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PETA
PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Subject: Public Comments on the HPV Challenge Program Test Plan for sec-Butyl Ether (sBE; CAS No. 6863-58-7) by ExxonMobil Chemical Company.

The following comments on the HPV Challenge Program test plan for sec-butyl ether by ExxonMobil Chemical Company are submitted on behalf of People for the Ethical Treatment of Animals, the Physicians Committee for Responsible Medicine, 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.

sBE is a small molecular weight ether. ExxonMobil Chemical Company proposes no additional testing for sBE. Mammalian toxicity endpoints are characterized by existing analog and metabolite data, and adequate calculated data were developed to characterize the aquatic toxicity of sBE.

sBE has the potential to hydrolyze, resulting in two molecules of sec-butyl alcohol (sBA). Data are available for sBA on acute toxicity, reproductive toxicity, developmental toxicity, and genotoxicity. Several studies in humans and animals are cited indicating that, in mammalian systems, sBA is readily absorbed and metabolized to methyl ethyl ketone (MEK) and other subsequent metabolites. Data are available for MEK for repeated dose toxicity and genotoxicity. It is unclear from the test plan, however, under what conditions the hydrolysis of sBE to sBA occurs. This should be established to support the appropriateness of the data on sBA to characterize the toxicity of sBE.

sBA has low acute toxicity to mammals. Oral LD50 values range from approximately 2.2 to 6.5 g/kg body weight. No significant adverse effects are reported for repeated-dose toxicity of sBA or MEK at any exposure level tested. In addition, the weight of evidence presented indicates that sBA does not produce reproductive or teratogenic toxic effects. sBA and MEK are negative in mutation and chromosomal aberration genotoxicity tests. Finally, a test plan for an analogous chemical, diisopropyl ether (DIPE), has already been submitted by the Isopropanol Panel of the American Chemistry Council. DIPE is a low-molecular-weight ether similar in structure to sBE. The existing mammalian toxicity data identified for DIPE can be used to support the characterization of mammalian toxicity for sBE, as their inherent toxicities are expected to be similar.

No existing aquatic toxicity data for sBE were identified. However a QSAR model that applies an equation for neutral organics to estimate aquatic toxicity is judged to be appropriate for sBE, and modeling was performed using ECOSAR. Based on the

calculated values, sBE is expected to be moderately toxic to aquatic species. Experimental data for an analogous ether, n-butyl ether (nBE) support using the calculated data for sBE and suggest that the modeled data may be conservative.

ExxonMobil Chemical Company use of existing data, including human data, for sBE's metabolites, sBA and MEK, and analogs, DIPE and nBE, together with data calculated by ECOSAR is consistent with the HPV Challenge Program's goal of obtaining screening level hazard information, and this approach saves animals' lives by avoiding duplicative tests. Thank you for your attention to these comments. I may be reached at 610-586-3975, or via e-mail at josephm@peta.org.

Sincerely,

Joseph Manuppello
Research Associate
Research & Investigations