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Subject: Public Comments on the HPV Challenge Program Test Plan for Gases, Petroleum, Extractive, C4-6 Isopentene Rich Reaction Products with Methanol, Ether Fraction, Hydrogenated, Cracked, Isopentene Fraction (C4-6 IRRP Fraction; CAS No. 108083-44-9) by ExxonMobil Chemical Company.

The following comments on the HPV Challenge Program test plan for the C4-6 IRRP Fraction 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 IRRP Fraction 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 constituent chemical groups of the C4-6 IRRP Fraction stream include C6 to C7 Aliphatics which comprise as much as 80% of the stream. The remaining individual constituents are present at levels between <1% and 4% and are not expected to contribute to greater adverse biological effects than those resulting from the two major groups. The sponsor proposes to evaluate data for n-hexane, 2,4-dimethylpentane and cyclohexane. Further, the sponsor recently submitted a test plan for the C4-6 Isopentene-Rich Ether Fraction (IRF) stream, in which data for cyclohexane and n-heptane and tert-amyl methyl ether (TAME) were summarized. n-Heptane is presented as an analog of 2,4-dimethylpentane for ecotoxicity and health effects data, so the only new data summarized relevant to these comments are those for n-hexane. Please refer to our comments on the IRF stream test plan for additional discussion of cyclohexane and n-heptane data. In addition, TAME is representative of the methoxypentanes, the largest of the minor chemical groups present, which constitutes 5.2% of the C4-6 IRRP Fraction stream.

Measured acute toxicity to fish data are available for n-hexane and cyclohexane. As previously noted in our comments on the sponsor's IRF stream test plan, n-heptane data are available for a freshwater invertebrate species and the measured n-heptane data compares favorably with data calculated by the ECOSAR model which is considered

appropriate to estimate aquatic toxicity for this class of chemicals. In addition, 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 reiterate that a search of TOXNET yielded two studies which may contain relevant data on aquatic toxicity[1,2] and that LC50 values for several fish species are available from the ECOTOX database on heptane.[3,4,5,6] We ask that these data be evaluated prior to any proposal of additional acute toxicity testing on fish.

Data are available for n-hexane, cyclohexane, and n-heptane to characterize the potential acute mammalian toxicity, genetic toxicity and repeated dose toxicity of the C4-6 IRRP Fraction stream. These data demonstrate a low order of acute oral, dermal, and inhalation toxicity and no strong evidence for genotoxicity. As noted in the test plan, the C4-6 IRRP Fraction stream is also expected to have a low order of repeated dose toxicity, although there is some concern based on evidence for peripheral neuropathy resulting from n-hexane exposure. In addition, we note that a search of TOXNET yielded a study which may address repeated dose toxicity for 2,4-dimethylpentane directly.[7] We ask that this study be evaluated prior to any proposal of additional repeated dose toxicity testing.

Data are available for n-hexane and cyclohexane to characterize the potential reproductive and developmental toxicity of the C4-6 IRRP Fraction stream and this potential toxicity is considered to be low. Again, we commend ExxonMobil Chemical Company for conducting a thoughtful, qualitative analysis of existing data and concluding that there is sufficient data, given the totality of what is known about a chemical, that no further reproductive and developmental toxicity testing is needed. This 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). We also note that a search of TOXNET yielded a study which may contain relevant data on the developmental toxicity of n-heptane.[8] We ask that these data, along with any additional data regarding possible effects on sex organs observed in the summarized repeated dose studies for n-heptane and in the repeated dose toxicity for 2,4-

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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] Halder CA, Holdsworth CE, Cockrell BY, Piccirillo VJ. Hydrocarbon nephropathy in male rats: identification of the nephrotoxic components of unleaded gasoline. *Toxicol Ind Health*. 1985. 1(3):67-87.

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

dimethylpentane referenced above,[9] be evaluated prior to any proposal of additional reproductive or developmental toxicity testing.

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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[9] Halder CA, et al. 1995.