

# **Malathion in Drinking-water**

Background document for development of  
WHO *Guidelines for Drinking-water Quality*

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## Preface

One of the primary goals of WHO and its member states is that “all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water.” A major WHO function to achieve such goals is the responsibility “to propose ... regulations, and to make recommendations with respect to international health matters ....”

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as *International Standards for Drinking-water*. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO *Guidelines for Drinking-water Quality* (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite, in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.

## Acknowledgements

The first draft of Malathion in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, was prepared by Dr P. Toft, Canada, to whom special thanks are due.

The work of the following working group coordinators was crucial in the development of this document and others in the third edition:

Mr J.K. Fawell, United Kingdom (*Organic and inorganic constituents*)  
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Ms M. Giddings, Health Canada (*Disinfectants and disinfection by-products*)  
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Prof. Y. Magara, Hokkaido University, Japan (*Analytical achievability*)  
Mr P. Jackson, WRc-NSF, United Kingdom (*Treatment achievability*)

The contribution of peer reviewers is greatly appreciated. The draft text was posted on the world wide web for comments from the public. The revised text and the comments were discussed at the Final Task Force Meeting for the third edition of the GDWQ, held on 31 March to 4 April 2003, at which time the present version was finalized. The input of those who provided comments and of participants in the meeting is gratefully reflected in the final text.

The WHO coordinators were as follows:

Dr J. Bartram, Coordinator, Water Sanitation and Health Programme, WHO Headquarters, and formerly WHO European Centre for Environmental Health  
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Ms C. Vickers provided a liaison with the International Chemical Safety Programme, WHO Headquarters.

Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comment are greatly appreciated.

### **Acronyms and abbreviations used in the text**

ADI	acceptable daily intake
ATSDR	Agency for Toxic Substances and Disease Registry
CAS	Chemical Abstracts Service
FAO	Food and Agriculture Organization of the United Nations
IARC	International Agency for Research on Cancer
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LD <sub>50</sub>	median lethal dose
NOAEL	no-observed-adverse-effect level
USA	United States of America
WHO	World Health Organization

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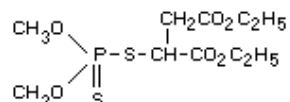


## 1. GENERAL DESCRIPTION

### 1.1 Identity

CAS No. 121-75-5  
Molecular formula: C<sub>10</sub>H<sub>19</sub>O<sub>6</sub>PS<sub>2</sub>

The chemical name of malathion is *S*-[1,2-di(ethoxycarbonyl)ethyl] dimethyl phosphorothiolothionate. Its chemical structure is shown below:



### 1.2 Physicochemical properties (FAO/WHO, 1977)

<i>Property</i>	<i>Value</i>
Appearance	clear, light, amber-coloured liquid
Boiling point	60 °C (decomposes)
Vapour pressure	5 × 10 <sup>-3</sup> Pa at 30 °C
Log <i>n</i> -octanol–water partition coefficient	2.36–2.89
Solubility in water	145 mg/litre at 25 °C

### 1.3 Major uses

Malathion is commonly used to control mosquitos and a variety of insects that attack fruits, vegetables, landscaping plants and shrubs. It can also be found in other pesticide products used indoors and on pets to control ticks and insects, such as fleas and ants. It is also used to control human head and body lice.

### 1.4 Environmental fate

In the open environment, malathion degrades rapidly by hydrolysis, biodegradation and photolysis, roughly in that order of importance. If released to air, malathion is degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals; the half-life for this reaction in air is estimated to be approximately 5 h. In other environmental compartments, the rate of transformation is heavily dependent on pH and organic content of the environmental medium. For example, studies indicate that hydrolysis is not significant in water at pH 5. At pH 7, however, malathion may completely hydrolyse in 6–7 days, whereas hydrolysis is complete in less than 12 h at pH 9. Under least favourable conditions (i.e., low pH and little organic content), malathion may persist with a half-life of months or even years. However, under most conditions, the half-life appears to be roughly 7–14 days (ATSDR, 2000).

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### ***2. ANALYTICAL METHODS***

Malathion in water may be determined by extracting into dichloromethane, drying the extract, redissolving in hexane and analysing by gas-liquid chromatography, phosphorus mode. The detection limit is 0.1 µg/litre (Health Canada, 1989).

### ***3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE***

#### ***3.1 Air***

In the USA, concentrations of malathion found in ambient air range from 6.2 ng/m<sup>3</sup> (in rural areas) to 220 ng/m<sup>3</sup> (ATSDR, 2000).

#### ***3.2 Water***

Malathion was not detected in surveys of municipal and private drinking-water supplies conducted in Canada between 1971 and 1986 (Health Canada, 1989). It was detected in 4 of 949 stream samples in southern Ontario agricultural watersheds at concentrations of 0.24–1.8 µg/litre (Health Canada, 1989). In the USA, malathion has been reported in surface water at levels up to 0.18 µg/litre and in drinking-water at 0.1 µg/litre (ATSDR, 2000).

#### ***3.3 Food***

Based on residue data from a market basket survey in Canada, the average daily intake of malathion in food for adults has been estimated to be 0.012 µg/kg of body weight per day (McLeod et al., 1980). In the USA, the average daily intake from food has been estimated to be 5.1 µg for an adult from a market basket survey carried out in 1982–1984 (Gunderson, 1988).

### ***4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS<sup>1</sup>***

Malathion is rapidly absorbed, biotransformed and excreted, predominantly in the urine but also in the faeces, largely as its two monocarboxylic acids and the dicarboxylic acid.

### ***5. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS<sup>2</sup>***

The oral LD<sub>50</sub> values for malathion in laboratory rodents were 1000–10 000 mg/kg of body weight, the observed differences probably being due to impurities. The most recent LD<sub>50</sub> values tend to be higher. The cholinesterase-inhibiting metabolite of

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<sup>1</sup> This section is taken from FAO/WHO (1998).

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malathion, malaoxon, has much lower oral LD<sub>50</sub> values of 100–220 mg/kg of body weight. WHO (1996) has classified malathion as “slightly hazardous.”

In a study of neurotoxicity in rats receiving single doses of 0, 500, 1000 or 2000 mg/kg of body weight, there was no NOAEL, as clinical signs were present at all doses. In a 13-week study of neurotoxicity, also in rats, at dietary concentrations of 0, 50, 5000 or 20 000 mg/kg, the NOAEL was 5000 mg/kg, equal to 350 mg/kg of body weight per day, on the basis of inhibition of brain acetylcholinesterase at the highest dose.

In a 30-day study of toxicity in rats receiving malathion in the diet at concentrations of 0, 50, 100, 500, 10 000 or 20 000 mg/kg, the NOAEL was 500 mg/kg, equal to 52 mg/kg of body weight per day, on the basis of increased liver weight and histopathological changes in the liver (periportal hepatocyte hypertrophy) at the next highest dose.

In a 90-day study of toxicity in rats, malathion was given at dietary concentrations of 0, 100, 500, 5000, 10 000 or 20 000 mg/kg. The NOAEL was 500 mg/kg, equal to 34 mg/kg of body weight per day, on the basis of decreased mean corpuscular volume and mean corpuscular haemoglobin, increased liver weights and relative kidney weights and chronic nephropathy in males and decreased mean cell volume, hepatocyte hypertrophy and increased relative kidney weight in females at the next highest dose.

A 21-day study of dermal toxicity was carried out in which rabbits were treated with malathion at doses of 0, 50, 300 or 1000 mg/kg of body weight per day for 6 h per day, 5 days per week. The NOAEL was 300 mg/kg of body weight per day on the basis of inhibition of brain acetylcholinesterase activity at the highest dose.

In a 28-day study of toxicity in dogs, malathion was fed in gelatin capsules at doses of 0, 125, 250 or 500 mg/kg of body weight per day for 28 days. There was no NOAEL because of clinical signs at all doses.

In a 1-year study of toxicity in dogs, malathion was administered orally in capsules at doses of 0, 62.5, 125 or 250 mg/kg of body weight per day, 7 days per week. The NOAEL was 125 mg/kg of body weight per day on the basis of body weight depression and changes in haematological and clinical chemistry parameters at the highest dose.

A number of long-term studies of toxicity and carcinogenicity have been carried out on malathion in both rats and mice. The earlier ones were reviewed by a working group convened by IARC, which concluded that the available data did not provide evidence that malathion was carcinogenic.

In an 18-month study in mice, malathion was administered at dietary concentrations of 0, 100, 800, 8000 or 16 000 mg/kg. The NOAEL was 800 mg/kg, equal to 140 mg/kg of body weight per day, on the basis of inhibition of brain acetylcholinesterase

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activity at termination and an increased incidence of liver adenomas in animals of both sexes at the next highest dose.

In a 2-year study in rats, dietary concentrations of 0, 100, 1000 or 5000 mg/kg were used. The NOAEL was 100 mg/kg, equivalent to 5 mg/kg of body weight per day, on the basis of reduced erythrocyte acetylcholinesterase activity and body weight. In another long-term study in rats, malathion was given at doses of 0, 100/50, 500, 6000 or 12 000 mg/kg for 2 years. The NOAEL was 500 mg/kg, equal to 29 mg/kg of body weight per day, on the basis of decreased survival and body weight gain, changes in haematological parameters, decreased brain acetylcholinesterase activity, increased  $\gamma$ -glutamyl transpeptidase activity, increased liver, kidney and thyroid/parathyroid weights and changes in the olfactory epithelium at the next highest dose.

Numerous tests have been carried out for genotoxicity both *in vitro* and *in vivo*. Most of the evidence indicates that malathion is not genotoxic, although some studies indicate that it can produce chromosomal aberrations and sister chromatid exchange *in vitro*. There was no evidence that malathion induces chromosomal aberrations *in vivo*. Malaoxon did not induce reverse mutation in bacteria, but it caused sister chromatid exchange in two tests in mammalian cells and induced sex-linked recessive lethal mutation in *Drosophila in vivo*. The four common impurities of malathion, isomalathion, *O,O,S*-trimethyl phosphorothioate, *O,S,S*-trimethyl phosphorodithioate and *O,O,O*-trimethyl phosphorothioate, did not induce reverse mutation in bacteria. The Meeting concluded that malathion is not genotoxic.

A number of studies of reproductive toxicity have been carried out, only some of which showed NOAELs. In a study in rats, malathion was administered by gavage to groups of pregnant animals on days 6–15 of gestation at doses of 0, 200, 400 or 800 mg/kg of body weight per day. The NOAEL was 400 mg/kg of body weight per day on the basis of maternal toxicity at the highest dose; no fetal toxicity was observed.

Malathion was administered orally at doses of 0, 25, 50 or 100 mg/kg of body weight per day to groups of pregnant rabbits on days 6–18 of gestation. The NOAELs were 25 mg/kg of body weight per day for maternal toxicity and 100 mg/kg of body weight per day for fetal toxicity; teratogenicity was not seen at any dose.

A two-generation study was undertaken in rats in which malathion was given at dietary concentrations of 0, 550, 1700, 5000 or 7500 mg/kg. The NOAEL was 7500 mg/kg, equal to 600 mg/kg of body weight per day, for reproductive toxicity and 1700 mg/kg, equal to 130 mg/kg of body weight per day, for developmental toxicity, the latter being based on reduced pup weights.

Two studies on the neurotoxicity of malathion in hens were reviewed. In neither was there evidence that malathion can cause delayed neuropathy, although some inhibition of neuropathy target esterase activity was found in the brains of birds at 2000 mg/kg of body weight.

## **6. EFFECTS ON HUMANS<sup>3</sup>**

In a study in volunteers with doses of 8, 16 or 24 mg of malathion per day, the NOAEL was 16 mg per day (equivalent to 0.27 mg/kg of body weight per day) on the basis of inhibition of plasma and erythrocyte cholinesterase activity. Several cases of exposure to impure malathion have been reported, none of which resulted in delayed neuropathy.

## **7. CONCLUSIONS**

An ADI of 0.3 mg/kg of body weight was established by JMPR in 1997 on the basis of the NOAEL of 29 mg/kg of body weight per day in the 2-year study of toxicity and carcinogenicity in rats, with a safety factor of 100. This ADI is supported by the NOAEL of 25 mg/kg of body weight per day in the study of developmental toxicity in rabbits. The alternative approach of basing the ADI on the study in humans was not taken, as the study was old and the material was therefore likely to contain toxic impurities.

A health-based value of 0.9 mg/litre can be calculated based on an allocation of 10% of the ADI of 0.3 mg/kg of body weight to drinking-water. However, as the chemical occurs in drinking-water at concentrations much lower than the health-based value, the presence of malathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, it is considered unnecessary to derive a guideline value for malathion in drinking-water.

## **8. REFERENCES**

ATSDR (2000) *Toxicological profile information sheet — Malathion. Draft for public comment.* Atlanta, GA, US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry.

FAO/WHO (1977) *Malathion.* Geneva, World Health Organization (Data Sheet on Pesticides No. 29).

FAO/WHO (1998) *Pesticide residues in food — 1997 evaluations. Part II — Toxicological and environmental.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/98.6).

Gunderson EI (1988) FDA Total Diet Study April 1982–April 1984, dietary intakes of pesticides, selected elements, and other chemicals. *Journal of the Association of Official Analytical Chemists*, 71(6):1200.

Health Canada (1989) Malathion. In: *Guidelines for Canadian drinking water quality — supporting documents.* Available at <http://www.hc-sc.gc.ca/hecs-sesc/water/pdf/dwg/malath.pdf>.

McLeod HA, Smith DC, Bluman N (1980) Pesticide residues in the total diet in Canada. V. 1976–1978. *Journal of Food Safety*, 2:141.

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<sup>3</sup> This section is taken from FAO/WHO (1998).

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WHO (1996) *The WHO recommended classification of pesticides by hazard and guidelines to classification 1996–1997*. Geneva, World Health Organization, International Programme on Chemical Safety (WHO/PCS/96.3).