

8EHQ-0204-14970



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February 10, 2004

Via Federal Express

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 20460

CONTAINS NO CBI

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2004 FEB 23 AM 8:

Dear 8(e) Coordinator:



8EHQ-01-14970

This letter is to inform you of the results of a recently conducted range-finding oral developmental toxicity study in rats with the above referenced test substance.

Groups of 8 time-mated CrI:CD®(SD)IGS BR rats were administered daily oral dosages of 0, 250, 500, or 1000 mg/kg/day of the above referenced test substance by gavage during gestation days 6-20 (day 6-20G). Controls were similarly administered the vehicle (deionized water). During the in-life portion of the study, maternal body weights, food consumption, and clinical signs data were collected. On day 21G, dams were euthanized and subjected to a gross external and internal examination. Uterine contents were described; all fetuses were removed and individually weighed, sexed, and examined for external alterations.

Maternal toxicity was observed at 1000 mg/kg/day, which was characterized by maternal mortality, and by statistically significant, test substance-related reductions in maternal body weight, weight gain, and food consumption. Two dams in the 1000 mg/kg/day group were found dead, and one dam in the 1000 mg/kg/day group was sacrificed *in extremis* during the dosing period. Clinical observations of stained fur, hunched over posture, and diarrhea were observed in one rat found dead on gestation day 12. Gasping was observed in the rat sacrificed *in extremis* on gestation day 13. There were no abnormal clinical signs observed for the rat found dead on gestation day 18. Both rats that were found dead had bloated stomachs, and thin lining of the non-glandular stomach. The rat sacrificed *in extremis* did not have any grossly observable abnormalities. Other clinical observations noted in rats dosed at 1000 mg/kg/day that survived to the scheduled sacrifice included stained and/or wet fur. No mortality and no compound-related clinical observations were observed in rats dosed at 250 and 500 mg/kg/day.



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Fetuses in the 1000 mg/kg/day group had a 5.8% reduction in mean fetal weight compared to the mean control value; however, due to the small number of litters evaluated in the 1000 mg/kg/day group, and the variability in the litter weights, the biological significance of this decrease is equivocal. There were no test substance-related external observations at any dose level. The number of live fetuses per litter, implantations, corpora lutea, sex ratio, and resorptions, were comparable across all groups.

The NOEL (no observed effect level) for both maternal and fetal effects in this range-finding developmental toxicity study was 500 mg/kg/day.

Under these experimental conditions, the findings described above appear to be reportable, based upon guidance given in the EPA TSCA Section 8(e) Reporting Guide (June, 1991).

Sincerely,

A handwritten signature in black ink that reads "A. Michael Kaplan". The signature is fluid and cursive, with a long horizontal stroke at the end.

A. Michael Kaplan, Ph.D.
Director – Regulatory Affairs and Occupational Health

AMK/LAM:clp
(302) 366-5260