

Reason for not establishing a guideline value	Not considered appropriate to set guideline values for pesticides used for vector control in drinking-water
Assessment date	2007
Principal references	FAO/WHO (2002) <i>Pesticide residues in food—2001 evaluations</i> WHO (2008) <i>Diflubenzuron in drinking-water</i>

Diflubenzuron is considered to be of very low acute toxicity. The primary target for toxicity is the erythrocytes, although the mechanism of haematotoxicity is uncertain. There is no evidence that diflubenzuron is either genotoxic or carcinogenic. It also does not appear to be fetotoxic or teratogenic and does not show significant signs of reproductive toxicity. There is evidence that young animals are not significantly more sensitive than adults to the effects of diflubenzuron.

It is not considered appropriate to set a formal guideline value for diflubenzuron used as a vector control agent in drinking-water. Where diflubenzuron is used for vector control in potable water, this will involve considerably less than lifetime exposure. The ADI determined by JMPR in 2001 was 0–0.02 mg/kg body weight. The maximum dosage in drinking-water of 0.25 mg/l would be equivalent to approximately 40% of the upper limit of the ADI allocated to drinking-water for a 60 kg adult drinking 2 litres of water per day. For a 10 kg child drinking 1 litre of water, the exposure would be 0.25 mg, compared with an exposure of 0.2 mg at the upper limit of the ADI. For a 5 kg bottle-fed infant drinking 0.75 litre per day, the exposure would be 0.19 mg, compared with an exposure of 0.1 mg at the upper limit of the ADI. Diflubenzuron 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.

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

### **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/l under WHOPES.

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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 body weight to correct for the purity of the racemate tested. The basis for the ADI was the NOAEL of 500 mg/kg diet, equivalent to 8.6 mg/kg 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 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/l would be equivalent to approximately 66% of the upper limit of the ADI (0.033 mg/kg 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 body weight, and for a 5 kg bottle-fed infant, the exposure would be approximately 0.15 mg/kg body weight, compared with the upper limit of the ADI of 0.05 mg/kg body weight. However, the low solubility and the high log octanol–water partition coefficient 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.

### **Novaluron**

Novaluron has been registered as an insecticide for food crops and ornamentals in a number of countries. WHO has assessed novaluron for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. The recommended dosage of novaluron in potable water in containers should not exceed 0.05 mg/l under WHOPES.

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In view of the absence of a carcinogenic potential in rodents and the lack of genotoxic potential in vitro and in vivo, JMPR concluded that novaluron is unlikely to pose a carcinogenic risk to humans. JMPR also concluded that novaluron is not a developmental toxicant. JMPR established an ADI of 0–0.01 mg/kg body weight on the basis of the NOAEL of 1.1 mg/kg body weight per day for erythrocyte damage and