Draft EFSA Scientific Opinion on the evaluation of the safety of preparations from the fruits of sweet and bitter fennel (Foeniculum vulgare Mill. and Foeniculum piperitum (Ucria) C.Presl)

Hazard characterisation (Section 3.6)

In this guide

41. Estragole, methyleugenol and safrole are considered genotoxic carcinogens (SCF, 2001b, a, 2002; EMA HMPC, 2005, 2023, 2024a, d) and EFSA considered only a single 2-year carcinogenicity study for methyleugenol sufficient to derive a dose response. The study exposed, rats and mice to methyleugenol by oral gavage at 0, 37, 75 or 150 mg/kg bw for 5 days per week (equivalent to 0, 26.4, 53.6 or 107.1 mg/kg bw per day) and rats to a second higher dose of 300 mg/kg bw per day (NTP, 2000).

42. EFSA had previously identified a lower confidence limit for a benchmark response of 10 % (BMDL10) for methyleugenol of 22.2 mg/kg bw per day as reference point for the entire *p*-allylalkoxybenzene group for the safety assessment of a feed additive (EFSA, 2022b). The BMDL10 had been derived by Suparmi et al. (2019) based on the incidence of liver tumours in male rats in the NTP study.

43. For this draft EFSA opinion on the safety of fennel fruit preparations EFSA decided to repeat the Suparmi et al. (2019) benchmark dose (BMD) analysis using Bayesian approaches as implemented in EFSA's Benchmark Dose modelling software and using sex as a covariate to increase power. To identify the BMDL10, data from male rats was used as they were more sensitive to hepatocarcinoma than the females. After model averaging the BMD identified was 32.4 mg/kg bw per day with a 90 % credible interval of 21.0 to 48.2 mg/kg bw per day. Therefore, the revised BMDL10 for methyleugenol was 21.0 mg/kg bw per day and in line with the EFSA approach this BMDL10 was applied to the whole *p*-allylalkoxybenzene group.