Dichlorvos 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 on selected chemicals in 1998 and on microbial aspects in 2002. The third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2005, and the second addendum to the third edition was published in 2007.

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 and 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 of potential health concern in drinking-water. In the first and second editions, these constituted Volume 2 of the GDWQ. Since publication of the third edition, they comprise a series of free-standing monographs, including this one.

For each chemical contaminant or substance considered, a lead institution prepared a background 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 documents for the third edition and addenda.

Under the oversight of a group of coordinators, each of whom was responsible for a group of chemicals considered in the GDWQ, 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. The draft documents were also released to the public domain for comment and submitted for final evaluation by expert meetings.

During the preparation of background documents and at expert 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 contributing to the second addendum to the third edition:

- Dr J. Cotruvo, J. Cotruvo Associates, USA (Materials and chemicals)
- Mr J.K. Fawell, United Kingdom (Naturally occurring and industrial contaminants)
- Ms M. Giddings, Health Canada (Disinfectants and disinfection by-products)
- Mr P. Jackson, WRe-NSF, United Kingdom (Chemicals – practical aspects)
- Prof. Y. Magara, Hokkaido University, Japan (Analytical achievability)
- Dr Aiwerasi Vera Festo Ngowi, Tropical Pesticides Research Institute, United Republic of Tanzania (Pesticides)
- Dr E. Ohanian, Environmental Protection Agency, USA (Disinfectants and disinfection by-products)

The draft text was discussed at the Working Group Meeting for the second addendum to the third edition of the GDWQ, held on 15–19 May 2006. The final version of the document takes into consideration comments from both peer reviewers and the public. The input of those who provided comments and of participants in the meeting is gratefully acknowledged.

The WHO coordinator was Dr J. Bartram, WHO Headquarters. Ms C. Vickers provided a liaison with the International Programme on Chemical Safety, WHO Headquarters. Mr Robert Bos, Public Health and the Environment Programme, WHO Headquarters, provided input on pesticides added to drinking-water for public health purposes.

Ms Penny Ward provided invaluable administrative support at the Working Group Meeting and throughout the review and publication process. 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>Definition</th>
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<tr>
<td>ADI</td>
<td>acceptable daily intake</td>
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<tr>
<td>CAS</td>
<td>Chemical Abstracts Service</td>
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<tr>
<td>FAO</td>
<td>Food and Agriculture Organization of the United Nations</td>
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<tr>
<td>GDWQ</td>
<td>Guidelines for Drinking-water Quality</td>
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<tr>
<td>IUPAC</td>
<td>International Union of Pure and Applied Chemistry</td>
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<tr>
<td>JMPR</td>
<td>Joint FAO/WHO Meeting on Pesticide Residues</td>
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<tr>
<td>$K_{ow}$</td>
<td>octanol–water partition coefficient</td>
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<tr>
<td>LD$_{50}$</td>
<td>median lethal dose</td>
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<tr>
<td>NOAEL</td>
<td>no-observed-adverse-effect level</td>
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<tr>
<td>UV</td>
<td>ultraviolet</td>
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<td>World Health Organization</td>
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6. REFERENCES
This document is based on the following reviews: WHO (1978), IPCS (1988), IARC (1991), and FAO/WHO (1994).

1. GENERAL DESCRIPTION

1.1 Identity

CAS No.: 62-73-7
Molecular formula: C₄H₇Cl₂O₄P

The IUPAC name for dichlorvos is 2,2-dichlorovinyl dimethylphosphate.

1.2 Physicochemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Melting point</td>
<td></td>
</tr>
<tr>
<td>Density</td>
<td>1.415</td>
</tr>
<tr>
<td>Water solubility</td>
<td>~10 g/l at 20 °C</td>
</tr>
<tr>
<td>Log octanol–water partition coefficient (log $K_{ow}$)</td>
<td>1.47</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>1.6 Pa</td>
</tr>
</tbody>
</table>

1.3 Major uses and sources in drinking-water

Dichlorvos is a volatile organophosphorus insecticide that is used against a wide range of mite and insect pests of plants, farm animals and humans and as an anthelminthic. It has agricultural, public health and domestic uses. It is also used to control parasites in fish farming.

1.4 Environmental fate

Dichlorvos breaks down rapidly in humid air, water and soil, by both abiotic and biotic processes. On hard dry surfaces, such as wood, it may persist for a longer time (39% remaining after 33 days). It degrades mainly to dichloroethanol, dichloroacetaldehyde, dichloroacetic acid, dimethylphosphate, dimethylphosphoric acid and other water-soluble compounds, which are eventually mineralized. Dichlorvos is rapidly lost from leaf surfaces by volatilization and hydrolysis.

2. HUMAN EXPOSURE

Exposure of the public through food and drinking-water is normally expected to be very low. However, public health and household use of dichlorvos will give rise to local exposure.

3. TOXICOLOGICAL SUMMARY

Dichlorvos is rapidly absorbed by all routes of exposure and rapidly degraded. The metabolic pathways of dichlorvos are similar in mammalian species, including

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1 After FAO/WHO (1994).
Dichlorvos has a marked acute oral toxicity with typical cholinergic signs and has been classified by WHO as highly hazardous. Rat erythrocyte and brain cholinesterase inhibited by dichlorvos spontaneously reactivates with a half-life of about 2 h both in vitro and in vivo.

Several carcinogenicity studies in mice and rats using routes other than gavage were negative, even when doses causing signs of toxicity were used. It should be noted that two squamous cell carcinomas of the oesophagus were observed in treated mice in one study. IARC (1991) has classified dichlorvos in group 2B.

Dichlorvos has been adequately tested in a series of in vitro and in vivo genotoxicity assays. These data indicate that dichlorvos is genotoxic in bacteria and cultured mammalian cells, but that it is not clastogenic in vivo except under conditions where an unusually high tissue dose can be attained. Dichloroacetaldehyde, a major metabolite of dichlorvos, is a weak bacterial mutagen. Positive results have been reported in mice given a dose of dichloroacetaldehyde far greater than that which could derive from sublethal doses of dichlorvos. Dichlorvos has been shown to methylate DNA in vitro at a rate that is 8–9 orders of magnitude lower than the rate of phosphorylation. Therefore, DNA alkylation is not likely to occur at doses of dichlorvos that are not inhibitory to erythrocyte/brain cholinesterase.

A three-generation reproduction study in rats was negative at doses up to 235 mg/kg in the diet, equivalent to 12 mg/kg of body weight per day. A one-litter, one-generation study in mice in which dichlorvos was administered by inhalation at doses that caused >90% plasma cholinesterase inhibition, but no signs of toxicity, was negative. Dichlorvos caused reversible damage of seminiferous tubules, Leydig cells and Sertoli cells at oral doses of 10 mg/kg of body weight daily for 18 days in mice and at 5 mg/kg of body weight and above every other day for 8 weeks in rats.

Dichlorvos appeared not to be teratogenic in mice, rats, and rabbits at doses that caused maternal toxicity.

Dichlorvos caused delayed polyneuropathy in hens at doses much higher than the unprotected LD₅₀. Cases of delayed polyneuropathy also have been reported in humans after severe intoxications.

In humans, the rate of dichlorvos hydrolysis by plasma is similar to that in rats. The rate of recovery of inhibited erythrocyte and plasma cholinesterase activity in humans given dichlorvos is much slower than in rats. Half-lives of recovery are about 15 days in humans and about 2 h in rats. A daily dose of 1 mg/kg of body weight to male human volunteers for 7 days caused 5–30% inhibition of erythrocyte cholinesterase. The NOAEL in humans, based on absence of erythrocyte cholinesterase inhibition in 12 volunteer males for 21 days, was 0.04 mg/kg of body weight per day.

In assessing the potential hazard to humans of residues of dichlorvos, the following considerations were taken into account in view of the weakly positive results in the gavage carcinogenicity study in mice.
Organophosphorus esters used as insecticides react with biological molecules by means of phosphorylation of serine hydrolases and of alkylation of macromolecules. Phosphorylation of acetylcholinesterase and alkylation of DNA are considered to account for the acute cholinergic toxicity and initiation of the carcinogenic process, respectively. These biochemical reactions occur at different rates. When the rate of phosphorylation is substantially higher than the rate of alkylation, in vivo genotoxic effects are unlikely to occur because effective doses cannot be achieved due to acute toxicity. Dichlorvos meets these criteria, the rate of phosphorylation of acetylcholinesterase being much faster (8 orders of magnitude) than that of alkylation of several macromolecules, including DNA. Hence, positive mutagenicity tests were seen only in vitro and, as indicated in the 1986 Joint Meeting report, carcinogenicity studies are unlikely to give more information. The weak carcinogenic response of dichlorvos obtained in mice in a corn oil gavage study should be interpreted as a local effect of dichlorvos.

Information on comparative cholinergic toxicity might be of critical relevance for the extrapolation of toxic effects (other than acute effects) of organophosphates in experimental animals to humans. The characteristics of the interactions of a given compound with acetylcholinesterase (rates of phosphorylation, spontaneous reactivation and ageing) from different species can be compared in vitro. Also, the in vivo rate of reappearance of blood acetylcholinesterase activity can be measured. In some cases, metabolic degradation of organophosphates can be assessed comparatively by measuring the level of serum A esterase, which hydrolyses a given compound. All these data enable an improved assessment of cholinergic toxicity of organophosphates in different species. This knowledge may be of special significance in the case of dimethyl phosphates, since the rates of in vivo reactivation vary substantially across species. Therefore, chronic dosing is more critical for extrapolation from animal data to humans. In a repeated-dose regime, the longer the half-life of reactivation, the more rapid and/or more toxic will be the resulting effect (i.e. in a chronic dosing regime, humans will survive much lower doses of dichlorvos causing, when given alone, peak erythrocyte/brain cholinesterase inhibition than those that can be reached in rodents). Therefore, comparison between the in vivo rates of recovery of enzyme activity will enable an assessment of the repeated doses of compounds and the resulting cholinesterase inhibition, which would represent the limiting factors for other toxicities (including mutagenicity and carcinogenicity).

In the case of dichlorvos, JMPR considered the extrapolation of carcinogenicity data derived in rodents and its applicability to human safety and concluded that the compound would not result in chronic human health hazards at doses below those that result in acetylcholinesterase inhibition.

JMPR maintained the ADI of 0–0.004 mg/kg of body weight (4 µg/kg of body weight), which is based on a 21-day study in humans with a NOAEL of 0.04 mg/kg of body weight per day, using a 10-fold safety factor.
4. PRACTICAL ASPECTS

4.1 Analytical methods and analytical achievability

[to be completed]

4.2 Treatment and control methods and technical achievability

A dichlorvos concentration of 220 mg/l was reduced to 0 mg/l within 20 min by batch treatment with ozone at 1 mg/l, but the dichlorvos molecule was not destroyed completely. In the presence of microporous silica, which caused ozone to decompose to form hydroxyl radicals, destruction was more complete (Kim et al., 2002).

It is reported that photocatalytic oxidation of dichlorvos is more effective using 254-nm light compared with 360-nm light. The addition of hydrogen peroxide resulted in a decrease in the rate of oxidation (Lu et al., 1994). Photocatalytic degradation of dichlorvos was achieved using thin films of titanium dioxide and a short illumination time (Mengyue et al., 1995). Laboratory experiments using a batch reactor have evaluated the adsorption of dichlorvos onto hydrous titanium dioxide from aqueous solution (Lu et al., 1996). Irradiation of a 110 mg/l solution with a 125-W medium-pressure mercury lamp in the presence of titanium dioxide gave approximately 95% removal after 80 min (Rahman & Muneer, 2005). In another study, complete degradation of a 10 mg/l solution was achieved after 20 min of irradiation with a 125-W lamp in the presence of titanium dioxide (Evgenidou et al., 2005). The removal of dichlorvos from a 22 mg/l solution by UV/titanium dioxide was enhanced by the addition of hydrogen peroxide (Shifu & Gengyu, 2005).

Dichlorvos (25–100 mg/l) was degraded by hydrogen peroxide plus ferrous iron; with a 25 mg/l solution, 80% destruction was achieved within 30 s, but complete removal required 60 min (Lu et al., 1999). Hydrogen peroxide alone had no effect on dichlorvos (Lu et al., 1997).

All of the above results suggest that dichlorvos should be removable by other advanced oxidation processes, such as ozone plus hydrogen peroxide.

Dichlorvos (concentration not stated) was 40–60% removed by different nanofiltration membranes and 95% removed by a polyamide reverse osmosis membrane (Košutič et al., 2005). Nanofiltration using different membranes gave 4–87% removal from a 1 mg/l solution; adsorption onto the membrane was an important contributor to removal (Kiso et al., 2000). A concentration of 0.01 µg/l was reduced by 98–99% by different ultra-low reverse osmosis membranes (Hofman et al., 1997).

No other information has been found on treatment of dichlorvos. However, this compound belongs to a group of organophosphorus pesticides that have generally been shown to be amenable to treatment by coagulation (10–20% removal), activated carbon and ozone.
5. CONCLUSION

It is not considered necessary to derive a formal guideline value for dichlorvos because it is not normally expected to occur in drinking-water. Nevertheless, in the event of a spill or similar event, it would be useful to have guidance on concentrations of dichlorvos in water that are not associated with adverse health effects, and so a health-based value is derived below.

Based on the JMPR ADI of 0–0.004 mg/kg of body weight and assuming a 60-kg adult drinking 2 litres of water per day with an allocation of 20% of the ADI to drinking-water, a health-based value for dichlorvos in drinking-water of 0.02 mg/l (rounded value) can be derived.

6. REFERENCES


