HBM4EU project

Outline of occupational health study on worker's exposure to chromium

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- Biomonitoring of hexavalent chromium
- Specific biomarkers for Cr(VI)
- Effect biomarkers for Cr(VI)
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Background

Chromium Species

Metallic element that has various oxidation states and forms a number of natural and antropogenic compounds.

- *Trivalent chromium [Cr(III)] form, abundant in nature and does not shown significant health hazard to humans.*

- *Hexavalent chromium form[Cr(VI)], rarely occurs naturally and poses human health hazards*

Exposure to hexavalent chromium compounds are associated with lung cancer, damage to the nasal epithelia and skin, …

Background

Uses of Cr(VI) compounds

- Chrome plating and metal finishing
- Stainless steel production
- Pigments in dyes, in paints
- Anticorrosive agent

Workplace exposures

by inhalation, direct contact with the skin

- Welding on stainless steel
- Operating chrome plating bath, surface treatment
- Use of spay paints…

Legal background

Companies using Cr(VI) compounds (for some specific reasons) have to apply for an authorization under Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) .
Authorizations are granted with the recommendations of strict conditions for risk management in these work tasks, which include relevant exposure monitoring methods.

Occupational exposure limit values were set in several countries. In France, an OEL of 1 µg/m^3 has been set for Cr(VI). This is the lowest OEL in Europe.
The European Commission has recently proposed to add Cr(VI) to the Carcinogens and Mutagens Directive (CMD, 2004/37/EC) and proposed a binding limit value of 0.005 mg/m^3 after a transition period.

No human biomonitoring guidance has been adopted under CMD. However, biomonitoring can support the exposure assessment under both REACH and CMD since it gives information on the real intakes and e.g. on the effectiveness of the respiratory protection to reduce exposure.

Biomonitoring of hexavalent chromium

The principal biomarker used for the biomonitoring of Cr(VI) exposure at the workplace is urinary (total) Cr.

The main problem with this biomarker is that it is not specific for Cr(VI) since it measures all chromium species

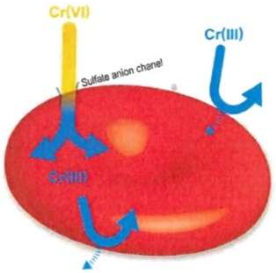
- *Cr(VI), Cr(III), …*
- *Occupational and dietary exposure*

For example in welding, exposure to both Cr(III) and Cr(VI) occurs, which makes it challenging to interpret urinary Cr levels.

Therefore, it seems important to develop more specific biomarkers for Cr(VI). It would be important to test how well urinary Cr correlates with more specific biomarkers in different work tasks, given that urinary Cr will probably remain the gold standard for the routine biomonitoring of Cr(VI) exposure.

Specific biomarkers for Cr(VI)

1. Chromium in Red Blood Cells – Cr-RBC



Only Cr(VI) is able to pass though the red cell membrane.

Levels of Cr inside the red blood cells would reflect exposure specifically to Cr(VI).
Levels of Cr in plasma would reflect the exposure to Cr(III) (Goldoni et al., 2010)

2. Chromium in exhaled breath condensate – Cr-EBC

Cr(VI) in EBC samples is an important new biomarker since it can give specific information on the Cr(VI) levels in the main target tissue (lungs) *(Leese et al., 2017).*

Cr(VI) and Cr(III) can be analyzed separately from the EBC samples.

Effect biomarkers for Cr(VI)

The characterization of effect biomarkers is of the utmost importance to establish a relationship between the exposure to Cr (VI) and its impact on human health.

Effect biomarkers reflect early biochemical changes (subclinical changes) before the onset of disease.

Oxidative stress, **inflammation**, and **DNA lesions** have been associated with exposure to Cr(VI) and have been recognized as crucial events in the carcinogenic process as well as **epigenetic modifications** (e.g. DNA methylation, histone modification)

Cr-RBC, CR-EBC and effect biomarkers seem promising but data is still very limited.

There is clearly a need for further studies, which would integrate and evaluate Cr-RBC, Cr-EBC and effect biomarkers as biomarkers for occupational exposure to Cr(VI).

Objectives of chromate study

To contribute to building a sound scientific basis for the regulatory EU institution to set-up occupational exposure limits and related biological limit values for chromium.

- To give a more accurate picture on Cr(VI) exposure by using specific biomarkers for Cr(VI) exposure, Cr-RBC and Cr-EBC, and to study correlation between biomarkers in different matrices.
- To create representative EU-wide data on the occupational exposure to Cr(VI) in Europe
- To provide recommendations on the use of different biomarkers for the assessment of occupational exposure to Cr(VI).
- To assess the suitability of effect biomarkers to reflect early subclinical effects that can be predictors of disease development.

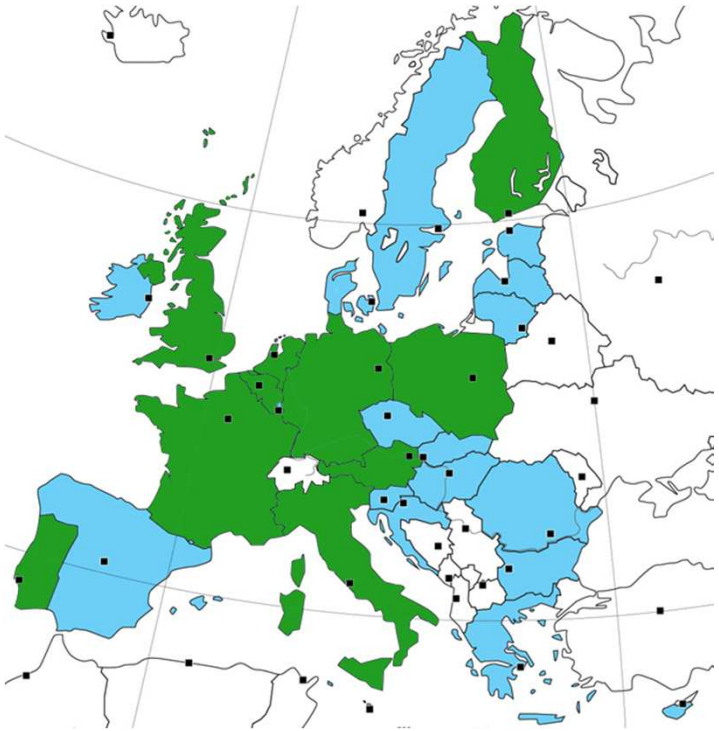
In addition

- To study the exposure of welders to other relevant metals, especially to nickel and manganese.
- To collect information on the exposure of chrome platers to bioaccumulative perfluoroalkylated substances (PFAS; like perfluorooctyl sulfonate, PFOS) via the use of mist suppressants. Information on PFAS is important, since PFAS exposure may be a confounder when interpreting the health effects of Cr(VI), such as cancer.

Conduction of chromate study

Participating countries (green)

Samples will be collected from Finland, Belgium, Netherlands/Austria, Portugal, France, Poland, Germany, UK and Italy.



Conduction of chromate study

Target population

Workers from companies performing stainless steel welding and surface treatment with Cr(VI) (chrome plating in baths, surface treatment by spraying or painting)

A **control group** will be recruited from the companies or elsewhere.

The target population size is

- 50 workers/country
- 3-5 companies/country
- 25 controls/country

Conduction of chromate study

Sample to be collected

Biological samples

urine

blood

EBC

Industrial hygiene samples

Wipe

air

Conduction of chromate study

Biological samples and biomarkers

Exposure biomarkers

Urine: Cr-U; Ni-U; Mn-U

EBC: Cr(VI)/Cr(III)-EBC ; and optionally Ni, Mn-EBC

Plasma: Cr; PFAS

Red Blood cells: Cr-RBC

Effect biomarkers (optional)

Urine: oxidative stress (e.g. malondialdehyde, 8-isoprostane, 8-hydroxy-2-deoxyguanosine) and epigenetic changes (e.g. DNA methylation).

Whole blood: genotoxicity (micronucleus assay), oxidative stress and epigenetic changes (e.g. DNA methylation).

Conduction of chromate study

Industrial hygiene samples

Investigated in order to get an overview on the Cr level at workplace and the principal routes of exposure to Cr

Personal air samples will be collected from workers given that exposure through inhalation is important when considering lung cancer risk.

air

Wipe samples will be collected from the hands of the workers since skin contamination may represent a significant exposure route to Cr resulting in gastrointestinal absorption via hand-to-mouth exposure. Cr can be absorbed in the skin.

Wipe

Conduction of chromate study

Questionnaire

The form was developed to collect contextual information on exposure.

The first part will report general information on the operating conditions and risk management measures.

HBM4EU WP8 ÉTUDE sur l'exposition au chrome hexavalent et à d'autres substances chimiques

QUESTIONNAIRE SUR LES LIEUX DE TRAVAIL (à remplir soi-même)

Nous vous serions reconnaissants si vous pouviez remplir ce bref questionnaire concernant les activités de votre entreprise en lien avec le chrome hexavalent et d'autres substances chimiques. Veuillez le renvoyer directement au chercheur une fois complété.

Entreprise et information en matière de médecine du travail

Nom et fonction du représentant de l'entreprise:

Nom de l'entreprise/de l'organisation:

Nom du département:

Adresse du site:

Pays:

Secteur industriel:

Code NACE Rév. 2 (à compléter par le chercheur):

Description du lieu de travail (nature des activités, produits fabriqués, organisation du travail):

Décrivez, de manière générale, la formation, le suivi, et les pratiques en matière de santé et sécurité au travail en lien avec l'exposition aux substances chimiques dangereuses au sein de votre entreprise:

Nom et adresse de la médecine du travail:

Personne de contact et coordonnées (adresse électronique, numéro de téléphone) du département «Santé et sécurité au travail»:

Conditions opératoires

(Choisissez entre chromage, pulvérisation/peinture ou soudage)

Activité	Se déroule sur votre site? (cochez la case si c'est le cas)	Répondez aux questions des sections
Chromage	☐	1 et 4

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The second part is a post-shift form for workers

- job description
- specific work tasks
- risk management measures (PPE)
- background exposure from other sources due to living habits, smoking, implants, food supplements

Conduction of chromate study

Ethical issues and Information materials

Ethical approval has to be applied nationally and obtained from the Ethics Committee prior to the start of the study.

Information materials will be provided for workers and companies.

Subject must be adequately informed of the aims, methods, the anticipated benefits and potential risks of the study and any other relevant aspects of the study.

- leaflet information on Cr(VI)
- information letter for the companies,
- information letter for the participating workers,
- informed consent form for the companies
- informed consent form for the workers

Conduction of chromate study

Sample analyses

Urinary and RBC or plasma Cr, PFAS analyses will be done under WP9 of HBM4EU in the selected laboratories after their successful participation in the QA program.

The analysis of Cr from exhaled breath condensates is under development, and a QA program will be designed. For effect markers, sample analyses will be done by the participating country.

Data analyses will be done under WP10 of HBM4EU.

Conduction of chromate study

Reporting of the results and data protection

All collected data will be anonymised before any treatment

Any information will be presented in a strictly anonymous format so that no one will be able to identify anyone (or any company) who took part in the study.

The workers will receive their personal results including some basic interpretation of what the results indicate. In addition, they will receive a summary of the results of the whole study.

The participating companies will receive their specific report considering environmental monitoring and collective biomonitoring results. They will be also provided with the electronic copy of the whole study report.

The results of the study will be reported within the reporting policy of the HBM4EU project, and a general report will be publicly accessible via the project website. The results (or part of the results) can be published as a scientific publication in a peer-reviewed scientific journal, and presented at scientific meetings.

More information

HBM4EU: Additional Deliverable AD 8.2 Research plan for chromates study under HBM4EU

at https://www.hbm4eu.eu/deliverables/

Thank you for your attention

Institut National de Recherche et de Sécurité

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