# USE OF MALATHION FOR VECTOR CONTROL

**REPORT OF A WHO MEETING GENEVA, 16–17 MAY 2016** 

WHO PESTICIDE EVALUATION SCHEME, DEPARTMENT OF CONTROL OF NEGLECTED TROPICAL DISEASES

GLOBAL MALARIA PROGRAMME

DEPARTMENT OF PUBLIC HEALTH, ENVIRONMENTAL AND SOCIAL DETERMINANTS OF HEALTH

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#### 1. INTRODUCTION

The World Health Organization (WHO) convened a group of experts to review the risk of malathion used in public health and discuss the implications of WHO's recommendations on the use of malathion in vector control following the evaluation of malathion as "probably carcinogenic to humans" by the International Agency for Research on Cancer (IARC). A particular concern was the potential implication of the availability or non-availability of malathion for vector control in the context of Zika virus disease.

The IARC monograph concluded that there was "limited evidence" in humans for carcinogenicity, based on observations of positive associations with the incidence of non-Hodgkin lymphoma and aggressive cancer of the prostate. It also concluded that there was "sufficient evidence" for carcinogenicity in experimental animals, and mechanistic and other relevant data supported the classification of malathion in Group 2A ("probably carcinogenic to humans").

In consideration of the IARC's classification and the availability of a significant number of new studies, an extraordinary Joint FAO/WHO Meeting on Pesticide Residues (JMPR) was held on 9-13 May 2016 at WHO headquarters in Geneva, Switzerland. The outcome of this meeting, at which the risk to consumers from exposure to malathion via residues in food following its agricultural use was assessed, informed the assessment by the experts of the risk from its vector control uses.

The JMPR reaffirmed the acceptable daily intake (ADI) of 0–0.3 mg/kg bw and the acute reference dose (ARfD) of 2 mg/kg bw established in 1997 and 2003 respectively on the basis of inhibition of acetylcholinesterase activity in both cases. Inhibition acetylcholinesterase activity was the most sensitive, relevant adverse effect of malathion identified.

The meeting reviewed two formulations of malathion: emulsion, oil in water (EW) and ultralow volume (UL). Both formulations are currently recommended by WHO for outdoor space spraying via vehicle-mounted and hand-held equipment. It was noted that these malathion products are not recommended by WHO for indoor space spraying and this scenario was therefore not considered further at the meeting.

Malathion wettable powder (WP) formulation is recommended by WHO for malaria vector control by indoor residual spraying (IRS). No specification of a malathion WP formulation, including toxicologically significant impurities<sup>1</sup> such as malaoxon and isomalathion, has been proposed to WHO by any manufacturer<sup>2</sup> and therefore it was not possible to undertake a risk assessment for this IRS scenario.

The health-based guidance values for malathion established by the JMPR are for the oral route of exposure. As the oral absorption of malathion is extensive (80%) and the ADI and ARfD are based on a systemic end-point, the experts concluded that the ADI and ARfD

<sup>&</sup>lt;sup>1</sup> Joint FAO/WHO meeting on pesticide residues. Geneva: World Health Organization; 2016 (http://www.who.int/foodsafety/areas\_work/chemical-risks/jmpr/en/, accessed May 2016).

The current WHO specification is available for the technical material and EW and UL formulations, but not for WP (http://who.int/entity/whopes/quality/en/Malathion\_specs\_eval\_WHO\_March\_2013.pdf, accessed May 2016).

without adjustment for oral absorption would be applicable for other routes of exposure, following adjustment for absorption by those routes, if necessary.

The JMPR noted that the only two tumours considered to be treatment-related following dietary exposure of rodents to malathion were liver adenomas in one study in mice and nasal adenomas in one study in rats. The JMPR concluded that these tumours were secondary to other toxicological effects in the target tissues and had a clear threshold and were secondary to other effects in the target tissues. The upper-bound of the ADI provided a margin of exposure of three orders of magnitude for the doses causing these tumours, and hence the experts concluded that the risk to humans from these carcinogenic effects was unlikely at exposures below the ADI.

The JMPR concluded that the genotoxic effects observed in some test systems with both malathion and malaoxon occur secondary to the formation of reactive oxygen species which will exhibit a threshold, and therefore malathion and malaoxon are unlikely to be genotoxic at anticipated dietary exposures.

The meeting of experts was opened by Dr Dirk Engels, Director, WHO Department of Control of Neglected Tropical Diseases. He welcomed participants and recalled that the extraordinary meeting of the JMPR (Geneva, 9–13 May 2016) had re-assessed the risk of malathion, as well as of glyphosate and diazinon, and that the conclusions from that meeting would be discussed in this specific meeting. He noted that IARC's classification of malathion as probably carcinogenic could have some implications on continuing the use of malathion for vector control, especially in the control of *Aedes* spp. in the context of the Zika virus outbreak. WHO is committed to recommending the use of low-risk pesticide products for public health and vector control, and Dr Engels hoped that the advice given to WHO would help the Organization in making an evidence-informed decision to advise Member States on the use of malathion.

Dr Raman Velayudhan, Coordinator, Vector Ecology and Management, further briefed the

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