

201-14867

Anh Nguyen

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To: NCIC HPV@EPA

CC:

Subject: Environmental Defense comments on the Polyphenyls (3 and 4-Phenyl Rings) Category

----- Forwarded by Anh Nguyen/DC/USEPA/US on 12/02/2003 06:59 AM -----

Richard\_Denison@environmentaldefense.org on 12/01/2003 05:52:46 PM



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Subject: Environmental Defense comments on the Polyphenyls (3 and 4-Phenyl Rings) Category

(Submitted via Internet 12/1/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and dalede@Solutia.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for the Polyphenyls (3 and 4-Phenyl Rings) Category.

The test plan and robust summaries submitted by Solutia, Inc. address two CAS Numbers; mixed terphenyls (CAS# 26140-60-3) and quaterphenyls (CAS# 29036-02-0). According to the sponsor, these substances are manufactured at a single site in an essentially closed and continuous process and then presumably are either sold to other customers for unspecified uses or used by Solutia for production of commercial products such as heat storage and transfer agents.

The terphenyls are comprised of at least three individual congeners; o-, m- and p-terphenyl. The composition of the quaterphenyls was not specified, although all constituents represent various mixtures of four phenyl rings without any other functional groups. The sponsor states that it does not separate and sell or use individual congeners, but it is not clear whether the buyers of the mixture separate and use individual congeners in their products.

According to the information provided in the test plan characterizing Solutia's production and use, there are minimal opportunities for environmental releases and worker exposure to these substances. However, customers of Solutia may use these substances in ways that lead to environmental releases and consumer exposure. In any event, releases and human exposure could occur from accidents or leakage from products containing terphenyls or quaterphenyls.

The test plan provides a convincing justification for establishing a category for the terphenyls and quaterphenyls, and we support it. The sponsor states that available data are available to fulfill HPV requirements with the exception that a combined reproductive/developmental toxicity study is proposed. We agree with these conclusions and proposal. We also commend the sponsor on preparing a complete and objective test plan. Specific comments on the test plan and robust summaries are as follows:

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1. The formation of the proposed category is justified because of similarities in chemical structure, physiochemical properties, the lack of functional groups on any of the mixture constituents, expected free rotation of the ring structures although there be some steric differences, expected similarities in metabolism and similarities in existing toxicological data. We do note, however, that category formation and justification in general would benefit from gene array data demonstrating that proposed members of a category elicit the same pattern of gene expression changes in appropriate biological systems.

2. The structure for m-terphenyl is incorrect on page 6 of the test plan, as it mistakenly depicts the structure for o-terphenyl.

3. The terphenyls and quaterphenyls possess high toxicity (in the range of 20-100 ug/l) to fish, aquatic toxicity and aquatic invertebrates, but the available data are adequate for screening level purposes. These findings do, however, raise concern given the potential for releases to occur from accidents or leakage from various products, and from the unknown uses of the substances by customers of Solutia.

4. Can the sponsor offer an explanation for the finding that the p-terphenyl congener exhibits much lower toxicity in aquatic systems than the other congeners?

5. On page 17 of the test plan, it is stated that these chemicals are resistant to water hydrolysis. However, they are biodegradable. What are the degradation products and are those products responsible for the high degree of ecological toxicity caused by the terphenyls and quaterphenyls?

6. Neither the terphenyls nor the quaterphenyls appear to possess genotoxic properties and we support the read-across approach where it is used.

7. The repeat dose studies are adequate to fulfill HPV requirements but we do note that the NOEL for the 265-day study is 3 mg/kg/day, whereas the NOELs for the 30-day studies are 100-250 mg/kg/day. Is this difference caused by a buildup of the terphenyls in the animals? Are there any available toxicokinetic studies that could address this issue? If so, they should be included in the robust summaries. Are the terphenyls hydroxylated and are the hydroxyl metabolites conjugated and cleared from the body? Also, the test substance used in the 265-day study contained 5% biphenyl. Could the biphenyl have caused the observed difference in NOELs as well as the observed kidney toxicity?

8. The sponsor proposes to conduct a reproductive/developmental study on a terphenyl mixture. We support this proposal because no such studies are available, in vitro studies demonstrate that the terphenyls are embryotoxic and it can be hypothesized that in vivo hydroxylation of both the terphenyls and quaterphenyls could produce estrogenic metabolites; this occurs with some biphenyl molecules. For this reason, we also propose that the sponsor conduct an estrogenic screen on the terphenyl mixture using a metabolic activating system. We agree with the proposal to use a terphenyl mixture to conduct the reproductive/developmental study but we do recommend that the mixture used be one that contains significant amounts of

m-terphenyl, as it appears to be the most toxic of the congeners.

Thank you for this opportunity to comment.

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