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December 20, 2001

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on HPV Test Plan and Robust Summary for 1,1-Difluoroethane

Dear Administrator Whitman:

The following comments on the DuPont SHE Excellence Center's test plan for 1,1-difluoroethane 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 nine million Americans.

DuPont's test plan and robust summary provide data for all the HPV SIDS endpoints, and DuPont appropriately does not call for additional testing. We support the conclusion that no animal testing is warranted.

However, the test plan violates principles #1 and #3 of the October 1999 Agreement among the EPA, industry, animal protection organizations, and environmental groups, which delineated certain principles for eliminating unnecessary testing on animals. These principles are as follows:

1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach.
3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships.

To provide a more comprehensive analysis of potential health hazards associated with 1,1-difluoroethane and to reduce the number of animals who could be killed to test similar chemicals, DuPont should have included much more of the existing information on 1,1-difluoroethane and structurally similar haloalkanes, and should have presented 1,1-difluoroethane in the context of a chemical category.

Additional Available Information

DuPont neglected to describe the application of 1,1-difluoroethane. 1,1-difluoroethane is part of a well-studied class of halogenated alkane chemicals used as propellants and refrigerants. These chemicals are

associated with bronchoconstriction, respiratory depression, and cardiac abnormalities at high concentrations. These effects vary among species.¹ Halogenated hydrocarbons, such as the fluorocarbons and the hydrochlorofluorocarbons, have been researched extensively because of their impact on environmental health, ozone destruction, and global warming.

Solubilities of fluorocarbon aerosol propellants have been determined in the blood and plasma of humans, monkeys, dogs, rats, and mice. Differences as large as approximately 4-fold in blood and 33-fold in plasma were found in different species. The partitioning of fluorocarbons between blood cells and plasma showed even greater differences between species. These pharmacokinetic differences among species demonstrate some of the limitations of inter-species extrapolation of toxicity data from nonhuman animals to humans.²

The uncertainties introduced by relying on animal data to identify human hazards can be avoided by examining the vast amount of existing information in humans, none of which was presented by DuPont. Although this chemical generally is characterized by low toxicity, much clinical data on the abuse of volatile substances, such as 1,1-difluoroethane, provide detailed information on acute toxic effects in humans.^{3,4} Human clinical data have demonstrated this chemical to cause confusion, pulmonary irritation, and tremors at high concentrations.

Intentional direct exposure to this chemical can cause freezing of airway soft tissue, oxygen displacement, or sensitization of myocardium. Human data also indicate that 1,1-difluoroethane is irritating to the eyes, nose, and throat. A case of severe oral mucosal frostbite injury from intentional abuse of 1,1-difluoroethane has been reported in the literature.⁴ This acute toxicity information is much more relevant to characterizing human hazards than a rat LD-50 value. Human clinical data also include the quantification of difluoroethane in biological samples.³ The metabolism of several halogenated ethanes has also been studied, since chlorofluorohydrocarbons presented environmental health challenges, and replacement aerosols have been investigated.⁵

1,1-difluoroethane's production and use as a refrigerant, aerosol propellant, and synthesis intermediate for 1-chloro-1,1-difluoroethane may lead to its release to the environment through various waste streams. Exposure may also occur in the occupational environment. The American Industrial Hygiene Association has recommended exposure to 1,1-difluoroethane not exceed an eight-hour time-weighted average of 1,000 parts per million, indicating these chemicals are known to be toxic to people only at relatively high exposure concentrations.

Category Analysis

DuPont should have formed a chemical category with other halogenated hydrocarbons it is sponsoring in the HPV program, such as 2,2-dichloro-1,1,1-trifluoroethane (CAS # 306832); 1,1,2-trichloro-1,2,2-trifluoroethane (CAS # 76131); 1,1-dichlorotetrafluoroethane (CAS # 374072); and 2,2-dichloro-1,1,1-trifluoroethane (CAS # 306832).

DuPont should also have coordinated with other sponsoring organizations, such as the Halogenated Solvents Alliance to maximize the use of all available data on structurally similar chemicals. Presentation of a chemical category provides greater insight into the relationship between chemical structure and toxicity, and provides the opportunity for reducing testing and the use of fewer animals. Other HPV chemicals that could be analyzed within the context of a category of haloalkanes are: 1-chloro-1,1-difluoroethane (CAS#75683, sponsored under the ICCA); 1,1-difluoroethene (CAS # 75387, sponsored under ICCA); 1,1-dichloroethylene

(CAS# 75354, sponsored by the Halogenated Solvents Alliance, Inc.); 1,1,1,2-tetrafluoroethane (CAS # 811972, sponsored by the European Fluorocarbon Technical Committee); 2-chloro-1,1,1,2-tetrafluoroethane (CAS # 2837890, sponsored by the European Fluorocarbon Technical Committee); 1,1-dichloro-1-fluoroethane (CAS # 1717007, sponsored under the ICCA); difluoromethane (CAS # 75105); and dichloromethane (CAS # 75092, sponsored by the Halogenated Solvents Industry Alliance, Inc.).

In conclusion, we support DuPont's conclusion that all data gaps have been filled under the HPV program and no animal testing is warranted. However, DuPont has done a poor job of summarizing and presenting the extensive amount of existing data on difluoromethane and related chemicals, which would present a complete picture of their potential hazards.

Thank you for your attention to these comments. I can be reached at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

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3. Broussard LA, Brustowicz T, Pittman T, Atkins KD, Presley L. Two traffic fatalities related to the use of difluoroethane. *J Forensic Sci* 1997;42(6):1186-7.
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