PREDICTIONS OF DEVELOPMENTAL NEUROTOXICITY POTENTIAL OF TDCPP

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Tris(1,3-dichloro-2-propyl)phosphate (TDCPP) is an organophosphate flame retardant with widespread usage and documented human exposures through food, inhalation, dust ingestion, and breast milk. Concern for neurodevelopmental effects in infants and children has been raised by findings of decreased neural proliferation in cell culture as well as abnormal development and altered thyroid hormones in larval zebrafish assays. We evaluated the potential for developmental neurotoxicity of TDCPP using in vitro and in vivo studies. With 1-hr exposure in vitro, decreased neuron firing rate was observed in micro-electrode arrays in rat cortical cell cultures at concentrations that did not impact cell viability. In larval zebrafish, 1-hr exposure produced concentration-related increases then decreases in motor activity. Longer exposures (48 hr) in developing human hN2 cells produced <30% decrease in neurite outgrowth and cell viability only at high concentrations, and no changes were noted in rat cortical neurite outgrowth. Pregnant Long-Evans rats were orally dosed (0, 15, 50, or 150 mg/kg/d) from gestational day 10 to weaning, and offspring were evaluated on several physical and neurological parameters. Serum thyroid hormones were unaffected in offspring on postnatal day (PND) 6 or 22, and in dams post-weaning. Brain weight was unaltered in offspring at both ages, but liver weight was increased in high-dose dams. There were no differences in body weight or litter size at birth, but starting at PND6 the high-dose group showed a persistent impairment in weight gain. The ontogeny of righting reflex (PND 2-4) and of motor activity (PNDs 13, 17, 21) was not altered by treatment. Thus, acute exposures produced effects on larval zebrafish behavior and rat neuronal cell activity. Exposure during developmental processes in rat cortical cells and in rats during the preweaning period showed little to no evidence of specific developmental neurotoxicity. *This is an abstract of a proposed presentation and does not reflect US EPA policy.*