Evaluation of Hydroxyatrazine in the Endocrine Disruptor Screening and Testing Program's Male and Female Pubertal Protocols.

ABSTRACT

Two critical components of the validation of any in vivo screening assay are to demonstrate sensitivity (ability to detect weak endocrine actives) and the specificity (the ability to correctly identify an inactive or "negative" chemical). Although the Endocrine Disruptor Screening Program's (EDSP) Tier 1 Male and Female Pubertal Protocols have been shown to be fairly sensitive assays for the detection of endocrine disrupting chemicals (EDCs), there are concerns that these assays lack specificity for effects when a chemical induces systemic toxicity. A lack of specificity, or the ability of an assay to correctly identify an inactive or "negative" chemical, would increase the probability of identifying false positives. In this study, we addressed this concern by treating rats with hydroxyatrazine (OH-ATR), a biotransformation by-product of the chlorotriazine herbicides known to produce nephrotoxicity following a 13 week dietary exposure in the rat. OH-ATR was administered by oral gavage to male (PND 23 to 53) and female rats (PND 22 to 42) as described in the EDSP pubertal protocols. Based on a previous study in our lab, males were dosed with 11.4 to 183.4 mg/kg OH-ATR and females were dosed with 45.75 to 183.4 mg/kg OH-ATR. Following exposure, there was a dose-responsive increase in the mean kidney weights of both the male and female. As the dose of OH-ATR was increased, there was a corresponding rise in both the incidence

and severity of kidney lesions, including the deposition of mineralized renal tubule material (concretions), hydronephrosis, renal tubule dilatation, and pyelonephritis. However, there were no differences in body weight, liver weight, or reproductive tissue weights, hormone concentrations or the age of pubertal onset in either the male or female rats as compared to controls. Additionally, there were no histological changes in the epididymides, testes, thyroids or ovaries. Therefore, based on the results of this study OH-ATR would not have been identified as an active endocrine disruptor in either pubertal assay.