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April 15, 2004

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

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Subject: Comments on the HPV Test Plan for Benzyltrimethylammonium chloride

Dear Administrator Leavitt:

The following comments on Bayer's test plan for Benzyltrimethylammonium chloride 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.

Bayer Chemicals Corporation LLC submitted its test plan on December 17, 2003 for the chemical Benzyltrimethylammonium chloride (CAS No. 56-93-9), or BTMAC. This substance is used to manufacture polyester resins, acrylics, and cellulose. A substantial number of physicochemical, fate, and toxicity studies have been conducted with BTMAC. Bayer fully utilizes existing studies, as well as structure activity relationship programs and models, to fulfill most SIDS endpoints in the HPV screening program. In particular, ECOSAR is used to estimate toxicity to fish, and a weight-of-evidence analysis of two subchronic studies, with detailed analysis of reproductive parameters, is used to meet the SIDS requirement for a reproductive toxicity study. This is a scientifically valid analysis and avoids a checklist approach to toxicology.

At the same time, we object to Bayer's proposal to conduct a separate developmental toxicity test. It is alarming that Bayer is proposing to conduct an OECD 414 test, when the combined reproduction/developmental screen, OECD 421, will reduce animal deaths by half and is adequate for a screening level program such as HPV. We ask that Bayer use the combined study in order to spare the lives of numerous animals.

If Bayer plans to conduct further animal testing, we request that it also conduct the *in vitro* rodent embryonic stem cell test (EST). Although doing so in parallel would not spare any animals at this point in time, it would assist with building the database for this non-animal method. The EST has recently become commercially available in the U.S., and was validated by the European Centre for the Validation of Alternative Methods last

year. The Centre's Scientific Advisory Committee concluded that the EST was ready to be considered for regulatory purposes (Genschow 2002). We are hopeful that Bayer will contact us for advice about laboratories in the U.S. that are currently conducting this test. This would be a great opportunity for Bayer to work with EPA and the animal welfare community to incorporate this validated non-animal test into the HPV program.

Lastly, Bayer did not identify compounds with structural similarity to BTMAC in its test plan. In the robust summaries, ECOSAR modeling grouped BTMAC within the Neutral Organics class of chemicals. We would like to inquire if Bayer has been able to identify other Neutral Organic compounds that can be expected to be of similar toxicity to BTMAC, as data for similar chemicals may be used to bridge data gaps for developmental toxicity, as well as other toxicological endpoints, in the SIDS battery.

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,

Megha Even, M.S.  
Research Analyst

Chad Sandusky, Ph.D.  
Director of Toxicology and Research

## References

Genschow, E., *et al.*, "The ECVAM international validation study on *in vitro* embryotoxicity tests: Results of the definitive phase and evaluation of prediction models", *Alternatives to Laboratory Animals* 30: 151-76, 2002.