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December 17, 2003

Michael O. Leavitt, Administrator  
U.S. Environmental Protection Agency  
Ariel Rios Building, 1101-A  
1200 Pennsylvania Ave., N.W.  
Washington, DC 20460

Subject: Comments on the HPV Test Plan for Polyphenyls category

Dear Administrator Leavitt:

The following comments on Solutia's test plan for the chemical category Polyphenyls (3- & 4-Phenyl rings) 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.

Solutia, Inc. submitted its test plan on July 24, 2003 for the Polyphenyls category, which consists of multiple isomers of both Mixed Terphenyls (CAS No. 26140-60-3) and Quaterphenyls (CAS No. 29036-02-0). Commercial products containing Mixed Terphenyls and Quaterphenyls, such as SANTOWAX R, THERMINOL 88, and SANTOTAR 9, are used as heat storage and transfer agents. These two members of the Polyphenyls category are mixtures of aromatic hydrocarbons containing 3 and 4 benzene rings. For instance, Mixed Terphenyls contain higher levels of 3-ring moieties and less 4-ring moieties while the reverse is true for Quaterphenyls. With a minor structural difference in the placement of the secondary or tertiary benzene rings, the physicochemical and toxicological properties of these two chemicals are very similar, as supported by existing data. We applaud Solutia's effort in comparing data for both chemicals and we support the formation of a category for these chemicals.

A 235-day chronic repeated dose toxicity study with Mixed Terphenyls, as well as multiple studies with each of the three isomers: meta-, ortho-, and para-terphenyl, all indicate no effects on reproductive organs after histopathological examination. Similarly, no effects were reported on rat gonads following 30 days oral exposure to m-, p-, or o-terphenyl. We concur with Solutia's assessment that there is no evidence that these compounds would be expected to affect reproductive performance. This is a thoughtful application of toxicology and appropriate for a screening level program such as HPV.

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At this time, however, we do question Solutia's assessment that a combined reproductive/developmental toxicity study (OECD 421) is necessary **simply** to address the developmental toxicity endpoint. If carried out, this test will result in the death of at least 675 animals, without adequately interpreting data from existing studies.

*In vitro* tests with all three terphenyl isomers indicate that there could be embryotoxic effects. With positive results reported for the terphenyl isomers in the mouse *in vitro* fertilization (IVF) studies, Mixed Terphenyls should be treated as a developmental toxicant/teratogen. When the above studies are considered together, these data should be sufficient for a screening level program and no further testing should be carried out. We question the proposal to kill 675 animals in an attempt to "check-the-box" for the developmental toxicity endpoint in the SIDS battery. As indicated in the October 1999 letter and the December 2000 *Federal Register* notice, "participants may conclude that there are sufficient data, given the totality of what is known about a chemical that certain endpoints need not be tested". The data showing positive results for terphenyl isomers in embryotoxicity studies should be adequate for a **screening level program** such as HPV, making further testing of these compounds wasteful and unnecessary.

Before moving to animal tests, we strongly urge Solutia to conduct the rodent embryonic stem cell test (EST), a validated protocol for assessing embryotoxicity, for comparison with IVF results. As you are aware, the EST has been validated by the European Centre for the Validation of Alternative Methods, and the Centre's Scientific Advisory Committee has concluded that this test is ready to be considered for regulatory purposes.

We again applaud Solutia's efforts on a well-thought out test plan, drawing on all available information and use of estimation modeling programs, to meet most of the SIDS endpoints for the Polyphenyls category. This approach is consistent with the EPA's stated goals of maximizing the use of existing data in order to limit additional animal testing. However, we are hopeful that Solutia will reconsider their proposal to kill 675 animals in a study which is inconsistent with this principle. Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at [meven@pcrm.org](mailto:meven@pcrm.org).

Sincerely,

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Research Analyst

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