Cluster overview for Reproductive and developmental toxicity - (BPA) in foodstuffs – Reproductive and Developmental Toxicity

In this guide

259. The CEP panel noted that the effects BPA are reported over a huge range of effective concentrations/doses (low nM and mg/kg bw per day to high µM and >1,000 µg/kg). This range needed consideration since there could be qualitative as well as quantitative differences in mechanisms, depending on dose.

260. It was considered clear that many of the reported effects of BPA on male reproductive endpoints are measuring downstream intermediate pleiotropic effects (e.g. altered expression of many genes and proteins, DNA methylation and histone changes, activation of MAPK, PI3K, PKA, Akt/mTOR pathways, INSL3, StAR, etc.). It was stated that details of upstream mechanisms, which are more likely to be BPA specific, are unclear in many cases. For example, mechanisms for BPA-induced sperm mitochondrial membrane potential changes could include altered ion channels, receptors (and receptor cross-talk) and ROS.

261. Receptor interactions are an obvious candidate mechanism for early BPA effects (AR, ERα, ERβ, GPER, ERRg, PPARg, etc.). Some studies have reported receptor-dependency of BPA effects, but the results are difficult to generalise, because steroid receptor properties and interactions are dynamic; substance effects can vary by e.g. tissue, life-stage and dose.

262. A plausible upstream mechanism for BPA effects is oxidative stress generation, at both low and high doses.

263. In summary, it seems plausible that BPA-induced oxidative stress (with modulation of androgen and oestrogen pathways, and downstream inflammation) is an early key event in the adverse effects of BPA on adult male and female reproductive organs.