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Steve 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 the chemical Tris(hydroxymethyl)aminomethane

Dear Administrator Johnson:

The following are comments on the test plan for the chemical Tris(hydroxymethyl)aminomethane (CAS# 77-86-1) (Tris Amino) for the HPV program, submitted by the Dow Chemical Company (Dow). These comments 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 animal, health and environmental protection organizations have a combined membership of more than ten million Americans.

This test plan, submitted by Dow late last year, is confusing to us. On the outset, it appears that Dow will be able to fulfill all HPV data endpoints with existing toxicity information and surrogate chemical data. In fact, Tris Amino is an ingredient in a whole host of consumer products and pharmaceuticals, leading one to believe that a full set of safety data should be available. Dow in fact states that it has conducted a Freedom of Information Act (FOIA) request in order to obtain Food and Drug Administration Data, which likely exist. We must stop short of commending Dow's efforts to describe available data for Tris Amino and its stated analogs (AMPD and AMP) and to obtain such data however, since Dow then commits to conducting a study if it cannot find data likely located at the FDA.

Despite histopathology data from several repeated-dose studies of Tris Amino, reproductive and developmental data from AMP, and the expected FDA data, Dow states that it will conduct a study according to OECD TG 421 if it does not receive adequate reproductive and developmental toxicity data for Tris Amino. It is very unclear why such a study, which would cause pain and suffering to approximately 675 animals, would ever be conducted. Even in the highly unlikely event that FDA data is not available, histopathological data from reproductive organs, together with developmental data from the surrogate AMP, should suffice to fulfill the reproductive and developmental toxicity endpoints for the HPV program and is in fact a strategy that the EPA itself has suggested for other test plans. In its test plan, Dow gives three pages of discussion on the suitability of AMPD and AMP as surrogates for Tris Amino, including solubility, physicochemical properties, patterns of excretion, etc. The test plan states: "based upon the properties, uses and toxicities of Tris Amino, AMPD, and AMP, the use of AMPD and AMP as surrogate substances to fulfill any data gaps for tris animo is warranted." It is very unclear from this test plan why an additional OECD TG 421 would be conducted.

In addition, a TOXLINE search found the following information: "USE OF **TROMETHAMINE** IS CONTRAINDICATED IN PREGNANT WOMEN OR PT WITH UREMIA OR CHRONIC RESPIRATORY ACIDOSIS. IT SHOULD NOT BE GIVEN FOR LONGER THAN 1 DAY." [Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc.,

1975., p. 775]. Perhaps this source contains more information to support the statement, and can help in the weight-of-evidence approach started, but not taken full advantage of, by Dow.

Thank you for your attention to these comments. We can be reached at 202-686-2210 ext. 335 or via e-mail at kstoick@pcrm.org with any questions or concerns.

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad B. Sandusky, PhD
Director of Research