

Single-Dose and Chronic Dietary Neurotoxicity Screening Studies on 2,4-Dichlorophenoxyacetic Acid in Rats¹ (Abstract)

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Forms of 2,4-dichlorophenoxyacetic acid (collectively known as 2,4-D) are herbicides used to control a wide variety of broadleaf and woody plants. Single-dose acute and 1-year chronic neurotoxicity screening studies in male and female Fischer 344 rats (10/sex/dose) were conducted on 2,4-D according to the U.S. EPA 1991 guidelines. The studies emphasized a Functional Observational Battery (which included grip performance and hindlimb splay tests), automated motor activity testing, and comprehensive neurohistopathology of perfused tissues. Dosages were up to 250 mg/kg by gavage for the single-dose study, and up to 150 mg/kg/day in the diet for 52 weeks in the repeated-dose study. In the acute study, gavage with 250 mg/kg test material caused slight transient gait and coordination changes and clearly decreased motor activity at the time of maximal effect on the day of treatment (day 1). Mild locomotor effects occurred in one mid-dose rat (75 mg/kg), on Day 1 only. No gait, coordination, or motor activity effects were noted by day 8. In the chronic study, the only finding of neurotoxicologic significance was retinal degeneration in females in the high-dose group (150 mg/kg/day). Body weights of both sexes were slightly less than controls in the mid-dose group, and 10% less than controls in the high-dose group. In summary, the findings of these studies indicated a mild, transient locomotor effect from high-level chronic exposure. Based on the results from these two studies, the no-observed-adverse-effect level for acute neurotoxicity was 15 mg/kg/day and for chronic neurotoxicity was 75 mg/kg/day. © 1997 Society of Toxicology.

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