WoE approach

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7. The WoE approach applied to the evaluation of genotoxicity data is based on EFSA Scientific Committee recommendations (EFSA Scientific Committee, 2011, 2017). As recommended by the EFSA Scientific Committee (EFSA Scientific Committee, 2011, 2017), a documented WoE approach for the evaluation and interpretation of genotoxicity data' has been applied, taking into account not only the quality and availability of the data on genotoxicity itself, but also all other relevant data that may be available. The main steps of the WoE approach applied in the genotoxicity assessment of BPA are described below.

Assembling of the evidence into lines of evidence of similar type

8. In a first step, the CEP Panel evaluated all available in vitro and in vivo studies addressing the three main endpoints of genotoxicity: gene mutations, structural and numerical chromosomal aberrations (CA) in addition to DNA damage endpoint (evaluated by Comet assay). The study results addressing each of these endpoints were grouped into lines of evidence. Only the studies of high and limited relevance were included.

9. Studies investigating the BPA MoA were considered, e.g. DNA oxidation, ROS (when genotoxicity was also investigated in the same study), DNA binding, interference with proteins involved in chromosome segregation during cell division, modulation of expression of genes involved in DNA repair or in chromosome segregation and markers of DNA double strand breaks (DSBs) (e.g. γH2AX). Evidence from the mechanistic studies may support the lines of evidence for the genotoxicity endpoints

Weighting of the evidence

10. A quantitative method to weight the evidence was not considered appropriate due to the quantity and heterogeneity of the evidence to be integrated. A qualitative method based on expert judgment was applied. All studies evaluated for reliability and relevance (as described above) were listed in tables below). The evaluation of the studies of high and limited relevance was described in the opinion, including the conclusion for each line of evidence. The consistency of the evidence was assessed and presented in the opinion.

Integrating all the evidence

11. Integrating evidence from the MoA with lines of evidence from genotoxicity endpoints allows a reduction in the uncertainty on the potential genotoxicity. In case genotoxic effects were observed, evidence from the MoA may allow clarification if the genotoxicity is due to a direct or indirect mechanism.