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Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

Re: Cyclohexanol (CAS No. 108-93-0)
Registration No.

Subject: Reply to EPA Comments on the IHF Cyclohexanol HPV Submission

Dear Ms. Whitman,

Under the EPA HPV Challenge Program, available cyclohexanol toxicity information was evaluated, data gaps were identified, and a decision was made to conduct repeated-exposure toxicity and reproductive/developmental toxicity studies.

The IHF Committee on Cyclohexanol initially proposed to conduct a 90-day inhalation toxicity study in rats (OECD 413) and to enhance the histopathological examination of rats in the 90-day study by placing special emphasis on testes and ovaries. Sperm analyses and examination of estrus cycle were also to have been conducted. If adverse effects on gonads or sperm were observed in the proposed 90-day study, a one-generation rat inhalation study (OECD 415) would have been conducted on cyclohexanol to assess functional effects on fertility and on the reproductive performance of male and female rats. If no adverse gonadal or spermatogenic effects were seen in the proposed 90-day study, an inhalation teratology study (OECD 414) in rats would have been conducted to determine hazard to the unborn fetus.

EPA recommended a single screening study (OECD 422; combined repeated-dose toxicity with reproductive/developmental toxicity screening) to satisfy testing needs. The IHF Committee on Cyclohexanol has decided to accept EPA's recommendation to conduct a study using OECD 422 guidelines. The IHF Committee on Cyclohexanol will modify the OECD 422 protocol to provide for a longer exposure (at least ten weeks prior to mating to encompass one complete sperm cycle in male rats) and a fuller evaluation of male reproductive organs to address potential reproductive concerns identified in prior studies. The Committee also feels the longer exposure will provide for a better estimation of repeat dose toxicity. Results from such a study will satisfy HPV Challenge requirements.

In addition to conducting a study following OECD 422 guidelines, the IHF Committee on Cyclohexanol will conduct a study (OECD 111, for example) to measure the stability (hydrolysis) of cyclohexanol in water and an acute study for invertebrate

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toxicity (OECD 202) to more accurately determine an EC50 for cyclohexanol. Finally, the robust summaries will be amended to include additional information requested by the agency where it is available.

The committee appreciates this opportunity to respond to comments from the EPA. Please address any questions or comments concerning this letter to: Henry Trochimowicz, Sc.D., 14 Lamatan Road, Newark, DE 19711; Phone: (302) 239-4725; E-mail: hjtroch@aol.com.

Sincerely,

Marianne C. Kaschak
Project Coordinator



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