food-borne alkenylbenzene apiol from parsley using physiologically based kinetic (PBK) modelling and read-across from safrole

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The present study developed physiologically-based kinetic (PBK) models for the alkenylbenzene apiol in order to facilitate risk assessment based on read-across from the related alkenylbenzene safrole. Model predictions indicate that in rat liver the formation of the 1′-sulfoxy metabolite is about 3 times lower for apiol than for safrole. These data support that the lower confidence limit of the benchmark dose resulting in a 10% extra cancer incidence (BMDL10) that would be obtained in a rodent carcinogenicity study with apiol may be 3-fold higher for apiol than for safrole. These results enable a preliminary risk assessment for apiol, for which tumor data are not available, using a BMDL10 value of 3 times the BMDL10 for safrole. Based on an estimated BMDL10 for apiol of 5.7–15.3 mg/kg body wt per day and an estimated daily intake of 4 × 10−5 mg/kg body wt per day, the margin of exposure (MOE) would amount to 140,000–385,000. This indicates a low priority for risk management. The present study shows how PBK modelling can contribute to the development of alternatives for animal testing, facilitating read-across from compounds for which in vivo toxicity studies on tumor formation are available to compounds for which these data are unavailable.

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