

8EHQ - 0299 - 13955

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Via Federal Express

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Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street SW
Washington, D. C. 20460-0001

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Dear 8(e) Coordinator:

8EHQ-97-13955
[Substituted Heterocycle]

This letter is to inform you of the preliminary results of a recently completed acute neurotoxicity study in rats with the above referenced test substance.

The test substance was administered once via gavage on test day 1 to adult male and female rats (12 rats/dose/gender) at dosages of 0, 20, 500, or 2000 mg/kg. Clinical observations, body weights, and food consumption were recorded periodically throughout the test period. Neurobehavioral assessments (functional observational battery and motor activity tests) were recorded the week prior to treatment (baseline), 1-3 hours post-dosing on test day 1, and again on test days 8 and 15. Six rats/gender/group were sacrificed and tissues were fixed with in situ perfusion techniques on test day 17. Tissues from the control and 2000 mg/kg rats were processed and examined for neuropathological effects.

Statistically significant test substance-related decrements in body weight, weight gain, and food consumption were observed in 2000 mg/kg males. There were no test substance-related adverse effects on body weight, weight gain, or food consumption in females at any dosage.

One male rat dosed with 2000 mg/kg was found dead on test day 2. There were no clinical signs of toxicity or gross lesions observed in this animal.

Male and female rats dosed with 2000 mg/kg had test substance-related decreases in motor activity on test day 1. There were no test substance related changes in either males or females at any dose for forelimb or hindlimb grip strength, foot splay, or any of the 34 other neurobehavioral parameters evaluated. There were no test substance-related morphological changes observed in males or females at any dosage.

In the absence of other corroborative evidence of neurotoxicity from the functional observational battery, clinical signs of neurotoxicity, and morphological changes in the nervous system, the lower motor activity was considered to be secondary to systemic toxicity and/or general malaise.

Under these experimental conditions, the findings described above would appear to be reportable, based on EPA guidance regarding the reportability of such data under TSCA Section 8(e) criteria.

Sincerely,

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