HBM4EU occupational biomonitoring study on hexavalent chromium and other harmful chemicals

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To contribute to building a sound scientific basis for the regulatory EU institution to set-up occupational exposure limits and related biological limit values, as well as reference values for the general population and to study the impact of the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON46007

Source
ToetsingOnline

Brief title
HBM4EU Chromium Study

Condition

- Other condition

Synonym
not applicable

Health condition

niet van toepassing

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: biomonitoring, chromium, exposure, occupation

Outcome measures

Primary outcome

Cr in inhalable and respirable dust sample collected from the air in the breathing zone of the worker by personal air sampling

Cr in hand wipe samples collected during the shift

Urinary Cr - Cr-U (pre-shift samples, at the end of shift / end of work week)

Cr in plasma (collected post-shift and preferably in the end of work week or at least after 1-2 days at work)

Cr in red blood cells - Cr-RBC (collected post-shift and preferably in the end of the work-week or after after 1-2 days at work)

Hexavalent and trivalent Cr in exhaled breath condensate - Cr(VI)-EBC (before and during the work shift, just before the end of the shift)

Secondary outcome

Plasma - PFAS (at the end of the shift / end of the work week) only from chromium platers working with chromium baths in which PFAS containing mist suppressants could have been used

Urinary nickel and manganese - Ni-U, Mn-U (at the end of the shift). Urinary nickel levels are suggested to be analysed from welders and those platers performing nickel plating. Urinary manganese levels are analysed from stainless

steel welders.

Nickel and manganese levels will be analysed in exhaled breath condensate - Ni, Mn - EBC (before and during the work shift, just before the end of the shift).

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

Effects biomarkers in whole blood: genotoxicity (micronucleus assay or chromosomal aberrations in peripheral blood reticulocytes or lymphocytes and DNA comet assay plus FPG-modified comet assay), oxidative stress (malondialdehyde, 8-isoprostane, 8-hydroxy-2-deoxyguanosine, Glutathione) and epigenetic changes (e.g. DNA methylation).

Cotinine, creatinine

Study description

Background summary

HBM4EU (Human Biomonitoring for Europe, www.hbm4eu.eu/about-hbm4eu) is a European study, which aims to harmonise and use human biomonitoring to understand people*s exposure to chemicals in the environment, via their occupation or use of consumer products and the related health risks, in order to improve chemical risk management. It is funded by the European Commission and national governments and includes experts from 28 countries and European Union agencies and will run from 2017 to 2021.

HBM4EU includes both the use of biomonitoring in the characterisation of the exposure and risks to the general population and to workers. Occupational exposure to specific chemicals may in many instances be several times higher than the exposure of the general populations from the environment from the use of consumer products. Human biomonitoring gives important information on the combined exposure via all routes of exposure; via inhalation, oral, dermal contact and via hands-to-mouth. It usually complements environmental measurements and can inform us on the effectivity of preventive and protective

measures (including personal protective equipment).

Within the HBM4EU project, several priority chemicals were identified (https://www.hbm4eu.eu/thesubstances/), which may be of concern for the European population. Several of those are also relevant at European workplaces, such as hexavalent chromium, Cr(VI). According to IARC (IARC 2012), Cr(VI) compounds are carcinogenic to humans (Group I). They are known to cause lung cancer in humans. The European Commission has recently proposed to add Cr(VI) to the Carcinogens and Mutagens Directive (CMD, 2004/37/EC) and has proposed a binding limit value for exposure to hexavalent chromium (EC, 2017). In addition, the use of hexavalent chromium compounds in various applications, including in the surface treatment of metals, is authorized under EU REACH regulation (EC1907/2006). Based on this, the need to collect new data on human exposure in the European countries has been emphasised.

A principal biomarker used for the biomonitoring of Cr(VI) exposure at the workplace is urinary (total) chromium (Cr). The main .limitation of this biomarker is that it is not specific for Cr(VI) since it measures exposure to both trivalent and Cr(VI). Especially in welding, exposure to both trivalent and Cr(VI) occurs, which makes it challenging to interpret urinary Cr levels. Also in surface treatment activities, part of the Cr(VI) present in air may be reduced to trivalent form. Therefore, it is important to develop more specific biomarkers for Cr(VI). In addition, it is important to test how well these more specific biomarkers correlate with the routine *gold standard* urinary (total) Cr method. The new, more specific markers include Cr in red blood cells and Cr(VI) in exhaled breath condensates (EBCs). Cr in red blood cells reflects the exposure specifically to Cr(VI) since only Cr(VI) is able to pass though the red blood cell membrane, with the levels of Cr in plasma reflecting the exposure to trivalent Cr (Goldoni et al., 2010). 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 i.e. in lungs (Leese et al., 2017). It is also a less invasive biomarker than blood. Cr(VI) and Cr(III) can be analyzed separately from the EBC samples.

The correlations between air Cr(VI), wipe samples, EBC, blood and urinary Cr levels allows further study of the fate and transformation of Cr(VI) to trivalent form when entered to the body. Additionally, the establishment of a relationship between exposure biomarkers and effect biomarkers in biological samples of Cr(VI)-exposed workers in EU is expected to provide meaningful data for a comprehensive risk assessment.

In the HMB4EU, hexavalent chromium occupational exposure study exposed workers and controls from companies performing chrome plating, surface treatment with chromates or stainless steel welding will be recruited from nine countries, namely: Austria Belgium, Finland, France, Germany, Italy, Poland, Portugal, The Netherlands and United Kingdom. In order to achieve comparable data in a harmonised way, the enclosed Standard Operating Procedures (SOPs) are intended

to be used. Every participating country is obliged to, as far as is reasonable possible, follow these procedures. The SOPs for the selection of participants and recruitment, information to the participants, informed consent (annex 1), completion of questionnaires (annex 2) and instructions for blood, EBC, urine, air and wipe sampling (annexes 3-7) provided separately. The general objective of the HMB4EU hexavalent chromium occupational study is to contribute to building a sound and valid scientific basis to propose biological limit values for occupational Cr(VI) exposure. In addition, the study will provide reference values for the general population (from data collected from controls) and study the impact of the recent regulatory measures to the exposure at European workplaces.

Study objective

To contribute to building a sound scientific basis for the regulatory EU institution to set-up occupational exposure limits and related biological limit values, as well as reference values for the general population and to study the impact of the recent regulatory measures to the exposure at European workplaces.

Study design

Cross sectional survey in 10 Eureopean countries

Study burden and risks

The burden for the participants consists of :
- the effort of collection of urine samples (two times)
- undergoing blood collection by vena puncture (one time)
- breathing in an apparatus for collection of end-exhaled condensate (two times)
- participating in taking of hand wipes (five times)
- carrying air sampling equipment during work hours (5 times)
- participating in an interview related to collect contextual information such as information on lifestyle and work-related determinants of exposure to chromium and other metals
- participating in a short daily interview regarding the tasks performed during the shift.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein 21N

Nijmegen 6525 HE
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein 21N
Nijmegen 6525 HE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Employment in one of the participating companies
Access to occupational healthcare

Exclusion criteria

None

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	10-09-2018
Enrollment:	75
Type:	Anticipated

Ethics review

Approved WMO

Date:	20-01-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL67044.091.18