Hazard Characterisation - Microcystins in Fish

A WHO review established a provisional tolerable daily intake (TDI) for MC-LR based on the subchronic (90 day) toxicity study in mice by Fawell et al. (1999), in which hepatic lesions were observed at higher doses, supported by the 28-day study in rats by Heinze (1999) (WHO, 2020). An uncertainty factor of 1000 was applied to the no-observed-adverse-effect-level (NOAEL) of 40 µg/kg bodyweight per day in the study in mice. This included uncertainty factors of 10 each for interspecies differences and intraspecies variability in the human population and a further factor of 10 for the use of a subchronic, rather than chronic, study and other limitations in the toxicological data. The resulting provisional TDI is 0.04 µg/kg bodyweight.

The WHO also recommended a provisional short term guidance value for water, based on the same data but applying an uncertainty factor of 100 rather than 1000, omitting the extra uncertainty factor of 10 as the data limitations were considered to primarily affect longer term risks. This is equivalent to a short-term health-based guidance value of 0.4 µg/kg bodyweight. However, it was noted that it was only intended to address risks over very short time periods. This is presumably to ensure that long term intakes remained within the provisional TDI.

The WHO review recommended that exposures to total microcystins, expressed as the equivalent amounts of microcystin-LR, should be compared to the provisional TDI and shorter term guidance value, since while these were based on toxicology data for microcystin-LR, the microcystins occur as mixtures. The WHO review noted the significant uncertainties due to differences in the potencies and toxicokinetics of different microcystins, which can be expected to result in large differences in potency following oral dosing.