

Lindane was toxic to the kidney and liver after administration orally, dermally or by inhalation in short-term and long-term studies of toxicity and reproductive toxicity in rats. The renal toxicity of lindane was specific to male rats and was considered not to be relevant to human risk assessment, as it is a consequence of accumulation of α_{2u} -globulin, a protein that is not found in humans. Hepatocellular hypertrophy was observed in a number of studies in mice, rats and rabbits and was reversed only partially after recovery periods of up to 6 weeks. Lindane did not induce a carcinogenic response in rats or dogs, but it caused an increased incidence of adenomas and carcinomas of the liver in agouti and pseudoagouti mice, but not in black or any other strains of mice, in a study of the role of genetic background in the latency and incidence of tumorigenesis. JMPR concluded that there was no evidence of genotoxicity. In the absence of genotoxicity and on the basis of the weight of the evidence from the studies of carcinogenicity, JMPR concluded that lindane is not likely to pose a carcinogenic risk to humans. Further, in an epidemiological study designed to assess the potential association between breast cancer and exposure to chlorinated pesticides, no correlation with lindane was found.

Malathion

Malathion (CAS No. 121-75-5) is commonly used to control mosquitoes and a variety of insects that attack fruits, vegetables, landscaping plants and shrubs. It can also be found in other pesticide products used indoors, on pets to control ticks and insects and to control human head and body lice. Under least favourable conditions (i.e. low pH and little organic content), malathion may persist in water with a half-life of months or even years. However, under most conditions, the half-life appears to be roughly 7–14 days. Malathion has been detected in surface water and drinking-water at concentrations below 2 µg/l.

Reason for not establishing a guideline value	Occurs in drinking-water at concentrations well below those of health concern
Assessment date	2003
Principal references	FAO/WHO (1998) <i>Pesticide residues in food—1997 evaluations</i> WHO (2003) <i>Malathion in drinking-water</i>

Malathion inhibits cholinesterase activity in mice, rats and human volunteers. It increased the incidence of liver adenomas in mice when administered in the diet. Most of the evidence indicates that malathion is not genotoxic, although some studies indicate that it can produce chromosomal aberrations and sister chromatid exchange in vitro. JMPR has concluded that malathion is not genotoxic.

A health-based value of 0.9 mg/l can be calculated for malathion based on an allocation of 10% of the upper limit of the JMPR ADI—based on a NOAEL of 29 mg/kg body weight per day in a 2-year study of toxicity and carcinogenicity in rats, using an uncertainty factor of 100 for interspecies and intraspecies variation and supported by a NOAEL of 25 mg/kg body weight per day in a developmental toxicity study in rabbits—to drinking-water. However, intake of malathion from all sources is generally low

and well below the upper limit of the ADI. As the chemical occurs in drinking-water at concentrations much lower than the health-based value, the presence of malathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, it is considered unnecessary to derive a formal guideline value for malathion in drinking-water.

Manganese¹

Manganese is one of the most abundant metals in Earth's crust, usually occurring with iron. It can exist in 11 oxidation states, often as chloride, oxides and sulfates. The most common oxidation states for manganese in natural water are manganese(II) and manganese(IV). Manganese is used principally in the manufacture of iron and steel alloys, and manganese compounds such as potassium and sodium permanganate are ingredients in various products used for cleaning, bleaching and disinfection. Manganese compounds are additionally used in some locations for potable water treatment and can also be an impurity in coagulants used during water treatment. Manganese occurs naturally in many surface water and groundwater sources; although naturally occurring manganese is usually the most important source for drinking-water, anthropogenic activities can also contribute to high levels of manganese in water. Manganese also occurs naturally in many food sources, and the greatest exposure to manganese is usually from food.

Provisional guideline value	<p><i>Total manganese:</i> 0.08 mg/l (80 µg/l), to be protective against neurological effects in the most sensitive subpopulation—bottle-fed infants—and consequently the general population</p> <p>This guideline value is provisional because of the high level of uncertainty, as reflected in the composite uncertainty factor of 1000</p>
Occurrence	<p>Levels in fresh waters vary widely. They are typically in the range 1–200 µg/l. Higher levels are usually associated with groundwater, lakes and reservoirs under acidic or reducing conditions, or in aerobic waters with industrial pollution. Very high concentrations (up to 10 mg/l) have been reported in acidic groundwater. In treated drinking-water, concentrations are typically less than 50 µg/l.</p>
TDI	<p>0.025 mg/kg bw, derived by applying an uncertainty factor of 1000 to a LOAEL of 25 mg/kg bw per day identified from studies that reported neurological effects in rats exposed to manganese from birth to postnatal day 21. The uncertainty factor takes into account interpecies variation (10), intraspecies variation (10) and database uncertainties (10, including use of a LOAEL).</p>
Limit of detection	<p>0.002 µg/l by ICP-MS; 0.005–50 µg/l by ICP-AES and GFAA spectrometry; and 10–70 µg/l by colorimetric methods. None of these methods distinguish between the different oxidation states of manganese.</p>

¹ As naturally occurring manganese in drinking-water is a chemical of concern in many areas, its chemical fact sheet has been expanded.