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June 4, 2010

Via Federal Express

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Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency, ICC Building
1201 Constitution Ave., NW
Washington, DC 20004



8EHQ-0610-17966A
DCN: 88100000295

Dear 8(e) Coordinator:



1,1,1-Tris(p-hydroxyphenyl) ethane
CAS # 27955-94-8

This letter is to inform you of the results of two mouse micronucleus assays with the above referenced test substance.

The effect of the test substance on the incidence of micronucleated polychromatic erythrocytes was evaluated in mice administered with 627, 1254, or 2508 mg/kg bodyweight as a single intraperitoneal injection. Preliminary toxicity testing was carried out to determine the toxicity of the test substance. Based on the results of this test, a maximum tolerable dose of the test substance was estimated to be 2508 mg/kg. Negative and positive control groups were dosed in an identical manner, by intraperitoneal injection. The negative control group received the vehicle, aqueous 1% methylcellulose. The positive control group was treated with mitomycin C, at 4 mg/kg bodyweight.

Bone marrow smears were obtained from the negative control and test substance groups at 24, 48, and 72 hours after dosing. Bone marrow smears were obtained from the positive control group 24 hours after dosing. One smear from each animal was examined for the presence of micronuclei in 1000 polychromatic erythrocytes. The ratio of polychromatic to normochromatic erythrocytes was assessed by examination of at least 1000 erythrocytes from each animal. A record of the incidence of micronucleated normochromatic erythrocytes was also kept.

In preliminary testing to determine toxicity of the test substance, two mice/sex/dose were treated with the test substance at dose levels of 625, 1250, 2048, 2500, 2560, 3200, 4000 or 5000 mg/kg and observed for 72 hours. Piloerection and hunched posture were observed in all animals. While these clinical signs were observed until 6 and 30 hours at 625 and 1250 mg/kg, respectively, the signs at other dose levels persisted until 72 hours. Lethargy was observed in one male dosed at 2560 mg/kg, in one male and both females dosed 4000 mg/kg, and in both males and females dosed at 5000 mg/kg. All the animals at 5000 mg/kg were found dead by 46 hours. In the main study, 15 mice/sex/dose were treated with the test substance at 627, 1254, and 2508 mg/kg. At 627 mg/kg piloerection was observed sporadically in all animals, at 1254 mg/kg, piloerection was observed in all animals until 72 hours, and at 2508 mg/kg, piloerection, hunched posture and lethargy were observed in all animals until 72 hours.

At all sampling times, mice treated with the test substance showed no significant increase in the frequency of micronucleated polychromatic erythrocytes. A dose-related decrease in the ratio of polychromatic to normochromatic erythrocytes was obtained for mice treated with the test substance at the 72 hour sampling time. This decrease may be evidence of bone marrow cell toxicity/depression, although no other such decreases were obtained at the other two sampling times. It is concluded that the test substance showed no evidence of mutagenic potential when administered as a single intraperitoneal injection in this *in vivo* test procedure.

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In the second assessment of the effect of the test substance on the incidence of micronucleated polychromatic erythrocytes in mice, five daily doses were administered to mice by intraperitoneal injection.

Preliminary toxicity testing was conducted at 500, 1000, 2000, or 4000 mg/kg (2 male and 2 female mice per dosage by intraperitoneal injection for 5 days). Piloerection was observed in all animals dosed at 500 mg/kg and piloerection, lethargy and/or hunched posture were noted in mice dosed at 1000, 2000 and 4000 mg/kg.

Additional preliminary toxicity testing (phase II) was conducted at 540, 900, 1500, or 2500 mg/kg (2 male and 2 female mice per dosage by intraperitoneal injection for 5 days) to confirm the results of the phase I testing. Piloerection was observed in all animals dosed at 540, 900, 1500, or 2500 mg/kg. Hunched posture was observed in one male dosed at 540 mg/kg and in all animals dosed at 900, 1500, or 2500 mg/kg. Lethargy was observed in males and females dosed at 900, 1500 and 2500 mg/kg.

In the definitive study, piloerection was observed in all animals dosed at 125, 250, 500, or 1000 mg/kg. Hunched posture was observed in all animals dosed at 500 or 1000 mg/kg. Under the conditions of the definitive study, the test substance did not show any evidence of mutagenic activity or bone marrow cell toxicity/depression when administered as 5 daily intraperitoneal doses to mice.

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 handwritten signature in black ink that reads "A. Michael Kaplan". The signature is written in a cursive, flowing style.

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

AMK/CC: clp
(302) 366-5260

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