

Methoprene

WHO has assessed methoprene for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. The recommended dosage of methoprene in potable water in containers should not exceed 1 mg/litre under the WHO Pesticides Evaluation Scheme.

In 2001, JMPR reaffirmed the basis of the ADI for racemic methoprene established in 1987, but lowered the value to 0–0.09 mg/kg of body weight to correct for the purity of the racemate tested. The basis for the ADI was the NOAEL of 500 mg/kg, equivalent to 8.6 mg/kg of body weight per day (corrected for purity), in a 90-day study in dogs (the main effect was increased relative liver weight) and a safety factor of 100. Young animals do not appear to be significantly more sensitive than adults. As no bridging studies with repeated doses were available for (*S*)-methoprene, JMPR made the conservative assumption that, in the absence of any information to the contrary, all the toxicity of the racemate was due to the *S* enantiomer. On this basis, JMPR established an ADI for (*S*)-methoprene of 0–0.05 mg/kg of body weight, equal to one-half the ADI for the racemate (which is a 1:1 mixture of the *R* and *S* enantiomers).

It is not considered appropriate to set a formal guideline value for methoprene used as a vector control agent in drinking-water. Where methoprene is used for vector control in potable water, this will involve less than lifetime exposure. The maximum dosage in drinking-water of 1 mg/litre would be equivalent to approximately 66% of the ADI (0.033 mg/kg of body weight) for a 60-kg adult drinking 2 litres of water per day. The exposure for a 10-kg child drinking 1 litre of water would be approximately 0.1 mg/kg of body weight, and for a 5-kg bottle-fed infant, the exposure would be approximately 0.15 mg/kg of body weight, compared with the ADI of 0–0.05 mg/kg of body weight. However, the low solubility and the high log K_{ow} of methoprene indicate that it is unlikely to remain in solution at the maximum recommended applied dose, and the actual levels of exposure are likely to be much lower than those calculated. Exposure from food is considered to be low.

Consideration should be given to using alternative sources of water for small children and bottle-fed infants for a period after an application of methoprene, where this is practical. However, exceeding the ADI will not necessarily result in adverse effects.

History of guideline development

Methoprene was not considered in the WHO *International Standards for Drinking-water* or in the first or second editions of the WHO *Guidelines for Drinking-water Quality*.

Assessment date

The risk assessment was conducted in 2007.

Principal references

FAO/WHO (2002) Methoprene and *S*-methoprene. In: *Pesticide residues in food – 2001 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/02.1; <http://www.inchem.org/documents/jmpr/jmpmono/2001pr09.htm>)

WHO (2008) *Methoprene in drinking-water: Use for vector control in drinking-water sources and containers. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/HSE/AMR/08.03/14).