

Aldicarb 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.

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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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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

ADI	acceptable daily intake
CAS	Chemical Abstracts Service
EPA	Environmental Protection Agency (USA)
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 ₅₀	median lethal dose
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
USA	United States of America
WHO	World Health Organization

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1. GENERAL DESCRIPTION

1.1 Identity

CAS No.: 116-06-3
Molecular formula: $C_7H_{14}N_2O_2S$

Aldicarb is the common name for 2-methyl-2(methylthio)propionaldehyde *O*-methylcarbamoyloxime.

1.2 Physicochemical properties (WHO, 1991)

<i>Property</i>	<i>Value</i>
Vapour pressure	13 Pa at 25 °C
Water solubility	6 g/litre at 20 °C
Log octanol–water partition coefficient	1.359

1.3 Major uses

Aldicarb is a systemic carbamate insecticide used to control nematodes in soil and insects and mites on a wide variety of crops, including citrus fruits, grain, peanuts, potatoes, soy beans, sugar-beet and tobacco.

1.4 Environmental fate

Aldicarb is oxidized by microorganisms in soil to the sulfoxide and sulfone (Lightfoot & Thorne, 1987); its degradation half-life ranges from a few days to more than 2 months. Aldicarb and its degradation products are generally mobile in soil; leaching is most extensive in soils with a low organic matter content (Cohen et al., 1984; US EPA, 1988).

Aldicarb is very persistent in groundwaters, particularly those that are acidic; the half-life for degradation to non-toxic products ranges from a few weeks to as long as several years (US EPA, 1984). The primary mode of degradation is chemical hydrolysis, although there may also be some microbial decay in shallow groundwater (Jones, 1986).

2. ANALYTICAL METHODS

Aldicarb and its degradation products in water may be determined by high-performance liquid chromatography (WHO, 1991). When followed by post-column derivatization to form fluorescent compounds, this method has detection limits of about 1.3, 0.8 and 0.5 µg/litre for aldicarb, the sulfoxide and the sulfone, respectively (Foerst & Moye, 1985). Aldicarb and its oxidation products can also be determined as their nitrile derivatives by capillary gas chromatography with a nitrogen–phosphorus detector (Zhong et al., 1984).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Water

Aldicarb was detected in 111 of 1017 samples in surveys of private and municipal drinking-water supplies in Canada (detection limits 0.01–3.0 µg/litre); the maximum concentration was 28 µg/litre (Hiebsch, 1988). Aldicarb has been detected in well water in the USA at concentrations ranging from less than 10 to 500 µg/litre (US EPA, 1984). Neither aldicarb nor its metabolites were detected in over 700 community groundwater drinking supplies in Florida, USA (detection limit 2–5 µg/litre for each compound) (Miller et al., 1989). Concentrations in groundwater near potato fields to which it had been applied were detectable (≥ 1 µg/litre) in 31.3% of samples taken in Long Island, New York, USA; 0.9% of samples contained aldicarb at concentrations above 100 µg/litre (Jones & Marquardt, 1987). Aldicarb sulfoxide and aldicarb sulfone residues are found in an approximately 1:1 ratio in groundwater (US EPA, 1988).

3.2 Food

Aldicarb was detected in 94% of potatoes analysed in the USA in 1980 at concentrations ranging from 50 to 520 µg/kg (US EPA, 1985). Aldicarb sulfoxide was found in 1981–1986 in 7 of 6391 samples of domestic agricultural commodities at levels at or below 1.0 mg/kg (Hundley et al., 1988).

3.3 Estimated total exposure and relative contribution of drinking-water

Based on maximum residue limits for aldicarb established by the Codex Alimentarius Commission (1993), the theoretical maximum daily intake of aldicarb from food is about 0.09 mg for a 60-kg adult (1.5 µg/kg of body weight per day). The average daily intake for a male aged 25–30 years has been estimated to be 0.2 µg/kg of body weight, based on residues in foods in the USA (Gunderson, 1988).

Based on a concentration of aldicarb in drinking-water of 5 µg/litre and consumption of 2 litres of drinking-water per day by a 60-kg adult, the daily intake by this route can be estimated to be 10 µg (0.2 µg/kg of body weight), which is about the same as that from food.

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS¹

Aldicarb is rapidly absorbed, widely distributed in the body and rapidly excreted. Metabolism appears to be similar in all species studied, aldicarb being rapidly metabolized to aldicarb sulfoxide, which is more slowly degraded to aldicarb sulfone. All metabolites are quickly eliminated from the body, 80–90% being excreted within

¹ This section has been taken from FAO/WHO (1993).

24 h. Elimination was complete by the fifth day after dosing, and no bioaccumulation was seen.

5. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS²

Aldicarb has high acute toxicity in a wide variety of mammalian species. Signs of toxicity are those commonly associated with acetylcholinesterase inhibition by a carbamate insecticide: cholinergic signs of poisoning, which are alleviated rapidly on cessation of exposure. Aldicarb sulfoxide is a more potent inhibitor of acetylcholinesterase than aldicarb itself, while aldicarb sulfone is considerably less toxic than either aldicarb or the sulfoxide. WHO (2001) has classified aldicarb as extremely hazardous.

Short-term and long-term studies have been performed in rats, mice and dogs with aldicarb and aldicarb metabolites, both individually and in combination. Toxicity tests employing mixtures of aldicarb or aldicarb sulfoxide with aldicarb sulfone are of interest because aldicarb sulfoxide and aldicarb sulfone are the terminal residues potentially consumed by humans. Cholinesterase depression is the most significant indicator of toxicity that can be evaluated. However, considerable attention must be paid to the methods of sample collection and determination of cholinesterase activity. Continuous administration of aldicarb to the test animals until collection of samples for analysis is important, as is rapid analysis under carefully controlled conditions.

It is now considered inappropriate to use no-adverse-effect levels from many of the earlier repeat-dose studies for the derivation of an ADI, because animals were not dosed for 24–48 h prior to collection of tissue samples for measurement of cholinesterase activity. In the most recent dog studies, which were conducted in a manner designed to maximize detection of cholinesterase depression, the overall NOEL was 0.02–0.03 mg/kg of body weight per day, but the NOAEL (which discounts inhibition of plasma cholinesterase only) was 0.05–0.06 mg/kg of body weight per day.

Results of repeat-dose studies with aldicarb demonstrate that the method of administering the test material to the test animals can greatly modify the apparent toxicity of aldicarb and its metabolites. Mice, rats and dogs have tolerated daily doses equal to the LD₅₀ incorporated into the diet for 7 days to 2 years. Doses that caused death in less than 2 h when administered as a bolus caused no death and only moderate cholinesterase depression when given in the diet.

Two dietary carcinogenicity studies have been conducted with aldicarb in rats, and three in mice. A dermal carcinogenicity study has also been conducted with aldicarb in mice, and dietary studies have been carried out with aldicarb sulfone in mice and aldicarb sulfoxide in rats. Aldicarb was not carcinogenic in mice or rats.

² This section has been taken from FAO/WHO (1993).

Two reproduction studies have been conducted in rats with aldicarb, and one with aldicarb sulfone. There were no effects on reproductive performance at doses up to 0.7 mg/kg of body weight per day for aldicarb or 9.6 mg/kg of body weight per day for aldicarb sulfone. Aldicarb did not display any teratogenic potential in rats or rabbits in studies that included maternally toxic doses.

After reviewing the available genotoxicity data, the Meeting concluded that aldicarb, aldicarb sulfoxide and aldicarb sulfone are not genotoxic.

In a range of special studies in animals (involving delayed neurotoxicity, behaviour, antagonistic agents and pesticide interactions), aldicarb displayed no results that gave cause for concern. There was no evidence of immunotoxicity in mice in a number of functional assays of cell-mediated immunity and in host resistance to respiratory infection.

6. EFFECTS ON HUMANS³

Epidemiological studies provided no convincing evidence that aldicarb could significantly alter immunological function in humans.

In addition to the above epidemiological studies, studies conducted in 1982 and 1983 attempted to correlate any potential adverse health effects with the occurrence of aldicarb in drinking-water. Although the authors concluded that further study was needed, there was no clear evidence that aldicarb contamination of drinking-water generally at concentrations of about 4–12 µg/litre, but at a maximum concentration of 400 µg/litre, was related to any health effects.

The anticholinesterase potential of aldicarb has been extensively investigated in humans. These studies revealed the same pattern of rapid cholinesterase inhibition and rapid recovery seen in experimental animals. Transient erythrocyte cholinesterase depression was seen at single doses of 0.05 mg/kg of body weight, and the NOAEL for cholinesterase depression (discounting changes in plasma enzyme activity) was 0.025 mg/kg of body weight.

A number of poisoning incidents have been reported in the agricultural use of aldicarb, but there has been no indication that the workers exposed were harmed once removed from the exposure source. Although several deaths have been reported, all of these have been attributed to suicide or gross neglect.

A number of food-borne aldicarb intoxications have been reported in the literature. These have all been associated with misuse, and reliable quantification of the dose of aldicarb involved has always proved difficult, if not impossible.

³ This section has been taken from FAO/WHO (1993).

7. GUIDELINE VALUE

IARC (1991) has concluded that aldicarb is not classifiable as to its carcinogenicity (Group 3).

In 1992, JMPR recommended an ADI of 0.003 mg/kg of body weight, based on a single oral dose study in human volunteers with a NOAEL of 0.025 mg/kg of body weight per day for depression of erythrocyte cholinesterase activity and an uncertainty factor of 10 (FAO/WHO, 1993). The calculated guideline value would, therefore, be 9 µg/litre, assuming an allocation of 10% of the ADI to drinking-water. Because this is very similar to the guideline value of 10 µg/litre derived in the second edition, the guideline value of 10 µg/litre is retained.

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