HISTORY OF GUIDELINE DEVELOPMENT

Trichloroethene

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to trichloroethene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a tentative guideline value of 0.03 mg/L was recommended. The guideline value was designated as tentative because, although carcinogenicity was observed in one species only, the compound occurred relatively frequently in drinking-water. The second edition of the Guidelines (1993) established a provisional health-based guideline value of 0.07 mg/L for trichloroethene. The value was provisional because an uncertainty factor of 3000 was used in its derivation. This provisional guideline value was brought forward to the third edition. In the first addendum to the third edition, published in 2006, a guideline value of 0.02 mg/L was established, which was designated as provisional due to deficiencies in the toxicological database. This guideline value was brought forward to the fourth edition of the Guidelines, published in 2011. The fourth edition of the Guidelines incorporating the first and second addenda, published in March 2022 (based on the 2020 assessment as a background document to the Guidelines), recognized that the prior study used for guideline value derivation had several significant methodological limitations. A revised approach for guideline value derivation was therefore implemented resulting in the amendment of the health-based guideline value to 0.008 mg/L. The guideline value was based on the use of physiologically-based pharmacokinetic modelling to identify human-equivalent points of departure from three key studies conducted in rodents. Respectively, these studies reported increased incidence of heart malformations in rats, decreased thymus weights in mice, and increased incidence of developmental immunotoxic effects in mice. Selection of multiple critical effects, rather than the lowest point of departure, as the basis of the guideline value helped overcome possible limitations of individual studies. It was also noted that this guideline value is considered protective of both cancer and non-cancer effects.