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Stephen Johnson, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for Trifluoromethane (HFC-23)

Dear Administrator Johnson:

The following comments on DuPont's test plan for Trifluoromethane (Flouroform, R-23, HFC-23, Freon®-23, CAS RN 75-46-7) 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.

We support DuPont's test plan for Trifluoromethane, a gas used for refrigeration, fire suppression systems, and plasma etching. The plan uses existing data for Trifluoromethane and other chemical/functional analogs, along with computational models, to fulfill the Screening Information Data Set (SIDS) endpoints requested by the High Production Volume (HPV) Challenge Program. This is in keeping with the EPA's 1999 "Letter to Manufacturers/Importers [of HPV chemicals]," which encourages program participants to use existing data, chemical categories, structure activity relationships, and human experience to minimize additional *in vivo* testing.

Trifluoromethane and its analogs demonstrate low toxicity in various aquatic and mammalian organisms. ECOSAR modeling of Trifluoromethane and analogs HFC-134a and HFC-125, along with experimental fish and daphnia data, indicate a low hazard to aquatic organisms. Plentiful acute and repeat inhalation toxicity data from both Trifluoromethane and analogs indicate low toxicity in rats, dogs, and humans. Other studies presented indicate that Trifluoromethane is not a developmental, reproductive, or genetic toxicant. Data from a developmental rat study indicate no maternal or fetal effects. In conjunction with the developmental data, DuPont has used histopathology from subchronic studies of Trifluoromethane and its analog HFC-32,

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to address reproductive toxicity, according to guidance in the HPV manual¹. For genotoxicity, the test plan cites the weight of evidence from negative *in vitro* and *in vivo* genotoxicity assays. Additionally, in a study with human volunteers, those exposed to trifluoromethane showed no clinically significant physiological or neurobehavioral effects, with volunteers experiencing relatively minor and short-lived symptoms including lightheadedness, anesthetic effects, and sensitivity to noise.²

As experimental and computational data indicate, Trifluoromethane demonstrates low toxicity towards aquatic and mammalian species. The environmental impact of this greenhouse gas is perhaps of far greater concern than its (low) toxicity. Because of Trifluoromethane's global warming potential, DuPont limits environmental and human exposure through careful monitoring for leaks, capture and destruction of excess product via incineration, and use of personal protective equipment by workers. Trifluoromethane is handled in closed pressurized systems; therefore, there is no direct contact with workers. In the case of a leak, the greatest concern to workers as stated in the test plan is frostbite. As mentioned above, volunteers in an exposure study demonstrated no clinically significant physiological or neurobehavioral effects.² We regard the low likelihood of human exposure combined with low toxicity in human and non-human animals as sufficient grounds to preclude additional mammalian testing. In addition, Trifluoromethane, one of the most abundant HFCs, has been regulated since 1997 under the Kyoto protocol and plans are underway to phase out its use along with CFCs, HCFCs, other greenhouse gases and ozone depleting substances.

In summary, DuPont has made good use of existing and computational data in order to satisfy the requirements of the HPV Challenge program and we concur with the current proposal not to conduct any additional animal testing. Thank you for your attention to these comments. We may be reached at 202-686-2210, ext. 345, or via e-mail at nbeck@pcrm.org.

Sincerely,

Nancy Beck, Ph.D.
Policy and Science Advisor

Chad B. Sandusky, Ph.D.
Director of Research

¹ OECD Secretariat (2004) Manual for Investigation of HPV Chemicals. (Section 4.3) See <http://www.oecd.org/dataoecd/35/38/31179717.pdf>

² Subcommittee on Exposure Guidance Levels for Selected Hydrofluorocarbons, Committee on Toxicology, Board on Environmental Studies and Toxicology, National Research Council. (2000) Submarine Exposure Guidance Levels for Selected Hydrofluorocarbons: HFC-236fa, HFC-23, and HFC-404a. 29-35