Guideline value derivation	
• allocation to water	10% of TDI
• weight	60 kg adult
• consumption	2 litres/day
Assessment date	1993
Principal reference	WHO (2004) *Methoxychlor in drinking-water*

The genotoxic potential of methoxychlor appears to be negligible. In 1979, IARC assigned methoxychlor to Group 3. Subsequent data suggest a carcinogenic potential of methoxychlor for liver and testes in mice. This may be due to the hormonal activity of proestrogenic mammalian metabolites of methoxychlor and may therefore have a threshold. The study, however, was inadequate, because only one dose was used and because this dose may have been above the maximum tolerated dose. The database for studies on long-term, short-term and reproductive toxicity is inadequate. A teratology study in rabbits reported a systemic NOAEL of 5 mg/kg body weight per day, which is lower than the LOAELs and NOAELs from other studies. This NOAEL was therefore selected for use in the derivation of a TDI.

Methyl parathion

Methyl parathion (CAS No. 298-00-0) is a non-systemic insecticide and acaricide that is produced throughout the world and has been registered for use on many crops, in particular cotton. It partitions mainly to air and soil in the environment. There is virtually no movement through soil, and neither the parent compound nor its breakdown products will reach groundwater. By far the most important route for the environmental degradation of methyl parathion is microbial degradation. Half-lives of methyl parathion in water are in the order of weeks to months. Concentrations of methyl parathion in natural waters of agricultural areas in the USA ranged up to 0.46 µg/l, with highest levels in summer. The general population can come into contact with methyl parathion via air, water or food.

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 (1996) *Pesticide residues in food—1995 evaluations.* IPCS (1992) *Methyl parathion* WHO (2004) *Methyl parathion in drinking-water*

A NOAEL of 0.3 mg/kg body weight per day was derived from the combined results of several studies conducted in humans, based on the depression of erythrocyte and plasma cholinesterase activities. Methyl parathion decreased cholinesterase activities in long-term studies in mice and rats, but did not induce carcinogenic effects. Methyl parathion was mutagenic in bacteria, but there was no evidence of genotoxicity in a limited range of studies in mammalian systems.

A health-based value of 9 µg/l can be calculated for methyl parathion on the basis of an ADI of 0–0.003 mg/kg body weight, based on a NOAEL of 0.25 mg/kg body weight per day in a 2-year study in rats for retinal degeneration, sciatic nerve demyelination, reduced body weight, anaemia and decreased brain acetylcholinesterase activity, using an uncertainty factor of 100 for interspecies and intraspecies variation. As the toxicological end-points seen in experimental animals were other than acetylcholinesterase inhibition, it was considered more appropriate to use these data rather than the NOAEL derived for cholinesterase inhibition in humans.

Intake of methyl parathion from all sources is generally low and well below the upper limit of the ADI. As the health-based value is much higher than concentrations of methyl parathion likely to be found in drinking-water, the presence of methyl parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a formal guideline value for methyl parathion is not deemed necessary.

Methyl tertiary-butyl ether

The major use of methyl *tert*-butyl ether, or MTBE, is as a gasoline additive. Surface water can be contaminated by gasoline spills; however, owing to the high volatility of MTBE, most is lost to evaporation. Spills and leaking storage tanks can cause more serious problems in groundwater, where MTBE is more persistent. MTBE has been detected in groundwater and drinking-water at concentrations in the nanogram to microgram per litre range.

Reason for not establishing a guideline value	Any guideline that would be derived would be significantly higher than concentrations at which MTBE would be detected by odour
Assessment date	2004
Principal references	IPCS (1998) *Methyl tertiary-butyl ether* WHO (2005) *Methyl tertiary-butyl ether (MTBE) in drinking-water*

No human cancer studies have been published for either the general population or occupationally exposed cohorts. There have been a number of human studies of neurological and clinical effects of exposure to MTBE by inhalation, with mixed results. In general, no objective changes could be seen at levels of MTBE normally found, even in such microenvironments as gasoline filling stations.

The weight of evidence suggests that MTBE is not genotoxic. A large number of studies using in vitro and in vivo mammalian and non-mammalian systems have been conducted to assess the mutagenicity of MTBE, almost all of which have produced negative results. These results suggest that the mechanism of action of MTBE is more likely to be non-genotoxic than genotoxic, although no one mechanism appears to explain all of the observed effects.

It has been concluded that MTBE should be considered a rodent carcinogen but that it is not genotoxic, and the carcinogenic response is evident only at high levels of exposure that also induce other adverse effects. The available data are therefore considered inconclusive and prohibit their use for human carcinogenic risk assessment.