WHO/SDE/WSH/03.04/38
English only

MCPA in Drinking-water

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

Originally published in **Guidelines for drinking-water quality**, 2nd ed. Vol.2. *Health criteria and other supporting information.* World Health Organization, Geneva, *1996.*

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 work of the following coordinators was crucial in the development of this background document for development of WHO *Guidelines for drinking-water quality*:

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The efforts of all who helped in the preparation and finalization of this document, including those who drafted and peer reviewed drafts, are gratefully acknowledged.

The convening of the experts meetings was made possible by the financial support afforded to WHO by the Danish International Development Agency (DANIDA), Norwegian Agency for Development Cooperation (NORAD), the United Kingdom Overseas Development Administration (ODA) and the Water Services Association in the United Kingdom, the Swedish International Development Authority (SIDA), and the following sponsoring countries: Belgium, Canada, France, Italy, Japan, Netherlands, United Kingdom of Great Britain and Northern Ireland and United States of America.

GENERAL DESCRIPTION

Identity

CAS no.: 94-74-6
Molecular formula: $C_9H_9ClO_3$
MCPA is the common name for 4-chloro-2-methylphenoxyacetic acid.

Physicochemical properties (*1–4*)

Property	*Value*
Melting point	118–119 °C
Water solubility	825 mg/litre at room temperature
Vapour pressure	0.2×10^{-3} Pa at 21 °C
Octanol–water partition coefficient	26
Organic carbon–water partition coefficient	110
Density	1.56 g/cm^3 at 25 °C
pK_a	3.07

Major uses

MCPA is a systemic hormone-type selective herbicide, readily absorbed by leaves and roots. Its uses include the control of annual and perennial weeds in cereals, grassland, and turf (*1*).

Environmental fate

MCPA did not volatilize from an aqueous solution (pH 7.0) heated for 13 days at 34–35 °C, nor was it hydrolysed at neutral pH (*5*). In aqueous solution at pH 8.3, MCPA had a photolytic half-life of 20–24 days in sunlight. In rice paddy water in the dark, it was totally degraded by aquatic microorganisms in 13 days (*6*). It undergoes various metabolic reactions [Source: Hazardous Substances Data Bank. Bethesda, MD, National Library of Medicine].

MCPA can be expected to leach readily in most soils (*7*). Mobility increases as organic matter content decreases. Its half-life in soil was 15–50 days (*5,6*). It degrades twice as quickly (6–12 days) when applied a second time to soil than after one application (15–28 days) (*8*).

ANALYTICAL METHODS

MCPA in water can be determined by a gas chromatographic method, after extraction with dichloromethane and esterification with diazomethane. The method sensitivity is about 0.1 µg/litre (*9*).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Water

In the USA, MCPA was found, at levels of 0.04–0.54 µg/litre in four of 18 surface water samples analysed, but in none of 118 groundwater samples (*4*). It was detected in some groundwaters in Montana (maximum level 5.5 µg/litre) (*4*) and in two of 237 wells in Ontario (*10*).

Food

In surveys conducted during 1965–68 in the USA, MCPA was detected in food composites at a maximum concentration of less than 0.4 mg/kg. It was not detected in food composites of adult total diet samples during 1971–76 or in infant or toddler diet samples during 1974–75 (*11*).

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

MCPA is readily absorbed from the gut of mice. After rats were exposed to MCPA, it was detected in all the organs tested (*12*). It is metabolized by the liver (*13*), 5-chloromethyl-catechol being one of its metabolites (*14*). Induction of microsomal oxidation by phenobarbital increases the rate of breakdown (*13*). Rats treated orally with MCPA excreted nearly all of it during the first 24 h after intake (90% in urine, 7% in faeces) (*12*). In rabbits and cattle, it is excreted rapidly, largely unchanged (*15,16*). In humans, 50% of the total dose was detected in the urine within 48 h (*17*).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Acute oral LD_{50}s for MCPA of 550 and 700 mg/kg of body weight have been reported in mice and rats, respectively (*1*).

Short-term exposure

After administration of MCPA (80.6% active ingredient) in the diet for 90 days to SPF weanling rats at doses of about 0, 2.5, 20, or 160 mg/kg of body weight per day, no compound-related effects were reported except for growth retardation and elevated relative kidney weights at the two highest doses. A NOAEL of 2.5 mg/kg of body weight per day was identified (*18*).

MCPA administered in the diet of CD rats for 3 months at doses of 0, 4, 8, or 16 mg/kg of body weight per day did not cause any adverse effects, except for increases in kidney weight in males at 16 mg/kg of body weight per day. A NOAEL of 8 mg/kg of body weight per day was identified from this study (*19*).
MCPA (94% a.i.) was administered orally to beagle dogs in two separate 13-week studies at dosing regimens of 0, 3, 12, or 48 mg/kg of body weight per day and 0, 0.3, 1, or 12 mg/kg of body weight per day. Decreased kidney and liver function, characterized by increases in blood urea, SGPT, and creatinine, were observed at doses as low as 3 mg/kg of body weight per day. Low prostatic weight and mucopurulent conjunctivitis were observed at higher doses. A NOAEL of 1 mg/kg of body weight per day was identified from these studies (*20*).

Beagle dogs were given oral doses of MCPA (95% a.i.) of 0, 0.15, 0.75, or 1.5 mg/kg of body weight per day for 1 year. Kidney toxicity was observed at the two highest doses. A NOAEL of 0.15 mg/kg of body weight per day was identified (*21*).

Long-term exposure

In a study in which Wistar rats (50 per sex per dose) were given MCPA (purity 84.8%) in their food at levels of 0, 20, 80, or 320 mg/kg for 2 years, a decrease in body weight gain, alterations of chemical and clinical parameters, and nephropathy were observed at the highest dose (*22*). In a study in which B6C21BRF$_1$ mice (50 per sex per dose) were given MCPA orally at levels of 0, 20, 100, or 500 mg/kg for 2 years, a greater frequency of renal lesions as a result of chronic nephropathy was observed at the highest dose (*23*).

Reproductive toxicity, embryotoxicity, and teratogenicity

No effects on reproduction were found in rats exposed to MCPA (95% a.i.) at 0, 3.3, 10, or 30 mg/kg of body weight per day in the diet over two generations (*24*). After oral administration of MCPA (75% a.i.) at 0, 5, 25, or 100 mg/kg of body weight per day to mice on days 6–15 of gestation, significantly reduced fetal weights and delayed skeletal ossification were observed at the highest dose (*25*).

MCPA (purity not specified) was administered (0, 20, 50, or 125 mg/kg of body weight per day) by gavage to pregnant CD rats (16–38 per dose) on days 6–15 of gestation. No maternal or fetal toxicity or teratogenic effects were observed (*26*). The intragastric administration of technical MCPA (700 mg/kg) on days 9 or 10 of gestation to female Wistar rats caused an increase in the frequency of resorption, a reduction of fetal weight, and the appearance of major malformations (*13*).

After MCPA was administered (0, 5, 12, 30, or 75 mg/kg of body weight per day) by gavage to rabbits on days 6–18 of gestation, no fetotoxicity or teratogenicity was observed at any of the dose levels tested. Body weights of the does were markedly reduced in the group given 75 mg/kg of body weight per day. A fetal NOAEL of 75 mg/kg of body weight per day and a maternal NOAEL of 30 mg/kg of body weight per day were identified (*27*).

Mutagenicity and related end-points

MCPA is slightly mutagenic at the gene level in yeast and *Drosophila* (*28,29*). It induces sister chromatid exchange in *in vitro* tests but has given contradictory results *in vivo* (*30*). It is inactive in gene mutation tests on bacteria and in *in vivo* cytogenetic tests (micronucleus and chromosomal aberrations) (*31–34*).

Carcinogenicity

MCPA (purity 84.8%) was administered to Wistar rats (50 per sex per dose) in their food at levels of 0, 20, 80, or 320 mg/kg for 2 years. No significant differences in the distribution of the various types of tumours in treated as compared with control animals were evident (*22*). Similarly, the oral administration of MCPA to $B6C21BRF_1$ mice (50 per sex per dose) at levels of 0, 20, 100, or 500 mg/kg for 2 years did not cause any significant differences in the distribution of the various types of tumours as between the treated and control groups (*23*).

EFFECTS ON HUMANS

Epidemiological investigations on MCPA have involved both the producers and users of chlorophenoxyacetic weedkillers, so that exposure to this product is generally accompanied by exposure to 2,4-D, 2,4,5-T, mecoprop, and dichlorprop. IARC carried out a comprehensive evaluation related to occupational exposures to chlorophenoxy herbicides, which were considered to show "limited evidence" of carcinogenicity (*35*).

GUIDELINE VALUE

There are only limited and inconclusive data on the genotoxicity of MCPA. IARC evaluated MCPA in 1983 and concluded that the available data on humans and experimental animals were inadequate for an evaluation of carcinogenicity (*11*). In further evaluations by IARC on chlorophenoxy herbicides in 1986 and 1987 it was concluded that evidence for their carcinogenicity was limited in humans and inadequate in animals (Group 2B) (*35,36*). No adequate epidemiological data on exposure to MCPA alone are available. Recent carcinogenicity studies on rats and mice (*22,23*) did not indicate that MCPA was carcinogenic.

A 1-year feeding study in dogs indicated a NOAEL of 0.15 mg/kg of body weight per day, based on the renal and liver toxicity observed at higher dose levels (*21*). Using this value and applying an uncertainty factor of 300 (100 for inter- and intraspecies variation and 3 for the inadequacy of the database), a TDI of 0.5 µg/kg of body weight can be calculated. An allocation of 10% of the TDI to drinking-water gives a guideline value of 2 µg/litre (rounded figure).

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