

Propanil in Drinking-water

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

© World Health Organization 2004

Requests for permission to reproduce or translate WHO publications - whether for sale or for non-commercial distribution - should be addressed to Publications (Fax: +41 22 791 4806; e-mail: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damage incurred as a result of its use.

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 first draft of Propanil in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, was prepared by Dr P. Toft, Canada, to whom special thanks are due.

The work of the following working group coordinators was crucial in the development of this document and others in the third edition:

Mr J.K. Fawell, United Kingdom (*Organic and inorganic constituents*)
Dr E. Ohanian, Environmental Protection Agency, USA (*Disinfectants and disinfection by-products*)
Ms M. Giddings, Health Canada (*Disinfectants and disinfection by-products*)
Dr P. Toft, Canada (*Pesticides*)
Prof. Y. Magara, Hokkaido University, Japan (*Analytical achievability*)
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:

Dr J. Bartram, Coordinator, Water Sanitation and Health Programme, WHO Headquarters, and formerly WHO European Centre for Environmental Health
Mr P. Callan, Water Sanitation and Health Programme, WHO Headquarters
Mr H. Hashizume, Water Sanitation and Health Programme, WHO Headquarters

Ms C. Vickers provided a liaison with the International Chemical Safety Programme, WHO Headquarters.

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
HSDB	Hazardous Substances Data Bank
LD ₅₀	median lethal dose
MCPA	4-(2-methyl-4-chlorophenoxy)acetic acid
NOAEL	no-observed-adverse-effect level
TCAB	3,3',4,4'-tetrachloroazobenzene

Table of contents

1. GENERAL DESCRIPTION	1
1.1 Identity	1
1.2 Physicochemical properties	1
1.3 Major uses	1
1.4 Environmental fate.....	1
2. ANALYTICAL METHODS	1
3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE.....	2
3.1 Water	2
4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	2
5. EFFECTS ON LABORATORY ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS	2
5.1 Acute exposure.....	2
5.2 Short-term exposure.....	2
5.3 Long-term exposure.....	2
5.4 Reproductive and developmental toxicity	3
5.5 Mutagenicity and related end-points.....	3
5.6 Carcinogenicity	3
6. EFFECTS ON HUMANS.....	3
7. CONCLUSIONS.....	3
8. REFERENCES	4

1. GENERAL DESCRIPTION

1.1 Identity

CAS No.:	709-98-8
Molecular formula:	C ₉ H ₉ Cl ₂ NO

Propanil is the common name for 3',4'-dichloropropionanilide.

1.2 Physicochemical properties (1)

<i>Property</i>	<i>Value</i>
Physical state	Colourless solid
Melting point	91.5 °C
Vapour pressure	0.026×10^{-3} Pa at 20 °C
Water solubility	130 mg/litre at 20 °C

1.3 Major uses

Propanil is a contact post-emergence herbicide used mainly in rice to control broad-leaved and grass weeds. It is also used mixed with MCPA in wheat (1).

1.4 Environmental fate

Propanil is hydrolysed in acidic and alkaline media to 3,4-dichloroaniline and propionic acid. In water, propanil and 3,4-dichloroaniline are rapidly degraded by sunlight to phenolic compounds, which then polymerize (1). Propanil is biodegraded in soil to various metabolites, including 3,4-dichloroaniline, which rapidly binds to soil; propionic acid, which is further metabolized to carbon dioxide; 3,3',4,4'-tetrachloroazoxybenzene; and two isomeric forms of tetrachloroazobenzene (1).¹ Propanil's half-life in soil is less than 5 days (1).

2. ANALYTICAL METHODS

Capillary gas chromatography with a selective nitrogen–phosphorus detector may be used for the determination of propanil, following extraction with methylene chloride. Confirmation by a second capillary column of different polarity is strongly recommended.

¹ Also from Hazardous Substances Data Bank (HSDB), National Library of Medicine, Bethesda, MD.

PROPANIL IN DRINKING-WATER

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Water

Residues of less than 0.03 mg/litre were detected in 162 water samples collected from 16 rice fields treated with 0.4–2.8 kg of propanil per ha, 1–120 days after application (2). Propanil has only occasionally been detected in groundwater.

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Propanil and its metabolites do not appear to accumulate in tissues. Propanil is hydrolysed by hepatic acylamidase, forming 3,4-dichloroaniline and propionic acid. Six metabolites have been detected in urine (3). When propanil was fed to a cow, 1.4% of the total dose was recovered in the faeces, but none was detected in urine or milk.²

5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS

5.1 Acute exposure

Propanil is of moderate acute toxicity; the oral LD₅₀ is over 2500 mg/kg of body weight in the rat (1).

5.2 Short-term exposure

Groups of albino rats (10 per sex per dose) were given the technical product in doses of 100, 330, 1000, 3300, 10 000 or 50 000 mg/kg in the diet (equivalent to 5, 17, 50, 165, 500 or 2500 mg/kg of body weight per day) for 3 months. All the animals in the highest dose group died. There was an increase in polychromatophilia at dose levels of 330 mg/kg and higher as well as evidence of haemolytic anaemia at 3300 and 10 000 mg/kg. From this study, a NOAEL of 100 mg/kg (equivalent to 5 mg/kg of body weight per day) was identified (4).

5.3 Long-term exposure

Propanil was administered at concentrations of 0, 100, 400 or 1600 mg/kg in the diet to albino Wistar rats (25 per sex per dose) for 2 years. At 1600 mg/kg, rats exhibited increased mortality (males only), significant decreases in body weight, slightly lower haematocrit and haemoglobin values and changes in spleen to body weight ratio (females only). The NOAEL in this study was 400 mg/kg, equivalent to 20 mg/kg of body weight per day (4).

In a 2-year study, beagle dogs were given propanil at concentrations of 0, 100, 600 or 3000 (raised to 4000 at the start of the 5th week) mg/kg in the diet. Significantly

² HSDB, National Library of Medicine, Bethesda, MD.

decreased body weight gains were evident at the highest dose level. No other effects attributable to propanil were observed (4).

5.4 Reproductive and developmental toxicity

Wistar rats administered technical-grade propanil in the diet (0, 100, 300 or 1000 mg/kg) for 11 weeks before mating and pregnancy did not exhibit any alterations in reproductive parameters (3).

5.5 Mutagenicity and related end-points

Propanil was inactive in *in vitro* tests on gene mutation, mitotic recombination and repair and damage of DNA in prokaryotic and eukaryotic cells (4,5). It gave results that were essentially negative in the cytogenetic test on mice (induction of structural chromosomal aberrations) (4,6) and positive in radical apex barley cells (7). Its metabolite 3,3',4,4'-tetrachloroazobenzene (TCAB) induces gene mutations in bacteria and fungal cells, as well as DNA repair synthesis in hepatic cultures in the rat (4,5,8).

5.6 Carcinogenicity

In a study in which groups of 50 Wistar rats were given oral propanil doses of 100, 400 or 1600 mg/kg for 24 months, histopathological tests did not reveal any carcinogenic effects. However, this study was limited and does not allow the evaluation of the carcinogenic potential of propanil (4).

6. EFFECTS ON HUMANS

The probable oral lethal dose is 0.5–5 g/kg of body weight. Exposure produces local irritation and central nervous system depression. Ingestion causes local irritation with a burning sensation in the mouth, oesophagus and stomach, gagging, coughing, nausea and vomiting, followed by headache, dizziness, drowsiness and confusion.³

Workers from a pesticide plant who were exposed to the propanil metabolite 3,4-dichloroaniline showed signs of methaemoglobinaemia. Of the 28 workers exposed to 3,4-dichloroaniline and propanil, 17 showed signs of chloracne, which is attributed to the presence of the contaminants TCAB or 3,3',4,4'-tetrachloroazoxybenzene (9).

7. CONCLUSIONS

Propanil is not persistent, being easily transformed under natural conditions to several metabolites. Two of these metabolites, 3,4-dichloroaniline and TCAB, are more toxic and more persistent than the parent compound. Although used in a number of countries, propanil has only occasionally been detected in groundwater.

³ HSDB, National Library of Medicine, Bethesda, MD.

PROPANIL IN DRINKING-WATER

Although a health-based value for propanil can be derived, this has not been done, because it is readily transformed into metabolites that are more toxic; therefore, a guideline value for the parent compound is considered inappropriate, and there are inadequate data on the metabolites to derive a guideline value for them. Authorities should consider the possible presence in water of more toxic environmental metabolites.

8. REFERENCES

1. Worthing CR, ed. *The pesticide manual*, 9th ed. Farnham, British Crop Protection Council, 1991.
2. Cabras P et al. Herbicide residues in waste waters from ricefields. *Pesticide Science*, 1983, 14:130–134.
3. US National Research Council. *Drinking water and health*. Washington, DC, 1977.
4. Rohm and Haas Co. *Project summary 600/53-83-097*. Philadelphia, PA, 1983–1984 (registration documents submitted to the Italian Ministry of Health).
5. Waters MD et al. Study of pesticide genotoxicity. *Basic Life Science*, 1982, 21:275–326.
6. Pilinskaja MA et al. Pervicnaja ocenka citogeneticeskoj aktivnosti i potencial'noj mutagennoj opasnosti 22 pesticidov. [Primary evaluation of the cytogenetic activity and potential mutagenic hazard of 22 pesticides.] *Citologija i genetika*, 1980, 14(6):41–47 (English abstract).
7. Das K et al. Cytological aberrations induced by Lasso, Machete & Stam F-34 in barley *Hordeum vulgare*. *Indian Journal of Experimental Biology*, 1978, 16:446–449.
8. Gilbert P et al. Genetic effects of chlorinated anilines and azobenzenes on *Salmonella typhimurium*. *Archives of Environmental Contamination and Toxicology*, 1980, 9(5):533–541.
9. Morse DL et al. Propanil-chloracne and methomyl toxicity in workers of a pesticide manufacturing plant. *Clinical Toxicology*, 1979, 15(1):13–21.