MX is a potent mutagen in bacteria and in cells in vitro and has undergone a lifetime study in rats in which some tumorigenic responses were observed. These data indicate that MX induces thyroid and bile duct tumours. IARC has classified MX in Group 2B (possibly carcinogenic to humans) on the basis of rat tumorigenicity and its strong mutagenicity.

A health-based value of 1.8 μg/l can be calculated for MX on the basis of the increase in cholangiomas and cholangiocarcinomas in female rats using the linearized multistage model (without a body surface area correction). However, this is significantly above the concentrations that would be found in drinking-water, and, in view of the analytical difficulties in measuring this compound at such low concentrations, it is considered unnecessary to propose a formal guideline value for MX in drinking-water.

Nickel

Nickel is a naturally occurring element, which is used mainly in the production of stainless steel and nickel alloys. Food is the dominant source of nickel exposure in the non-smoking, non-occupationally exposed population; water is generally a minor contributor to the total daily oral intake. However, the nickel contribution from water may be significant where there is heavy pollution, where nickel that occurs naturally in groundwater is mobilized, or where nickel leaches from nickel- or chromium-plated taps or stainless steel devices or materials that are in contact with water. The primary source of nickel in drinking-water is leaching from metals that are in contact with drinking-water.

Guideline value	0.07 mg/l (70 μg/l)
Occurrence	Concentration in drinking-water are typically less than 25 μg/l, although concentrations may be elevated (up to 5 mg/l) where nickel is released from metal alloys that are in contact with drinking-water, such as fittings, including taps, or as a result of anthropogenic contamination or mobilization from natural deposits
Basis of guideline value derivation	The guideline value is based on achievability by available source control measures and treatment technologies, measurability by analytical methods and toxicology. Reproductive toxicity (increased incidence of rat litters with post-implantation loss) was considered the most sensitive end-point and is therefore the basis for the TDI derivation of 13 μg/kg body weight. An uncertainty factor of 100 was applied to account for interspecies differences (10) and intraspecies variation (10) to the BDML10 of 1.3 mg/kg bw per day, from a two-generation study in rats. Although the 2021 risk assessment supports a health-based value of 80 μg/l based on this TDI, the guideline value was retained at 70 μg/l considering the above factors. Further, 80 μg/l is only slightly higher than the previous guideline value of 70 μg/l (established in 2014); factoring in the imprecision inherent in risk assessment procedures, this difference is not judged significant enough to warrant a revised, minimally relaxed guideline value.
Limit of detection	0.5–5 μg/l for ICP-MS, ICP-AES and graphite furnace AAS; 0.1 mg/l for flame AAS

Prevention and treatment	For surface water, conventional water treatment (coagulation, sedimentation, filtration) may be effective under certain circumstances, depending on a number of factors, including the coagulant dosage and pH. For groundwater, ion-exchange resins have been shown to be effective. The most important means of control is by product specifications through an appropriate certification scheme for materials in contact with drinking-water. Consumers, particularly nickel-sensitive people, should flush chromium- or nickel-plated taps before using the water, particularly after periods of stagnation.
Health-based value derivation	
• allocation to water	20% of TDI
• weight	60 kg adult
• consumption	2 litres/day
Additional comments	The guideline value is also protective of any possible acute effects, including systemic contact dermatitis
	As nickel is usually found in drinking-water below the guideline value, monitoring and inclusion in drinking-water regulations and standards would usually only be necessary if there were indications that a specific pollution or problem might exist
Assessment date	2021
Principal reference	WHO (2021) *Nickel in drinking-water* EFSA (2020) *Update of the risk assessment of nickel in food*

IARC concluded that inhaled nickel compounds are carcinogenic to humans (Group 1) and that metallic nickel is possibly carcinogenic (Group 2B). However, there is a lack of evidence of a carcinogenic risk from oral exposure to nickel. In a well-conducted two-generation reproductive study in rats administered nickel by gavage, an increase in the frequency of litters with post-implantation loss was reported; thus, reproductive and developmental toxicity was identified as the relevant and sensitive end-point for derivation of the health-based value.

Exposure to nickel through the skin or by inhalation may lead to nickel sensitization. Whereas oral ingestion of nickel is not known to lead to systemic contact dermatitis (SCD) in the general population, it can elicit SCD in nickel-sensitized individuals. However, the guideline value of 70 µg/L is considered adequately protective of SCD that may result from drinking-water exposure based on a margin of exposure (MOE) assessment. Acute consumption of water containing nickel at the chronic health-based value of 80 µg/l would result in an MOE of approximately 16. The MOE of 16 was calculated from an acute LOAEL for SCD of 4.3 µg/kg bw and an acute exposure of 0.27 µg/kg bw (based on a scenario of a person weighing 60 kg, drinking a glass of tap water (about 200 ml) containing nickel at the health-based value of 80 µg/l). The guideline value is further considered adequately protective considering that SCD elicitation was associated with a bolus exposure, in contrast to the intermittent nature of a drinking-water exposure scenario.