HBM4EU science and policy for a healthy future

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2 Background and the objectives of the study

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 general population and to the workers. Occupational exposure to specific chemicals may in many instances be several times higher than the exposure of general populations via the environment or via 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).

HBM4EU has identified several priority chemicals, which may be of concern for the European population. Several of those are also relevant at European workplaces. Hexavalent chromium Cr(VI) is one of the priority substances under HBM4EU. It is one of the most important occupational carcinogens, which has been shown to cause lung cancer in humans. It is currently an issue in the EU since Cr(VI) compounds are authorised under Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and the Commission has published a proposal to set a binding limit value for Cr(VI) under the Carcinogens and Mutagens Directive (CMD) i.e. EU Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work.

2.1 Legislative background

According to REACH legislation all companies using Cr(VI) compounds (for example for surface treatment) have to apply an authorisation under REACH for their uses. All the applications submitted to the European Chemicals Agency (ECHA) have been published on ECHA's website (https://echa.europa.eu/applications-for-authorisation-previous-consultations). Some of the applications cover only single use from a single company but some of those are large, so-called upstream applications covering hundreds end-user companies or sites across Europe. More than 100 authorisations for different uses of chromates have already been requested. This means that thousands of workers are still in contact with Cr(VI). Exposure to Cr(VI) levels of more than 1 µg/m^3 result in cancer risks of > 4 extra lung cancers per 1000 workers (ECHA, 2013). In many cases, exposure data which has been provided to support authorisation was limited. Although ECHA's scientific committees, Risk Assessment Committee (RAC) and Socio-Economic Analysis Committee (SEAC) have in most cases supported granting an authorisation for these uses in the lack of viable, ready-to-use alternatives, they have usually recommended strict conditions for risk management in these work tasks, which include monitoring of exposure using relevant exposure monitoring methods.

It should be noted that REACH concerns only the use of chromates for specific purposes, and it does not cover process-generated fumes like welding fumes. In welding, Cr(VI) is formed together with less toxic trivalent chromium Cr(III). Management of Cr(VI) formed during the welding process is achieved by compliance with occupational limit values. 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 (EC, 2017). The proposal is 0.010 mg/m^3 for a period of 5 years after the date of transposition of the directive; after that period a limit of 0.005 mg/m^3 will apply.

There is a derogation for welding or plasma-cutting processes or similar work processes that generate fumes: for these processes the exposure limit value is 0.025 mg/m^3 until 5 years after the transposition date and after that period the limit will be 0.005 mg/m^3. A higher limit for welding and plasma-cutting is proposed because of the socio-economic reasons. In France, an OEL of 1 µg/m^3 has been set for Cr(VI) together with a corresponding biological limit value (BLV) of 2.5 µg/L or 1.8 µg/g creatinine (end of the week and end of shift) for urinary Chromium (Cr) (ANSES, 2017). This is the most stringent OEL (and corresponding biological limit values) currently set in workplace in EU and since this BLV is close to background urinary Cr levels in occupationally non-exposed populations, the need for new and more specific exposure biomarkers is emphasised.

2.2 Biomonitoring of hexavalent chromium

No human biomonitoring guidance have been adopted under CMD, although 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. Since principal biomarker used for the biomonitoring of Cr(VI) exposure at the workplace is urinary (total) Cr, different biological limit values have been set on a national basis such as in Spain, UK and Germany. However, the main problem with this biomarker is that it is not specific for Cr(VI) since it measures exposure both to Cr(III) 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 would be important to develop more specific biomarkers for Cr(VI). Even if urinary Cr will remain the gold standard for the routine biomonitoring of Cr(VI) exposure, it would be important to test how well it correlates with more specific biomarkers in different work tasks. These new, more specific markers include Cr in red blood cells and Cr(VI) in exhaled breath condensates (EBC). Cr in red blood cells reflects the exposure specifically to Cr(VI) since only Cr(VI) is able to pass though the red cell membrane. Levels of Cr in plasma reflects the exposure to trivalent Cr whereas levels inside the red blood cells reflects exposure to Cr(VI) (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) and it is a less invasive biomarker than blood. Cr(VI) and Cr(III) can be analysed separately from the EBC samples and the correlations between air Cr(VI), EBC, blood and urinary Cr levels allow further study of the fate and transformation of Cr(VI) to Cr(III) when in the human body.

2.3 Biomonitoring of effect biomarkers

The characterisation of effect biomarkers is of utmost importance to establish a relationship between the exposure to Cr (VI) and its human health impact, given that they comprise sensitive endpoints that reflect early biochemical changes (subclinical changes) before the onset of disease (Annangi et al., 2016). In addition, it has been suggested using effect biomarkers into the risk assessment process for several toxic metals, like Cr (Ray et al., 2014). In fact, oxidative stress, inflammation, and DNA lesions have been associated with exposure to Cr(VI) and have been recognised as crucial events in the carcinogenic process (Arita and Costa, 2009; Annangi et al., 2016). Furthermore, it has been suggested that, other than the induced genotoxic effects, epigenetic modifications (e.g. DNA methylation, histone modification) may contribute to the carcinogenicity of Cr(VI) compounds (Salnikow and Zhitkovich, 2008; Arita and Costa, 2009, Ray et al., 2014). As an example of the utilisation of Cr associated epigenetic modification to inform the risk assessment process, Cr has been associated with histone modifications in a dose-dependent manner in an in vitro model (Sun et al., 2009, Ray et al., 2014). Thus, the establishment of a relationship between exposure biomarkers and effect biomarkers in biological samples of Cr(VI)-exposed workers is expected to provide meaningful data for a comprehensive risk assessment.

Due to the REACH authorisation and the proposed addition of Cr(VI) to CMD it is important to gather EU-wide data on the current exposures, their potential subclinical effects (measured by effect biomarkers) and the impact of these regulatory actions to the occupational exposure to Cr(VI) and the potential health risks.

2.4 Objectives

2.4.1 General objective

The general objective of the study is 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.

2.4.2 The specific aims of the study are

- To support recent regulatory measures (REACH and CMD) related to occupational exposure to Cr(VI)
- To create representative EU-wide data on the occupational exposure to Cr(VI) in Europe
- To give a more accurate picture on Cr(VI) exposure by using specific biomarkers for Cr(VI) exposure, Cr-Red Blood Cells (RBC) and Cr-Exhaled Breath Condensate (EBC), and to study correlation between biomarkers for Cr levels in different matrices.
- To compare the levels of the HBM4EU occupationally exposed and non-exposed population with the levels of the general population using samples from the wider distribution.
- 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 (e.g. genotoxicity and epigenetic endpoints) to reflect early subclinical effects in somatic cells that can be predictors of disease development.
- To study the exposure of welders to other relevant metals, especially to nickel (U-Ni, EBC-Ni) and manganese (U-Mn EBC-Mn). Data would support the setting of binding limit value for nickel compounds under CMD.
- In addition, information on the exposure of chrome platers to bioaccumulative perfluoroalkylated substances (PFAS; like perfluorooctyl sulfonate, PFOS) via the use of mist suppressants will be obtained from the collected blood samples. Since PFAS has a long half-life, analysis represents exposure for a longer period. Information on PFAS is important, since PFAS exposure may be a confounder when interpreting the health effects of Cr(VI), such as cancer.
- To create a framework to follow regarding the use of biomonitoring in occupational health context.

3 What are the benefits for the companies and workers participating in the study?

Potentially exposed workers and controls from companies performing chrome plating, surface treatment with chromates or stainless steel welding will be recruited.

Because of the recent legislative actions including authorisation of Cr(VI) under REACH and the setting of a binding limit value (BOELV) for Cr(VI) under CMD there is a need to monitor the exposure to Cr(VI). Both chromate authorisations and CMD oblige employers to conduct measurements of exposure, and it is very likely that chromate uses are also followed by occupational health and safety regulations in different countries. Air monitoring can bring information on the airborne levels at the work place but not necessarily on the real exposure of the workers if personal protective equipment (PPE) is used and is effective. On the other hand, traditional biomonitoring methods (urinary Cr) may overestimate the exposure since it cannot differentiate exposure to hexavalent from the exposure to less hazardous trivalent Cr. Therefore, new methods used in the study can bring more accurate information on the worker's exposure to Cr and help to improve the occupational risk assessment and, consequently, to adapt the representative risk management measures (RMMs) if needed. The information created in this study can be also used to support exposure assessment e.g. in the scope of the REACH authorisation process.

In the case of companies performing stainless steel welding, the study will give them information on their compliance with the EU BOELV given under CMD.

In addition, companies will receive recommendations for the health surveillance of workers and information on the applicability of different monitoring methods and risk management measures in different situations. This could even result in cost savings when monitoring activities are properly focused. Participating companies are provided with an electronic copy of the report with the collective results of the study published on the website of the HBM4EU project. They will receive company-specific hygienic report which includes recommendations for the surveillance and monitoring procedures and can also choose to receive the collective urinary biomonitoring results of their workers.

4 Conduction of the study

4.1 Operational plan and schedule

Samples will be collected under HBM4EU work package 8 (WP8) during the year 2018 from at least eight of the following participating countries; France, Netherlands/Austria[1], Finland, Belgium, Poland, Portugal, Germany, UK and Italy. Samples to be collected are listed in Table 1.

Table 1: Samples collected in the study

Samples	Sample source	Personal data (yes/no)	Ethics statement (yes/no)*
Urine samples of workers exposed to Cr(VI)	Voluntary exposed workers	yes	yes
Urine samples of persons non-occupationally exposed (controls)	Voluntary non-exposed workers	yes	yes
Blood samples of workers exposed to Cr(VI)	Voluntary exposed workers	yes	yes
Blood samples of persons non-occupationally exposed (controls)	Voluntary non-exposed workers	yes	yes
EBC samples of workers exposed to Cr(VI)	Voluntary exposed workers	yes	yes
EBC samples of persons non-occupationally exposed (controls)	Voluntary non-exposed workers	yes	yes
Air samples	Personal breathing zone samples of the voluntary workers / stationary samples collected at the workplaces	yes / no	no
Wipe samples	From the hands of the voluntary workers	yes	no

**Ethics statements are applied nationally from the local ethics board of the participating countries*.

[1] Netherlands and Austria will recruit all together 5 companies.

Analysis of samples will be made under WP 9 in the selected laboratories after their successful participation in the QA program along 2019. Data analysis is performed under WP 10 in 2019. If considered useful, the biological samples can be used also for effect biomarker analyses under WP14. These will be planned and reported separately. Detailed schedule is given in Figure 1.

Task	Q1/18	Q2/18	Q3/18	Q4/18	Q1/19	Q2/19	Q3/19	Q4/19
Detailed SOPs								
Ethical approvals								
Samplings								
U-Cr QA								
U-/RBC-/P- Cr analyses								
EBC-Cr method development & analyses								
Statistical analyses								
Reporting								

Figure 1: Time schedule of the chromate study

4.2 Biomarkers to be studied

The exposure biomarkers investigated in this project will be:

- Urinary Cr - Cr-U (pre-shift samples, at the end of the shift / end of the work week)
- Cr in plasma (collected post-shift and preferably in the end of the 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 at least after 1-2 days at work)
- Hexavalent and trivalent Cr in exhaled breath condensate – Cr(VI)-EBC (before exposure/work and during the work shift, just before the end of the shift)

In addition to Cr analyses, following exposure biomarkers will be also studied from the collected samples:

- Plasma – PFAS (at the end of the shift / end of the work week) only from chrome platers working with chrome 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. These analyses can be made simultaneously with U-Cr analyses and do not cause any significant extra work.
- Optionally, nickel and manganese levels will be analysed in exhaled breath condensate – Ni, Mn-EBC (before exposure/work and during the work shift, just before the end of the shift)

Optionally, the following effect biomarkers can be investigated from the following samples if sample quantities collected allow it (refer paragraph 4.5 below for the total matrix quantity needed):

- 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).

Since it is possible to collect only at maximum 16 ml of blood, this may be a limiting factor for the number of effect markers analysed from blood samples.

4.3 Industrial hygiene samples suggested to be collected

In order to get an overview on the Cr level at workplace and the principal exposure routes to Cr, Cr(VI) and total Cr levels in personal air samples will be investigated.

Wipe samples from the hands of the workers will be also collected, since skin contamination may represent a significant exposure route to Cr resulting in gastrointestinal absorption via hand-to-mouth exposure. Thus, these samples are important for the interpretation of the biomonitoring results. Whereas, inhalation exposure is important when considering lung cancer risk, secondary ingestion via the contaminated hands affects the whole body burden and may increase the risk for gastrointestinal cancers as suggested by animal studies and also by some epidemiological studies (ECHA, 2013, Keller et al., 1993). Cr does not easily pass through the skin, but Cr can be absorbed in the skin and Cr compounds are known to cause skin sensitisation.

These samplings and their analyses are performed under WP8. Analyses are primarily performed by those institutes collecting the samples, if possible. Those analyses will be performed without the supervision of WP9 and consequently, WP9 will not be responsible for the quality of those data. Aim is to collect these samples from all participating companies. Detailed sampling strategy for these samples will be included in standard operating procedures produced in the beginning of 2019.

4.4 Target population - Companies recruitment

The target population are workers from companies performing surface treatment with Cr(VI) (chrome plating in baths, surface treatment by spraying or painting) and stainless steel welding. The exact welding and surface treatment techniques used in the companies and by workers will be specified when collecting contextual information.

A control group will be needed mainly for blood samples and EBC samples from Cr non-exposed population recruited from the companies or elsewhere. Also urine samples are collected from the control persons unless there is a representative control dataset for urinary Cr already available in the country. Control population will consist of men and women of working age from administrative staff or non-metal exposed workers and includes both smokers and non-smokers.

Participating countries

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

National companies will be recruited by each country. List of companies who have applied for an authorisation for the use of Cr(VI) in surface treatment activities can be found from ECHA webpages and can be used to help identifying potential interested targets. European metal industry

association, Eurometaux (which is the member of HBM4EU stakeholder forum), will distribute information on the study and can provide a support letter to help to recruit companies.

Population size

The target population size for this project is 50 workers/country and 3-5 companies/country.

The target number of controls/country is 25 for RBC and EBC samples. The number of involved workers will enable to significantly differentiate the exposed population from the controls and the pre-shift of the beginning of the work week from the post-shift of the end of the work week.

Although some countries already have good control datasets for urinary Cr, urine samples may also needed to be collected e.g. to ensure the adequacy and the representativeness of the control samples.

4.5 Sample collections and storage

The main issues to be considered for the sample collections (urine, blood, EBC, air, wipe) are listed in Table 2.

The collected biological samples will be stored at – 20°C before dispatch to the laboratories which will proceed with the analysis. For effect biomarkers, freshly collected samples will be sent immediately to the laboratories that will analyse them. The air/wipe samples are aimed to be analysed after the collection by those institutes collecting the samples.

Table 2: Detailed sample collection plan for 9 participating countries*

<table>
<tr><th rowspan="2">Samples</th><th colspan="3">Sampling period</th><th rowspan="2">Volume of sample</th><th rowspan="2">Number of workers</th><th rowspan="2">Number of controls</th><th rowspan="2">Overall Number of samples (9 countries)</th></tr>
<tr><th>No of days of sampling</th><th>Pre-shift / Beginning work week</th><th>Post-shift / End work week</th></tr>
<tr><td>Urine</td><td></td><td>X</td><td>x</td><td>20 ml</td><td>50</td><td>-</td><td>900</td></tr>
<tr><td>plasma+RBC</td><td></td><td colspan="2" rowspan="2">At any time in the work week
except the first work day</td><td>6 ml</td><td>25</td><td>25</td><td>450</td></tr>
<tr><td>Whole blood</td><td></td><td>10 ml</td><td>25</td><td>25</td><td>450</td></tr>
<tr><td>EBC</td><td></td><td>X</td><td>x</td><td>1.5 – 2 ml</td><td>25</td><td>25**</td><td>675</td></tr>
<tr><td>Air</td><td>1day/worker</td><td></td><td></td><td></td><td>25</td><td>-</td><td></td></tr>
<tr><td>Wipe</td><td>1day/worker</td><td></td><td></td><td></td><td>25</td><td>-</td><td></td></tr>
</table>

**all matrices will not necessary be collected from all participants*

***one EBC sample from each control.*

4.6 Questionnaire to collect contextual information on exposure

The general questionnaire developed for occupational studies under HBM4EU WP7 has been used as a basis and modified for the purposes of the current study. The questionnaire is attached here as Annex 1.

It includes a separate questionnaire for the workplace to collect general information on the operating conditions and risk management measures. This can be filled by the researcher (occupational hygienist) visiting the company. Post-shift questionnaire for workers includes detailed questions on the job description and the specific work tasks, risk management measures including the use of personal protective equipment, background exposure from other sources due to living habits, smoking, implants, food supplements (including Cr containing weight losing pills) etc. Slightly different questionnaires have been prepared for welders and surface treatment operators.

Researchers will support the filling of the questionnaire by the workers in order to ensure that workers understand all the questions and all the relevant information will be received.

4.7 Information materials and ethical issues

Under WP7 the following materials have been provided to assist with company and worker recruitment into the study;

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

These are annexed as **Annexes 2-6.**

Ethical permissions are applied nationally from the national ethics boards of participating countries, and managed according to the rules set up in the WP1.5 concerning ethical aspects of the HBM4EU. Ethical application will be sent in the beginning of 2018 to the ethical committees of the participating countries.

4.8 Standard Operating Procedures

Detailed SOPs for sample collection and sample storage (urine, blood, EBC, air, wipe) for participating institutes are to be done by March 2018 by INRS, KuLeuven, IPASUM, HSL, IOM, DPH, INSA and FIOH, under coordination of WP7 (task 7.2).

4.9 Sample analyses

Urinary and RBC or plasma Cr analyses will be done under WP9 of HBM4EU in the selected laboratories after their successful participation in the QA program. The Inter-laboratory Comparison Investigations (ICI) and External Quality Assurance Schemes (EQUAS) for the urinary, RBC and plasma Cr will be performed under WP9 during the year 2018, and after finalising the program and the approval of the candidate laboratories the analyses of the urinary samples will start in the beginning of 2019.

Since the analyses of manganese and nickel can be easily made simultaneously with U-Cr analyses and do not cause any significant extra work, also these should be analysed at least from stainless steel welders but nickel also from those metal surface treatment operators who are performing nickel surface treatments. However urinary nickel and manganese analyses will not be performed under the QA scheme since neither nickel nor manganese is on list of prioritized chemicals. Thus WP9 will not be responsible for the quality of those data.

Since the analysis of Cr from exhaled breath condensates is not well-established, it is currently not suitable for HBM4EU ICI/EQUAS scheme. It will need some method development and validation. For this, laboratories with possible earlier expertise on these methods and capability for further method development should be selected. These can be found among the members of WP8.5 partners. The method development and analyses of these samples will start in the third quarter of 2018. Once the method will be ready for use, a tailor made QA program will be designed by QAU-WP9.

PFAS analyses are performed by the selected laboratories with proven capability for PFAS analyses in 2019 after the finalisation of the ICI/EQUAS program for PFAS analyses.

For possible effect marker analyses samples (optional) are sent to the laboratories and analyses are performed under WP14 depending on the funding available.

4.10 Data analyses

Data analyses will be done under WP10 of HBM4EU. For the HBM biomarker variables and some main accompanying variables (eg. age, sex…) a data template and harmonised codebook (available at https://www.hbm4eu.eu/data-management/) has been developed by WP10 for the data collections to transfer their data to the HBM4EU repository. Data analysis requirements (see objectives) have to be specified later among the partners involved in WP10. KU Leuven, FIOH and SDU (PFAS data analyses) are responsible on the data analyses related to the occupational exposure studies under WP10. Statistical plans for each specific biomarker will include the definition and harmonisation of the variables (codebook), the statistical test to be applied, specific exclusion/partitioning criteria for calculating reference values, sample size calculations, uncertainty analysis, data descriptions, and visualisations.

4.11 Reporting of the results and data protection

All collected data will be anonymised before any treatment by replacing participant and company names with a code and protecting all electronic and paper records from unauthorised access.

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 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.

The participants (workers) will receive their personal urinary Cr results including some basic interpretation of what the results indicate. In addition, they will receive a summary of the results of the whole study as described in the consent form.

The participating companies will receive their specific report considering environmental monitoring and collective urinary Cr biomonitoring results. This option is detailed in the consent. They will be also provided with the electronic copy of the whole study report. These aspects can be confirmed once ethical approval has been given.

5 Research team

The responsible personnel from different countries involved in the study are listed in Table 3.

Table 3: Introduction of the research group

Country	Company	Responsible persons
France	INRS SP-France	Sophie Ndaw Alain Robert Ogier Hanser Mounia El Yamani Nadine Fréry
Finland	FIOH	Tiina Santonen Simo Porras
UK	HSL	Kate Jones Liz Leese
	IOM	Karen Galea John Cherrie Miranda Loh
Germany	IPASUM	Thomas Göen
Portugal	ESTeSL INSA	Susana Viegas Edna Ribeiro Maria João Silva Henriqueta Louro
Italy	DPH ISS	Ivo Iavicoli Flavia Ruggieri
Poland	NIOM	Wojtek Wasowicz Beata Janasik
Belgium	KU Leuven	Radu - Corneliu Duca Matteo Creta Lode Godderis
Netherlands	RUMC	Paul Scheepers
Austria	MUW	Hanns Moshammer

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7 Annexes

7.1 Annex 1: Questionnaires to collect contextual information

QUESTIONNAIRE FOR WORKPLACES (self-administered)

We would be grateful if you can complete this short questionnaire concerning your companies' activities relating to hexavalent chromium and other chemicals. Please return it directly to the researcher once completed.

Company and Occupational Health care information

Name and position of the company representative: .....

Name of the Company/Organisation: .....

Name of the department: .....

Site address: .....

Country: .....

Industrial sector: .....

NACE Rev.2 code (to be filled by researcher): .....

Description of the workplace (nature of the business, what is being manufactured, how the work is organized):

.....

.....

Describe the general training, monitoring, and occupational health and safety practices related to exposure to hazardous chemicals in your company:

.....

.....

Name and address of the Occupational health care: .....

.....

Contact person and contact details (e-mail, phone number) of the Occupational Health and Safety department:

.....

.....

Operational conditions

(Select those that apply from chrome plating, spraying/painting or welding)

Job	**Take place at your site?** **(tick if apply)**	**Complete questions in Sections**
Chrome plating	☐	1 and 4
Spraying/painting	☐	2 and 4
Welding	☐	3 and 4

1. Chrome plating in baths

a. Used quantities of hexavalent chromium in % (or g/l) in the baths? (please tick box/specify)
☐ ≤5; ☐ >5-10; ☐ >10-50% or ……. grams/litre (g/l)

b. The frequency of hexavalent chromium plating operations? (categories: daily, days/week or days/month)

c. Does the work include also nickel plating? (please circle) Yes / No / Don't know

d. If nickel is used what is the used quantity in % (or g/l) in the baths?
…….% or ……. grams/litre (g/l)

e. The frequency of nickel plating operations? (categories: daily, days/week or days/month)

f. Does the work include also coating with trivalent chromium? (please circle) Yes / No / Don't know

g. If trivalent chromium is used what is the used quantity in % (or g/l) in the baths?
…….% or ……. grams/litre (g/l)

h. The frequency of trivalent chromium plating operations? (categories: daily, days/week or days/month)

i. Does the work include also coating with cadmium? (please circle) Yes / No / Don't know

j. If cadmium is used, what is the used quantity in % (or g/l) in the baths?
…….% or ……. grams/litre (g/l)

k. The frequency of cadmium plating operations? (categories: daily, days/week or days/month)

l. Size of the parts treated? (please describe)

---

m. How many employees work on these activities?

Risk management measures for chrome plating (please circle)

Enclosure of the bath	Total	Partial	No
Local exhaust ventilation (LEV) present at bath	Yes	No	
Use of bubble dispersers on the liquid surface	Yes	No	
The use of mist suppressants		Yes	No

- PFAS (Perfluoroalkylated substances) suppressant use
Yes (please specify) No Don't know

- Other suppressant use Yes (please specify) No

2. Surface treatment by spraying or painting

a. Used quantities of hexavalent chromium in % the paint? (please tick box)
☐ ≤0.01; ☐ >0.01-0.1; ☐ >0.1-0.5; ☐ >0.5-1; ☐ >1-5; ☐ >5-10; ☐ >10-15; ☐ >15 %

b. Average quantity of paint used per month (litres or gallons)? ..... litres / ..... gallons

c. Frequency of spraying or painting and machining operations? (categories: daily, weekly, monthly, other)

d. Size of the parts sprayed or painted? (please describe)

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e. How many employees work on these activities?

3. Welding

a. The frequency of welding operations? (categories: daily, weekly, monthly, other)

b. Size of the parts welded? (please describe)

---

c. How many employees work on these activities?

➢ **What welding method is used?** (please tick box) ➢	☐ MMA (manual metal arc) ☐ MAG (metal active gas) ☐ MIG (metal inert gas) ☐ TIG (tungsten inert gas) ☐ SAW (submerged arc welding) ☐ Plasma - plasma gas ☐ Flux-cored welding ☐ Other (please specify) ..... ☐ .....

4. Previous measurements

Have any of the following types of measurements been collected from your workers at the site?

Measurements	Tick all that apply	Years collected
Air samples	☐	
Dermal exposure measurements	☐	
Blood samples from workers	☐	
Urine samples from workers	☐	
Other (please specify)	☐	
	☐	

Would you be willing to allow the researchers to have access to these results (in a confidential manner)? (please circle) Yes No

If yes, contact person and contact details (e-mail, phone number):

Thank you for filling the questionnaire!

Please return it directly to the researcher once completed.

POST-SHIFT QUESTIONNAIRE FOR WORKERS (interviewed by researcher)

Background information about worker

Urine sample	**Date collected:** **Time:**	
EBC sample	**Date collected:** **Time:**	
Blood sample	**Date collected:** **Time:**	
Air sample (personal)	**Date collected:**	
Wipe sample (personal)	**Date collected:**	
Company name and name of department		
Worker name and position		
Sex (please circle)	**Male** **Female**	
Date of birth (dd/mm/yyyy)		
What is your height (cm or feet/inches)	..... **cm / ..... ft ..... inches**	
What is your current weight (kg or stones/lb)	..... **kg / ..... St ..... lb**	
Occupation	**Free description:**	**ISCO08 code**
Is the work done predominantly (please circle)	**Inside** **Outside**	
Duration of work shifts (hours)		
Type of work shifts (please tick box)	☐ **Fixed day** ☐ **Fixed night** ☐ **Rotating day/back** ☐ **Rotating day/back/night** ☐ **Other** (please specify).....	
Home address		
Home location and related characteristics (please circle)	**Urban** **Rural**	

Are there industrial plants, incinerators or landfill sites in the surroundings of house? (please circle)	**Yes** **No** **If yes, approximately how far away from your house is the closest one (km)?**
Please describe the vehicular traffic density in the surroundings of your home address (please circle)	**Quiet street (low density)** **Residential road (medium density)** **Main Road (heavy density)**
Cigarette smoking (please circle)	**Yes** **No** **Former smoker**
Cigarette smoking (continues)	**Approximate number of cigarettes/day** **Number of years you have smoked** **If former smoker, how many years ago did you stop smoking?** **Approximate number of cigarettes/day you smoked** **Number of years you smoked**
Do you smoke electronic cigarettes? (please circle)	**Yes** **No** **Former smoker**
E-cigarettes (continues)	**Approximate number of e-cigarettes/day** **Number of years you have smoked e-cigarettes** **If former e-cigarettes smoker, how many year ago did you stop smoking?** **Approximate number of e-cigarettes/day you smoked** **Number of years you smoked e-cigarettes**
Do you use any other tobacco products? (please circle)	**Yes** **No** **Former user** **If yes or former user, please specify**
Other tobacco products (continues)	**Approximate number of tobacco product/day** **Number of years you have used** **If former user, how many years ago did you stop?** **Approximate number of product/day you used** **Number of years used**

Do you have implants which may contain metals? (please circle)	**Yes** **No** **Don't know** **If yes, how long?** **Do you know what type of implants?** (please specify)
Do you have dental fillings? (please circle)	**Yes** **No** **If yes, do you know what material they are made of?** (please specify)
Alcohol consumption	**Yes** **No** **How often do you typicially drink alcohol?** (please circle) **daily weekly monthly**
Alcohol consumption (continues)	**On average, how many days in a month do you have at least one alcoholic beverage?** **On a typical day that you drink alcohol, how many drinks do you usually have?**
Consumption of other beverages (please circle)	**Coffee** **Tea** **Energy drinks** **On average, how many times in a typical day?** **Coffee** ..... **Tea** ..... **Energy drinks** .....
Dietary habits (please circle)	**Mixed** **Vegetarian** **Vegan** **Other** (please specify)
Use of food supplements (e.g. diet pills) (please circle)	**Yes** **No** **If yes, please specify:**
Recreational activities or hobbies which may cause additional chromate exposure (e.g. welding, paint spraying, metal works) (please circle)	**Yes** **No** **If yes, please specify:**

Occupational history

Occupation/job title	Did the work involve any of the following activities (tick that apply)				Start time (year)	Finish time (year)
	metal plating	painting or spraying	welding	other metal works		
	☐	☐	☐	☐		
	☐	☐	☐	☐		
	☐	☐	☐	☐		
	☐	☐	☐	☐		

Job description

What job were you doing today?

Job	(Tick if apply)	Complete questions in Section
Chrome plating	☐	1
Spraying/painting	☐	2
Welding	☐	3

1. Job description in chrome plating in baths

(please list the type of work tasks you have been involved in today)

	Work task	**Duration of the task in a work shift** (hours/ minutes)	**Frequency of the task** (x times per week)	**Process type** (manual or auto-matic)	**PPE* used** (add the corresponding numbers)	**LEV** used** (yes, no)
1	**Readjustment of the electrolyte**: decanting and weighing, mixing, re-filling of baths					
2	**Application in baths**: loading of jigs, chemical pre-treatment, application by dipping or immersion, rinsing and drying, chemical post treatment, cleaning and unloading of jigs, cleaning of equipment, regular maintenance of equipment					
3	**Infrequent maintenance activities**					
4	**Drawing of sample and transfer to laboratory**					
5	**Laboratory analysis**					
6	**Waste management**					
7	**Other** (please specify)					

*PPE (Personal protective equipment) worn:
1. Powered or air-fed, filtering respirator
2. Reusable half or full face mask respirator (without powered or air-fed respirator)
3. Disposable face mask
4. Other Respiratory Protection Equipment (please specify)
5. Coveralls
6. Reusable Gloves
7. Disposable gloves
8. Other (please specify)

** LEV=local exhaust ventilation

Has your respiratory protection equipment (mask) been fit tested? (please circle)	**Yes** **No** **If yes, when?**
Have you received information, instruction or training on the use of safe work practices when carrying out this activity? (please circle)	**Yes** **No**
Hygiene facilities in the company (please tick box if apply)	☐ **Possibility to wash hands** ☐ **Take shower** ☐ **Separate place for working clothes** ☐ **Specific place for the storage of respiratory protective equipment** ☐ **Other** (please specify)..... ☐ .....
Have the work conditions been normal during the work day? (please circle)	**Yes** **No** **If not normal, please specify (e.g. problems with mask or extraction not working):**

2. Job description in surface treatment by spraying or painting

(please list the type of work tasks you have been involved in today)

	Work task	**Duration of the task in a work shift** (hours/ minutes)	**Frequency of the task** (x times per week)	**PPE* used** (add the correspond-ding numbers)	**LEV** used** (yes, no)
1	**Preparation tasks**: Decanting, Mixing of paints, Re-filling of apparatus				
2	**Spraying in spray cabin/spray booth**				
3	**Spraying outside of spray booth**				
4	**Surface treatment in automatic spray tunnel**				
5	**Surface treatment by rolling (small to medium sized areas)**				
6	**Surface treatment by brushing or pen stick (small areas/touch-up)**				
7	**Drying/self-curing (activities of workers outside one meter distance to the drying part) with no LEV**				
8	**Cleaning and maintenance of equipment**				
9	**Infrequent maintenance activities**				
10	**Machining operations (grinding) on parts containing chromium**				

11	**Machining operations (grinding) on parts covered with chromium paint**				
12	**Waste management**				
13	**Other** (please specify)				

*PPE (Personal protective equipment) worn:
1. Powered or air-fed, filtering respirator
2. Reusable half or full face mask respirator (without powered or air-fed respirator)
3. Disposable face mask
4. Other Respiratory Protection Equipment (please specify)
5. Coveralls
6. Reusable Gloves
7. Disposable gloves
8. Other (please specify)
** LEV=local exhaust ventilation

Has your respiratory protection equipment (mask) been fit tested? (please circle)	**Yes** **No** **If yes, when?**
Have you received information, instruction or training on the use of safe work practices when carrying out this activity? (please circle)	**Yes** **No**
Hygiene facilities in the company (please tick box if apply)	☐ **Possibility to wash hands** ☐ **Take shower** ☐ **Separate place for working clothes** ☐ **Specific place for the storage of respiratory protective equipment** ☐ **Other** (please specify)…… ☐ ……
Have the work conditions been normal during the work day? (please circle)	**Yes** **No** **If not normal, please specify (e.g. problems with mask or extraction not working):**

3. Job description in welding (please list the type of work tasks you have been involved in today)

	Work task	**Duration of the task in a work shift** (hours/ minutes)	**Frequency of the task** (x times per week)	**PPE* used** (add the corresponding numbers)*	**LEV** used:** 1. Gun fixed extraction 2. Movable welding hood 3. Extracted work bench 4. Extracted welding booth 5. General ventilation 6. Other (please specify)
1	**Manual welding**				
2	**Manual tack-welding**				
3	**Robot welding**				
4	**Other manual tasks**: Cleaning, Grinding, Cutting etc.				
5	**Cleaning and maintenance of equipment**				
6	**Waste management**				
7	**Other** (please specify)				

*PPE (Personal protective equipment) worn:
1. Welding helmet with powered or air-fed, filtering respirator
2. Welding helmet with half mask re-usable dust respirator
3. Welding helmet with disposable particulate respirator
4. Welding helmet without any respirator
5. Welding helmet with other respiratory protection equipment (please specify)
6. Fire/flame resistant clothing
7. Welding gloves
8. Other gloves
9. Other (please specify)
** LEV=local exhaust ventilation

Has your respiratory protection equipment (mask) been fit tested? (please circle)	**Yes** **No** **If yes, when?**
Have you received information, instruction or training on the use of safe work practices when carrying out this activity? (please circle)	**Yes** **No**
Hygiene facilities in the company (please tick box if apply)	☐ **Possibility to wash hands** ☐ **Take shower** ☐ **Separate place for working clothes** ☐ **Specific place for the storage of respiratory protective equipment** ☐ **Other** (please specify)..... ☐ .....
Have the work conditions been normal during the work day? (please circle)	**Yes** **No** **If not normal, please specify (e.g. problems with mask or extraction not working):**

Operational conditions in welding

What material was welded? (please circle) ➢	➢ **Stainless steel** **Other** (please specify) ➢
➢ **What welding method was used?** (please tick box) ➢	☐ **MMA (manual metal arc)** ☐ **MAG (metal active gas)** ☐ **MIG (metal inert gas)** ☐ **TIG (tungsten inert gas)** ☐ **SAW (submerged arc welding)** ☐ **Plasma - plasma gas** ☐ **Flux-cored welding** ☐ **Other** (please specify)..... ☐ .....
➢ **Chromium and nickel content of the welded material?**	➢ **Chromium content:** .....**%** ➢ ➢ **Nickel content:** .....**%** ➢ ➢ **Don't know** (please circle if apply) ➢
Was the welded material painted with chromium containing paints? (please circle)	➢ **Yes** **No** **Don't know**
Material and type of the welding rod? ➢	➢ ➢ ➢
Material of the welding flux? ➢	➢ ➢ ➢
Where do you weld? (please tick box if apply)	☐ **Outdoor** ☐ **Outdoor in a ventilated confined space of** ..... **m^3** ☐ **with no/natural ventilation** ☐ **with forced ventilation** ☐ **with LEV*** ☐ **Indoor in a space >1000 m^3** ☐ **Indoor in a confined space of** ..... **m^3** ☐ **with no/natural ventilation** ☐ **with forced ventilation (e.g. ship building)** ☐ **with LEV***

* LEV=local exhaust ventilation

7.2 Annex 2: Information for Participating Companies

HBM4EU occupational biomonitoring study on chromium and other harmful chemicals

Information for Participating Companies

Introduction

We would like to invite your company to take part in HBM4EU (Human Biomonitoring for Europe), a pan-European study which aims to investigate workers' exposure to hazardous chemicals in the workplace.

HMB4EU is a European project running from 2017 to 2021 and including experts from 28 European countries and European Union agencies. It is funded by the European Commission's Horizon 2020 Program and by our national governments. Further details can be found at https://www.hbm4eu.eu/about-hbm4eu/.

We are reaching out to companies authorised to use hexavalent chromium Cr(VI) under the EU REACH Regulation and affected by the proposition to limit workers' exposure to Cr(VI) and other chemicals under the EU Directive on carcinogens or mutagens at work (Directive 2004/37/EC). Your participation can further benefit your company's risk assessment & management and corporate responsibility practices. Our role is completely funded and participation into the project does not result in any out-of-pocket costs for your company.

About the study

The aim of this study is to evaluate the exposure to carcinogenic Cr(VI)at the European workplaces and to evaluate if the current safety and control measures are able to protect workers from harmful exposure. Secondly, we are testing the utility of new, more specific methods to assess the worker's exposure to Cr(VI)from the human samples. These methods will avoid the confounding effect caused by the exposure to less harmful trivalent chromium Cr(III).

We will also evaluate the exposure to nickel, manganese, and perfluoroalkylated substances if exposure to such chemicals is anticipated in your company. Biological monitoring in urine, blood and breathing samples will be the main method in the assessment of exposure, but industrial hygienic sample (air and hand wipe) measurements might be also carried out.

From each participating company, we will need up to a total of 15 workers, as follows:

(a) up to 10 workers whose duties involve welding or surface treatment activities (however, if the company has e.g. multiple sites or multiple processes falling under the scope of the study, also higher number of participating workers is possible), and

(b) up to 5 workers who do not have such duties, to be used as a comparison group.

What does my company have to do if we agree to take part?

Once your company agrees to participate, the next steps are:

1) Following your signed consent, our Research Team will contact you to arrange a suitable time for our team members to visit your premises and speak to you and your workers about our study. An information leaflet will be given to your workers. Workers will then have to agree to participate by signing their own consent forms.
2) Our research team will visit your company on an agreed date to take biological and hygienic samples from participating workers and to ask them a few questions about their background and working routines, and to collect information on the relevant processes and work activities.
3) If we have your permission, we may take photographs of relevant processes and work activities, which will be amended such that workers or the company cannot be identified. This material may be also used for demonstration purposes in the information session in which results of the study are presented in your company.
4) Samples and information will be taken from your workers during working hours.
5) The duration of sampling and information collection will depend on the category of the participant, i.e. exposed versus unexposed. For chromium exposed worker's it will take two times 15 minutes to give a breath sample and about 10-15 minutes to fill the questionnaire. Time will be needed also for two blood samplings and urine samples. For unexposed workers each sample is given only once.
6) Once samples are gathered, information regarding your company and workers' names will be coded and anonymity will be guaranteed.
7) Samples and information gathered from your workers will then go for analysis.

What are the benefits for the companies participating to the study?

This Pan-European study will help you to comply with your possible obligations under EU chemical legislation (REACH) and/or your obligations under the EU Directive on carcinogens or mutagens at work (Directive 2004/37/EC), which will set an EU-wide binding limit value (BOELV) for the exposure to hexavalent chromium exposure at work.

By participating, your company will:

- Receive an electronic copy of the report with the collective results of the study published on the website of the HBM4EU project. The report will not contain any information identifying your company or your workers.
- Receive your company-specific hygienic report electronically. The report will include recommendations for the surveillance and monitoring procedures of your workers.
- You can also choose to receive an electronic report of the collective urinary chromium biomonitoring results of your workers, but will not receive individual results. Your workers will receive their personal chromium exposure results.
- Your workers will gain awareness regarding the safety measures that they need to follow when carrying out activities involving exposure to hexavalent chromium

Does our company have to take part?

No, it is entirely up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign a consent form.

However, even if you sign the consent form you are still free to withdraw at any time and without giving reason and we will not approach any member of your staff to participate in the study. However, we will retain right to use any samples collected prior to the withdrawal in a confidential manner.

Are there any risks if my company joins HBM4EU?

There are no risks involved if your company joins HBM4EU, and your company's name will not be disclosed no matter what the results regarding chemical exposure.

How will my company's privacy be guaranteed?

- Participants are anonymous as their names are replaced with a code, and therefore cannot be traced as working for your company.
- Any information that may lead to the identification of a worker or your company will not be stated in any published reports i.e. country or company name.
- Computer security will be used to block any unauthorised access and all paper records will be securely stored.
- Information or samples provided to researchers will not include your company's registration numbers.
- Any results reported by this study will not contain information that may identify your company or staff. Only anonymous results of research conducted by the research team will be published and made available on the study's website: https://www.hbm4eu.eu/

Are there any costs involved?

There are no costs involved except brief working time of your staff members allocated for this study.

Who has reviewed the study?

The study is reviewed by the Bioethics committees and the Data protection commissioners of [Country]

Who do I contact if I would like more information about the hexavalent chromium study?

You can always reach out to [Name Surname of Research Coordinator of the Country]

Tel: [xxxxxxx] Email: [xxxxxxxx]

7.3 Annex 3: Information for Participating Workers

HBM4EU Occupational biomonitoring study on hexavalent chromium and other harmful chemicals

Information for Participating Workers

You are invited to take part in a research study. Please read the following information to understand why the research is being done and what it involves. We are happy to answer any questions or concerns you may have.

About HBM4EU

People are exposed to a complex mixture of chemicals throughout their daily lives. These chemicals can be found in the environment, consumer products, food and drinking water and at workplaces.

Human biomonitoring involves collecting samples from people, e.g. blood, hair, saliva or urine, and measuring the levels of indicators of chemicals that are of interest. HBM4EU (Human Biomonitoring for Europe) is a European study, which aims to harmonise and use human biomonitoring to understand people's exposure to such chemicals and the related health risks, in order to improve chemical risk management. At workplaces, human biomonitoring can inform us on the need to reduce exposure. HBM4EU is funded by the European Commission and national governments. It includes experts from 28 countries and European Union agencies and will run from 2017 to 2021. Learn more at https://www.hbm4eu.eu/.

About this study

We want to check if the current safety and control measures used at the workplaces across Europe can protect from the exposure to hexavalent chromium (Cr(VI)) and other harmful chemicals. In addition, we want to study new methods to assess the exposure to these chemicals.

The study has been approved by the [*national Bioethics Committee*] and complies with the Data Protection Regulation.

Why did you choose me?

We are inviting workers whose duties involve possible exposure to hexavalent chromium (Cr(VI)) (welding, plating and surface treatment activities) and workers without such duties, for comparison. You were chosen because you work in a workplace in which you may be exposed to hexavalent chromium (Cr(VI), or we consider you as a suitable control person since your work tasks do not include such exposures. Your employer has consented to participate in the study and has agreed to you participating if you decide to do so.

What do I have to do if I agree to take part?

You don't have to change your usual routine since the study will take place during normal working hours. If you decide to participate, you will confirm your agreement by completing and signing the enclosed consent form.

We will then find a suitable time to perform the study. You will meet the researchers during the work week for the collection of samples.

If your duties involve stainless steel welding or chromate plating or surface treatment, you will be asked to provide:

- Exhaled breath samples, by breathing normally into a sterile disposable tube for about 15 minutes, at both the beginning and end of your working week
- Urine samples before the work shift at the beginning of your working week and after the work shift at the end of your working week. We will provide you with a collection bottle which you can give to the researcher.
- Two small samples of blood (16 ml) will be collected from the vein in your arm. These will be collected post-shift preferably in the end of the work week or at least after one or two days of work.
- You will also need to fill a questionnaire which includes questions on your work tasks, personal protection and lifestyle aspects which may affect the results of the chemical analyses.

From some (not all) participants, we may also wish to collect personal air samples, which are collected by wearing a specific air sampling device on your work clothes, while you carry out your normal work tasks during one single work day. Wipe samples from your hands might also be collected in order to measure hand contamination.

Optionally and only if you consent to, we may take photographs or video to document your work area and practices. We will blur these materials to protect your identity and your company. You can still participate in the study without being present in photographs or video recordings.

If your duties ***don't*** involve chrome plating, surface treatment or stainless steel welding, you will be asked to provide the following:

- A sample of the urine you pass first thing in the morning before meeting with the researcher. We will provide you with a collection bottle which you can give to the researcher.
- An exhaled breath sample, by breathing normally into a sterile disposable tube for about 15 minutes.
- Two small samples of blood (16 ml) will be collected from the vein in your arm,

at any time during the working week.

The blood and exhaled breath samples will be collected from you by a trained health professional.

What will happen to my samples, data and results?

We will replace your name with a code to protect your privacy and will transfer the samples to specialised laboratories for analysis.

Your samples will be examined to measure your exposure to hexavalent chromium. Depending on your work tasks they will be also examined for nickel and manganese (if you are working as a welder), or nickel (if you are performing nickel plating) or for polyfluorinated substances (if you are working with chrome baths), which may also be significant chemical contaminants in these work tasks. Urine and blood samples might be additionally analysed for the early, reversible cellular effects caused by the chromium in order to study the utility of these tests in the health surveillance of workers.

Your samples will not be analysed for alcohol, prescription or illegal drugs.

A*nonymised* data collected from you and other participants will be stored and used for research purposes and may be combined with other data from different sources. Your anonymised samples

will be stored at [specify place and length of storage] for use in future ethically approved biomonitoring studies to study chemical exposure.

Your *personal* results for urinary chromium will be reported to you [in approximately XX weeks/months by NNNN], unless you tell us you do not wish to receive them. When the results of the whole study will be finished, you will receive the summary of the collective results from the all participating companies.

Your employer will receive the collective results of all the workers, but will not receive individual results. The *collective* results from all the participating companies will be published as a study report which will be openly accessed at https://www.hbm4eu.eu/

How will my privacy be guaranteed?

HBM4EU complies with the European Data Protection Regulation. We guarantee your anonymity by replacing your name with a code and protecting all electronic and paper records from unauthorised access. Published reports of the study will not contain information that can trace back to you or your company. Your employer or other third parties will not have access to your personal results, unless you consent to.

Why do you need my written consent?

Your written consent confirms that you volunteer to take part in the study, understand what is required from you and why. You will also confirm that we can contact you in the future to tell you about your personal results or for scientific, statistical or historical purposes.

How will I benefit if I participate?

The study will help to develop the safe working practices at your workplace. You will learn about your personal exposure to chromium and get guidance how to reduce it.

Are there any risks if I join the HBM4EU study?

All sampling will be conducted by qualified and specially trained health professionals. There are no risks, other than possible minor discomfort during sample collection.

Can I quit the study?

We encourage you to discuss with us any concerns you may have, but you are free to withdraw the study at any time without consequences. We will, however, retain right to use any samples collected prior to the withdrawal in a confidential manner.

Are there any costs to me?

There are no costs to you. Your participation in the study will take place during your normal working hours (with the exception of the collection of urine samples first thing in the morning). You will not face salary deductions for your time commitment to the study.

Who do I contact if I'm unsure about anything or would like further information about the hexavalent chromium study?

Please contact [Name, Institute of National study Coordinator]

Tel: [xxxxxxx] **Email** [xxxxxxx]

7.4 Annex 4: Informed consent form for the companies

EMPLOYER CERTIFICATE OF INFORMED CONSENT

Study description		
Title	HBM4EU occupational biomonitoring study on chromium and other harmful chemicals	Code

Researcher identifier	
Name	Telephone
Institution	Email
Company information	
Name	
Street Address	Telephone
Country	Email
Company contact person	
Name	Telephone
Position	Email

Company Code		**Initials**
1	I have read the companion “Information for participating companies” leaflet. I have had the opportunity to consider the information, ask any questions regarding it and have received satisfactory answers.	
2	I understand that my company’s participation is voluntary and we are free to withdraw at any time without giving any reason, and without my company’s legal rights being affected. The HBM4EU research team will retain the right to use any samples collected from the workers prior to the withdrawal in a confidential manner.	
3	I understand that my company will not benefit financially from taking part in this study.	
4	I consent that the HBM4EU research team will enter my company’s premises to collect biological and industrial hygienic samples and exposure related information from workers who have agreed to participate in this study by signing their own consent form.	
5	I confirm that my workers’ salary will not be affected due to their participation in this study, which will take place during working hours.	
6	I consent to the use of cameras by the HBM4EU research team as follows: ☐ I **do not** give permission for any photography during the research visit ☐ I give permission for photography to document work areas and practices, under the condition that the photographs will be blurred to protect the identity of my company and my workers in any published reports.	

7	I understand that my company has the right to receive the *collective* chromium biomonitoring results of our workers via the nominated company contact, but will *not* receive *individual* results. I indicate my company's preference as follows: ☐ My company wishes to **receive the collective biomonitoring results of our workers** ☐ My company does **not to** wish to receive the collective biomonitoring results of our workers My company will also receive electronic copies of our company specific industrial hygienic report and the overall findings of this research study.	

.....	.....	.....
Name and position of company representative	Date	Signature of Company Representative

7.5 Annex 5: Informed consent form for the workers

WORKER CERTIFICATE OF INFORMED CONSENT

Study description	
Title	HBM4EU occupational biomonitoring study on chromium and other harmful chemicals

Participant identifier	
Name	Telephone
Company	Email

Participant Code		Initials
1	I have read the companion “Information for Participating Workers” leaflet. I have had the opportunity to consider the information, ask any questions I wished to and received satisfactory answers.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, and without my medical care or legal rights being affected. The research team will, however, retain right to use any samples collected prior to the withdrawal in a confidential manner.	
3	The [*Specify organisation*] will be able to contact me during working hours to collect my personal samples and information after I have consented to participate in this study.	
4	I consent that the [*Specify organisation*] has the right transfer my sample(s) and/or personal data, in coded form to protect my identity, to specialised laboratories to analyse the chemicals and markers specified in the “Information for Participating Workers” leaflet.	
5	I consent that the [*Specify organisation*] has the right to store my sample(s) and personal data in a biobank for [*no of years*] for future ethically approved biomonitoring studies. I understand that the [*Specify organisation*] may contact me in the future regarding the use of my stored sample(s) and personal data. My contact details may be stored exclusively for this purpose and will not be disclosed to any third party.	
6	I consent to the use of cameras by the [*Specify organisation*] as follows: ☐ I **do not** wish to be photographed during the research visit ☐ I give permission for photography, under the condition that the photographs will be blurred to protect my identity in any published reports.	
7	I understand that I will not benefit financially by taking part in this study.	
8	I understand that I will receive information on my personal results for urinary chromium. I will receive this information from [*Specify for each country]*.	

	In addition, when the whole study is completed, I will receive the summary of the final collective results of the study. I want to receive this by email/by post to the following address: _____	

.....	.....	.....
Name of Participant	Date	Signature of Participant

Statement by the researcher/person taking consent

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

.....	.....	.....
Name of Researcher / person taking the consent	Date	Signature of Researcher / person taking the consent

7.6 Annex 6: Information leaflet on Cr(VI)

Working safely with chromium

Working with some forms of chromium (Cr) may affect health. This leaflet tells you about the possible health effects, the preventative measures your employer must apply and the precautions you should take to protect your health.

What is chromium (Cr)?

Cr is a relatively common chemical element. It is found naturally in rocks, soil, plants, animals and volcanic dust and gases. Cr compounds form a large and varied group of chemicals. They can be solid, liquid or gas and have no taste and no odor. The most significant forms of Cr are metallic chromium (Cr(0)), trivalent chromium (Cr(III)) and hexavalent chromium (Cr(VI)). Under some conditions, Cr forms can change from one to another.

- Cr metal is steely-grey and shiny. It has high corrosion resistance and hardness and is used mostly in the production of stainless steel and chrome plating. Cr metal is not harmful to human health.
- Cr(III) occurs naturally in living organisms. It is an essential nutrient in trace amounts. It is found in some industrial processes and has a low toxicity.
- Cr(VI) is very toxic. It is classified as a carcinogen, which means that it can cause cancer.

In which industrial processes and products can Cr(VI) be found?

- Production and use of stainless steel and other chromium alloys (and during the welding and cutting of these).
- Electroplating.
- Production of dyes, paints, inks, pottery and plastics using Cr pigments.
- Leather tanning.
- Wood treatment.
- Chromate-containing primers and other surface coatings.
- Smelting of ferrochromium ore.
- Impurities in portland cement, etc.

How can Cr(VI) get into your body?

- By inhaling airborne Cr(VI) in contaminated dust, fumes or mist.
- Skin contact through handling solutions, coatings or cements containing Cr(VI).
- Swallowing it, through handling food contaminated with dust on your hands.

How can Cr(VI) harm you?

As with all chemical exposures, the risk related to Cr(VI) exposure depends on your personal traits and habits, how much of the chemical you were exposed to, how you were exposed, how long and how often the exposure occurred, and whether other chemicals were present.

Single exposures to Cr(VI) compounds may cause:

- Irritation and inflammation of the nose and upper respiratory tract.
- Irritation, burns or ulcers of the skin, if your exposure is through the skin.
- Eye damage from splashes.

Repeated or prolonged exposure to Cr(VI) compounds may cause:

- Cancer of the lung.
- Damage to the nose, inc. ulcers and holes in tissue flap separating the nostrils.
- Inflammation of the lungs.
- Allergic reactions in the skin (dermatitis) and respiratory tract (e.g. wheezing).
- Kidney damage.
- Potential effects on reproduction (e.g. male fertility, fetal development).

What must employers do to protect their workers?

The [*refer to EU/national*] law requires employers to:

- Assess the risks to your health and the precautions needed for your protection
- Prevent you from getting exposed to Cr(VI), or where this cannot reasonably be done, adequately control your exposure
- Reduce your exposure to airborne Cr and its compounds so far as reasonably practicable, and in any case to below the following workplace exposure limits:
- for Cr (VI) compounds, XX milligrams per cubic metre (mg.m3) of air, averaged over an 8-hour period
- for other chromium compounds, XX mg.m3 averaged over an 8-hour period
- Maintain all fume and dust controls in efficient working order
- Provide fit testing of any tight-fitting respirators
- Find out how much Cr you are exposed to, normally through a monitoring programme, and tell you the results
- Arrange any health checks that are necessary
- Inform, instruct and train all employees who may be exposed to chromium

What must you do, if you work with processes involving Cr(VI)?

- Use the extraction equipment or other control measures correctly,
- Use the protective clothing and equipment provided.
- Always use the washing facilities provided, which should be adequate and suitable for your needs.
- If you have to wear a respirator make sure:
    - it fits properly
    - if it is a tight-fitting mask, that you have been fit tested and are clean shaven
    - it is clean and in good working order
    - the filter is changed regularly
    - stored in a clean/dry place, preferably a locker.
- Report defects in enclosures, extraction equipment or other control measures to your employers.
- Don’t eat, drink or smoke in work areas where chromium may be present.

How can you get more information?

[*Adopt at national level, as you find appropriate. May refer to the national competent authority for occupational health and safety or other appropriate official body*].