How can HBM4EU support fight against occupational cancer?

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German Environment Agency
The CAS Registry currently (2019) contains more than 155 million unique organic and inorganic chemical substances.

EU chemical sales increased by more than 50% in 20 years (Cefic, 2018).

In many countries, chemical industry is one of the largest branches of the manufacturing industries.

About 215 million tons of chemicals hazardous to health have been consumed in EU-28 in 2016, including 34 million tons of carcinogenic, mutagenic and reprotoxic (CMR) chemicals (Eurostat).
Answer open policy-relevant questions as defined by EU Services and partner countries

Give policy makers a fast and easy access to results and data

Bridge the gap between science and policy
HBM4EU Consortium

5 years (2017-2021)
European Joint Programme under Horizon 2020
Total budget: ~ 74 million €

30 countries (24 EU Member States, 5 associated countries, Switzerland) and the European Environment Agency

117 Partners

Coordinated by the German Environment Agency (UBA)
HBM4EU Structure

**Pillar 1: Science to Policy**
- WP4: Prioritisation and input to the annual work plan
- WP5: Translation of results into policy
- WP6: Sustainability and capacity building

**Pillar 2: European HBM Platform**
- WP7: Survey design and fieldwork preparation
- WP8: Targeted field work surveys and alignment at EU level
- WP9: Laboratory analysis and quality assurance
- WP10: Data management and analysis

**Pillar 3: Exposure and Health**
- WP11: Linking HBM, health studies, and registers
- WP12: From HBM to exposure
- WP13: Establishing exposure health relationships
- WP14: Effect Biomarkers
- WP15: Mixtures, HBM and human health risks
- WP16: Emerging Chemicals

**Scientific and Administrative Management**
- WP1: Programme management and coordination
- WP2: Knowledge Hub
- WP3: Internal Calls

**National and EU Stakeholders; Advisory Board**

**Governing Board**
Prioritisation of chemicals

Mapping of policy needs in participating countries and external bodies → research questions and nomination of chemicals

Scoring of chemicals based on **prioritisation criteria**

Consultation:
- EU policy board
- National Hubs
- Stakeholders

Scoping documents for prioritised chemicals & research plans

1. Hazard properties
2. Exposure characteristics
3. Regulatory status
4. Public concern
5. Technical feasibility

https://www.hbm4eu.eu/
https://www.hbm4eu.eu/the-substances
Prioritisation at national and EU level

Second round
Prioritisation 2018

9 substance groups:

1. Acrylamide
2. Aprotic solvents
3. Arsenic
4. Diisocyanates
5. Lead
6. Mercury
7. Mycotoxines
8. Pesticides
9. UV filters
### Carcinogenic priority substances or substance groups

**First round Prioritisation 2016**
- 1. Phthalates/DINCH
- 2. Bisphenols
- 3. Per-/Polyfluorinated compounds
- 4. Flame Retardants
- 5. Cadmium & Chromium
- 6. PAHs and air pollutants
- 7. Anilin family: MOCA
- 8. Chemical mixtures
- 9. Emerging chemicals

**Second round Prioritisation 2018**
- 1. Acrylamide
- 2. Aprotic solvents
- 3. Arsenic
- 4. Diisocyanates
- 5. Lead
- 6. Mercury
- 7. Mycotoxines
- 8. Pesticides
- 9. UV filters

Large number of carcinogenic substances: What does that mean for our bodies?
Policy-related questions

• Exposure of the general population – and of workers?
• What is the exposure of sensitive sub-groups?
• Exposure differences in Europe?
• Is exposure driven by diet, consumer habits, occupation or environmental contamination?
• Health impact?
• Drivers of mixture risks/substances contributing to certain types of cancer?
Collection of HBM data for general EU population

Schedule:

- **Today**: 10-11 PSU selected proportional to the population in each region
- **2021**: 300 participants per PSU

Information on internal exposure of the general EU population allows for a better assessment of workplace exposures.
### Standard operating procedures for better assessment of occupational exposure

<table>
<thead>
<tr>
<th>SOP No.</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SOP for <em>selection of participants and recruitment</em>, information to the participants, <em>informed consent</em></td>
</tr>
<tr>
<td>2</td>
<td>SOP for completion of <em>company and worker</em> questionnaires</td>
</tr>
<tr>
<td>3</td>
<td>SOP for <em>blood sampling</em>, including sample storage and transfer</td>
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<tr>
<td>4</td>
<td>SOP for the <em>collection of exhaled breath condensate samples</em></td>
</tr>
<tr>
<td>5</td>
<td>SOP for <em>urine sampling</em>, including sample storage and transfer</td>
</tr>
<tr>
<td>6</td>
<td>SOP for <em>air sampling</em> of inhalable and respirable dust fraction and (hexavalent) chromium</td>
</tr>
<tr>
<td>7</td>
<td>SOP for obtaining <em>dermal wipe samples</em></td>
</tr>
<tr>
<td>8</td>
<td>Procedure for <em>comparing occupational hygiene measurements with exposure estimates</em> generated using exposure models</td>
</tr>
</tbody>
</table>

HBM4EU is aiming to deliver practical guidance for better use of HBM in workplace settings!
QA/QC program: the HBM4EU ICI/EQUAS scheme

73 exposure biomarkers,
4 biological matrices
25 countries with participating laboratories,
7 laboratories involved in the organisation

- Bisphenols: 24 laboratories
- Phthalates: 20 laboratories
- DINCH: 7 laboratory
- PFAS: 21 laboratories
- PAHs: 23 laboratories
- Phosphorous FRs: 1 laboratory
- Brominated FRs: 15 laboratories
- Cadmium: 33 – urine, 22 – blood
- Chromium: 16, 19, 21 laboratories
Data management in HBM4EU

- Safeguard prior consent of the data owners
- Collect existing HBM data from partner countries
- Integrate HBM data generated within HBM4EU
- Grant access to data to work packages for undertaking analysis
- Make data available via IPCHEM as the European Commission’s reference access point for chemical monitoring data

EU General Data Protection Regulation
Activities on mixtures in HBM4EU

More than 100 researchers and stakeholders co-signed the position paper.

Position Paper: Preventing risks for people and environment from hazardous chemical mixtures

Rationale for action - Background

Man-made has changed the natural prerequisites for sustainable development of life through innovations of new chemicals (pharmaceuticals, pesticides, polymers, detergents and more) and by refining natural products (e.g. crude oil, wood, natural rubber, fragrances and much more). This has both directly and indirectly influenced and changed human lives, ecosystems and the planet's environment. While many of the innovations have improved the quality of life, there has also been an increased understanding that exposure to many hazardous chemicals and their mixtures can reduce the number of deaths, pollution and other adverse effects.
Targeted occupational study: Chromium VI and others (lead: FIOH - Finland)

**Exposure:** workers during welding activities, Cr (VI) electroplating, other surface treatment activities

**Study info:** 8 countries (BE, FI, FR, IT, NL, PL, PT, UK), 50 workers/country in 3-5 companies/country; analysis of Chromium VI, PFAS, Ni and Mn (where relevant)

**Time schedule:**

- **2017:** Research plan developed
- **2018:** Harmonised methodology & beginning of sampling
  - Urine, blood, exhaled breath & industrial hygiene samples
- **2019:** Finalisation of sampling & analysis
  - Analysis for HBM4EU priority Substances in labs that have passed WP9 QA/QC

**Outlook:** preparation of next occupational study for exposure to diisocyanates and others in plastics and construction sectors
Collection of HBM data for workers

1st targeted occupational study

Focus in companies performing surface treatment and stainless steel welding

Main aims:

- **Support** recent **regulatory measures** (REACH and CMD) related to occupational exposure to Cr(VI)
- Create **representative EU-wide data** on the **occupational exposure to Cr(VI)**
- Give a more accurate picture on Cr(VI) exposure and compare different matrices.
- Provide **recommendations** on the use of biomarkers for the **assessment of occupational exposure** to Cr(VI).

<table>
<thead>
<tr>
<th>Exposure biomarker</th>
<th>Exposure biomarker</th>
<th>Effect Biomarker</th>
<th>Personal air samples and dermal wipe samples</th>
<th>Context infos for modelling study</th>
<th>Questionnaires</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr(VI) (urine), EBC (blood)</td>
<td>P-PFAS, Ni/Mn (urine), EBC (blood)</td>
<td>(genotox and epigenetic) – blood</td>
<td>Modelling study</td>
<td>of health</td>
<td>Company</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Workers</td>
</tr>
</tbody>
</table>

50 workers/country | 25 controls/country

Data and measurements collected

Sample analysis | Data entry

Data analysis and reporting
Case studies on effects of substances classified as carcinogens

Work Package 5: Derivation of Health-based guidance values (HBM-GV)

Work Package 13: Effect biomarkers - exposure and cancer relationships

Work Package 15: Mixtures - Chromium VI, Nickel, PAHs and lung cancer
Derivation of Health-based guidance values (HBM-GV)

HBM-GV for carcinogenic substances for which a threshold on exposure-effect relationship can be identified

Example: Cadmium (Deliverable 5.15)

• Cd and Cd compounds are carcinogenic to humans (Group 1, IARC)
  
  – lack of consistent relationship between exposure and effect in epidemiological studies (confounders: smoking and other carcinogenic factors)
  
  – derivation of HBM-GV is based on nephrotoxicity (most sensitive endpoint)
Establishing exposure and cancer relationships

PAHs and air pollutants
• Investigating mechanisms and AOPs beyond carcinogenic outcomes

Cd and Cr (VI)
• Collating mechanistic explanations for the effects and effect biomarkers of carcinogenicity (lungs, kidney, prostate, breast)

HBM4EU contributes to risk assessment by generating knowledge on exposure-health relationships!

• critical assessment of possible associations of acrylamide with several endpoints including cancer

Diisocyanates
• collection of mechanistic information and AOPs relevant to diisocyanates-induced cancer
• exploration of the use of existing cohorts for linking diisocyanates to health via occupational exposures
Development of 5 case studies on mixtures and health outcomes

1. Developmental neurotoxicity beyond polybrominated diphenylethers (PBDEs)
2. Heavy metals and nephrotoxicity
3. Anti-androgeneric chemicals and male reproductive health
4. Chromium (VI), nickel and polycyclic aromatic hydrocarbons and lung cancer
5. Addressing exposure misclassification in mixture studies
## Case study: Chromium (VI), nickel and polycyclic aromatic hydrocarbons and lung cancer

<table>
<thead>
<tr>
<th>Substance</th>
<th>TLV-TWA* (mg/m³)</th>
<th>Exposure data TWA (mg/m³)</th>
<th>HQ</th>
<th>HI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr VI</td>
<td>0.005</td>
<td>0.011</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>[Carcinogenic and Mutagenic Directive]</td>
<td></td>
<td>(HSE, 2013)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soluble nickel compounds</td>
<td>0.5</td>
<td>0.077</td>
<td>0.154</td>
<td>2.369</td>
</tr>
<tr>
<td>[Chemical Agents Directive (98/24/EC)]</td>
<td></td>
<td>(HSE, 2013)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAHs</td>
<td>0.00007</td>
<td>1.03 X 10⁻⁶** benzo[a]pyrene</td>
<td>0.015</td>
<td>&gt;1</td>
</tr>
<tr>
<td>PAHs mixtures containing benzo[a]pyrene</td>
<td></td>
<td>(Jeffrey et al., 2000)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Cumulative exposures pose a risk for lung cancer that needs to be further analysed. Cr (VI) is the driver substance.
Planned: 2nd Targeted Occupational Study

Focus on:

• Diisocyanates
  – In motor vehicle manufacturing and repair, in the use of diisocyanate containing glues and in the various uses in construction sector

• Waste management – specifically electronic waste (E-waste)
  – Metals (Cr, Cd, Hg), flame retardants, phthalates
• 4-5 countries/region
• Both exposure and effect biomarkers
• E.g. genotoxicity markers relevant for both regions
• Research plan and sampling in 2020, analysis of the results in 2021
Communication tools: https://www.hbm4eu.eu

HBM4EU Website
Leaflet
Newsletter
Online Library
Scoping documents
Introduction for Stakeholders
Deliverables
Fact Sheets
Introductory video
Contribution of HBM4EU to protect workers health

HBM4EU

- collects internal exposure data on European level from various health-relevant chemicals of the general EU population and workers.

- allows better comparisons of background exposure data with occupational exposures.

- creates practical guidance for the use of HBM in workplaces.

- investigates links of chemical exposures and mixtures to health effects such as cancer and derivation of HBM-GV.

- supports the knowledge on exposure routes which may help to improve protective measures for workplaces.
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