Health based guidance values - Statement on the guidance levels for the fortificants in the Bread and Flour Regulations

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15. No tolerable upper levels (TUL) or safe upper levels (UL) have been established for calcium, iron, niacin and thiamin by the EVM due to the lack of sufficient animal and human data (EVM, 2003).

16. However, the EVM stated that “1,500 mg/day of supplemental calcium would not be expected to result in any adverse effect, but that higher doses could result in adverse GI symptoms in a few people” (EVM, 2003). The Scientific Committee on Food (SCF) established a TUL of 2,500 mg/day for calcium in 2003 (SCF, 2003). This TUL was based on long duration intervention studies of different time periods in which total daily calcium intakes of 2,500 mg from both diet and supplements were tolerated without adverse effects and was endorsed by EFSA in 2012 (EFSA, 2012).

17. The EVM proposed that a supplemental intake of 17 mg/person/day (0.22 mg/kg bw per day for a 78.6 kg adult) (based on the average body weight in the UK National Diet and Nutrition Survey (NDNS) data) (Bates *et al.*, 2014, 2016, 2020; Roberts *et al.*, 2018) for iron would not be expected to produce adverse effects in the majority of individuals. However, this guidance value does not apply to individuals who have an increased susceptibility to iron overload, a condition which is associated with a homozygous haemochromatosis genotype (with an estimated prevalence of up to 0.4% in the Caucasian population). An UL for iron has not been established by EFSA**.** The National Institutes of Health Office of Dietary Supplements in the United States have advised ULs of 40 mg/day/person for individuals aged 0 months to 13 years and 45 mg/day for individuals aged 14 years and over (Institute of Medicine, 2001). However, it has been reported that ingestion <20 mg/kg of elemental iron is non-toxic and moderate symptoms of iron toxicity can occur between 20 to 60 mg/kg (Yuen and Becker, 2022).

18. The EVM proposed that a guidance level of 17 mg/day for niacin would not be expected to result in any adverse effects. However, it was noted by the EVM that this guidance level is for supplementation only, as adverse effects from niacin seem to be related to acute, bolus intakes. Adverse effects from long term exposure of niacin in food would be less likely as free niacin levels in food are low. Additionally, the EVM noted that the guidance level is based on intakes of conventional formulations of niacin. This would not be applicable to sustained release preparations but niacin contained in dietary supplements is not in the sustained release form (EVM, 2003). In 2002, the SCF set an UL of 10 mg/day for niacin based on flushing of skin (EFSA, 2014).

19. The EVM proposed a guidance level for supplemental thiamin of 100 mg/day, which would not be expected to result in adverse effects. The EVM noted

however that this guidance level was applicable only to the water-soluble forms of thiamin. Furthermore, the study by Gokhale *et al*. (1999), used to derive the guidance level, was conducted in young women (EVM, 2003) who may not be representative of the population in general. An UL for thiamin was not established by the SCF as there were only limited data on adverse effects in humans and lack of dose-response studies (EFSA, 2016). Whilst there is a lack of evidence of toxicity from a high intake of thiamin from food or supplements (Martel *et al*., 2021), symptoms such as headache, nausea, irritability, insomnia, rapid pulse and weakness have been observed at high oral doses of ≥7,000 mg/day thiamin hydrochloride (EVM, 2003).