outlined above and include data from additional analogs. This would strengthen the test plan in keeping with the EPA's 1999 "Letter to Manufacturers/Importers [of HPV chemicals]," which encourages program participants to use chemical categories, and structure activity relationships to minimize additional *in vivo* testing. This guidance also states that "animal experiments should not be performed if another validated method- not involving the use of animals- is reasonably and practically available". Therefore, should the justification for Tribufos fail to meet EPA standards and other analogs with existing data can not be identified, we urge Bayer CropScience to use *in vitro* methods to fulfill requested data wherever possible.

Thank you for your attention to these comments. We may be reached at 202-686-2210, ext. 345, or via e-mail at nbeck@pcrm.org.

Sincerely,

Nancy Beck, Ph.D.
Policy and Science Advisor

Chad B. Sandusky, Ph.D.
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