Dicofol in Drinking-water

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

Access to safe drinking-water is essential to health, a basic human right and a component of effective policy for health protection. A major World Health Organization (WHO) function to support access to safe drinking-water is the responsibility “to propose ... regulations, and to make recommendations with respect to international health matters ...”, including those related to drinking-water safety and management.

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 third edition of the GDWQ was published in 2004, the first addendum to the third edition was published in 2006 and the second addendum to the third edition was published in 2008. The fourth edition was published in 2011, and the first addendum to the fourth edition was published in 2017.

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 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 background document evaluating the risks for human health from exposure to the particular chemical in drinking-water was prepared. The draft health criteria document was submitted to a number of scientific institutions and selected experts for peer review. The draft document was also released to the public domain for comment. Comments were carefully considered and addressed as appropriate, taking into consideration the processes outlined in the *Policies and Procedures Used in Updating the WHO Guidelines for Drinking-water Quality* (http://apps.who.int/iris/bitstream/10665/70050/1/WHO_HSE_WSH_09.05_eng.pdf) and the *WHO Handbook for Guideline Development* (http://www.who.int/publications/guidelines/handbook_2nd_ed.pdf), and the revised draft was submitted for final evaluation at expert consultations.

During the preparation of background documents and at expert consultations, 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 Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting 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 website and in the current edition of the GDWQ.
Acknowledgements

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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 comments are greatly appreciated.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ADI</td>
<td>acceptable daily intake</td>
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<tr>
<td>ARfD</td>
<td>acute reference dose</td>
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<tr>
<td>bw</td>
<td>body weight</td>
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<tr>
<td>DCBP</td>
<td>dichlorobenzophenone</td>
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<tr>
<td>DDT</td>
<td>dichlorodiphenyltrichloroethane</td>
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<tr>
<td>DIN</td>
<td>Deutsches Institut für Normung (German Institute for Standardization)</td>
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<tr>
<td>ECD</td>
<td>electron capture detection</td>
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<tr>
<td>EU</td>
<td>European Union</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>GC-MS</td>
<td>gas chromatography with mass spectrometry</td>
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<tr>
<td>HBV</td>
<td>health-based value</td>
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<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
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<td>JMPR</td>
<td>Joint FAO/WHO Meeting on Pesticide Residues</td>
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<tr>
<td>$K_{oc}$</td>
<td>soil adsorption coefficient</td>
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<tr>
<td>$K_{ow}$</td>
<td>octanol–water partition coefficient</td>
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<tr>
<td>LOAEL</td>
<td>lowest-observed-adverse-effect level</td>
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<tr>
<td>NOAEL</td>
<td>no-observed-adverse-effect level</td>
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<tr>
<td>USA</td>
<td>United States of America</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<td>WHOPES</td>
<td>World Health Organization Pesticide Evaluation Scheme</td>
</tr>
</tbody>
</table>
Contents

1. MAJOR USES .............................................................................................................................................. 1
2. POTENTIAL FOR OCCURRENCE IN WATER ................................................................................................. 1
3. TOXICITY .................................................................................................................................................. 1
4. DERIVATION OF A HEALTH-BASED VALUE ............................................................................................ 2
5. CONSIDERATIONS IN APPLYING THE HEALTH-BASED VALUE ............................................................... 3
6. ANALYSIS IN WATER .................................................................................................................................. 3
7. TREATMENT TECHNOLOGIES .................................................................................................................... 3
8. CONCLUSION ............................................................................................................................................. 3
9. REFERENCES ................................................................................................................................................ 3
Dicofol is the International Organization for Standardization (ISO)–approved common name for 2,2,2-trichloro-1,1-bis(4-chlorophenyl) ethanol. It is a non-systemic acaricide that acts by stimulating axonal transmission of nervous signals. Dicofol is structurally similar to dichlorodiphenyltrichloroethane (DDT). Its Chemical Abstracts Service number is 115-32-2.

1. MAJOR USES

Dicofol is an organochlorine acaricide that has been used in agriculture since the late 1950s (WHO/FAO, 1996). Products containing dicofol have been registered for broad-spectrum contact, non-systemic control of plant-eating mites in cotton, tea and a wide variety of fruit, vegetable and ornamental crops (FAO/WHO, 1993). Dicofol is manufactured from DDT; in the 1980s, restrictions were placed on the amount of DDT permitted as an impurity (USEPA, 1998). As a result of the re-registration process, dicofol products are being phased out in the United States of America (USA) and are no longer approved for use in the European Union (EU) (European Commission, 2008; USEPA, 2011a,b).

2. POTENTIAL FOR OCCURRENCE IN WATER

Dicofol is only slightly soluble in water (0.8 mg/L at 25 °C; Kidd & James, 1991), has a high octanol–water partition coefficient (log $K_{ow}$ 4.28; IPCS, 2003) and binds strongly to soil (soil adsorption coefficient $[K_{oc}] > 5000$; Tillman, 1992). It has a half-life of about 40–50 days in soil. Dicofol is unlikely to reach water, but may do so if bound to particulate matter subject to runoff. Its persistence in water is pH dependent, being higher at lower pH. Dichlorobenzophenone (DCBP) is a major metabolite in both soil and water (Worthing, 1991; USEPA, 1998).

There are few data on the occurrence of dicofol in water. Limited groundwater monitoring in four states in the USA found no detectable concentrations of dicofol (USEPA, 1992). Dicofol was released from a manufacturing site in the USA in 1980, and subsequent investigation by the United States Environmental Protection Agency reported dicofol and later DCBP in groundwater, although there was some uncertainty over the dicofol detections (USEPA, 2000). This scenario is unlikely to be representative of contamination that may arise from normal use. Dicofol is included as a priority hazardous substance under the EU Water Framework Directive, so it is likely that more occurrence data will be gathered under this legislation (European Commission, 2012).

Dicofol has been proposed as a persistent organic pollutant under the Stockholm Convention (UNEP, 2013).

3. TOXICITY

The Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting on Pesticide Residues (JMPR) evaluated dicofol in 2011 (FAO/WHO, 2012; WHO, 2012). The primary effects of dicofol after short- or long-term exposure of experimental animals were body weight reduction associated with decreased feed intake and increased liver weight accompanied by increased hepatic mixed-function oxidase activity and liver hypertrophy, increased serum alanine aminotransferase and serum alkaline phosphatase activities and hepatocellular necrosis at higher doses. At high doses, changes in the kidneys, adrenals, heart and testes were also observed in rodents. Reduced serum cortisone levels were seen in dogs, indicating disturbances in adrenocorticoid metabolism. Dicofol caused liver tumours in male mice at doses associated with significant enzyme induction and liver hypertrophy, which are anticipated to exhibit a threshold response. Dicofol gave a negative response in an adequate range of in vitro genotoxicity and in vivo chromosomal aberration tests. On the basis of the
absence of genotoxicity, the absence of carcinogenic effects in rats and the expectation that the adenomas present in mice will exhibit a threshold, JMPR concluded that dicofol was unlikely to pose a carcinogenic risk to humans at anticipated dietary exposure levels. In a one-generation study on reproduction in rats, no reproductive or offspring toxicity was observed at the highest dose tested. In developmental toxicity studies in rats and rabbits, no effects on embryo or fetal toxicity were noted at the highest doses tested. JMPR reported that dicofol was not teratogenic.

JMPR established an acceptable daily intake (ADI) of 0–0.002 mg/kg body weight (bw) (FAO/WHO, 2012; WHO, 2012). This was derived from a no-observed-adverse-effect level (NOAEL) of 0.22 mg/kg bw per day in a 2-year toxicity and carcinogenicity study in rats, based on histopathological changes in the liver and adrenal gland (Hazelton & Harris, 1989; Quinn & Hazelton, 1990). A safety factor of 100 was applied. The ADI was supported by a NOAEL of 0.2 mg/kg bw per day from a 90-day neurotoxicity study in rats (Foss, 1993). There was a margin of 20 000 between the upper bound of the ADI and the lowest-observed-adverse-effect level (LOAEL) for liver adenomas in the male mouse (NCI, 1978; Nave & Hurt, 2000).

JMPR established an acute reference dose (ARfD)\(^1\) of 0.2 mg/kg bw on the basis of a NOAEL of 15 mg/kg bw in an acute neurotoxicity study in rats (Foss, 1993), based on decreased body weight and decreased feed intake at 75 mg/kg bw. This ARfD was supported by a NOAEL of 15 mg/kg bw in a single-dose oral toxicity study in rats, based on decreased feed intake and hypertrophy of the adrenal gland at 75 mg/kg bw (Parno, Anderson & Donofrio, 2000). Although these effects were mild, they were observed in two studies, and therefore 75 mg/kg bw was considered a marginal LOAEL. A safety factor of 100 was applied.

### 4. DERIVATION OF A HEALTH-BASED VALUE\(^2\)

Pesticides provide a special case for establishing health-based values (HBVs) for drinking-water in terms of the potential exposure from other sources, because they are deliberately applied to food crops. JMPR concluded that the daily intake of dicofol in food was between 1% and 30% of the upper bound of the ADI (FAO/WHO, 2013), which suggests that exposure from food varies widely and will depend on local circumstances and usage.

With an allocation of 20% of the upper bound of the JMPR ADI of 0.002 mg/kg bw to drinking-water and the assumption that a 60 kg adult drinks 2 L of water per day, an HBV of 0.01 mg/L (10 µg/L) can be derived for dicofol. The default allocation factor of 20% has been used to account for the fact that available food exposure data, which suggest that exposure via this route is low, do not generally include information from developing countries, where exposure via this route may be higher (for further information, see section

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\(^1\) The estimate of the amount of a substance in food or drinking-water, expressed on a body weight basis, that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer.

\(^2\) Formal guideline values are established when one of the following criteria has been met: 1) there is credible evidence of occurrence of the chemical in drinking-water combined with evidence of actual or potential toxicity, 2) the chemical is of significant international concern or 3) the chemical is being considered for inclusion or is included in the World Health Organization Pesticide Evaluation Scheme (WHOPES). For some chemicals, no formal guideline values are established when occurrence is likely to be well below a level that would be of concern for health. Establishing a formal guideline value for such substances may encourage Member States to incorporate a value into their national standards when this may be unnecessary. When a formal guideline value is not established, a “health-based value” may be determined in order to provide guidance to Member States when there is reason for local concern. This reference value provides both a means of judging the margin of safety in the absence of a specific guideline value and a level of interest for establishing analytical methods.

5. CONSIDERATIONS IN APPLYING THE HEALTH-BASED VALUE

The HBV for dicofol is protective against health effects resulting from lifetime exposure from drinking-water. Small exceedances above the HBV for short periods are unlikely to have an impact on health. If these exceedances are due to massive contamination, however, such as that found in emergency or spill situations, the acute HBV of 6 mg/L (derived from the JMPR ARfD) would provide a useful point of reference for the provision of advice to consumers. This acute HBV indicates the concentration of dicofol in drinking-water that a person could consume for 24 hours without appreciable health risk (for further information, see section 8.7.5 of the Guidelines for Drinking-water Quality; WHO, 2017).

Routine monitoring of dicofol is not considered necessary. However, Member States should consider local usage and potential situations such as spills in deciding whether and where to monitor. In the event that monitoring results show levels above the HBV on a regular basis, it is advisable that a plan be developed and implemented to address the situation.

As a general principle, efforts should be made to keep the concentration of pesticides in water as low as possible and to not allow concentrations to increase up to the HBV.

6. ANALYSIS IN WATER

There is no standard method for analysis of dicofol in water, although it is likely to be amenable to the methods used for organochlorine pesticides, such as liquid–liquid extraction followed by gas chromatography with electron capture detection (ECD). There is a report of German method DIN 38407-2, which involves solvent extraction, gas chromatographic separation and ECD detection, with a limit of quantification of 5 ng/L (Deutsches Institut für Normung, 1993). Other methods reported in the literature include the determination of dicofol in seawater by large-volume solid-phase extraction followed by gas chromatography with mass spectrometric determination (GC-MS) and in breast milk using GC-MS after liquid–liquid extraction and cleanup (Loos, 2012).

7. TREATMENT TECHNOLOGIES

No information is available on removal of dicofol during water treatment. However, the relatively low aqueous solubility and high octanol–water partition coefficient suggest that dicofol should be removed by adsorption onto activated carbon, and any dicofol adsorbed onto particulate matter would likely be removed during coagulation.

8. CONCLUSION

It is not considered necessary to establish a guideline value for dicofol, as it is unlikely to be found in drinking-water sources or drinking-water. Where monitoring results show the presence of dicofol in drinking-water on a regular basis, an HBV of 0.01 mg/L can be applied. In an emergency or spill situation, an acute HBV of 6 mg/L may provide useful guidance.

9. REFERENCES


DICOFOL IN DRINKING-WATER

report no. 86R-190 from Rohm and Haas Company, Spring House, PA, USA. Submitted to WHO by Rohm and Haas Company, Spring House, PA, USA [cited in WHO, 2012].


