HUMAN HEALTH RISK ASSESSMENT FOR METALLIC CHROMIUM AND TRIVALENT CHROMIUM IN ACCORDANCE WITH EUROPEAN UNION LEGISLATION

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ABSTRACT

*The Unit of Toxicological Risk Assessment of the Finnish Institute of Occupational Health (FIOH) is conducting a 'Health Risk Assessment for Metallic Chromium and Trivalent Chromium' under the sponsorship of the International Chromium Development Association (ICDA) and the International Stainless Steel Forum (ISSF). This risk assessment will be conducted in accordance with the current European Union legislation in force (Council Regulation 793/93/EEC, Commission Regulation 1488/94/EEC, Dir. 67/548/EEC), but also to meet the regulatory obligations as set out in the European Commission REACH legislation proposal (Consultation Document, the **R**egistration, **E**valuation, **A**uthorisation and Restrictions of **CH**emicals). Further aims include outlining the criteria for the setting of occupational exposure limits for metallic chromium and trivalent chromium compounds.*

Human Health Risk Assessment according to the current legislation shall entail hazard identification of the toxic end points (acute toxicity, irritation/corrosivity, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity, reproductive toxicity) including, as appropriate, dose (concentration) - response assessment, and derivation of the N(L)OAELs (No (Lowest) Observed Adverse Effect Level) and/or DNELs (Derived No Effect Level). Exposure assessments for workers, consumers and humans exposed via the environment take into account all the known intended uses. Risk characterisation will compare the typical and/or reasonable worst case exposure estimates to the N(L)OAELs or DNELs to determine Margins of Safety (MOS) for all human populations by each exposure scenario and type of effect, followed by conclusions about the presence or absence of risk.

Although all of the key elements of existing legislation remain in REACH, the principal change is that, the burden of proof will be transferred from the member state authorities to industry. The new proposed format of Chemical Safety Report (CSR) will include Risk Management Measures (RMM) as an essential part of the report in addition to the risk assessment. The RMM plays a role in the evaluation of further testing needs and advocating reasons for possible waiwer of requirements.

The research programme started in March 2002 and will be completed within the time frame of two years.

1. INTRODUCTION

In the European Union the Existing Substances Regulation (ESR) 793/93/EEC [1] has been in force since 1993 and the 'mother directive' Dir. 67/548/EEC [2] since 1967. Council Regulation 793/93/EEC [1] gives the framework for risk assessment of 140 priority substances (Com Regs. 1179/94 [3], 2268/95 [4], 143/97 [5], 2364/2000 [6]), among which chromium (VI) compounds (chromium trioxide, sodium chromate, sodium dichromate, ammonium dichromate, potassium dichromate) were included (Com Reg. 143/97 [5]. The Risk Assessment Report can be found in the Internet site of the European Chemicals Bureau (http://jrc.ecb.it) [7].

The Unit of Toxicological Risk Assessment of the Finnish Institute of Occupational Health (FIOH) is conducting a 'Health Risk Assessment for Metallic Chromium and Trivalent Chromium' under the sponsorship of the International Chromium Development Association (ICDA) and the International Stainless Steel Forum (ISSF).

This risk assessment will be performed according to the current European Union legislation in force, but also to meet the regulatory obligations as set out in the European Union Commission REACH legislation proposal (Consultation Document, the **R**egistration, **E**valuation, **A**uthorisation and Restrictions of **CH**emicals (later 'REACH'), Volumes I-VII (http://europa.eu.int/comm/enterprise/chemicals/chempol/whitepaper/reach.htm [8]). This new proposed legislation REACH [8] will be reviewed as regards the technical requirements for preparing the required Chemicals Safety Report (CSR).

Further aims are to recommend classification and labelling, and the setting of occupational exposure limits for metallic chromium and trivalent chromium species.

The research programme was started in March 2002 and will be completed within the time frame of two years.

2. EUROPEAN UNION EXISTING SUBSTANCES LEGISLATION

The risk assessment of metallic chromium and trivalent chromium compounds will be carried out according to the current existing substances legislation Council Reg. 793/93/EEC [1] and Commission Reg. 1488/94/EEC [9] as well as using the European Union recently revised Technical Guidance Document on Risk Assessment (TGD, 2003 [10]).

Because the risk assessment will be carried out as described, it will be easily transferred to the new report format of Chemicals Safety Report (later 'CSR') which is described in the future REACH [8] requirements specifying the obligations to manufacturers and importers of the substance(s).

Human Health Risk Assessment according to the current legislation shall entail hazard identification including, as appropriate, dose (concentration) - response (effects) assessment, exposure assessment for workers, consumers and humans exposed via the environment and risk characterisation for all these populations by different use categories and scenarios separately.

Although all of the key elements of existing legislation remain in REACH, the principal change is that the burden of proof will be transferred from member state authorities to industry. The new proposed format of CSR will include Risk Management Measures (RMM) as an essential part of the report in addition to the risk assessment. The RMM plays a role in the evaluation of further testing needs and advocating reasons for possible waiver of requirements.

According to the current legislation in force, the classification and labelling of the substance(s) will be reviewed by the EU Working Group on Classification and Labelling of Dangerous Substances in accordance with the revised criteria set out in the 28th ATP of the Dir 67/548/EEC i.e. Directive 2001/59/EC [11]. This classification is also an important part of the future REACH system, in which the industry is obliged to classify the substance in the CSR.

A duty to communicate information on substance(s) in the supply chain to the immediate downstream user(s) is one of the new obligations of REACH. This information package is defined and includes the safety data sheets (SDS) and the chemical safety reports (CSR). REACH encourages formation of industry consortia with a view to share data and produce joint submission of information regarding the intrinsic properties of substances, but excluding confidential business information of the registrants. Avoidance of unnecessary animal testing is one of the key objectives in the proposed REACH legislation.

3. RISK ASSESSMENT

The risk assessment will use the methodologies outlined in the revised Technical Guidance Document (TGD, 2003).

3.1 Special challenge to evaluate trivalent chromium compounds

Metallic chromium and trivalent chromium compounds are a special challenge for risk assessment. There are several trivalent chromium compounds: chromite, chromium hydroxide sulphate, chromium acetate (hydrate), chromium chloride (hexahydrate), chromium nitrate (7.5 hydrate, nonahydrate), chromium hydroxide, chromic oxide, chromium perchlorate, chromium phosphate (dihydrate), chromium potassium sulphate, (dodecahydrate), chromium carbide, chromium boride and chromium picolinate.

Among these the most relevant ones: chromium, chromic oxide and basic chromium sulphate will be discussed in more detail in the report.

Trivalent chromium is an essential trace metal for human health. Its role in the human physiology will be reviewed and discussed in the report and taken into account in the final Risk Characterisation.

Reference to a specific chemical species of chromium is not always clear in all exposure situations especially as both Cr(III) and Cr(VI) may be involved, and therefore it is not always possible to draw clear cut conclusions about the link between exposure and harmful effects.

3.2 Exposure

Human exposure must be assessed for workers, consumers and humans exposed via the environment according to the current legislation by each use category. In the proposed REACH legislation, special obligation is given to the manufacturer and importer to specify and assess all the exposure scenarios developed for the own use(s) and all known intended uses. When the downstream user introduces a new use, he is responsible for assessing the(se) scenario(s). Another new issue in the future REACH CSR is that the manufacturer and importer are required to recommend risk reduction measures (RMMs) to the downstream users to control the exposures of humans and the environment.

Relevant occupational exposure scenarios - if possible, all the intended uses - will be assessed for the metallic chromium and trivalent chromium compounds.

The following exposure scenarios have been identified so far by industrial and use categories:

- **Production:** Chromite ore mining, Ore processing (chromite sand), Separation of chromium from ore, Ferro-chrome production, Ferro-chrome slag production
- **Formulation and use:** Production of chromium metal, Production of chromium carbides, Production of alloys, Stainless steel production, Production of basic chromium sulphate, Chromium lignosulfonate production, Refractory production, Pigment production, Catalyst production, Leather tanning, Thermal spraying, Electroplating with trivalent chromium, Use of chromite sand, Pharmaceutical applications (dietary supplements), Cosmetic applications, Other chromium chemicals.
- **End uses:** Leather goods finishing, Working with CCA-impregnated wood, Catalyst handling, Paint manufacture and use, Manufacture of metal products.
- **Recycling:** Scrap handling, Chromium regeneration, Leather waste handling.

The measured exposure data will be presented as 90% percentile values whenever possible using the measured data provided by the industry and all additional data available from other relevant sources. Modelled data will be used for the scenarios lacking measured data concerning inhalation exposure. To estimate dermal exposure, modelled data will be used according to the TGD guidance. Both the typical values and the reasonable worst case exposure estimates will be taken into risk characterisation for the final conclusions. This will be done for all relevant routes of exposure (oral, dermal and/or inhalation) and the body burden will be estimated.

The measurement of total dust has been used as indicator of exposure to trivalent chromium compounds. The challenge concerning the exposure assessment for metallic chromium and trivalent chromium compounds is the knowledge about the characteristics of the total dust, i.e. the content of the chromium species, the particle size distribution and the portion of respirable dust in each exposure scenario.

Consumer exposure will introduce all the main known consumer uses of metallic chromium and trivalent chromium compounds. The following scenarios have been identified: stainless steel articles (e.g. kitchen utensils), chrome-tanned leather, chromium in detergents, cleaning agents/household chemicals and cosmetics, chromium in paints, pigments and varnishes.

The exposure of humans via the environment will also be reviewed: dietary intake of chromium, drinking water and contaminated soils as examples of the sources of exposure.

3.3 Hazard assessment

The hazard assessment will review and evaluate all the toxic end points [(Acute toxicity, Irritation/Corrosivity, Sensitisation, Repeated dose toxicity, Mutagenicity, Carcinogenicity and Toxicity for Reproduction (fertility and developmental toxicity)]. This will be done with guidance according to the current legislation [1, 9] and using the revised TGD [10].

Most of the toxic end points are so called 'threshold end points' for which the N(L)OAEL (No (Lowest) Observed Adverse Effect Level) will be derived. REACH [8] introduces the new concept of Derived No-effect Levels (DNELs) to be assessed for the risk characterisation.

3.4 Risk characterisation

In the Risk Characterisation the typical and reasonable worst case exposure estimates for each use scenario in each population (workers, consumers, humans exposed via the environment) will be compared to the derived N(L)OAEL (or DNEL in REACH) for each toxic end point separately. This ratio is the 'Margin of Safety' (MOS).

Whether the magnitude of MOS in a particular case is sufficient for indicating the absence of risk (or the contrary) is interpreted in the light of the severity of the effect, the extrapolations made from experimental data, intra- and interspecies variation, and overall confidence of the data base.

Many of the toxic end points for metallic chromium and trivalent chromium compounds are lacking test results from experiments performed with validated EU Dir. 67/548/EEC [2] Annex V methods or the corresponding OECD Testing Guidelines [12]. Most of the scientific literature results available show that experiments have tended not to follow the agreed testing protocols and GLP. Limited data on the speciation of chromium compounds causes an additional challenge for testing and use/interpretation of test results from a limited number of chromium species.

In the final conclusions the needs and rationale for possible further testing will be presented. End points under special consideration are sensitisation, mutagenicity and reproductive toxicity.

4. REFERENCES

[1] Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances. Official Journal No. L 84, 23/03/1993, p. 0001

[2] Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. Official .Journal No P196, 16. 8. 1967, p.1.

[3] Commission Regulation (EC) No 1179/94 of 25 May 1994 concerning the first list of priority substances as foreseen under Council Regulation (EEC) No 793/93. Official Journal No. L 131, 26/05/1994, p. 0003-0004.

[4] Commission Regulation (EC) No 2268/95 of 27 September 1995 concerning the second list of priority substances as foreseen under Council Regulation (EEC) No 793/93. Official Journal No. L 231, 28/09/1995, p. 0018-0019.

[5] Commission Regulation (EC) No 143/97 of 27 January 1997 concerning the third list of priority substances as foreseen under Council Regulation (EEC) No 793/93. Official Journal L 025, 28/01/1997, p.0013-0014.

[6] Commission Regulation (EC) No 2364/2000 of 25 October 2000 concerning the fourth list of priority substances as foreseen under Council Regulation (EEC) No 793/93. Official Journal L 273, 26/10/2000, p. 0005-0007.

[7] European Union Risk Assessment Report, Chromium trioxide (CAS No 1333-82-0), Sodium chromate (CAS No. 7775-11-3), Sodium trichromate (CAS No. 10588-01-9), Ammonium trichromate (CAS No. 7789-09-5), Potassium dicromate (CAS No 7778-50-9). (http://ecb.jrc.it/existing-chemicals/).
[8] REACH - Consultation Document, the Registration, Evaluation, Authorisation and Restrictions of CHemicals, Volumes I-VII (http://europa.eu.int/comm/enterprise/chemicals/chempol/whitepaper/reach.htm).
[9] Commission Regulation (EC) No 1488/94 of 28 June 1994 laying down the principles for the assessment of risks to man and the environment of existing substances in accordance with Council Regulation (EEC) No 793/93. Official Journal No. L 161, 28/06/1994, p. 0003.
[10] Technical Guidance Document on Risk Assessment (TGD) in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market (2003). (http://ecb.jrc.it/).
[11] Commission Directive 2001/59/EC of 6 August 2001 adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. Official Journal No. L 225, 21. 8. 2001, p.1.
[12] OECD Guidelines for the Testing of Chemicals (1993). (http://www.oecd.org/oecd/pages/home/displaygeneral/0,3380,EN-document-524-14-no-no-5647-0,00.html).