# CHEMICAL RISK ASSESSMENT AT THE INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

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## ABSTRACT

*Sustainable development is one of the central themes of the work of the World Health Organization; chemical safety is one of its important components. For more than 25 years, WHO has had specialized units for assisting member countries in dealing with their problems in chemical safety. For one of the units involved, International Programme on Chemical Safety, a reorientation is in progress to make best use of existing resources, and to prioritise the work to optimally correspond to the needs of the member countries. The risk assessment work of IPCS, and specifically, the work on chromium and chromium compounds, are discussed.*

## 1. INTRODUCTION

The sensitivity of humans to chemical effects varies, but the variation between individuals is usually as large as that between populations in different locations. The hazard identification and characterization are thus similar globally - while the other corner stone of risk characterization and management, exposure, may vary widely depending the industry and technology applied.

Prudent risk management decisions often require investments in short term, and bring economical gains in long term only. Thus when such decisions are influenced by organisations with a vested interest, short-term implications may become overemphasized. Only independent risk assessment is likely to provide sustainable risk management decisions.

Through work of independent expert groups, IPCS aims at providing assessments of the effects of chemicals on human health and environment; these can then be used, combined with relevant information on exposure level and pattern, in making informed risk management decisions.

## 2. INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

In World Health Organization, assessment of chemical safety on the global level is performed mainly in the Programme on Chemical Safety, and in the International Agency for Research on Cancer, the latter concentrating on qualitative assessment of the carcinogenicity of chemical and other exposures.

International Programme on Chemical Safety is a collaborative effort of the World Health Organization (WHO), International Labour Organization (ILO), and United Nations Environment Programme (UNEP), and was founded in 1980. At present, IPCS is reorienting its work to fully adapt to the changes in the world of chemical safety. Its mission has been newly revised to be that *IPCS tools and knowledge-bases contribute to the reduction of the global burden of disease related to chemicals.* The client of IPCS comprise countries, industry, non-government organisations (NGOs), government organisations, academia, research organization.

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IPCS activities have been crystallised into four elements:
1) Risk assessment, including harmonisation of methodology and support of normative functions used to establish guidance values (such as the WHO drinking-water and air-quality guidelines).
2) Poisons information, prevention and management, including epidemiology, follow-up of cases and collection and use of aggregated sets of human toxicology data.
3) Chemical incidents and emergencies, including public health preparedness, response, prevention and surveillance,
4) Capacity-building support, for the above activities. (Note that capacity-building activities are built into each of the other three elements).

The *intermediate goal* for the element one is to *Establish the basis for the assessment of risk through collecting and establishing the evidence for chemicals-related adverse effects, including the identification and quantification of chemical-related problems and determining the quality of the evidence, including risk assessments*, and the desired outcomes (impact on country level) are:

- Countries are better able to characterize and communicate risk information based on the clarity of presentation of IPCS outputs.
- IPCS outputs drive country-specific activities to eliminate/minimize exposure to hazardous chemicals.
- Countries are better able to measure progress towards chemical management goals using environmental health and occupational health indicators identified and characterized by IPCS.
- Academia/research organisations set priorities based on research needs identified in risk assessment products of IPCS.

The outputs, by which IPCS strives to reach these goals are:

- Chemical risk assessments (including Concise International Assessment Documents (CICADs), International Chemical Safety Cards (ICSCs) and Poisons Information Monographs (PIMs).
- Chemical risk assessments for Codex Alimentarius and Member States (JMPR, JECFA, Methodology for Evaluation of Chemicals in Food).
- Chemical risk assessments for WHO guidelines (including Air/Water Quality) and for Persistent Organic Pollutants (POPs).
- Methodologies for chemical risk assessments (including emerging health risks and harmonisation).

Other items in the first category above (risk evaluation of priority chemicals) are Environmental Health Criteria Documents (EHC), Health and Safety Guides (HSG), WHO Recommended Classification of Pesticides by Hazard, and Pesticide Data Sheets.

Environmental Health Criteria Documents are comprehensive documents on hazards and risks of chemicals to human health and the environment, and are designed for scientific experts responsible for giving advice to relevant authorities on suitable policies for ensuring safe use of chemicals. The International Chemical Safety Cards summarise essential health and safety information on chemicals and provide information for use at shop-floor level in factories, agriculture and other work places. The Concise International Chemical Assessment Documents are characterisations of hazard and dose-response with a sample risk characterisation intended for use in risk management at national but also on factory level.

IPCS Risk and Hazard assessments are based on the work of internationally acknowledged experts with a global participation. In the process, special attention is paid to avoiding potential conflicts of interest, and extensive peer review is an integral feature. The process is fully transparent and based on publicly available process and assessment guidelines.

IPCS Risk and Hazard assessment documents are available free of charge on the web at http://www.who.int/pcs/ inchem.htm (and the most recent ones as Acrobat pdf files at http://www.who.int/pcs/ra_main.html ), and at nominal cost in printed form (bookorders@who.int). They are further available on CDROM from the Canadian Centre for Occupational Safety and Health at clientservices@ccohs.ca

## 3. IPCS PRIORITY SETTING

Prerequisites for a chemical to be included in IPCS risk assessment programmes are, that there is probability of exposure (of humans or environment), and of significant toxicity or ecotoxicity. Thus a priority chemical typically is of transboundary concern, is of concern to a range of countries: developed, developing, in transition; is significantly traded internationally; has high production volume; has dispersive use; and is toxic and/or ecotoxic and/or accumulates in the body or environment. It should be noted that in IPCS view, mere production volume does not necessarily reflect exposure, and that chemical exposures without quantitatively important effects on a global basis, may be still very significant locally or for smaller groups of people. In setting priorities, IPCS also considers it important that sufficient information is available to perform a meaningful hazard / risk assessment, and that no other international assessment has been recently accomplished or is in process.

At its web site, http://www.who.int/pcs/ra_site/docs/RAdoc__proposal.htm, IPCS invites proposals for risk assessments.

## 4. CICAD SPECIAL FEATURES

CICADs are based on a high-quality peer-reviewed recent national /regional risk assessment document. The quality is checked in an extensive international peer review, adjusted to the contents of the document. Proper treatment of the peer review comments is verified in a meeting of a Final Review Board. Controversial issues are solved in *ad hoc* consultative groups.

CICADs contain hazard and risk identification, dose-response analysis and sample risk characterisation. In a CICAD, key end points and studies are dealt in depth: the purpose is that the reader can verify the adequacy of the basis of the hazard and risk characterisation, and follow the logic of selecting the key end point and the key studies. CICADs are concise on non-key end points and studies: they are either described very briefly or a reference is given to the source document only.

CICADs are based on recent source document. This makes it possible to produce a CICAD largely based on work already performed, and the process is cost-effective. Furthermore, a co-ordinating group between The Organisation of Economical Co-operation and Development (OECD) chemical programme ensures that duplication of effort is minimised.

## 5. PREPARATION OF A CICAD

A scheme for the preparation of a CICAD, and the role of the steering group in this process, are given in Fig 1. A description of the process and of the roles and responsibilities of those involved, is available (http://www.who.int/pcs/ra_main.html). A risk assessment steering group, an international group of experts in risk assessment, guides IPCS risk assessment work.

A proposal for an IPCS risk assessment is considered by the steering group, who advise IPCS on whether the criteria of priority are fulfilled, and also investigates whether there is a need to proceed to an IPCS assessment, *i.e.*, there is no adequate international risk assessment recently finalised, or in preparation. The steering group also advises on what would be the appropriate form of the document, i.e., CICAD or other, and suggests an author/author organisation.

The first draft document goes through an acceptance review by the secretariat, is revised if needed, and is sent to international peer review. This review comprises the IPCS focal points, plus additional *ad hoc* reviewers, as required. The comments received are tabulated, the authors consider them individually, and make appropriate changes in the document, and provide an explanation to changes made / points kept unchanged.

A Final Review Board is then convened to verify that the author has dealt with the peer review comments adequately, and when necessary, to give advice on how the possible questions that are still open, should be solved. The FRB also considers comments from stakeholders, knowing, which comments come from independent peer reviewers, and which come from individuals /organisations with a conflict of interest.

The final review board then eventually approves the document as an international assessment; the document is edited, and printed and made available on the web.

The first final review board meeting was held in November 1996, and at present, that is, May 2003, altogether 47 CICADs have appeared in printed form, nine are in press (summaries available on the web), and eight more are being reviewed (expected to be available on the web early 2004).

## 6. EVALUATION OF CHROMIUM COMPOUNDS AT WHO AND IPCS

The carcinogenicity of chromium and chromium compounds have been evaluated at IARC on several occasions, in 1972, 1979, 1982, 1982, 1987, 1990, and most recently, in 1999.

In 1990[1], the overall conclusion was that:

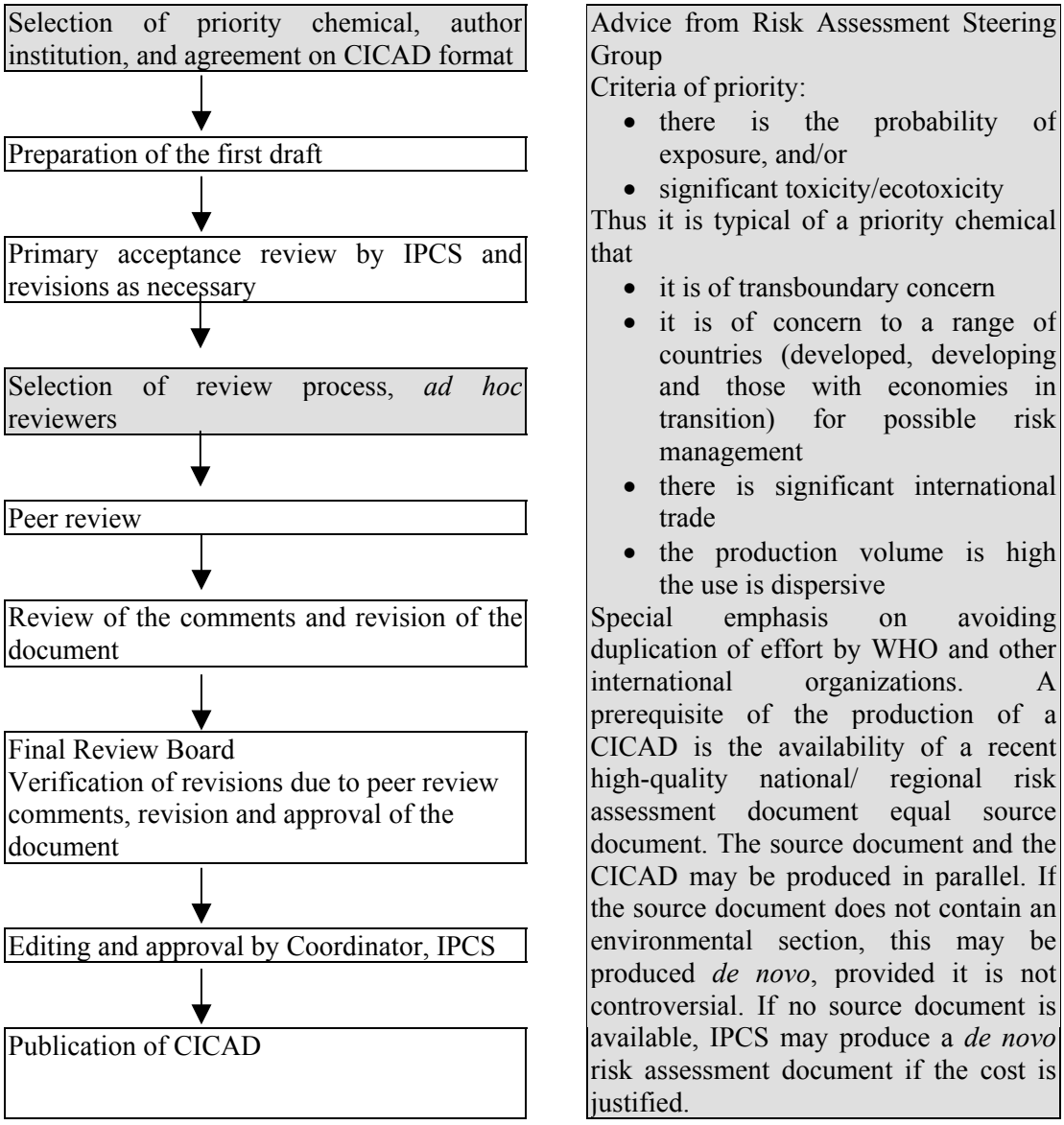
1) Chromium (VI) is carcinogenic to humans. This evaluations were based on sufficient evidence in humans for the carcinogenicity of chromium (VI) compounds as encountered in the chromate production, chromate pigment production and chromium plating industries, as well as on sufficient evidence in experimental animals for the carcinogenicity of calcium chromate, zinc chromates, strontium chromate and lead chromates, and limited evidence for the carcinogenicity of chromium trioxide (chromic acid) and sodium dichromate;
2) Metallic chromium and chromium(III)compounds are not classifiable as to their carcinogenicity to humans, based on inadequate evidence in humans and in experimental animals.

IARC made the above overall evaluation on chromium(VI)compounds on the basis of the combined results of epidemiological results of epidemiological studies, carcinogenicity studies in experimental animals, and several types of other relevant data which support the underlying concept that chromium(VI) ions generated at critical sites in the target cells are responsible for the carcinogenic action observed.

In 1999 IARC[2] separately assessed the carcinogenicity of surgical implants, and among them chromium and chromium containing alloys. The overall evaluation was that implanted foreign bodies of metallic chromium, chromium-based alloys and stainless steel [and several others] are not classifiable as to their carcinogenicity in humans. These evaluations were based on inadequate evidence of carcinogenicity both in humans and experimental animals. An alloy powder containing 66-67% nickel, 13-16% chromium and 7% iron was classified as possibly carcinogenic to humans, based on sufficient evidence of carcinogenicity in experimental animals

IPCS evaluated the effects of chromium compounds on human health and environment in 1988 - no summary is presented here, as the document is so old (and is available on the web at http://www.inchem.org/ documents/ehc/ehc/ehc61.htm). IPCS has just started to the preparation of a Concise International Chemical Assessment Document on trivalent chromium compounds, which will be based on a the Agency for Toxic Substances Registry (ATSDR) toxicity profile[3], and another document, prepared by the Finnish Institute of Occupational Health.

Figure 1. CICAD preparation flow-chart.




## 7. REFERENCES

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