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February 27, 2006

8EHQ-0206-16043 F

Via Federal Express

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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, ICC Building
1201 Constitution Ave., NW
Washington, DC 20460

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8EHQ-05-16043

Dear 8(e) Coordinator:

8EHQ-05-16043
Substituted Lactone

This letter is to inform you of the results of a recently completed *in vivo* mammalian erythrocyte micronucleus test in mice with the above-referenced substance.

An *in vivo* mammalian erythrocyte micronucleus test was conducted in male and female CrI:CD®(ICR) BR mice. The test substance, and the control substances were administered once by gavage, and animals were sacrificed 24 or 48 hours after the treatment. The test substance was delivered in corn oil. Concurrent negative (vehicle) controls were included at both sacrifice time points, as well as a positive cyclophosphamide control at the 24-hour sacrifice time point. The *in vivo* mouse micronucleus test was negative.

A rangefinder experiment using one group of 3 male mice was conducted for dosing concentration verification for the main study. The highest and only dose used for the rangefinder study was the limit dose of 2000 mg/kg body weight administered by gavage. The animals were observed for clinical signs of toxicity and mortality immediately after dosing and daily thereafter for two days (until approximately 48 hours post-dosing). 3/3 male animals showed ataxia at 5 and 15 minutes post-dosing, and 2/3 animals showed low posture 15 minutes post-dosing. No clinical signs of toxicity were observed at ≥30 minutes post-dosing. No weight loss, moribundity or mortality occurred.

In the main study, the dose levels of test substance were 500, 1000, or 2000 mg/kg body weight. Mice were observed for clinical signs of toxicity at 0-1 hour post-dosing, 3-5 hours post-dosing and prior to the scheduled sacrifice at 24 or 48 hours post-dosing. Slide evaluation was conducted at all dose levels at the 24-hour sacrifice point, and at the 2000 mg/kg dose level at the 48-hour sacrifice point.

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Mortality occurred in 1/14 females dosed at 2000 mg/kg. Clinical signs of toxicity were observed at all dose levels tested in male and female mice exposed to the test substance. At 2000 mg/kg, clinical observations included ataxia in 14/14 males and 14/14 females, and prostration in 2/14 females. At 1000 mg/kg, ataxia was observed in 7/10 males and 7/10 females. At 500 mg/kg, ataxia was observed in 1/10 males and 1/10 females. There were no significant changes in body weight or body weight gain in either male or female animals administered the test substance.

No statistically significant increases in micronucleated PCE frequency were observed in any evaluated test substance-treated group of male or female animals at either time point. There were no statistically significant decreases in PCEs among 1000 erythrocytes. However, a depression in the frequency of PCE/total erythrocytes was detected at the 48-hr time point in male animals exposed to the test substance at 2000 mg/kg. Although not statistically significant, and within the laboratory historical negative control range, this is considered as an indication of bone marrow toxicity, confirming that the test substance reached the target cells.

Under these experimental conditions, the clinical signs described above are being reported in accordance with the guidance given in the EPA TSCA Section 8(e) Reporting Guide (June 1991).

Sincerely,