ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ-10-17915	89110000001	10/1/10

COMMENTS:

DOES NOT CONTAIN CBI

mR#
330335

DuPont Haskell Global Centers
for Health and Environmental Sciences
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10 OCT -1 12:07

September 30, 2010

Via Federal Express

8EHQ-10-17915

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

8EHQ-0910-17915B
DCN:89110000001

89110000001

Dear 8(e) Coordinator:

8EHQ-10-17915
Terephthalic Acid
100-21-0

DuPont received information from a third party on the above-referenced substance. DuPont has reviewed the information for reportability under TSCA §8(e) and provides below a summary of the information that has been determined to meet EPA's TSCA §8(e) criteria for reporting. It is unknown whether the information reported below has been previously reported to EPA by any third party or is otherwise considered known to the Administrator under TSCA §8(e) guidance.

Mouse Micronucleus Test:

Male and female ICR mice were obtained from Harlan Sprague Dawley, Inc. In the pilot study, 5 mice/sex received 2000 mg/kg and 2 males/dose received 1, 10, 100 or 1000 mg/kg i.p. In the toxicity study, 5 mice/sex/dose received doses of 1200, 1400, 1600 or 1800 mg/kg i.p. In the main micronucleus study the controls consisted of 10 mice/sex; at 200 and 400 mg/kg i.p. there were 5 mice/sex/dose; at 800 mg/kg i.p. there were 15 mice/sex; and the positive controls consisted of 5 mice/sex/dose.

Mice were given a single intraperitoneal injection of the test substance or vehicle alone (corn oil). In the pilot study and toxicity study, mice were observed for signs of toxicity for 3 days after administration. In the micronucleus study, mice were sacrificed 24 hours later. Additional mice from the vehicle control and high dose groups were sacrificed 48 hours after dose administration. For the micronucleus study bone marrow cells were obtained from the femurs. The cells were prepared and evaluated for micronucleated polychromatic erythrocytes.

In the pilot study, 3/5 males and 5/5 females died within 2 days administration of 2000 mg/kg. Lethargy and piloerection were noted in males at 1000 mg/kg and males and females at 2000 mg/kg. Tremors were observed in the males at 2000 mg/kg, and convulsions, prostration and crusty eyes were observed in females at this dose. All other animals appeared normal. In the toxicity study, mortality occurred within 3 days of dosing as follows: 2/5 males and 1/5 females at 1200 mg/kg; 4/5 males and 3/5 males at 1400 mg/kg; 2/5 males and 4/5 females at 1600 mg/kg; and 4/5 males and 2/5 females at 1800 mg/kg. Lethargy, piloerection and crusty eyes were seen in all mice at all doses. Tremors were seen in females at 1200 mg/kg, and in males and females at 1400 and 1800 mg/kg. Convulsions were seen in males and females at 1600 and 1800 mg/kg, and prostration in males at 1200 and 1400 mg/kg and males and females at 1600 and 1800 mg/kg. The maximum tolerated dose chosen for the micronucleus assay was 800 mg/kg.

CONTAINS NO CBI

In the micronucleus study, 1 male mouse in the 800 mg/kg group was found dead the day after administration, but was replaced. Lethargy and piloerection were seen at all 3 doses in both sexes. Mice treated with vehicle alone and the positive control substance appeared normal throughout the study. Reductions of 2% to 9% in the ratio of polychromatic erythrocytes to total erythrocytes were observed in some of the treated groups compared to controls suggesting that erythropoiesis was not inhibited. There were no significant increases in the number of micronucleated polychromatic erythrocytes per 2000 polychromatic erythrocytes in treated groups compared to controls, irrespective of sex and time of bone marrow collection. The positive control substance induced a significant increase. Under the conditions of this study, terephthalic acid did not induce a significant increase in the incidence of micronucleated polychromatic erythrocytes in bone marrow and was concluded to be negative in the mouse micronucleus test.

In Vitro Cytogenetic Assay in Human Lymphocytes:

The test substance was evaluated in an *in vitro* cytogenetic assay using human lymphocytes with and without metabolic activation. Duplicate human peripheral blood cultures were exposed to the solvent (DMSO), test substance or positive control substances (mitomycin C and cyclophosphamide) at appropriate concentrations in two experiments. Concentrations used in this test were: 10, 50, 100, 175, 250, 500, 1000, 1300 or 1660 µg/ ml. In the first experiment (Experiment 1), cells were exposed to the test substance and control substances for a period of 3 hours both in the presence and absence of S9 mix. In the second experiment (Experiment 2), cells were exposed to the test substance and control substances for a period of 3 hours in the presence of S9-mix and 20 hours in the absence of S9 mix. Treatment of the cultures started approximately 48 hours after culture initiation. A single sampling time, 20 hours after the start of treatment (68 hours after culture initiation), was used. Cells were harvested, fixed and mounted on microscope slides for examination. The three concentrations chosen for chromosomal aberration analysis were 50, 250 and 500 µg/mL. The concentration of test substance above 500 µg/mL decreased the pH of the culture medium by 1.1 pH units and were not selected for chromosomal aberration analysis. No significant effect on osmolality was observed. A reduction in the mean mitotic activity, compared to the control, was observed in cultures from both Experiment 1 (34% +S9-mix; 26% -S9 mix) and Experiment 2 (35% +S9-mix, 59% -S9 mix), treated with the highest concentrations of terephthalic acid selected for chromosomal aberration analysis.

Statistically and biologically significant increases in the percentage of aberrant cells were observed in Experiment 2 following 20 hour treated in the absence of S9-mix. Small increases in the percentage of aberrant cells were observed following 3 hour treatment in Experiment 1 in the presence and absence of S9-mix and in Experiment 2 in the presence of S9-mix. The positive control materials, mitomycin C and cyclophosphamide, induced statistically and biologically significant increases in the percentage of aberrant cells, compared to the solvent control cultures. Clastogenicity observed in this study may be due to pH reductions from the acidic test substance.

Sincerely,

A. Michael Kaplan

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

AMK/RV: clp
(302) 366-5260

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