

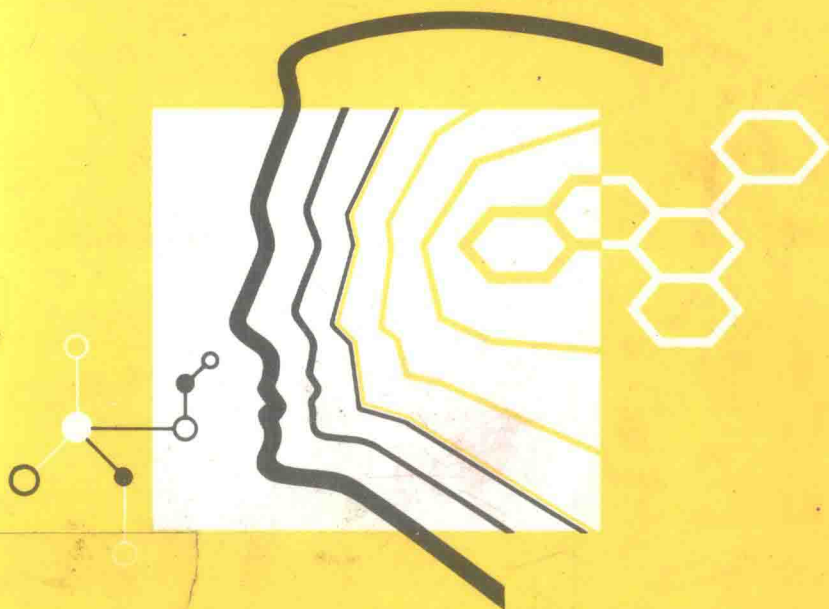
IPCS

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY



Environmental Health Criteria 214

Human Exposure Assessment



IOMC

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



WORLD HEALTH ORGANIZATION

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Environmental Health Criteria 214

HUMAN EXPOSURE ASSESSMENT

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The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (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, the United Nations Institute for Training and Research, 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.

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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).

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Environmental Health Criteria

P R E A M B L E

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 effect 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 only used 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 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.

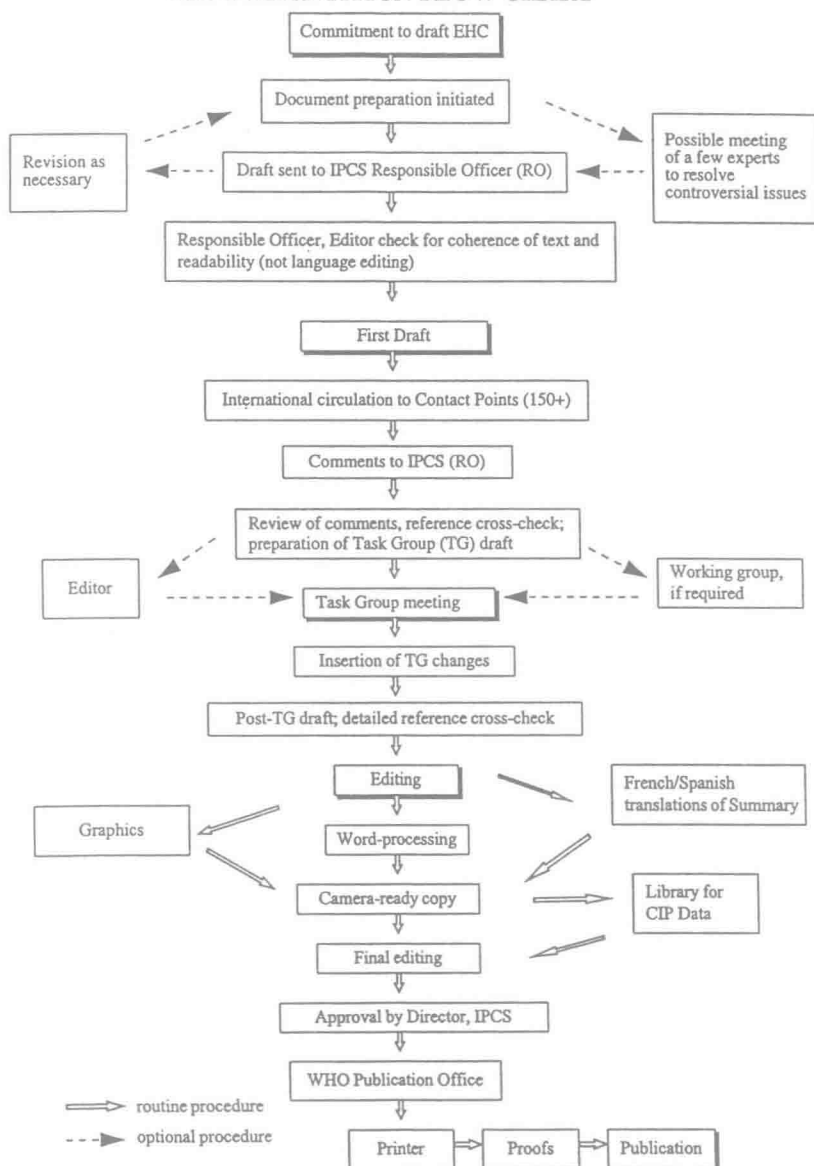
Procedures

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 reference data bases 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 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.

EHC PREPARATION FLOW CHART



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 only speak 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, it 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 HUMAN EXPOSURE ASSESSMENT

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ENVIRONMENTAL HEALTH CRITERIA FOR HUMAN EXPOSURE ASSESSMENT

A Task Group on the Environmental Health Criteria for Human Exposure Assessment met in Glion-sur-Montreux, Switzerland, from 16 to 20 February 1998. Dr M. Younes, IPCS, welcomed the participants on behalf of the Manager, IPCS, and the three IPCS cooperating organizations (UNEP/ILO/WHO). The Task Group reviewed and revised the final draft of the monograph. In preparation for the final draft a review meeting was held at the National Institute of Health Sciences (NIHS), Tokyo, from 17 to 19 July 1996.

The first draft was prepared by Dr D. L. MacIntosh, University of Georgia, USA and Professor J. D. Spengler, Harvard University, USA.

Dr K. Gutschmidt was responsible officer in IPCS for the overall scientific content of the monograph and the organization for the meetings, and Ms K. Lyle (Sheffield, United Kingdom) was responsible for the technical editing of the monograph.

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

ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
ADD	average daily dose
AI	acceptance intervals
ALAD	Δ -aminolaevulinic acid dehydratase
AMIS	Air Monitoring Information System
ANOVA	analysis of variance
AOAC	Association of Official Analytical Chemists
ASTM	American Society for Testing of Materials
CDF	chlorinated dibenzofurans; cumulative distribution function
CFU	colony-forming units
CI	confidence interval
DG18	dichloran 18% diglycerol agar
DVM	dust vacuum method
EDTA	ethylenediamine tetra-acetic acid
ELISA	enzyme-linked immunosorbent assays
EPS	extracellular polysaccharides
ETS	environmental tobacco smoke (exposure)
EU	endotoxin unit
FDA	US Food and Drug Administration
FFQ	food frequency questionnaire
GEMS	Global Environment Monitoring System
GerES	German Environmental Survey
GM	geometric mean
GSD	geometric standard deviation
HEAL	Human Exposure Assessment Location
HPLC	high-pressure liquid chromatography
HUD	US Department of Housing and Urban Development
IAEA	International Atomic Energy Agency
IAQ	internal air quality
ISEA	International Society of Exposure Analysis
ISO	International Organization for Standardization
LADD	lifetime average daily dose
LAL	<i>Limulus</i> amoebocyte lysate
LOD	limit of detection
LOQ	limit of quantification
LWW	Lioy-Weisel-Wainman
MAD	maximum allowable deviations
MCS	multiple chemical sensitivity
MDL	method detection limit
MEA	malt extract agar

NAAQS	National Ambient Air Quality Standard
NHEXAS	National Human Exposure Assessment Survey
NIOSH	National Institute for Occupational Safety and Health
NTA	nitriloacetic acid
OR	odds ratio
PAH	polycyclic aromatic hydrocarbons
PBPK	physiologically based pharmacokinetic (method)
PCB	polychlorinated biphenyls
PCDD	polychlorinated dibenzo- <i>p</i> -dioxin
PCP	pentachlorophenol
PDF	probability distribution function
PEM	personal exposure monitor
PM _n	particulate matter with aerodynamic diameter < <i>n</i> μm
PTEAM	particle total exposure assessment methodology
QA	quality assurance
QC	quality control
RAST	radioallergosorbent tests
RIA	radioimmunoassay
RSP	respirable particulate matter
SAM	stationary outdoor monitor
SBS	sick building syndrome
SD	standard deviation
SEM	scanning electron microscope
SIM	stationary indoor monitor
SOP	standard operating procedure
SVOC	semivolatile organic compound
TCCD	2,3,7,8-tetrachloro dibenzo- <i>p</i> -dioxin
TDS	US FDA Total Diet Study
TEQ	TCCD toxic equivalents
TSP	total suspended particulates
TWI	tolerable weekly intake
UNEP	United Nations Environment Programme
VOC	volatile organic compound
XRF	X-ray fluorescence

FOREWORD

The International Programme on Chemical Safety (IPCS), launched in 1980, is a joint collaborative programme of the International Labor Organization (ILO), the United Nations Environment Programme (UNEP), and the World Health Organization (WHO); WHO is the Administrating Organization of the Programme. The two main roles of the IPCS are to establish the scientific health and environmental risk assessment basis for safe use of chemicals (*normative function*) and to strengthen national capabilities for chemical safety (*technical cooperation*). In the field of methodology, the work of the IPCS aims at promoting the development, improvement, validation, harmonization and use of generally acceptable, scientifically sound methodologies for the evaluation of risks to human health and the environment from exposure to chemicals. The work encompasses the development of Environmental Health Criteria monographs on general principles of various areas of risk assessment covering various aspects related to risk assessment such as, in this publication, on exposure assessment.

The WHO and the World Meteorological Organization coordinate the assessment of climate, urban air and water pollution, and health status of populations. These measures provide the indicator of trends and status.

Until 1995, the basic source for internationally comparable urban air pollution data was the Global Environment Monitoring System (GEMS/Air) of UNEP and WHO. Started in 1974, shortly after the Stockholm Environment Conference, GEMS had built up a system that collected comparable ambient air pollution data in about 50 cities of 35 countries, varied in geography and income (UNEP/WHO, 1988, 1992). Typically, sulfur dioxide and total suspended particulates (TSP) had been monitored in three stations of each city, one each in industrial, commercial, and residential zones. Later, GEMS also collected monitoring data for carbon monoxide, nitrogen dioxide, and lead, and made emissions estimates for all five pollutants. The results were published periodically by GEMS, and also often appeared in other periodic international data sets, such as those of the World Bank (World Bank, 1992), the World Resources Institute (World Resources Institute, 1992), the United Nations (UN ESCAP, 1990) and UNEP itself (UNEP, 1991).

More recently, WHO created with the Air Management Information System (AMIS) the successor of GEMS/Air. Like GEMS/Air, AMIS

provides air quality data for major and megacities. Data on sulfur dioxide, nitrogen dioxide, carbon monoxide, ozone, black smoke, suspended particulate matter, PM₁₀, lead and others are available. AMIS also includes information on air quality management (WHO, 1997).

Much of what is known about contaminants in food, soils, water and air has become available through WHO and UNEP publications. For more than 20 years WHO/UNEP has been promoting an appreciation for improved assessments of human exposures through training sessions, workshops, demonstration projects, and published methodologies and reports. Through a series of WHO-sponsored studies in every populated continent, the principles of human exposure assessment have been illustrated for indoor and outdoor air pollutants, food contamination and water. In 1984, after some background reports (e.g., UNEP/WHO, 1982), WHO and UNEP conducted the Human Exposure Assessment Location (HEAL) Project, which facilitates research and information sharing among 10–15 institutions worldwide concerned with exposure assessment for a limited number of pollutants (Ozolins, 1989). Unfortunately, although providing important functions, the HEAL project has not had the mandate or anything approaching the resources required to actually make comparable international estimates of population exposures. HEAL projects, for the most part, have investigated exposures to conventional inorganic air pollutants such as carbon monoxide, nitrogen dioxide and general undifferentiated particle mass where inhalation is the primary route of exposures. However, the HEAL programme does offer examples of lead, cadmium and pesticide studies which illustrate multiple exposure pathways and demonstrate the necessity of extensive analytical training and quality programmes. An analytical quality control programme which involved all participating laboratories enabled reliable international comparisons of exposure despite differences in methodologies applied by the different laboratories.

Preceding this criteria document the UNEP, FAO and WHO have been actively advancing the concepts and methodologies for human exposures. GEMS/Air, GEMS/Water and GEMS/Food are establishing the uniformity among data collected worldwide to establish national and international status and trends. These efforts, together with others, such as the Codex Committee on Pesticide Residues, the several Joint FAO/WHO Consultations on food consumption, pesticide residues, veterinary drugs, additives and chemical contaminants, have been developing the basis of quantitative assessment of human exposures and