

# **Monochloroacetic Acid 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

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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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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:

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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**

CAS	Chemical Abstracts Service
DNA	deoxyribonucleic acid
EPA	Environmental Protection Agency (USA)
IARC	International Agency for Research on Cancer
IUPAC	International Union of Pure and Applied Chemistry
LD <sub>50</sub>	median lethal dose
LOAEL	lowest-observed-adverse-effect level
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program (USA)
TDI	tolerable daily intake
USA	United States of America

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## 1. GENERAL DESCRIPTION

### 1.1 Identity

CAS No.:	79-11-8
Molecular formula:	ClCH <sub>2</sub> COOH

The IUPAC name for monochloroacetic acid is monochloroethanoic acid.

### 1.2 Physicochemical properties<sup>1</sup>(Verschueren, 1977; Weast, 1988; Budavari et al., 1989; HSDB, 2001)

Property	Value
Boiling point (°C)	187.8
Melting point (°C)	52.5
Density (g/cm <sup>3</sup> )	1.58 at 20 °C
Vapour pressure (kPa)	0.0087 at 25 °C 0.133 at 40 °C
pK <sub>a</sub> at 25 °C	2.866
Water solubility	Very soluble
Log octanol–water partition coefficient	0.22

### 1.3 Organoleptic properties

No information is available on the taste or odour threshold of monochloroacetic acid in water.

### 1.4 Major uses

Monochloroacetic acid is used in research and development laboratories, in medical and surgical hospitals and in chemical and pharmaceutical preparations. It is also used in fabric mills, in communication equipment (television, radio, telegraph) and in automotive stamping (NIOSH, 1990).

## 2. ANALYTICAL METHODS

The chloroacetic acids can be detected in water by EPA Method 552.1, EPA Method 552.2 or Standard Method 6251B (APHA et al., 1998). In EPA Method 552.1, the haloacetic acids are extracted on a miniature anion exchange column and converted to methyl esters in the eluant prior to analysis. EPA Method 552.2 involves a liquid–liquid extraction procedure, after which the acetic acids are converted to methyl esters (US EPA, 1995). Both EPA methods use gas chromatography and electron capture detection. Standard Method 6251B uses a micro liquid–liquid extraction procedure combined with gas chromatography and electron capture detection. Method detection

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<sup>1</sup> Conversion factor in air: 1 ppm = 3.87 mg/m<sup>3</sup>.

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limits range from <0.1 to 0.4 µg/litre. The practical quantification level for monochloroacetic acid in all of the above methods is approximately 2 µg/litre.

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

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

Monochloroacetic acid can be formed as a combustion by-product of organic compounds in the presence of chlorine (Juuti & Hoekstra, 1998). Stack gases of municipal waste incinerators have been reported to contain monochloroacetic acid at concentrations in the range 3.2–7.8 µg/m<sup>3</sup> (Mower & Nordin, 1987). Some of the monochloroacetic acid in the atmosphere may be formed from the hydrolysis of monochloroacetanilide herbicides, such as alachlor, acetochlor, metazachlor, metolachlor, butachlor and propachlor (Reimann et al., 1996). No data are available for annual, 8-h and 24-h time-weighted average ambient air concentrations of monochloroacetic acid in the USA (NATICH, 1993) or elsewhere.

Reimann et al. (1996) reported levels of monochloroacetic acid in rainwater in the range 0.05–9 µg/litre. It can be assumed that the chlorinated acetic acids detected in rainwater are from the atmosphere.

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

Chlorinated acetic acids are formed from organic material during water chlorination (Coleman et al., 1980; IPCS, 2000). Data for drinking-water supplies in the USA (US EPA, 2001, 2002a,b) indicate that monochloroacetic acid is present in surface water distribution systems at <2–82 µg/litre, with a mean concentration of 2.1 µg/litre. In groundwater distribution systems, monochloroacetic acid is present at <2–59 µg/litre, with a mean concentration of 1.5 µg/litre.

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

As chlorine is used in food production and processing — including disinfection of chicken in poultry plants; processing of seafood, poultry and red meats; sanitizing equipment and containers; cooling heat-sterilized foods; and oxidizing and bleaching in the flour industry (US EPA, 1994) — monochloroacetic acid is likely to be found as a disinfection by-product in meat and other food products (US EPA, 2002a). Monochloroacetic acid can also be taken up from cooking water (Raymer et al., 2001).

Reimann et al. (1996) examined the concentrations of monochloroacetic acid and other chlorinated acetic acids in a limited number of samples from several vegetables, fruits, grains and beer. Monochloroacetic acid concentrations ranged from <0.7 to 5.3 µg/kg in vegetables, from 1.7 to 13.2 µg/kg in grains, from 2.3 to 11.8 µg/kg in flours/breads and from 0.2 to 2.6 µg/litre in beer. Monochloroacetic acid was not detected in fruits or tomatoes.

### ***3.4 Estimated total exposure and relative contribution of drinking-water***

Although the available data for monochloroacetic acid are sufficient to demonstrate that food and air are relevant exposure sources in addition to drinking-water, the data are not adequate to quantify the contributions of each source for an overall assessment of exposure.

## **4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS**

Cases of human systemic poisoning and/or lethality following acute dermal exposure to monochloroacetic acid via accidental splashing with molten or concentrated solution (up to 90% monochloroacetic acid) have been reported in the literature. These cases suggest that monochloroacetic acid is rapidly absorbed and systemically distributed following direct skin contact covering at least 10% of the skin surface (Millischer et al., 1988; Kusch et al., 1990; Kulling, 1992). Intravenous administration of radiolabelled monochloroacetic acid to rats resulted in rapid distribution into the tissues, and only 0.6–1% of the radiolabel remained in plasma 5 min following dosing (Saghir et al., 2001). In rats given monochloroacetic acid subcutaneously, levels in kidney and liver were approximately the same and 4–5 times higher than those in plasma, brain and heart (Hayes et al., 1973). Proposed metabolic pathways include dehalogenation to form oxalate and glycine and/or dehalogenation and reduction to thiodiacetic acid via glutathione conjugation (Bhat et al., 1990). Monochloroacetic acid has also been reported to bind to lipids (Bhat & Ansari, 1989). Approximately 90% of a single, orally administered dose was excreted in the urine within 24 h (Kaphalia et al., 1992).

## **5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS**

### ***5.1 Acute exposure***

The oral LD<sub>50</sub>s for monochloroacetic acid in mice, male rats and male guinea-pigs were estimated to be 255, 76 and 80 mg/kg of body weight, respectively (Woodard et al., 1941). Dosed animals exhibited no immediate symptoms but soon became apathetic and rapidly lost weight. When death occurred, it was within 1–3 days. Survivors appeared to recover completely. In another study in rats, an oral LD<sub>50</sub> of 2820 mg/kg of body weight in males and a dermal LD<sub>50</sub> of 8068 mg/kg of body weight were reported (Smyth et al., 1951). In other studies, oral LD<sub>50</sub>s in mice were found to be 165 mg/kg of body weight (Morrison, 1946) and 260 mg/kg of body weight (Berardi et al., 1987).

### ***5.2 Short-term exposure***

B6C3F<sub>1</sub> mice (20 per sex per dose) received monochloroacetic acid by gavage at 0, 25, 50, 100, 150 or 200 mg/kg of body weight per day for 13 weeks (Bryant et al., 1992; NTP, 1992). Mortality was increased at the highest dose, and females at this dose exhibited decreased body weight and increased relative liver weights.

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Cholinesterase levels were decreased in females at 150 and 200 mg/kg of body weight per day. The only treatment-related histopathology was the occurrence of hepatocellular cytoplasmic vacuolization in mice receiving 200 mg/kg of body weight per day that died during the study. Based on decreased cholinesterase level, the LOAEL was 150 mg/kg of body weight per day and the NOAEL was 100 mg/kg of body weight per day (Bryant et al., 1992; NTP, 1992).

Effects were seen at every dose level in F344 rats (20 per sex per dose) that received monochloroacetic acid by gavage at 0, 30, 60, 90, 120 or 150 mg/kg of body weight per day for 13 weeks. At 90 mg/kg of body weight per day and above, these effects included increased blood urea nitrogen levels, decreased cholinesterase levels, elevated serum thyroxine levels in males and accumulation of mononuclear inflammatory cells (mainly macrophages) and myofibre degeneration in both sexes. At 60 mg/kg of body weight per day, effects included decreased survival, decreased relative heart weight, increased relative liver weight and cardiomyopathy (degenerative and inflammatory changes) in both sexes. Increased blood urea nitrogen levels were seen in females only. At 30 mg/kg of body weight per day and above, effects included decreased relative heart weights in females, increased relative liver weights in male rats, increased relative kidney weights in males, decreased cholinesterase levels in both sexes and reduced lymphocyte counts. The LOAEL for this study was the lowest dose tested, 30 mg/kg of body weight per day (Bryant et al., 1992; NTP, 1992), based on decreased heart weight and reduced lymphocyte counts.

### ***5.3 Long-term exposure***

B6C3F<sub>1</sub> mice (60 per sex per dose group) were given monochloroacetic acid by gavage at 0, 50 or 100 mg/kg of body weight per day, 5 days per week, for 2 years (NTP, 1992). Effects were seen only at the highest dose and included decreased survival in males, decreased mean body weight and metaplasia of the olfactory epithelium in females and inflammation of the nasal mucosa and squamous hyperplasia of the forestomach in both sexes. The NOAEL for this study was 50 mg/kg of body weight per day (NTP, 1992).

F344 rats (70 per sex per dose group) received monochloroacetic acid by gavage at doses of 0, 15 or 30 mg/kg of body weight per day, 5 days per week, for 2 years. No effects on body weight or clinical findings were observed. However, survival was significantly decreased in male rats at 30 mg/kg of body weight per day and in female rats in both dose groups. The incidence of uterine polyps was marginally (non-significantly) increased in females at both doses. The LOAEL for this study was 15 mg/kg of body weight per day, based on reduced survival (NTP, 1992).

Male F344 rats (50 per dose) were administered monochloroacetic acid in drinking-water at concentrations of 0, 0.05, 0.5 or 2 g/litre (time-weighted average daily doses of 0, 3.5, 26 and 60 mg/kg of body weight per day) for 104 weeks. The highest concentration was reduced to 1.5 g/litre at 8 weeks and 1.0 g/litre at 24 weeks due to severely decreased body weight gain. At 60 mg/kg of body weight per day, effects included increased myocardial degeneration, increased chronic active inflammation of

the nasal cavities and mildly increased liver inflammation. At 26 mg/kg of body weight per day and above, effects included decreased body weights, decreased absolute and relative liver weight, decreased kidney weight, increased relative testes weights and decreased absolute and relative spleen weights. At 3.5 mg/kg of body weight per day, the only effect noted was a 74–80% increase in absolute and relative spleen weights relative to controls. The LOAEL for this study, based on increased spleen weights, was 3.5 mg/kg of body weight per day (DeAngelo et al., 1997). This LOAEL is considered to be minimal because of the marginal target organ effects at this dose, the confounding effects of decreased body weight at the two higher dose levels and the lack of a dose–response (US EPA, 2002a).

### **5.4 Reproductive and developmental toxicity**

Pregnant Sprague-Dawley rats were given monochloroacetic acid in drinking-water at concentrations of 0 or 1.57 g/litre (0 or 193 mg/kg of body weight per day) on gestation days 1–22. A significant decrease in body weight gain was observed in exposed dams relative to controls. No adverse reproductive, developmental or teratogenic effects were reported; however, a complete fetal examination for internal or skeletal abnormalities was not conducted. Based on decreased maternal weight gain, the LOAEL for maternal toxicity is the only dose tested, 193 mg/kg of body weight per day. This dose was a NOAEL for developmental toxicity (Johnson et al., 1998).

Monochloroacetic acid exhibited teratogenic potential in non-mammalian developmental toxicity screening assays with *Hydra attenuata* (Fu et al., 1990; Ji et al., 1998).

### **5.5 Mutagenicity and related end-points**

Monochloroacetic acid was not mutagenic for *Salmonella typhimurium* with or without metabolic activation (Mortelmans et al., 1986); it was positive in the mouse lymphoma cell forward mutation assay without metabolic activation (McGregor et al., 1987). It was positive for the induction of sister chromatid exchanges in Chinese hamster ovary cells without metabolic activation and negative with metabolic activation (Galloway et al., 1987), and it was negative in the Chinese hamster lung fibroblast system (Sawada et al., 1987), the SOS chromotest in *Escherichia coli* with and without activation and the fluctuation test in *S. typhimurium* TA100 with and without metabolic activation (Giller et al., 1997). It did not induce DNA strand breaks in rats or mice (Chang et al., 1991) or chromosomal damage in the newt (*Pleurodeles waltl* larvae) micronucleus test (Giller et al., 1997).

Although the data are somewhat conflicting, the weight of evidence suggests that monochloroacetic acid has neither significant mutagenic potential nor any structural alerts for mutagenicity. This conclusion is supported by the negative data in carcinogenicity bioassays in two species, discussed in the next section.

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### ***5.6 Carcinogenicity***

There was no evidence of carcinogenic activity in 2-year gavage bioassays in F344 rats and B6C3F<sub>1</sub> mice. Rats (70 per sex per dose) received monochloroacetic acid at 0, 15 or 30 mg/kg of body weight per day, and mice (60 per sex per dose) received 0, 50 or 100 mg/kg of body weight per day (NTP, 1992).

There was no evidence of carcinogenicity in a 2-year bioassay in male F344 rats (50 per dose group) administered monochloroacetic acid in drinking-water at concentrations of 0, 0.05, 0.5 or 2.0 g/litre (corresponding to time-weighted average daily doses of 0, 3.5, 26.1 and 59.9 mg/kg of body weight per day) (DeAngelo et al., 1997).

### ***6. EFFECTS ON HUMANS***

Most cases of human poisoning from monochloroacetic acid are due to accidental dermal exposures caused by unintentional splashing of concentrated solution onto the skin. Of the seven cases identified by Millischer et al. (1987) and the additional case discussed by Kusch et al. (1990), five resulted in fatality and two resulted in reversible coma. Clinical signs included skin burns, vomiting, neurological symptoms such as convulsions, cardiovascular irregularities (such as tachycardia, hypotension and abnormal electrocardiograph) and loss of consciousness. Biochemical changes observed included severe acidosis with hyperglycaemia and hypokalaemia, decreased urinary output and elevated phosphocreatinine levels. Death occurred 4–18 h following acute exposure; autopsy showed liver, brain, heart and kidney lesions (Millischer et al., 1987; Kulling et al., 1992). One patient was reported to have recovered 4 days following exposure, after being treated with intravenous fluid replacement, intravenous potassium chloride, high-dose corticosteroids and diuretics (Kusch et al., 1990). Under conditions of high acute dermal exposures, monochloroacetic acid is a systemic metabolic poison, possibly via inhibition of the Krebs cycle (Millischer et al., 1987).

### ***7. GUIDELINE VALUE***

No evidence of carcinogenicity was found in 2-year gavage bioassays with rats and mice (NTP, 1992). Monochloroacetate has given mixed results in a limited number of mutagenicity assays and has been negative for clastogenicity in genotoxicity studies. IARC has not classified the carcinogenicity of monochloroacetic acid. US EPA (2002a) has classified monochloroacetic acid as Group D, not classifiable as to human carcinogenicity, in accordance with the 1986 EPA Guidelines for Carcinogen Risk Assessment (US EPA, 1986); and as inadequate for an assessment of human carcinogenic potential, in accordance with the 1999 EPA Draft Guidelines for Carcinogen Risk Assessment (US EPA, 1999).

Because there is no evidence of significant *in vivo* mutagenic potential or carcinogenicity, a TDI of 3.5 µg/kg of body weight was calculated based on a LOAEL of 3.5 mg/kg of body weight per day from a study in which increased absolute and

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relative spleen weights were observed in male rats exposed to monochloroacetic acid in drinking-water for 2 years (DeAngelo et al., 1997), incorporating an uncertainty factor of 1000 (100 for intra- and interspecies variation and 10 for the use of a minimal LOAEL instead of a NOAEL and for database deficiencies, including the lack of a multigeneration reproductive toxicity study).

With an allocation of 20% of the TDI to drinking-water, and assuming a 60-kg adult ingesting 2 litres of drinking-water per day, the guideline value for monochloroacetic acid is 20 µg/litre (rounded figure). This guideline value is achievable using commonly available analytical methods.

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