

Part 4: Trace Elements

Boron

Function

Boron is essential to the life cycles of some animal species, but in regard to humans it is considered only probably essential. There is, however, clear evidence that dietary intake of this element is *beneficial* to humans (Nielsen 2000). Boron deprivation impairs calcium metabolism and bone health, as well as brain function and energy metabolism.

Safety Evidence

Boron has a low potential for causing obvious adverse effects in humans, as indicated by the widespread use of boric acid between 1870 and 1920 as a food preservative. This use of boric acid led to boron intakes of up to 500 mg per day without adverse effects other than nausea and loss of appetite (Nielsen 1996). In pregnant rats, dietary boric acid can cause fetal development defects and growth deficits (Price et al. 1996). In studies with dogs, high intakes of boric acid have caused testicular atrophy and moderately decreased sperm production (Weir and Fisher 1972). Intakes of 500 mg boric acid (72 mg of boron) per day for 50 days by adults have disturbed appetite and digestion (Nielsen 1996).

The Environmental Protection Agency (EPA) relied on one of the dog studies (Weir and Fisher 1972) in calculating a Reference Dose (RfD). Since adverse effects were found with an intake of 29 mg per kg per day over thirty-eight weeks of treatment, this level became the LOAEL. The next lower dose, of 8.8 mg per kg per day, produced no adverse effects; this intake level became the NOAEL. The EPA applied a hundredfold margin of safety to the NOAEL in dogs to calculate a “safe” intake (RfD) of 0.09 mg per kg per day, or 6.3 mg per day in a 70 kg man (Environmental Protection Agency 2004).

For humans, the data are too scant and the effects too vague to identify a specific LOAEL value. Although more information is needed, the gastrointestinal effects associated with intake of 500 mg of boric acid (72 mg of boron) may be considered undesirable rather than harmful. Moreover, these effects should be self-limiting due to consumer awareness. Thus, no LOAEL value for boron intake by humans can be identified.

Clinical trials with an upper intake of 3 mg per day produced no adverse effects but because so few other intake levels have been subjected to clinical study, 3 mg

may be lower than appropriate to identify as a NOAEL for humans. The EPA RfD of 0.09 mg per kg per day, or 6.3 mg per day in a 70 kg man, may be considered a safe level of human intake. This intake level cannot be identified as a NOAEL, however, because it is based on calculation rather than observation. For boron intake by adults, the RfD of 6.3 mg per day may be used instead of a human NOAEL because it is only a little above the range of clinical experiments and is far below the FNB UL and the EVM GL; that is, it does not require application of any additional safety factor (in other words, a safety factor of 1.0 is sufficient) to calculate a safe human intake.

Published Official Reviews of Boron Safety

The FNB found that most data on the adverse effects of boron in humans were associated with an accidental single episode or short-term ingestion of boric acid (Food and Nutrition Board 2001). In the absence of human dose-response data judged useful, FNB extrapolated from animal data to set a human UL. From the data of Price and coworkers (Price et al. 1996), FNB identified a NOAEL of 9.6 mg per kg per day for developmental toxicity in mice, and selected a composite UF of 30 (3 for interspecies variability and 10 for extrapolation from mice to humans) to derive a UL of 0.3 mg per kg per day. Correction to a reference adult weight of 61 kg gave FNB an adult UL of 20 mg boron per day.

The UK EVM found the long-term clinical study of Meacham and colleagues (Meacham et al. 1994) to be insufficient as the basis for an SUL or GL (Expert Group on Vitamins and Minerals 2003). Instead, using the same data on developmental toxicity in mice (Price et al. 1996) that FNB studied, UK EVM identified the NOAEL as 9.6 mg per kg per day, applied a composite UF of 60 (10 for interspecies and 6 for inter-individual), and derived an SUL of 9.6 mg per day for a 60 kg person.

The EPA applied a composite UF of 100 to the data of Price and coworkers to derive an RfD of 6.3 mg per day (Environmental Protection Agency 2004).

CRN ULS for Boron

A clinical trial (Meacham et al. 1994) with an intake of 3 mg per day produced no adverse effects. Other studies confirmed this observation (Nielsen 2000), and 3 mg may be considered as an OSL for supplemental intake. Intakes from conventional foods are almost always less than 3 mg per day (Expert Group on Vitamins and Minerals 2003).

The EPA RfD uses a UF that may be excessive, and the FNB UL applies to total intake from all data. In the face of these quantitative uncertainties, CRN believes

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that the ULS for boron should be 6 mg per day, based on the UK EVM SUL of 9.6 mg and the fact that food intakes rarely exceed 3 mg.

Comparison of Safety Values for Boron

CRN ULS	6 mg
US FNB UL	20 mg
EC SCF UL	Not reviewed (as of May 2004)
EC supplement maximum	Not established (as of May 2004)
UK EVM SUL	9.6 mg

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