

## **Hydroquinone: Acute and subchronic toxicity studies with emphasis on neurobehavioral and nephrotoxic effects**

Abstract: Hydroquinone (HQ) is a common water-soluble constituent of foods, an ingredient in skin lightening preparations, a photographic developer, and an antioxidant used in the preparation of industrial polymers. In this series of studies, aqueous solutions of HQ were given by gavage to male and female Sprague-Dawley rats to determine the acutely lethal dose, the clinical signs of behavioral toxicity associated with doses at or near a dose causing mortality, and the effects of the administration of dose levels resulting in acutely observable behavioral effects when administered 5 days/week for 13 weeks. The acute dermal toxicity of HQ in rabbits was also determined. For the acute oral toxicity study, groups of five male and five female rats were administered single oral doses of 375, 345, 315, or 285 mg/kg. At all dose levels, animals exhibited minor to moderate tremors and minor convulsions within the first hour after dosing. The acute oral LD50 value for both sexes combined was > 375 mg/kg. Dermal application of 2000 mg/kg HQ to rabbits under an occlusive wrap for 24 h did not result in neurobehavioral effects or mortality. Subchronic exposure was accomplished by administration of doses of 200, 64, 20, or 0 mg/kg/day of HQ in water to groups of male and female rats study (10/sex/group). A functional observational battery (FOB) was used to detect neurobehavioral effects prior to HQ exposure and postexposure at 1, 6, and 24 h and 7, 14, 30, 60, and 91 days. Daily clinical observations were also recorded for each animal. Doses of 200 or 64 mg/kg HQ resulted in acutely observable behavioral effects including tremors and reduced activity. Tremors occurred within one hour of dosing and resolved by the 6-h examination. Brain weights were not altered by HQ administration, but mean terminal body weight was reduced approximately 7% for the 200 mg/kg males. Neuropathologic examination of the CNS and PNS, including special stains for myelin and axonal process, did not reveal any morphologic lesions associated with HQ administration or secondary to repetitive CNS stimulation by HQ. The nephrotoxic effects observed in Fischer 344 rats after HQ exposure was not observed in this study with Sprague-Dawley rats. Oral doses of  $\geq 64$  mg/kg HQ resulted in acute neurobehavioral effects indicative of CNS stimulation; however, subchronic exposure to dose levels that produced repetitive CNS stimulation by HQ did not result in an exacerbation of acute stimulatory effects over time or morphologic changes in the CNS or PNS or nephrotoxicity.