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Michael O. Leavitt, 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 Benzenemethanethiol

Dear Administrator Leavitt:

The following are comments on the test plan for the chemical Benzenemethanethiol (BZM, CAS# 100-53-8) for the HPV program, submitted by Chevron Phillips Chemical Company LP (CPC). 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.

CPC proposes to do an OECD 407 on this chemical, which will kill approximately 40-80 mammals, an OECD 203, which will kill approximately 40-120 fish, and an OECD 473.

First, we want to ensure that CPC uses either human lymphocytes or mammalian cells obtained from established cultures for its proposed OECD 473, so as to avoid killing additional animals in order to supply the cells.

We are encouraged that CPC uses bridging data on a similar compound (Phenyl Mercaptan) to meet the SIDS endpoints for reproductive and developmental toxicity. However, CPC still proposes to conduct a repeat dose study using OECD 407. We believe we have found some information that may fulfill this endpoint. We urge CPC to look into EPA/OTS Document #86940000968, titled "Acute oral, acute and chronic dermal and vapor toxicity study of thiophenol, with cover letter dated 05/06/94." Although specific information is not immediately obvious, it is the responsibility of the submitter to ensure that all information on the test chemical and any surrogates (thiophenol is another name for Phenyl Mercaptan) is included in the robust summaries, in order for the public to evaluate all available data. It is imperative that this possible source of information is investigated before any animal testing is begun, as outlined in the Federal Register pertaining to the HPV program (Federal Register, 2000) and in the Letter to HPV participants (Wayland, 1999).

We would also like to question the need for an OECD 203. The TETRATOX assay could be combined with the ECOSAR data, eliminating the requirement to conduct a live fish test. In the TETRATOX assay, the protozoan *Tetrahymena pyriformis* is used as a biomarker for acute lethality in fish (Schultz 1997). The biochemistry and physiology of *T. pyriformis* have been thoroughly investigated since the 1950s, and this assay has been used, in various forms, for aquatic toxicity testing since the 1970s (Sinks & Schultz 2001). In this test, a range-finding study followed by three replicate definitive tests is performed for each test substance. Each treatment replicate consists of a minimum of five different concentrations per substance tested; thus, at least 30 data points comprise each analysis. The current, standardized protocol is for a 40-hour static test, which provides for multigenerational exposure. Range-finding tests are also included to allow an accurate approximation of both the highest concentration with no observed effect on population growth and the lowest concentration with total inhibition of cell replication. Output measures from the TETRATOX assay are the 50 percent inhibitory growth concentration (IGC50, mmol/L) and the 95 percent fiducial interval. The current TETRATOX database includes more than 2,000 industrial organic chemicals, including over 800 aliphatic chemicals, 900 aromatic chemicals, 400 neutral narcotics, and 400 direct-acting electrophiles, among others (Schultz, personal communication). The TETRATOX protocol has now been standardized and has undergone a preliminary ring test (Larsen *et al.*1997). The German EPA is currently funding a second, more elaborate ring test, with the goal of establishing an OECD Test Guideline. In the interim, data generated by TETRATOX demonstrate a consistently high degree of concordance to data from *in vivo* acute studies in fish, which supports the use of this assay as a prospective replacement for toxicity studies in fish (Seward *et al.*2001). When combined with results from ECOSAR, there is simply no justification for further fish toxicity testing.

Thank you for your attention to this issue. We look forward to a prompt and favorable response to our concerns. We can be reached at 202-686-2210 ext. 335 or via email at *kstoick@pcrm.org*.

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad B. Sandusky, PhD
Director of Research

EPA. 2000. "Data collection and development on high production volume (HPV) chemicals", Federal Register, Vol. 65, No. 248, Dec. 26.

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Schultz TW. 1997. TETRATOX: *Tetrahymena pyriformis* population growth impairment endpoint: a surrogate for fish lethality. *Toxicol Meth* 7:289-309.

Sinks GD & Schultz TW. 2001. Correlation of *Tetrahymena* and *Pimephales* toxicity: evaluation of 100 additional compounds. *Environ Toxicol Chem* 20:917-921.

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Wayland SH. Letters to manufacturers/importers. 1999. *http://www.epa.gov/chemrtk/ceoltr2.htm*.