Methyl Parathion in Drinking-water

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

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

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Ms M. Giddings, Health Canada (Disinfectants and disinfection by-products)
Dr P. Toft, Canada (Pesticides)
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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Mr H. Hashizume, Water Sanitation and Health Programme, WHO Headquarters

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.
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<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ADI</td>
<td>acceptable daily intake</td>
</tr>
<tr>
<td>ATSDR</td>
<td>Agency for Toxic Substances and Disease Registry</td>
</tr>
<tr>
<td>CAS</td>
<td>Chemical Abstracts Service</td>
</tr>
<tr>
<td>FAO</td>
<td>Food and Agriculture Organization of the United Nations</td>
</tr>
<tr>
<td>IUPAC</td>
<td>International Union of Pure and Applied Chemistry</td>
</tr>
<tr>
<td>JMPR</td>
<td>Joint FAO/WHO Meeting on Pesticide Residues</td>
</tr>
<tr>
<td>LC₅₀</td>
<td>median lethal concentration</td>
</tr>
<tr>
<td>LD₅₀</td>
<td>median lethal dose</td>
</tr>
<tr>
<td>LOAEL</td>
<td>lowest-observed-adverse-effect level</td>
</tr>
<tr>
<td>NOAEL</td>
<td>no-observed-adverse-effect level</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
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<tr>
<td>UV</td>
<td>ultraviolet</td>
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<td>WHO</td>
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1. GENERAL DESCRIPTION

1.1 Identity

CAS No.: 298-00-0  
Molecular formula: C₇H₁₀NO₅PS

The IUPAC chemical name of methyl parathion is O,O-dimethyl O-4-nitrophenyl phosphorothioate. Its chemical structure is shown below:

\[
\begin{array}{c}
\text{C}_7\text{N} \quad \text{PO(OCH}_3)_2 \\
\end{array}
\]

1.2 Physicochemical properties (IPCS, 1992)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point</td>
<td>35–38 °C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>143 °C</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>1.3 mPa at 20 °C</td>
</tr>
<tr>
<td>Water solubility</td>
<td>55–60 mg/litre at 25 °C</td>
</tr>
<tr>
<td>Log octanol–water partition coefficient</td>
<td>1.83–3.43</td>
</tr>
</tbody>
</table>

1.3 Major uses

Methyl parathion is produced throughout the world and has been registered for use on many crops. Data indicate that most methyl parathion is used for protecting cotton fields. It is a non-systemic insecticide and acaricide that controls numerous insects by contact and stomach action. It is generally applied as a spray, mainly from an emulsifiable concentrate formulation (IPCS, 1992).

1.4 Environmental fate

The distribution of methyl parathion in air, water, soil and organisms in the environment is influenced by several physical, chemical and biological factors. Studies using model ecosystems and mathematical modelling indicate that methyl parathion partitions mainly to air and soil in the environment, with lesser amounts in plants and animals. There is virtually no movement through soil, and neither the parent compound nor its breakdown products will reach groundwater (IPCS, 1992).

By far the most important route for the environmental degradation of methyl parathion is microbial degradation. Loss of the compound in the field and in model ecosystems is more rapid than predicted from laboratory studies. This is because of the presence of a variety of microorganisms capable of degrading the compound in different habitats and circumstances (IPCS, 1992).
METHYL PARATHION IN DRINKING-WATER

Methyl parathion can undergo oxidative degradation, to the less stable methyl paraoxon, in the presence of ultraviolet (UV) radiation or sunlight; sprayed films degrade under UV radiation with a half-life of about 40 h. However, the contribution of photolysis to total loss in an aquatic system was estimated to be only 4%. Hydrolysis of methyl parathion also occurs and is more rapid under alkaline conditions (IPCS, 1992).

The degradation of methyl parathion by hydrolysis and biodegradation was studied in four types of water (ultrapure, pH 6.1; river water, pH 7.3; filtered river water, pH 7.3; and seawater, pH 8.1) maintained at 6 ºC and 22 ºC in the dark. The half-lives of methyl parathion at 6 ºC in the four types of water were determined to be 237, 95, 173 and 233 days, respectively; at 22 ºC, the half-lives were 46, 23, 18 and 30 days, respectively (ATSDR, 1999).

2. ANALYTICAL METHODS

Analysis of water for methyl parathion in the µg/litre range has been done using gas chromatography with electron capture detector or flame photometric detector and with high-pressure liquid chromatography. With water samples, the primary problem is concentration of the samples, since they generally contain only trace amounts of methyl parathion. Several concentration, cleanup and separation techniques have been used in an attempt to improve the sensitivity and selectivity of the method (ATSDR, 1999).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

Background atmospheric levels of methyl parathion in agricultural areas range from not detectable to about 70 ng/m³. Air concentrations after spraying declined rapidly over 3 days and returned to background levels after about 9 days (IPCS, 1992).

3.2 Water

Concentrations in natural waters of agricultural areas in the USA ranged up to 0.46 µg/litre, with highest levels in summer. Levels in river water (in laboratory studies) declined to 80% of the initial concentration after 1 h and 10% after 1 week.

In a study to determine the residue levels of pesticides in shallow groundwater of the USA, water samples from 1012 wells and 22 springs were analysed for methyl parathion. No methyl parathion was detected in any of the water samples (ATSDR, 1999). In a study of water from near-surface aquifers in the US Midwest, no methyl parathion was detected in any of the water samples from 94 wells that were analysed for pesticide levels (ATSDR, 1999). However, methyl parathion was detected at a concentration of 0.01 µg/litre in another groundwater study where there was contamination due to a point source (ATSDR, 1999).
3.3 Food

There are only a small number of published reports on residues of methyl parathion in food throughout the world. In the USA, residues of methyl parathion in food have generally been reported at very low levels, with few individual samples exceeding maximum residue limits. Only trace residue levels of methyl parathion have been detected in the total dietary studies reported. Methyl parathion residues were highest in leafy (up to 2 mg/kg) and root vegetables (up to 1 mg/kg) in market basket surveys in the USA between 1966 and 1969. Food preparation, cooking and storage all cause decomposition of methyl parathion residues, further reducing human exposure. Raw vegetables and fruits may contain higher residues after misuse.

The average methyl parathion intake from food in the USA during 1988 was estimated to range from 0.1 to 0.2 ng/kg of body weight per day.

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Methyl parathion is absorbed through the skin and from the respiratory and digestive tracts. Observed differences between its oral and intravenous toxicity are believed to be associated with first-pass effects in the liver. The compound is rapidly excreted; negligible amounts of the labelled dose were present in the blood, tissues and organs at 48 h. Conversion of methyl parathion to methyl paraoxon has been shown to occur within minutes after oral administration to rats. Detoxification is achieved by O-demethylation or hydrolysis to p-nitrophenol. In humans, the primary urinary metabolites were p-nitrophenol and dimethyl phosphate.

5. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS

Methyl parathion is acutely toxic at low doses when administered either orally (LD_{50} = 4 mg/kg of body weight) or by inhalation (LC_{50} = 0.13 mg/litre). The compound is slightly irritating to the skin and the eyes but has not been shown to be a sensitizing agent. WHO has classified methyl parathion as “extremely hazardous.”

In a 90-day study in mice at dietary levels of 0, 10, 30 or 60 mg/kg, the NOAEL was 10 mg/kg (equivalent to 1.5 mg/kg of body weight per day) on the basis of significant decreases in absolute and relative testicular weights. Cholinesterase activity was not measured in this study. In a 90-day study in rats, the NOAEL was 2.5 mg/kg (equivalent to 0.12 mg/kg of body weight per day) on the basis of significant decreases in plasma, erythrocyte and brain cholinesterase activities at 25 mg/kg (equivalent to 1.2 mg/kg of body weight per day).

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1 This section is taken from FAO/WHO (1996).
2 This section is taken from FAO/WHO (1996).
Two 13-week studies were conducted in dogs, in which methyl parathion was administered at dietary levels of 0, 0.3, 1 or 3 mg/kg of body weight per day in one study and 0, 0.03, 0.3 or 3 mg/kg of body weight per day in the other. In both studies, the LOAEL was 3 mg/kg of body weight per day, on the basis of decreases in erythrocyte, plasma and brain cholinesterase activity. The NOAELs were 1 and 0.3 mg/kg of body weight per day, respectively. In a 1-year study in dogs, the NOAEL was also 0.3 mg/kg of body weight per day, the highest dose tested.

In a 1-year study in rats to determine the ocular and neurotoxic effects of methyl parathion, dietary levels of 0, 0.5, 2.5, 12 or 50 mg/kg were administered. Ocular toxicity was not observed. Degenerative changes of the sciatic nerve and its extensions consistent with demyelination were observed at the two highest doses. The LOAEL was 12 mg/kg, equal to 0.5 mg/kg of body weight per day. The NOAEL was 2.5 mg/kg, equal to 0.1 mg/kg of body weight per day.

In a 2-year study in mice, methyl parathion was not carcinogenic at dietary levels up to 50 mg/kg (equal to 9.2 mg/kg of body weight per day). The NOAEL was 7 mg/kg, equal to 1.6 mg/kg of body weight per day, on the basis of significant decreases in erythrocyte, plasma and brain cholinesterase activities. In a study of toxicity and carcinogenicity in rats fed methyl parathion at dietary levels of 0, 2, 10 or 50 mg/kg, there was no evidence of carcinogenicity. The NOAEL was 2 mg/kg (equivalent to 0.1 mg/kg of body weight per day), and the LOAEL was 10 mg/kg (equivalent to 0.5 mg/kg of body weight per day), on the basis of a reduction in brain acetylcholinesterase activity. In another 2-year study in rats, methyl parathion did not induce carcinogenic effects. The NOAEL was 5 mg/kg (equivalent to 0.25 mg/kg of body weight per day) on the basis of tremors, anogenital staining, reduced body weight, retinal degeneration, sciatic nerve degeneration, decreased packed cell volume and haemoglobin and erythrocyte counts, and decreased brain cholinesterase activity in males and females at 50 mg/kg (equivalent to 2.5 mg/kg of body weight per day).

Two studies of developmental toxicity were conducted in rats. In one study, animals received methyl parathion by gavage at doses of 0, 0.3, 1 or 3 mg/kg of body weight per day. The NOAEL for maternal and developmental toxicity was 1 mg/kg of body weight per day on the basis of increased numbers of deaths, ataxia and dyspnea in dams and delayed ossification in fetuses. In another study, the NOAEL for maternal and developmental toxicity was 0.3 mg/kg of body weight per day on the basis of significant decreases in maternal body weight gain during treatment and gestation and an increased incidence of stunted fetuses at 1 mg/kg of body weight per day. In studies of developmental toxicity in rabbits, decreased erythrocyte and plasma cholinesterase activities were reported in dams receiving 3 mg/kg of body weight per day by gavage. No developmental effects were reported that could be attributed to the administration of methyl parathion. The NOAEL for maternal toxicity was 1 mg/kg of body weight, and that for developmental toxicity was 3 mg/kg of body weight.

In a multigeneration study in rats, dietary levels of 0, 2, 10 or 50 mg/kg were administered. Slight effects on pup survival were reported in animals receiving 10 mg/kg, equivalent to 0.5 mg/kg of body weight per day. The NOAEL was 2 mg/kg,
Methyl parathion was mutagenic in bacteria, but there was no evidence of genotoxicity in a limited range of studies in mammalian systems.

**6. EFFECTS ON HUMANS**

The NOAEL derived from the combined results of several studies conducted in humans, based on the depression of erythrocyte and plasma cholinesterase activities, was 0.3 mg/kg of body weight per day.

**7. CONCLUSIONS**

An ADI of 0.003 mg/kg of body weight was established on the basis of the NOAEL of 5 mg/kg, equivalent to 0.25 mg/kg of body weight per day, in the 2-year study in rats for retinal degeneration, sciatic nerve demyelination, reduced body weight, anaemia and decreased brain acetylcholinesterase activity. A safety factor of 100 was used. Since the toxicological end-points seen in animals were other than acetylcholinesterase inhibition, a safety factor of 10 could not be applied to the NOAEL in humans.

A health-based value of 9 µg/litre can be calculated based on an allocation of 10% of the JMPR ADI of 0.003 mg/kg of body weight to drinking-water. As the health-based value is much higher than methyl parathion concentrations likely to be found in drinking-water, the presence of methyl parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a numerical guideline value for methyl parathion is not deemed necessary.

**8. REFERENCES**


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3 This section is taken from FAO/WHO (1996).