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July 27, 2007

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 2-propanone, Reaction Products with Phenol

Dear Administrator Johnson:

The following comments on General Electric Plastics' January 10, 2007 test plan for 2-propanone Reaction Products with Phenol 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.

The reaction of 2-propanone with phenol produces the desired product bisphenol A (pp-BPA), as well as several related linear and cyclic bis- and tris-phenols. Collectively, these products are termed "BPA Tars" (CAS RN 4767-03-7). The test plan submitted by Toxicology/Regulatory Services on behalf of General Electric Plastics is based on the data available on pp-BPA, given that pp-BPA is the major product of the reaction and the minor constituents produced are predicted to have biological reactivity similar to that of pp-BPA. The use of existing pp-BPA data to address gaps in the knowledge of related chemicals is in keeping with the EPA's agreement with the animal protection community to maximize the use of existing data in order to minimize further animal testing.

It is worthy to note that available oral, dermal, and genotoxicity data from spirobiindane (a minor constituent of BPA-Tars) are similar to that from pp-BPA, supporting the use of pp-BPA as a representative constituent of the BPA Tars mixture. To confirm that all of the reaction products share the same physicochemical properties as pp-BPA, and therefore that pp-BPA is an adequate representative of the group, water solubility and biodegradation testing on BPA-Tars is proposed. The results of the water solubility testing will be used to determine whether additional confirmatory ecotoxicity testing will be performed, in order to support the use of data from pp-BPA. If ecotoxicity testing is pursued, General Electric Plastics proposes testing on fathead minnows, claiming that a fish study is "technically more feasible" than studies using *Daphnia* or algae. In its October 1999 "Letter to Manufacturers/Importers [of HPV chemicals]," the EPA states that "animal experiments should not be performed if another validated method - not involving the use of animals- is reasonably and practically available". Based on this directive, we ask General Electric Plastics to use the lower order animal, *Daphnia,* or algae for any confirmatory testing, especially given that *Daphnia* and algae are usually more sensitive than fish to toxicity (Hutchinson et al., 2003). In addition, the fish test is intended to show whether exposure to BPA-Tars will result in large-scale fish death, thereby predicting economic loss and ecologic damage. If this exposure kills the food on which fish subsist, it could deplete fish populations even without direct

fish toxicity. Therefore, until the toxicity of BPA-Tars to aquatic plants and invertebrates is known, tests on fish are premature.

If testing on *Daphnia* or algae is truly not technically feasible, then General Electric Plastics must provide compelling evidence to support its claim. In the event that fish testing is performed, rather than a traditional (LC50) test, the company should conduct an acute threshold test in which fish testing would be performed at one concentration only—the lowest EC50 concentration obtained in the existing *Daphnia* and algae data for pp-BPA. Fish are rarely more sensitive to toxicity than algae and *Daphnia*, but in the event that fish demonstrate greater sensitivity to the BPA-Tars mixture than algae or *Daphnia* did to pp-BPA, testing with fish would be continued at lower concentrations using a step-down approach (Jeram et al., 2005; Hutchinson et al., 2003).

Numerous studies are cited showing that pp-BPA is not a genetic, reproductive, or developmental toxicant, and a study on spirobiindane also yielded negative genotoxicity results. Based on these data, the genetic, reproductive, and developmental toxicity testing requirements of the HPV program for BPA-Tars can be satisfied by accepting pp-PBA data as a surrogate for BPA-Tars. Nevertheless, General Electric Plastics proposes testing the BPA-Tars mixture for genotoxicity using the bacterial reverse mutation, chromosomal aberration, and mouse lymphoma assays. It is unclear why genotoxicity testing is proposed, but if GE Plastics does perform these tests, we strongly suggest that the chromosomal aberration assay be performed *in vitro*, as opposed to *in vivo*, following the Organization for Economic Coordination and Development (OECD) Test Guideline (TG) 473. The EPA, in its 1999 "Letter to Manufacturers/Importers" mentioned above, encourages HPV Challenge Program participants "to use in vitro genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use."

In conclusion, General Electric Plastics has made good use of existing data in order to satisfy the requirements of the HPV Challenge program. This approach greatly reduces animal testing, but further efforts could be made towards that goal by incorporating the suggestions outlined in this letter.

Thank you for your attention to these comments. I 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.
Director of Research

Hutchinson, TH, et al. (2003) A strategy to reduce the numbers of fish used in acute ecotoxicity testing of pharmaceuticals. Environ. Toxicol. Chem. 22: 3031-3036.

Jeram S, et al. (2005) A strategy to reduce the number of fish in acute ecotoxicity testing of new chemical substances notified in the European Union. Regul. Toxicol. Pharmacol. 42: 218-224.