Low-dose effects of bisphenol A on mammary gland development in rats

Bisphenol A (BPA) is widely used in food contact materials, toys, and other products. Several studies have indicated that effects observed at doses near human exposure levels may not be observed at higher doses. Many studies have shown effects on mammary glands at low doses of BPA, however, because of small number of animals or few doses investigated these data have not been used by EFSA as point of departure for the newly assessed tolerable daily intake (TDI). We performed a study with perinatal exposure to BPA (0, 0.025, 0.25, 5, and 50 mg/kg bw/day) in rats (n = 22 mated/group). One of the aims was to perform a study robust enough to contribute to the risk assessment of BPA and to elucidate possible biphasic dose–response relationships. We investigated mammary gland effects in the offspring at 22, 100, and 400 days of age. Male offspring showed increased mammary outgrowth on pup day (PD) 22 at 0.025 mg/kg BPA, indicating an increased mammary development at this low dose only. Increased prevalence of intraductal hyperplasia was observed in BPA females exposed to 0.25 mg/kg at PD 400, but not at PD 100, and not at higher or lower doses. The present findings support data from the published literature showing that perinatal exposure to BPA can induce increased mammary growth and proliferative lesions in rodents. Our results indicate that low-dose exposure to BPA can affect mammary gland development in male and female rats, although higher doses show a different pattern of effects. The observed intraductal hyperplasia in female rats could be associated with an increased risk for developing hyperplastic lesions, which are parallels to early signs of breast neoplasia in women. Collectively, current knowledge on effects of BPA on mammary gland at low doses indicates that highly exposed humans may not be sufficiently protected.

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Contributors: Egebjerg, K. M., Boberg, J., Isling, L. K., Christiansen, S., Hass, U.
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