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cc:

Subject: public comments on ACC's HPV test plan for the propylene category

Attached please find comments on the American Chemistry Council's test plan for the propylene category. The comments are submitted on behalf of Animal Protection Organizations.

Thank you.

Nicole Cardello, M.H.S.
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April 5, 2002

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the American Chemistry Council's HPV Test Plan for the Propylene Streams Category

Dear Administrator Whitman:

The following comments on the American Chemistry Council's (ACC's) test plan for the propylene category 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 nine million Americans.

The propylene streams consist mainly of propylene and propane, highly volatile gases with three carbons. We commend the ACC's sensible approach to using data on propane from the American Petroleum Institute's HPV submission and data on propylene from the ICCA program to characterize the toxicity of the propylene streams. We are also gratified by the consideration of physicochemical properties to avoid irrelevant ecotoxicity tests. Since propane and propylene are highly volatile and practically insoluble in water, these chemicals clearly do not pose a risk to the aquatic environment. The ACC has sensibly described these chemicals' properties and plans to use ECOSAR to predict aquatic toxicity.

While the ACC test plan does not propose any additional tests under the U.S. EPA HPV program, and the test plan reflects improvements in inter-industry and inter-program coordination, the CEFIC Lower Olefins Sector Group is sponsoring propylene through the ICCA program. A developmental toxicity test and an *in vivo* genetic toxicity test on propylene are planned under ICCA. The ACC does not describe which specific test methods are to be used nor does it discuss the rationale for doing additional tests.

Propylene is the raw material for the manufacture of several organic chemicals including acetone, isopropyl alcohol, acrylonitrile and polypropylene plastic. The gas displaces oxygen in inhaled air and is associated with adverse effects due to asphyxiation, including fatigue, confusion, and unconsciousness.

Genetic toxicity studies have been conducted with propylene. Propylene was not found to be mutagenic when tested in *Escherichia coli* or *Salmonella typhimurim.*[1,2] Since the *in vitro* genetic toxicity tests have suggested that propylene is not mutagenic, and since the *in vitro* genetic toxicity screening tests are more sensitive than the *in vivo* genetic toxicity tests, no further genetic toxicity tests on animals should be conducted under these screening level programs. If sponsors are interested in potential genetic toxicity effects, we recommend that nonanimal tests be conducted. The OECD decision tree for assessment of genetic toxicity screening states that two negative *in vitro* genetic toxicity tests are sufficient to obviate the need for further genetic toxicity testing at the screening level.

The toxicokinetics of propylene have been studied in different species, and physiological toxicokinetic models have been developed for inhaled propylene gas in the mouse, rat, and human.[3] The chemical sponsors should capitalize on the opportunity to use PBPK modeling to eliminate testing. For example, the developmental toxicity may not be relevant, as propylene gas is eliminated so rapidly in humans and other species that the likelihood of exposure to the fetus may be very low.

We are concerned that although ACC proposes no other testing under the HPV program, it instead refers to new testing proposed under other programs. This appears to represent a growing trend to export tests to other programs to avoid public scrutiny. By referring indirectly to this other testing, without providing the background regarding the tests, or making documents on the testing publicly available, it is difficult to determine the appropriateness of the testing by a third party reviewer.

In short, while we do recognize that ACC has coordinated with other test plans to reduce duplicative testing and is relying on ECOSAR and physicochemical properties to characterize ecotoxicity of the propylene category, we believe the additional animal tests proposed through ICCA are inappropriate. We believe it is incumbent upon ACC to coordinate with its European counterparts to ensure that duplicative or irrelevant animal testing is not conducted through the ICCA. In the spirit of transparency, we would appreciate the ACC informing us of its progress in this area.

Thank you for the opportunity to comment and your attention to these important issues. I can be reached via telephone at 202-686-2210, ext. 302, or via e-mail at *ncardello@pcrm.org.* Correspondence should be sent to my attention at the following address: PCRM, 5100 Wisconsin Ave., Suite 400, Washington, DC 20016.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

1. Clayton GD, Clayton FE (eds). *Patty's Industrial Hygiene and Toxicology: Vol. 2A, 2B, 2C: Toxicology.* 3rd ed. New York: John Wiley Sons, 1981-1982. 3200.

2. Victorin K, Stahlberg M. A method for studying the mutagenicity of some gaseous compounds in *Salmonella typhimurium. Environ Mol Mutagen* 1998;11(1):65-77.

3. Filser JG, Schmidbauer R, Rampf F, Baur CM, Putz C, Csanady GA. Toxicokinetics of inhaled propylene in mouse, rat, and human. *Toxicol Appl Pharmacol* 2000:169(1):40-51.