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PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Mr. Stephen Johnson, Administrator
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Subject: Public Comments on the HPV Challenge Program Test Plan for the C4-6 Isopentene Rich-Ether Fraction (IRF) stream by ExxonMobil Chemical Company.

The following comments on the HPV Challenge Program test plan for the C4-6 IRF stream 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.

We commend ExxonMobil Chemical Company for its thoughtful use of existing data on major constituents of the C4-6 IRF stream, the composition of which is well-defined, to fill all SIDS endpoints. The resulting reduction in proposed testing saves animals' lives and is consistent with the HPV Challenge Program's goal of obtaining screening level hazard information.

As noted in the test plan, the predominant chemical fraction in this stream is the methoxypentanes, which comprises from 43 to 60% of the stream. A second chemical fraction is the heptanes, which comprises from 18 to 24%. A third chemical fraction, cyclohexene, comprises from 6 to 9%. Together, these groups and constituents account for up to 91% of the stream. The remaining constituents, present at levels between 1% and 9%, are not expected to contribute to greater adverse effects than those resulting from the major groups or constituents. The sponsor proposes to use data from representative constituents from the methoxypentanes and heptanes along with cyclohexene to characterize the overall toxicity of the stream. The major methoxypentane is tert-amyl methyl ether (TAME). The heptanes will be represented by n-heptane.

Measured TAME acute toxicity data are available for a freshwater fish species. A 96-hour trout (Oncorhynchus mykiss) LC50 value of 580 mg/L is reported. Notably, the measured TAME data compare favorably with data calculated by the ECOSAR model (LC50 = 201 mg/L). Measured cyclohexene acute toxicity data are also available for a freshwater fish with a 96-hour medaka (Oryzias latipes) LC50 value of >10 mg/L reported. Again, the measured cyclohexane data compare favorably with data calculated by ECOSAR (LC50 = 7.6 mg/L).

Measured n-heptane data are available for a freshwater invertebrate species. A 48-hour invertebrate (Daphnia magna) EC50 value of 1.5 mg/L is reported. The measured n-

heptane data compare favorably with data calculated by the ECOSAR model (EC50 = 0.42 mg/L). ECOSAR applies an equation for neutral organics to estimate aquatic toxicity and is therefore considered appropriate to estimate aquatic toxicity for these classes of chemicals. ExxonMobil Chemical Company's use of structure activity relationships to minimize further testing is in accordance with the EPA's October 1999 letter to chemical sponsors addressing animal welfare concerns (http://www.epa.gov/oppt/chemrtk/pubs/general/ceoltr2.htm). It should also be noted that n-heptane is volatile and information on its environmental fate suggests that once in the atmosphere, it will be largely degraded through physical processes at a relatively rapid rate. Finally, we note that a search of TOXNET yielded two studies which may contain relevant data on aquatic toxicity.[1,2] In addition, LC50 values for several fish species are available from the ECOTOX database on heptane.[3,4,5,6] These data can be added to the information the sponsor has already summarized to further strengthen a weight-of-evidence approach to filling aquatic toxicity endpoints.

Data are available for each of the above three constituents to characterize the potential acute mammalian toxicity, genetic toxicity and repeated dose toxicity of the C4-6 IRF stream. These data demonstrate a low order of acute oral and inhalation toxicity and repeated dose toxicity. Further, cyclohexene and n-heptane demonstrated no evidence of genotoxicity, while the weight of evidence suggests that TAME is not genotoxic.

Data are available for TAME and cyclohexene to characterize the potential reproductive and developmental toxicity of the C4-6 IRF stream. Repeated exposure to these constituents is not expected to cause harm to reproduction or the developing fetus. ExxonMobil Chemical Company has conducted a thoughtful, qualitative analysis of existing data and concluded that there is sufficient data, given the totality of what is known about the C4-6 IRF stream that no further reproductive or developmental toxicity testing is needed. This is in accordance with the EPA's October 1999 letter to chemical sponsors (http://www.epa.gov/oppt/chemrtk/pubs/general/ceoltr2.htm). We also note that a search of TOXNET yielded a study which may contain relevant data on the developmental toxicity of n-heptane.[7] These data, along with any additional data regarding possible effects on sex organs observed in the summarized repeated dose studies for n-heptane, can be added to the information the sponsor has already

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[1] Shell Oil Co. Biodegradability, BOD Inhibition and Acute Toxicity to Fish of Chemical Compounds with Cover Letter. EPA/OTS; Doc #878210113.1982.

[2] Ghatak, DB and Konar, SK. Acute Toxicity of a Mixture of Anionic Detergent Parnol J and Petro-chemical n-heptane to Plankton Worm and Fish. *Impacts of Environment on Animals and Aquaculture*. Manna, GK and Jana, BB, eds. 1990. 233-236.

[3] Verschueren, K. LC50 Carassius auratus (Goldfish) 4mg/L/24 hr. *Handbook of Environmental Data on Organic Chemicals. Volumes 1-2, 4th ed.* 2001.1221.

[4] Juhnke I, Luedemann D. LC50 Leuciscus idus melanotus (Golden orfe) 2940 mg/L/48 hr. *Z.Wasser-Abwasser-Forsch.* 1978. 11(5): 161-164.

[5] Wallen IE, Greer WC, Lasater R. LC50 Gambusia affinis (Western mosquitofish) 4924 mg/L/24, 48, 96 hr. *Sewage Ind Wastes*. 1957. 29(6): 695-711.

[6] Ghatak DB, et al. LC50 Tilapia mossambica (Mozambique tilapia) 375 mg/L/96 hr. *Environ Ecol.* 1988. 6(4): 943-947.

[7] Brown-Woodman PD, et al. Induction of birth defects by exposure to solvents: an in vitro study. *Teratology*. 1995. 51(4):288.

summarized to further strengthen a weight-of-evidence approach to filling reproductive and developmental toxicity endpoints.

Thank you for your attention to these comments. I may be reached at (757) 622-7382, ext. 8001, or via e-mail at josephm@peta.org.

Sincerely,

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