

3-month study, and effects in a 2-year study included hepatocellular swelling, mild anaemia, increased incidence of brown pigment in the kidneys (possibly indicative of slight degeneration of the tubular epithelium) and decreased urinary specific gravity and protein.

Di(2-ethylhexyl)adipate

Di(2-ethylhexyl)adipate (DEHA) is used mainly as a plasticizer for synthetic resins such as PVC. Reports of the presence of DEHA in surface water and drinking-water are scarce, but DEHA has occasionally been identified in drinking-water at levels of a few micrograms per litre. As a consequence of its use in PVC films, food is the most important source of human exposure (up to 20 mg/day).

Reason for not establishing a guideline value	Occurs in drinking-water at concentrations well below those of health concern
Assessment date	2003
Principal reference	WHO (2003) <i>Di(2-ethylhexyl)adipate in drinking-water</i>

DEHA is of low short-term toxicity; however, dietary levels above 6000 mg/kg of feed induce peroxisomal proliferation in the liver of rodents. This effect is often associated with the development of liver tumours. DEHA induced liver carcinomas in female mice at very high doses, but not in male mice or rats. It is not genotoxic. IARC has placed DEHA in Group 3 (not classifiable as to its carcinogenicity to humans).

A health-based value of 80 µg/l can be calculated for DEHA on the basis of a TDI of 280 µg/kg body weight, based on fetotoxicity in rats, and allocating 1% of the TDI to drinking-water. However, because DEHA occurs at concentrations well below those of health concern, it is not considered necessary to derive a formal guideline value.

Di(2-ethylhexyl)phthalate

Di(2-ethylhexyl)phthalate (DEHP) is used primarily as a plasticizer. Exposure among individuals may vary considerably because of the broad nature of products into which DEHP is incorporated. In general, food will be the main exposure route.

Guideline value	0.008 mg/l (8 µg/l)
Occurrence	Found in surface water, groundwater and drinking-water in concentrations of a few micrograms per litre; in polluted surface water and groundwater, concentrations of hundreds of micrograms per litre have been reported
TDI	25 µg/kg body weight, based on a NOAEL of 2.5 mg/kg body weight per day for peroxisomal proliferation in the liver in rats, using an uncertainty factor of 100 for interspecies and intraspecies variation
Limit of detection	0.1 µg/l by GC-MS

Treatment performance	No information found on removal from water
Guideline value derivation	
• allocation to water	1% of TDI
• weight	60 kg adult
• consumption	2 litres/day
Additional comments	The reliability of some data on environmental water samples is questionable because of secondary contamination during sampling and working-up procedures. Concentrations that exceed the solubility more than 10-fold have been reported.
Assessment date	1993
Principal reference	WHO (2003) <i>Di(2-ethylhexyl)phthalate in drinking-water</i>

In rats, DEHP is readily absorbed from the gastrointestinal tract. In primates (including humans), absorption after ingestion is lower. Species differences are also observed in the metabolic profile. Most species excrete primarily the conjugated mono-ester in urine. Rats, however, predominantly excrete terminal oxidation products. DEHP is widely distributed in the body, with highest levels in liver and adipose tissue, without showing significant accumulation. The acute oral toxicity is low. The most striking effect in short-term toxicity studies is the proliferation of hepatic peroxisomes, indicated by increased peroxisomal enzyme activity and histopathological changes. The available information suggests that primates, including humans, are far less sensitive to this effect than rodents. In long-term oral carcinogenicity studies, hepatocellular carcinomas were found in rats and mice. IARC has concluded that DEHP is possibly carcinogenic to humans (Group 2B). In 1988, JECFA evaluated DEHP and recommended that human exposure to this compound in food be reduced to the lowest level attainable. JECFA considered that this might be achieved by using alternative plasticizers or alternatives to plastic material containing DEHP. In a variety of in vitro and in vivo studies, DEHP and its metabolites have shown no evidence of genotoxicity, with the exception of induction of aneuploidy and cell transformation.

Dimethoate

Dimethoate (CAS No. 60-51-5) is an organophosphorus insecticide used to control a broad range of insects in agriculture, as well as the housefly. It has a half-life of 18 hours to 8 weeks and is not expected to persist in water, although it is relatively stable at pH 2–7. A total daily intake from food of 0.001 µg/kg body weight has been estimated.

Guideline value	0.006 mg/l (6 µg/l)
Occurrence	Detected at trace levels in a private well in Canada, but not detected in a Canadian survey of surface water or drinking-water supplies
ADI	0–0.002 mg/kg body weight based on an apparent NOAEL of 1.2 mg/kg body weight per day for reproductive performance in a study of reproductive toxicity in rats, applying an uncertainty factor of 500 (100 for interspecies and intraspecies variation, 5 to take into consideration concern regarding whether the NOAEL could be a LOAEL)