

Adding permethrin directly to drinking-water for public health purposes is not recommended by WHO, as part of its policy to exclude the use of any pyrethroids for larviciding of mosquito vectors of human disease. This policy is based on concern over the possible accelerated development of vector resistance to synthetic pyrethroids, which, in their application to insecticide-treated mosquito nets, are crucial in the current global anti-malaria strategy.

### **Pirimiphos-methyl**

Pirimiphos-methyl is an organophosphorus compound that is used in a wide range of pesticidal applications. Pirimiphos-methyl is being considered by WHO for addition to potable water in containers as a mosquito larvicide treatment, particularly to control dengue fever. The manufacturer recommends the direct addition of 1 mg/l to water.

Reason for not establishing a guideline value	Not recommended for direct application to drinking-water unless no other effective and safe treatments are available
Assessment date	2007
Principal references	FAO/WHO (1993) <i>Pesticide residues in food—1992 evaluations</i> FAO/WHO (2008) <i>Pesticide residues in food—2006 evaluations</i> WHO (2008) <i>Pirimiphos-methyl in drinking-water</i>

The only biochemical effect consistently observed with pirimiphos-methyl in acute, short-term or long-term studies is cholinesterase inhibition. Studies with mice, rats and dogs showed NOAELs of 0.5 mg/kg body weight per day and above. Young animals do not appear to be significantly more sensitive than adults. In human studies, no cholinesterase inhibition was seen at 0.25 mg/kg body weight per day (the highest dose tested). On this basis, JMPR revised the ADI to 0–0.03 mg/kg body weight by applying a 10-fold safety factor to the NOAEL in the human studies.

At the maximum recommended dosage for drinking-water of 1 mg/l, a 60 kg adult drinking 2 litres of water would have an intake of 0.033 mg/kg body weight, compared with the upper limit of the ADI of 0.03 mg/kg body weight. The intake for a 10 kg child drinking 1 litre of water would be 0.1 mg/kg body weight; for a 5 kg bottle-fed infant drinking 0.75 litre, it would be 0.15 mg/kg body weight. There is uncertainty regarding the level that would cause effects in humans, as the NOAEL on which the ADI is based was the highest dose tested, and so the ADI may be more conservative than is at first apparent. These intake figures are all below the acute reference dose of 0.2 mg/kg body weight and would not result in an acute exposure risk from the initial application of pirimiphos-methyl to drinking-water containers at the recommended dose. In addition, the low solubility and the high log octanol–water partition coefficient of pirimiphos-methyl indicate that the larvicide is very unlikely to remain in solution at the maximum recommended applied dose, so the actual levels of exposure are expected to be lower than those calculated. Exposure from food is generally considered to be low, but occasional high exposures can be experienced.

Based on the above calculations, pirimiphos-methyl is not recommended for direct application to drinking-water unless no other effective and safe treatments are available. If pirimiphos-methyl is applied directly to drinking-water, consideration should be given to using alternative sources of water for bottle-fed infants and small children for a period after its application, where this is practical. However, it is noted that exceeding the ADI will not necessarily result in adverse effects.

### **Pyriproxyfen**

Pyriproxyfen is a broad-spectrum insect growth regulator with insecticidal activity against public health insect pests, including mosquitoes. WHO has assessed pyriproxyfen for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. The recommended dosage of pyriproxyfen in potable water in containers should not exceed 0.01 mg/l under WHOPES.

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 (2000) <i>Pesticide residues in food—1999 evaluations</i> WHO (2008) <i>Pyriproxyfen in drinking-water</i>

JMPR evaluated pyriproxyfen and concluded that it was not genotoxic and does not pose a carcinogenic risk to humans. Young animals do not appear to be significantly more sensitive than adults.

JMPR established an ADI of 0–0.1 mg/kg body weight on the basis of an overall NOAEL of 10 mg/kg body weight per day, based on increased relative liver weight and increased total plasma cholesterol concentration in male dogs in two 1-year studies of toxicity and using a safety factor of 100.

It is not considered appropriate to set a formal guideline value for pyriproxyfen used for vector control in drinking-water. The maximum recommended dosage in drinking-water of 0.01 mg/l would be equivalent to less than 1% 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 0.01 mg, compared with an exposure of 1 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 0.0075 mg, compared with an exposure of 0.5 mg at the upper limit of the ADI. The low solubility and the high log octanol–water partition coefficient of pyriproxyfen 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 even lower than those calculated.

### **Spinosad**

Spinosad is a natural product derived from the bacterium *Saccharopolyspora spinosa*. Spinosad DT is a mixture of spinosyn A and spinosyn D. It is used for mosquito control in potable water in containers.