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Concise International Chemical Assessment Document 50

ELEMENTAL MERCURY AND INORGANIC MERCURY COMPOUNDS: HUMAN HEALTH ASPECTS

Please note that the pagination and layout of this web version are not identical to the printed CICAD

First draft prepared by Dr J.F. Risher, Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, Georgia, USA

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World Health Organization Geneva, 2003 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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FOREWORD

Concise International Chemical Assessment Documents (CICADs) are the latest in a family of publications from the International Programme on Chemical Safety (IPCS) — a cooperative programme of the World Health Organization (WHO), the International Labour Organization (ILO), and the United Nations Environment Programme (UNEP). CICADs join the Environmental Health Criteria documents (EHCs) as authoritative documents on the risk assessment of chemicals.

International Chemical Safety Cards on the relevant chemical(s) are attached at the end of the CICAD, to provide the reader with concise information on the protection of human health and on emergency action. They are produced in a separate peer-reviewed procedure at IPCS. They may be complemented by information from IPCS Poison Information Monographs (PIM), similarly produced separately from the CICAD process.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents undergo extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are provided as guidance only. The reader is referred to EHC 170.¹

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact IPCS to inform it of the new information.

Procedures

The flow chart on page 2 shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world — expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment. The IPCS Risk Assessment Steering Group advises the Coordinator, IPCS, on the selection of chemicals for an IPCS risk assessment based on the following criteria:

- there is the probability of exposure; and/or
- there is significant toxicity/ecotoxicity.

Thus, it is typical of a priority chemical that

- it is of transboundary concern;
- it is of concern to a range of countries (developed, developing, and those with economies in transition) for possible risk management;
- there is significant international trade;
- it has high production volume;
- it has dispersive use.

The Steering Group will also advise IPCS on the appropriate form of the document (i.e., EHC or CICAD) and which institution bears the responsibility of the document production, as well as on the type and extent of the international peer review.

The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes primary review by IPCS to ensure that it meets the specified criteria for CICADs.

¹ International Programme on Chemical Safety (1994) Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits. Geneva, World Health Organization (Environmental Health Criteria 170) (also available at http://www.who.int/pcs/).

CICAD PREPARATION FLOW CHART





- \$ above + specialized experts
- above + spectalized expertsabove + consultative group

The second stage involves international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers' comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers' comments. At any stage in the international review process, a consultative group may be necessary to address specific areas of the science.

The CICAD Final Review Board has several important functions:

- to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
- to verify that the peer reviewers' comments have been addressed appropriately;
- to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
- to approve CICADs as international assessments.

Board members serve in their personal capacity, not as representatives of any organization, government, or industry. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.

1. EXECUTIVE SUMMARY

The source document upon which this CICAD is based is the *Toxicological profile for mercury (update)*, published by the Agency for Toxic Substances and Disease Registry of the US Department of Health and Human Services (ATSDR, 1999). Data identified as of January 1999 were considered in the source document. Data identified as of November 1999 were considered in the preparation of this CICAD. Information on the availability and the peer review of the source document is presented in Appendix 1. Information on the peer review of this CICAD is presented in Appendix 2. This CICAD was considered at a meeting of the Final Review Board, held in Helsinki. Finland, on 26-29 June 2000 and approved as an international assessment by mail ballot of the Final Review Board members on 27 September 2002. Participants at the Final Review Board meeting are presented in Appendix 3. The International Chemical Safety Cards for elemental mercury and six inorganic mercury compounds, produced by the International Programme on Chemical Safety, have also been reproduced in this document.

Mercury is a metallic element that occurs naturally in the environment. There are three primary categories of mercury and its compounds: elemental mercury, which may occur in both liquid and gaseous states; inorganic mercury compounds, including mercurous chloride, mercuric chloride, mercuric acetate, and mercuric sulfide; and organic mercury compounds. Organic mercury compounds are outside the scope of this document.

Elemental mercury is the main form of mercury released into the air as a vapour by natural processes.

Exposure to elemental mercury by the general population and in occupational settings is primarily through inhaling mercury vapours/fumes. The average level of atmospheric mercury is now approximately 3– 6 times higher than the level estimated for preindustrial automobile. No reliable data are currently available to determine the extent of such exposure.

Analytical methods exist for the specific assessment of organic and inorganic mercury compounds; however, most available information on mercury concentrations in environmental samples and biological specimens refers to total mercury.

Intestinal absorption varies greatly among the various forms of mercury, with elemental mercury being the least absorbed form (<0.01%) and only about 10% of inorganic mercury compounds being absorbed. For elemental mercury, the main route of exposure is by inhalation, and 80% of inhaled mercury is retained. Inorganic mercury compounds may be absorbed through the skin in toxicologically relevant quantities.

Elemental mercury is lipid soluble and easily penetrates biological membranes, including the blood-brain barrier. Metabolism of mercury compounds to other forms of mercury can occur within the tissues of the body. Elemental mercury can be oxidized by the hydrogen peroxide-catalase pathway in the body to its inorganic divalent form. After exposure to elemental mercury or inorganic mercury compounds, the main route of excretion is via the urine. Determination of concentrations in urine and blood has been extensively used in the biological monitoring of exposure to inorganic forms of mercury; hair mercury levels do not reliably reflect exposure to elemental mercury or inorganic mercury compounds.

Neurological and behavioural disorders in humans have been observed following inhalation of elemental mercury vapour, ingestion or dermal application of inorganic mercury-containing medicinal products, such as teething powders, ointments, and laxatives, and ingestion of contaminated food. A broad range of symptoms has been reported, and these symptoms are qualitatively similar, irrespective of the mercury compound to which one is exposed. Specific neurotoxic symptoms include tremors, emotional lability, insomnia, memory loss,

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