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DuPont Haskell Global Centers
for Health and Environmental Sciences
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June 30, 2009

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Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, DC 20004

DCN: 88090000296

Dear 8(e) Coordinator:

Octafluorocyclobutane
CAS # 115-25-3

This letter is to inform you of the results of a pre-1977 (1971) inhalation cardiac sensitization study in dogs which we recently became aware of with the test substance referenced above.

The study was designed to study the effects of varying concentrations of the test substance on dogs with simultaneous injection of epinephrine over a 30-minute exposure period. Twelve healthy, male beagle dogs were exposed to 100% test mixture consisting of 35% test substance and 65% nitrogen for 0-5 seconds, followed by exposure to 50% test mixture plus 50% air from 6 to 30 seconds. This was followed by exposure to an incremental decay from 16.6% to 8.3% test mixture, balance of air, from 31 seconds to 30 minutes. In another test, the same 12 dogs were exposed to a similar concentration profile substituting nitrogen for the test substance. During each 30-minute exposure, five challenge doses of epinephrine (0.008 mg/kg) were administered to the dogs at 15 second, and at 2, 10, 20, and 30 minutes. Electrocardiograms were recorded continuously throughout the entire exposure and heart rate tabulated.

During the 30-minute exposures to the test substance (100% test mixture consisting of 35% test substance and 65% nitrogen for 0-5 seconds, followed by exposure to 50% test mixture plus 50% air from 6 to 30 seconds; this was followed by exposure to an incremental decay from 16.6% to 8.3% test mixture, balance of air, from 31 seconds to 30 minutes), 1/12 dogs showed a serious cardiac arrhythmia (multiple consecutive ventricular beats) after the first challenge dose of epinephrine; a re-test of this dog yielded a similar result. When the dogs were exposed to the nitrogen regiment, no serious disturbance in cardiac rhythm occurred. No significant effect on heart rate was observed on any test animal due to the test substance or nitrogen exposure. Under the conditions of this experiment, the test substance is capable of sensitizing the dog's heart to intravenously administered epinephrine. In an additional experiment, the dog that showed the arrhythmia was exposed on two separate occasions to a mixture containing

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35% test substance and 65% nitrogen for 5 seconds and challenges with the standard dose of epinephrine. No significant disturbance in cardiac rhythm was observed during either exposure.

This information is submitted in accordance with current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act or, where it is not clear that reporting criteria have been met, it is submitted as a precautionary measure and because it is information in which EPA may have an interest.

Sincerely,

A. Michael Kaplan

A. Michael Kaplan, Ph.D.
Director - Regulatory Affairs

AMK: clp
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