Developmental toxicity studies of four fragrances in rats.

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Abstract

Four fragrances, 6-acetyl-1,1,2,4,4,7-hexamethyltetraline (AHTN), 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-gamma-2-ben zopyran (HHCB), musk ketone and musk xylene were tested for developmental toxicity in Sprague-Dawley rats (25/group, 3 groups/fragrance, 2 fragrances/corn oil control). Dosages tested were HHCB: 50, 150, 500 mg/kg per day; AHTN: 5, 15, 50 mg/kg per day; musk ketone: 15, 45, 150 mg/kg per day; musk xylene: 20, 60, 200 mg/kg per day. All dosages tested exceeded multiples of the estimated maximal daily human dermal exposure. Treatment (gavage, 5 ml/kg) occurred on GDs 7-17 and Caesarean-sectioning on GD 20. Based on the results of these studies, none of the four fragrances tested were more toxic in the conceptuses than in the dams. Maternal NOAELs were 50, 5, 15 and 20 mg/kg per day for HHCB, AHTN, musk ketone and musk xylene, respectively (150, 50, 45 and 60 mg/kg per day caused clinical signs and reduced weight gain and feed consumption). Developmental NOAELs were 150, 50, 45 and 200 mg/kg per day for HHCB, AHTN, musk ketone and musk xylene, respectively. No adverse effects on embryo-fetal viability, growth or morphology occurred at the highest dosages of AHTN (50 mg/kg per day) or musk xylene (200 mg/kg per day). Developmental toxicity occurred at the high-dosages of HHCB (axial skeletal malformations at 500 mg/kg per day) and musk ketone (increased postimplantation loss and reduced fetal body weight at 150 mg/kg per day). The results of this study indicate that under conditions of normal use, the tested fragrances do not pose a risk to human conceptuses.

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