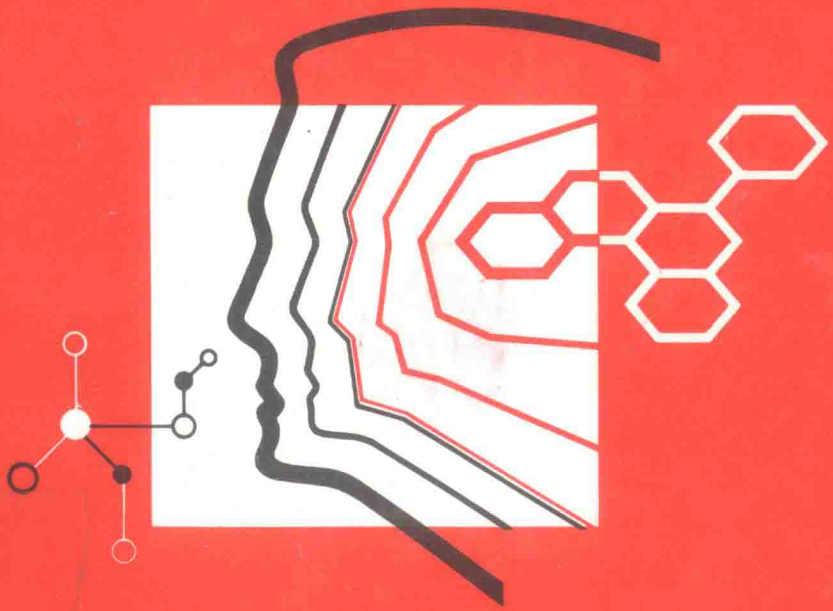
IPCS

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

UNEP

Environmental Health Criteria 216

Disinfectants and Disinfectant By-products



IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
A cooperative agreement among UNEP, ILO, FAO, WHO, UNIDO and OECD

WORLD HEALTH ORGANIZATION

Environmental Health Criteria 216

DISINFECTANTS AND DISINFECTANT BY-PRODUCTS

First draft prepared by G. Amy, University of Colorado, Boulder, Colorado, USA; R. Bull, Battelle Pacific Northwest Laboratory, Richland, Washington, USA; G.F. Craun, Gunther F. Craun and Associates, Staunton, Virginia, USA; R.A. Pegram, US Environmental Protection Agency, Research Triangle Park, North Carolina, USA; and M. Siddiqui, University of Colorado, Boulder, Colorado, USA

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

World Health Organization
Geneva, 2000

The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organisation (ILO) and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

WHO Library Cataloguing-in-Publication Data

Disinfectants and disinfectant by-products.

(Environmental health criteria ; 216)

1.Disinfectants - chemistry 2.Disinfectants - toxicity 3.Drinking water 4.Risk assessment 5.Epidemiologic studies I.Series

ISBN 92 4 157216 7 (NLM Classification: QV 220)
ISSN 0250-863X

Printed in Finland
2000/13145 – Vammala – 5000

NOTE TO READERS OF THE CRITERIA MONOGRAPHS

Every effort has been made to present information in the criteria monographs as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria monographs, readers are requested to communicate any errors that may have occurred to the Director of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case postale 356, 1219 Châtelaine, Geneva, Switzerland (telephone no. + 41 22 – 9799111, fax no. + 41 22 – 7973460, E-mail irptc@unep.ch).

Environmental Health Criteria

PREAMBLE

Objectives

In 1973, the WHO Environmental Health Criteria Programme was initiated with the following objectives:

(i) to assess information on the relationship between exposure to environmental pollutants and human health, and to provide guidelines for setting exposure limits;

(ii) to identify new or potential pollutants;

(iii) to identify gaps in knowledge concerning the health effects of pollutants;

(iv) to promote the harmonization of toxicological and epidemiological methods in order to have internationally comparable results.

The first Environmental Health Criteria (EHC) monograph, on mercury, was published in 1976, and since that time an ever-increasing number of assessments of chemicals and of physical effects have been produced. In addition, many EHC monographs have been devoted to evaluating toxicological methodology, e.g., for genetic, neurotoxic, teratogenic and nephrotoxic effects. Other publications have been concerned with epidemiological guidelines, evaluation of short-term tests for carcinogens, biomarkers, effects on the elderly and so forth.

Since its inauguration, the EHC Programme has widened its scope, and the importance of environmental effects, in addition to health effects, has been increasingly emphasized in the total evaluation of chemicals.

The original impetus for the Programme came from World Health Assembly resolutions and the recommendations of the 1972 UN Conference on the Human Environment. Subsequently, the work became an integral part of the International Programme on Chemical

Safety (IPCS), a cooperative programme of UNEP, ILO and WHO. In this manner, with the strong support of the new partners, the importance of occupational health and environmental effects was fully recognized. The EHC monographs have become widely established, used and recognized throughout the world.

The recommendations of the 1992 UN Conference on Environment and Development and the subsequent establishment of the Intergovernmental Forum on Chemical Safety with the priorities for action in the six programme areas of Chapter 19, Agenda 21, all lend further weight to the need for EHC assessments of the risks of chemicals.

Scope

The criteria monographs are intended to provide critical reviews on the effects on human health and the environment of chemicals and of combinations of chemicals and physical and biological agents. As such, they include and review studies that are of direct relevance for the evaluation. However, they do not describe *every* study carried out. Worldwide data are used and are quoted from original studies, not from abstracts or reviews. Both published and unpublished reports are considered, and it is incumbent on the authors to assess all the articles cited in the references. Preference is always given to published data. Unpublished data are used only when relevant published data are absent or when they are pivotal to the risk assessment. A detailed policy statement is available that describes the procedures used for unpublished proprietary data so that this information can be used in the evaluation without compromising its confidential nature (WHO (1990) Revised Guidelines for the Preparation of Environmental Health Criteria Monographs. PCS/90.69, Geneva, World Health Organization).

In the evaluation of human health risks, sound human data, whenever available, are preferred to animal data. Animal and *in vitro* studies provide support and are used mainly to supply evidence missing from human studies. It is mandatory that research on human subjects is conducted in full accord with ethical principles, including the provisions of the Helsinki Declaration.

The EHC monographs are intended to assist national and international authorities in making risk assessments and subsequent risk management decisions. They represent a thorough evaluation of risks and are not, in any sense, recommendations for regulation or standard setting. These latter are the exclusive purview of national and regional governments.

Content

The layout of EHC monographs for chemicals is outlined below.

- Summary — a review of the salient facts and the risk evaluation of the chemical
- Identity — physical and chemical properties, analytical methods
- Sources of exposure
- Environmental transport, distribution and transformation
- Environmental levels and human exposure
- Kinetics and metabolism in laboratory animals and humans
- Effects on laboratory mammals and *in vitro* test systems
- Effects on humans
- Effects on other organisms in the laboratory and field
- Evaluation of human health risks and effects on the environment
- Conclusions and recommendations for protection of human health and the environment
- Further research
- Previous evaluations by international bodies, e.g., IARC, JECFA, JMPR

Selection of chemicals

Since the inception of the EHC Programme, the IPCS has organized meetings of scientists to establish lists of priority chemicals for subsequent evaluation. Such meetings have been held in: Ispra, Italy, 1980; Oxford, United Kingdom, 1984; Berlin, Germany, 1987; and North Carolina, USA, 1995. The selection of chemicals has been based on the following criteria: the existence of scientific evidence that the substance presents a hazard to human health and/or the environment; the possible use, persistence, accumulation or degradation of the

substance shows that there may be significant human or environmental exposure; the size and nature of populations at risk (both human and other species) and risks for the environment; international concern, i.e., the substance is of major interest to several countries; adequate data on the hazards are available.

If an EHC monograph is proposed for a chemical not on the priority list, the IPCS Secretariat consults with the cooperating organizations and all the Participating Institutions before embarking on the preparation of the monograph.

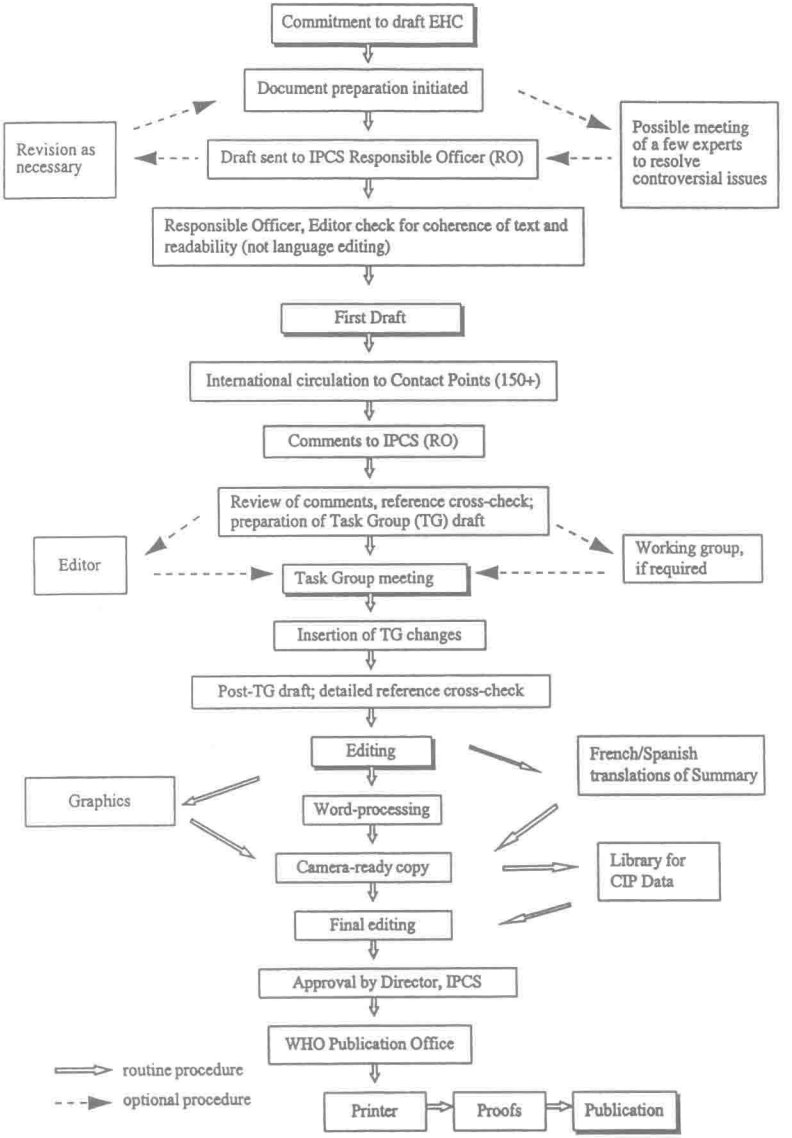
Procedures

The order of procedures that result in the publication of an EHC monograph is shown in the flow chart. A designated staff member of IPCS, responsible for the scientific quality of the document, serves as Responsible Officer (RO). The IPCS Editor is responsible for layout and language. The first draft, prepared by consultants or, more usually, staff from an IPCS Participating Institution, is based initially on data provided from the International Register of Potentially Toxic Chemicals and from reference databases such as Medline and Toxline.

The draft document, when received by the RO, may require an initial review by a small panel of experts to determine its scientific quality and objectivity. Once the RO finds the document acceptable as a first draft, it is distributed, in its unedited form, to well over 150 EHC contact points throughout the world who are asked to comment on its completeness and accuracy and, where necessary, provide additional material. The contact points, usually designated by governments, may be Participating Institutions, IPCS Focal Points or individual scientists known for their particular expertise. Generally, some four months are allowed before the comments are considered by the RO and author(s). A second draft incorporating comments received and approved by the Director, IPCS, is then distributed to Task Group members, who carry out the peer review, at least six weeks before their meeting.

The Task Group members serve as individual scientists, not as representatives of any organization, government or industry. Their function is to evaluate the accuracy, significance and relevance of the

EHC PREPARATION FLOW CHART



information in the document and to assess the health and environmental risks from exposure to the chemical. A summary and recommendations for further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting and by the need for a balanced geographical distribution.

The three cooperating organizations of the IPCS recognize the important role played by nongovernmental organizations. Representatives from relevant national and international associations may be invited to join the Task Group as observers. While observers may provide a valuable contribution to the process, they can speak only at the invitation of the Chairperson. Observers do not participate in the final evaluation of the chemical; this is the sole responsibility of the Task Group members. When the Task Group considers it to be appropriate, it may meet *in camera*.

All individuals who as authors, consultants or advisers participate in the preparation of the EHC monograph must, in addition to serving in their personal capacity as scientists, inform the RO if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a conflict of interest statement. Such a procedure ensures the transparency and probity of the process.

When the Task Group has completed its review and the RO is satisfied as to the scientific correctness and completeness of the document, the document then goes for language editing, reference checking and preparation of camera-ready copy. After approval by the Director, IPCS, the monograph is submitted to the WHO Office of Publications for printing. At this time, a copy of the final draft is sent to the Chairperson and Rapporteur of the Task Group to check for any errors.

It is accepted that the following criteria should initiate the updating of an EHC monograph: new data are available that would substantially change the evaluation; there is public concern for health or environmental effects of the agent because of greater exposure; an appreciable time period has elapsed since the last evaluation.

All Participating Institutions are informed, through the EHC progress report, of the authors and institutions proposed for the drafting

of the documents. A comprehensive file of all comments received on drafts of each EHC monograph is maintained and is available on request. The Chairpersons of Task Groups are briefed before each meeting on their role and responsibility in ensuring that these rules are followed.

WHO TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA FOR DISINFECTANTS AND DISINFECTANT BY-PRODUCTS

Members

Dr G. Amy, Department of Civil, Environmental, and Architectural Engineering, University of Colorado, Boulder, Colorado, USA

Mr J. Fawell, Water Research Centre, Marlow, Buckinghamshire, United Kingdom (***Co-Rapporteur***)

Dr B. Havlik, Ministry of Health, National Institute of Public Health, Prague, Czech Republic

Dr C. Nokes, Water Group, Institute of Environmental Science and Research, Christchurch, New Zealand (***Co-Rapporteur***)

Dr E. Ohanian, Office of Water/Office of Science and Technology, United States Environmental Protection Agency, Washington, DC, USA (***Chairman***)

Dr E. Soderlund, Department of Environmental Medicine, National Institute of Public Health, Torshov, Oslo

Secretariat

Dr J. Bartram, Water, Sanitation and Health Unit, Division of Operational Support in Environment Health, World Health Organization, Geneva, Switzerland

Dr R. Bull, Battelle Pacific Northwest Laboratory, Richland, Washington, USA

Mr G.F. Craun, Gunther F. Craun and Associates, Staunton, Virginia, USA

Dr H. Galal-Gorchev, Chevy Chase, Maryland, USA (***Secretary***)

Mr N. Nakashima, Assessment of Risk and Methodologies, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr R.A. Pegram, United States Environmental Protection Agency, Research Triangle Park, North Carolina, USA

Mr S.T. Yamamura, Water, Sanitation and Health Unit, Division of Operational Support in Environment Health, World Health Organization, Geneva, Switzerland

Representatives/Observers

Dr N. Drouot, Dept Toxicologie Industrielle, Paris, France (representing European Centre for Ecotoxicology and Toxicology of Chemicals)

Mr O. Hydes, Drinking Water Inspectorate, London, United Kingdom

Dr B.B. Sandel, Olin Corporation, Norwalk, Connecticut, USA (representing American Industrial Health Council/International Life Sciences Institute)

IPCS TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA FOR DISINFECTANTS AND DISINFECTANT BY-PRODUCTS

A WHO Task Group on Environmental Health Criteria for Disinfectants and Disinfectant By-products met in Geneva from 17 to 21 August 1998. Dr Peter Toft, Associate Director, IPCS, welcomed the participants on behalf of the three IPCS cooperating organizations (UNEP/ILO/WHO). The Task Group reviewed and revised the draft document and made an evaluation of risks for human health from exposure to certain disinfectants and disinfectant by-products.

The first draft of the chemistry section was prepared by G. Amy and M. Siddiqui, University of Colorado, Boulder, Colorado, USA; the toxicology section was prepared by R. Bull, Battelle Pacific Northwest Laboratory, Richland, Washington, USA, and R.A. Pegram, US Environmental Protection Agency, Research Triangle Park, North Carolina, USA; and the epidemiology section was prepared by G.F. Craun, Gunther F. Craun and Associates, Staunton, Virginia, USA.

The efforts of all who helped in the preparation and finalization of the monograph are gratefully acknowledged.

* * *

The preparation of the first draft of this Environmental Health Criteria monograph was made possible by the financial support afforded to IPCS by the International Life Sciences Institute.

A financial contribution from the United States Environmental Protection Agency for the convening of the Task Group is gratefully acknowledged.

ACRONYMS AND ABBREVIATIONS

ALAT	alanine aminotransferase
AP	alkaline phosphatase
ARB	atypical residual bodies
ASAT	aspartate aminotransferase
AWWA	American Water Works Association
BAN	bromoacetonitrile
BCA	bromochloroacetic acid/bromochloroacetate
BCAN	bromochloroacetonitrile
BDCA	bromodichloroacetic acid/bromodichloroacetate
BDCM	bromodichloromethane
BUN	blood urea nitrogen
bw	body weight
CAN	chloroacetonitrile
CHO	Chinese hamster ovary
CI	confidence interval
CoA	coenzyme A
C_{max}	maximum concentration
CMCF	3-chloro-4-(chloromethyl)-5-hydroxy-2(5H)-furanone
2-CP	2-chloropropionate
CPN	chloropropanone
CT	computerized tomography
CYP	cytochrome P450
DBA	dibromoacetic acid/dibromoacetate
DBAC	dibromoacetone
DBAN	dibromoacetonitrile
DBCM	dibromochloromethane
DBP	disinfectant by-product
DCA	dichloroacetic acid/dichloroacetate
DCAN	dichloroacetonitrile
DCPN	dichloropropanone
DHAN	dihaloacetonitrile
DOC	dissolved organic carbon
ECD	electron capture detector
ECG	electrocardiogram
EEG	electroencephalogram
EHEN	*N*-ethyl-*N*-hydroxyethylnitrosamine
EPA	Environmental Protection Agency (USA)

ESR	electron spin resonance
FAO	Food and Agriculture Organization of the United Nations
GAC	granular activated carbon
GC	gas chromatography
GGT	γ-glutamyl transpeptidase
GOT	glutamate–oxalate transaminase
GPT	glutamate–pyruvate transaminase
GSH	glutathione-SH
GST	glutathione-*S*-transferase
HAA	haloacetic acid
HAN	haloacetonitrile
HDL	high-density lipoprotein
HPLC	high-performance liquid chromatography
hprt	hypoxanthine phosphoribosyl transferase
IARC	International Agency for Research on Cancer
IC	ion chromatography
i.p.	intraperitoneal
IPCS	International Programme on Chemical Safety
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	median lethal dose
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LOAEL	lowest-observed-adverse-effect level
MA	3,4-(dichloro)-5-hydroxy-2(5H)-furanone
MBA	monobromoacetic acid/monobromoacetate
MCA	monochloroacetic acid/monochloroacetate
MNU	methylnitrosourea
MOR	mortality odds ratio
MRI	magnetic resonance imaging
MTBE	methyl *tert*-butyl ether
MX	3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone
NADP	nicotinamide adenine dinucleotide phosphate
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NOM	natural organic matter
NTP	National Toxicology Program (USA)
8-OH-dG	8-hydroxy-2-deoxyguanosine
OR	odds ratio

PAS	periodic acid/Schiff's reagent
PBPK	physiologically based pharmacokinetic model
PFBHA	*O*-(2,3,4,5,6-pentafluorobenzyl)-hydroxylamine
pK_a	log acid dissociation constant
PPAR	peroxisome proliferator activated receptor
PPRE	peroxisome proliferator responsive element
RR	relative risk
SCE	sister chromatid exchange
SD	standard deviation
SDH	sorbitol dehydrogenase
SE	standard error
SGOT	serum glutamate–oxaloacetate transaminase
SGPT	serum glutamate–pyruvate transaminase
SMR	standardized mortality ratio
SSB	single strand breaks
TBA	tribromoacetic acid/tribromoacetate
TBARS	thiobarbituric acid reactive substances
TCA	trichloroacetic acid/trichloroacetate
TCAN	trichloroacetonitrile
TCPN	trichloropropanone
TDI	tolerable daily intake
TGF	transforming growth factor
THM	trihalomethane
TOC	total organic carbon
TOX	total organic halogen
TPA	12-*O*-tetradecanoylphorbol-13-acetate
UDS	unscheduled DNA synthesis
UV	ultraviolet
UVA_{254}	UV absorbance at 254 nm
V_{max}	maximum rate of metabolism
WHO	World Health Organization