Absorption of cadmium compounds is dependent on the solubility of the compounds. Cadmium accumulates primarily in the kidneys and has a long biological half-life in humans of 10–35 years. There is evidence that cadmium is carcinogenic by the inhalation route, and IARC has classified cadmium and cadmium compounds in Group 2A (probably carcinogenic to humans). However, there is no evidence of carcinogenicity by the oral route and no clear evidence for the genotoxicity of cadmium. The kidney is the main target organ for cadmium toxicity.

In its recent evaluation of cadmium, JECFA found that data relating excretion of the biomarker β_2-microglobulin in urine to cadmium excretion in urine for individuals who are 50 years of age and older provided the most reliable basis on which to determine a critical concentration of cadmium in the urine. Urinary excretion of less than 5.24 µg of cadmium per gram creatinine was not associated with an increased excretion of β_2-microglobulin, and the dietary exposure that would result in a urinary cadmium concentration at the breakpoint of 5.24 µg/g creatinine was estimated to be 0.8 µg/kg body weight per day or about 25 µg/kg body weight per month. Because of cadmium's exceptionally long half-life, the previous PTWI of 7 µg/kg body weight was withdrawn, and a PTMI of 25 µg/kg body weight was established.

Carbaryl

Carbaryl (CAS No. 63-25-2) is a broad-spectrum carbamate insecticide that is used to control insect pests in crops, trees and ornamental plants. It also has some uses in public health and veterinary practice. Carbaryl has not been reported in drinking-water; however, it could occur following overspraying or spillage into surface water. Exposure through drinking-water is therefore considered to be low unless in exceptional circumstances. The major route of carbaryl intake for the general population is food, but residues are considered to be relatively low.

Reason for not establishing a guideline value	Occurs in drinking-water at concentrations well below those of health concern
Assessment date	2006
Principal references	FAO/WHO (2002) *Pesticide residues in food—2001 evaluations* WHO (2008) *Carbaryl in drinking-water*

Carbaryl acts through inhibition of brain cholinesterase, and this is also its primary mode of toxicity. However, carbaryl is also considered to be a non-genotoxic carcinogen in mice, in which it causes vascular tumours in males. On this basis, JMPR established an ADI of 0–0.008 mg/kg body weight. This was based on a lowest-observed-adverse-effect level (LOAEL) of 15 mg/kg body weight per day and application of a safety factor of 2000 (10 for interspecies variation, 10 for intraspecies variation and 20 to reflect the occurrence of the rare and malignant tumour for which a no-effect level could not be identified).

A health-based value of 50 µg/l (rounded value) can be determined from the JMPR ADI of 0–0.008 mg/kg body weight, assuming a 60 kg adult drinking 2 litres of water per day and allowing 20% of the upper limit of the ADI from drinking-

water. However, carbaryl does not appear to be found in drinking-water at significant concentrations, and so it is not considered necessary to propose a formal guideline value.

Carbofuran

Carbofuran (CAS No. 1563-66-2) is used worldwide as a pesticide for many crops. Residues in treated crops are generally very low or not detectable. The physicochemical properties of carbofuran and the few data on occurrence indicate that drinking-water from both groundwater and surface water sources is potentially the major route of exposure.

Guideline value	0.007 mg/l (7 µg/l)
Occurrence	Has been detected in surface water, groundwater and drinking-water, generally at levels of a few micrograms per litre or lower; highest concentration (30 µg/l) measured in groundwater
ADI	0–0.002 mg/kg body weight based on a NOAEL of 0.22 mg/kg body weight per day for acute (reversible) effects in dogs in a short-term (4-week) study conducted as an adjunct to a 13-week study in which inhibition of erythrocyte acetylcholinesterase activity was observed, and using an uncertainty factor of 100
Limit of detection	0.1 µg/l by GC with a nitrogen–phosphorus detector; 0.9 µg/l by reversed-phase HPLC with a fluorescence detector
Treatment performance	1 µg/l should be achievable using GAC
Guideline value derivation	
• allocation to water	10% of upper limit of ADI
• weight	60 kg adult
• consumption	2 litres/day
Additional comments	Use of a 4-week study was considered appropriate because the NOAEL is based on a reversible acute effect; the NOAEL will also be protective for chronic effects.
Assessment date	1998
Principal references	FAO/WHO (1997) *Pesticide residues in food—1996 evaluations* WHO (2004) *Carbofuran in drinking-water*

Carbofuran is highly toxic after acute oral administration. The main systemic effect of carbofuran poisoning in short-term and long-term toxicity studies appears to be cholinesterase inhibition. No evidence of teratogenicity has been found in reproductive toxicity studies. On the basis of available studies, carbofuran does not appear to be carcinogenic or genotoxic.

Carbon tetrachloride

Carbon tetrachloride is used mainly in the production of chlorofluorocarbon refrigerants, foam-blowing agents and solvents. However, since the Montreal Protocol on Substances that Deplete the Ozone Layer (1987) and its amendments (1990 and 1992) established a timetable for the phase-out of the production and consumption of