

8EHQ-0202-14970

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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 20460

COMPANY SANITIZED

Dear 8(e) Coordinator:

8EHQ-01-14970

This letter is to inform you of the results of a recently conducted 90-day oral gavage study in rats with the above referenced test material.

The test material was mixed with deionized water and administered to groups of 10 male and 10 female rats at dosages of 0, 25, 200, or 1000 mg/kg/day. The high dose level was reduced to 600 mg/kg/day during the fifth week of the study because of deaths and adverse clinical signs. The rats were observed for clinical signs at least twice daily and were weighed weekly. A detailed physical examination of each rat was performed weekly. Neurobehavioral screening (functional observational battery and motor activity) was performed before initiation of treatment and during week 12. A shortened battery was performed each week (except week 12), and food consumption was determined weekly. All rats were necropsied.

Salivation was observed throughout the study in all rats dosed at 1000/600 mg/kg/day and in some rats dosed at 200 mg/kg/day. Abnormal gait was observed during week 4 in 4 male and 2 female rats dosed at 1000 mg/kg/day. Paddling of the forepaws was observed during weeks 12 and 13 in one male and 4 female rats dosed at 600 mg/kg/day. While these clinical signs were noted during the study, no treatment-related neurobehavioral changes were observed in the functional observational battery or motor activity assessments.

Four rats in the 1000 mg/kg/day group were sacrificed week 3 or 4 because of adverse clinical signs and body weight loss. Abnormalities in the forestomach (non-glandular stomach) were observed during gross examinations for a majority of rats dosed with 1000/600 mg/kg/day. Macroscopically, effects were also seen in a variety of organs in the four rats dosed with 1000 mg/kg/day and sacrificed early in the study.

Microscopically, inflammatory, degenerative and hyperplastic changes mainly in the forestomach were observed in rats dosed at 1000/600 mg/kg/day. The principal findings were inflammation, epithelial necrosis and ulceration, and epithelial hyperplasia. In all 4 cases of decedent rats, necrotic and inflammatory lesions of the stomach and small intestine were considered to be factors contributory to death. Also considered to be associated with the clinical condition of these four animals was apoptosis, seen in various lymphoid tissues including spleen, mesenteric lymph node, mandibular lymph node and Peyer's patch in the ileum.

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 (1991).

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Sincerely,