

HBM4EU reflections on the European Commission's chemicals strategy for sustainability

Human biomonitoring is a key tool in supporting the design, delivery and evaluation of chemical regulation in Europe.

[HBM4EU](#) - the European Human Biomonitoring Initiative - is funded under the European Commission's Horizon 2020 programme and is investigating knowledge gaps regarding the exposure of the European population to priority chemical substance groups and resulting impacts on health. As a leader in research on exposure to chemicals and impacts on health in Europe, HBM4EU is well-positioned to provide scientific insights on key elements of the chemical's strategy for sustainability.

This document channels input from the [HBM4EU Management Board](#) to the European Commission on the **roadmap on the chemicals strategy for sustainability**. It provides some reflections on priorities for actions identified in the roadmap, highlights additional aspects seen as critical from the perspective of HBM4EU and identifies relevant lines of evidence produced under the initiative.

Fostering coherence across legislative silos - "one substance – one assessment"

HBM4EU supports a coherent and consistent approach to managing substances that are subject to regulation under two or more legislative silos. A first step involves undertaking one single risk assessment at European level, involving all relevant European agencies.

- The data on internal exposure generated using human biomonitoring data provides a complete picture of human exposure and can be used to enhance chemical risk assessment by providing information on actual human exposure via multiple exposure pathways likely to be regulated under separate policy silos. An understanding of the contribution that different exposure routes make to total exposure provides the starting point for deciding on risk management measures under legislative silos.
- HBM4EU is contributing to the discoverability, accessibility and availability of high quality, reliable and coherent exposure datasets at European level, in particular by making metadata available via the Information Platform for Chemical Monitoring (IPCHEM). This supports the sharing and reusing of data across legislative silos as required for the "one substance – one assessment" approach.

Understanding human exposure to chemicals in Europe

Human biomonitoring data is co-created through public participation in scientific research. It provides citizens with insight to their personal chemical body burdens. The zero-pollution agenda should depart from an understanding of how the bodies of European citizens are polluted with synthetic chemicals, and make reducing the chemical body burden and associated health impacts a key priority.

- Demonstrating the effectiveness of existing policies is essential for maintaining public trust and securing the ongoing collaboration of industry and stakeholders. Under HBM4EU, human biomonitoring conducted through harmonised approaches at European scale provides a platform for monitoring the exposure of the European population to chemicals. This data will allow us to track the efficacy of policies in minimising human exposure to [HBM4EU Priority Substances, as well as the trends in substitution of chemicals that are subjected to regulation](#).

- An understanding of population exposure and the exposure of vulnerable groups, against health-based human biomonitoring guidance values, provides the basis for effective cross-silo risk management aimed at reducing impacts on health.
- HBM4EU data will establish a baseline of exposure for the European population against which to measure the effectiveness of future risk management measures under a future strategy. Future biomonitoring activities will allow us to establish time trends in exposure, informing the evaluation of new risk management measures.
- Comparing human biomonitoring data from across Europe can highlight regional differences linked to variations in diet, environmental quality, climate, consumer behaviour and lifestyle. HBM4EU is also working to identify vulnerable groups, or higher exposure groups, to inform targeted measures to reduce exposure.
- Identifying exposure to new chemicals (e.g. substitutes of regulated compounds) in the population and their sources and determinant exposure factors. New planned HBM studies as well as the biobanked samples offer the possibility of a prompt alert of emerging risks and thus, providing valuable information to set the priorities in risk assessment and health protection.

Identifying routes of exposure

When exposure is a concern, the capacity to identify the main pathways and routes of exposure for chemicals is a *sine qua non* for effective risk management.

- HBM4EU is undertaking a thorough analysis of plausible routes and pathways of exposure for HBM4EU priority substances, taking into account differences in exposure modifiers, such as age and gender, as well as profession, across Europe.
- Using modelling tools, we relate internal exposure to environmental sources and identify external exposure pathways. Using validated models, we reconstructed external exposure levels and derived exposure estimates over the life-course for the general population across the EU for priority substances.

Human exposure to chemicals in products in a circular economy

Protecting citizens from hazardous chemicals in products, including products imported into the EU, is identified as a priority in the Roadmap. The transition to a circular economy is laying out new pathways for human exposure to chemicals in recycled material flows. To better protect consumers and workers, HBM4EU call on industry to make information on the chemicals in products, articles and waste and the respective use volumes transparently available through accessible online tools. This will support research to link evidence on human exposure to external exposure pathways.

- HBM4EU is improving access to data on human exposure to chemicals and identifying upstream exposure routes in various material flows – including in consumer products, via diet and in the occupational setting. This can inform targeted efforts to minimize exposure by eliminating chemicals from material flows.
- Over the long term, the availability of information on exposure to chemicals in specific material flows, including products, will stimulate the production of safer chemicals, products and materials.
- HBM4EU is producing data on the exposure of workers to chemicals in waste management installations, including recycling facilities. This evidence will help support the design of circular material flows that minimise human exposure at all stages of the product life cycle.

Informing chemical grouping and avoiding regrettable substitution

HBM4EU strongly encourages risk management procedures that explicitly avoid regrettable substitution, including thorough risk assessment of alternatives and the assessment and management of groups of substances.

- HBM4EU actively investigates human exposure to substitutes on the market, and emerging substitutes, as well as their health impacts, thereby addressing a well-known knowledge gap.
- When (certain) uses of chemical substances are prohibited or regulated, alternative substances should be subject to rigorous risk assessment. HBM4EU evidence will inform decisions on which substitutes have less impact on health – avoiding regrettable substitution. Examples include the flame retardants, bisphenols, per- and poly fluoroalkyl substances (PFAS) and phthalates, as well as cadmium or arsenic.
- HBM4EU evidence of exposure to and the health impacts of substitutes provides additional evidence to support grouping and can inform possible grouping of chemicals for regulatory purposes.
- Chemical grouping offers a means for accelerating risk assessment and risk management, in a context where we have an estimated 50,000 chemicals circulating on the market. HBM4EU research focusses on groups of chemicals, recognising that substances in a chemical family often have common functionalities, hazards and exposure pathways, and include older, current as well as new substances, often used to substitute substances subject to restrictions.
- Grouping is a particularly useful tool for the risk assessment and management of substances that are very persistent and very bioaccumulative (vPvB) and persistent, bioaccumulative and toxic (PBT), as well as chemicals of equivalent concern under REACH.
- HBM4EU developed a text mining tool based on artificial intelligence which screens the scientific literature as well as available data bases to rapidly identify putative health effects of substitutes.

Identifying and tackling chemicals of emerging concern

The need to strengthen the EU regulatory framework to rapidly react to the risk associated to chemicals of emerging concerns (CECs) and to the continuous new scientific information and evidence in this field is highlighted in the roadmap. It is critical to improve the availability of evidence on human exposure to CECs and their related health impact, to support effective prioritisation for risk assessment and management.

- HBM4EU is making available evidence on human exposure and associated health impacts through novel approaches to inform the identification of chemicals of concern under EU regulatory processes. This includes new large-scale suspect and non-targeted screening (NTS) approaches applied to human matrices to capture CECs, as well as unknown contaminants and their metabolites, in the scope of providing early warnings and broad support to exposure assessment.
- HBM4EU supports an approach to market access whereby chemicals undergo a rigorous screening before producers and importers are authorised to sell chemicals on the European market. This can be supported by the implementation of upstream approaches to ensure that chemical products are safe and sustainable by design.
- HBM4EU is providing the basis of a new expert network partnership to address this emerging chemical issue and support EU policies through a harmonized implementation of these NTS approaches.
- HBM4EU has connected high skilled HBM laboratories with emerging ones thus creating a network of analytical laboratories, that will guarantee the harmonization and comparability of HBM data. The links within this network have allowed for the implementation of a complete ICI/EQUAS program covering the substances in HBM4EU. The strengths and needs in analytical work in HBM

have been highlighted and expert laboratories have improved/developed analytical methods for the analytical gaps identified.

Tackling the combined effects of chemical mixtures

HBM4EU fully agrees with the need to address the combination effects of chemicals set out in the roadmap and has called for the stepwise translation of the latest science into the development of new approaches, methodologies and tools.

- HBM4EU is running a survey of human exposure to mixtures of pesticides using suspect screening analyses of citizens living in 'hot spot' areas in across six of our partner countries, with first results expected in the second semester of 2020. These analyses will inform whether 'hot spot' areas contribute to higher exposure groups and thus may require additional measures to safeguard public health. Additionally, this study will provide valuable knowledge regarding the utility of suspect screening as an innovative method for human biomonitoring.
- HBM4EU advances methodologies for assessing health effects due to exposure to chemical mixtures through real-life case studies cumulative risk assessment.
- Novel applications of *in vitro* assays combined with advanced high-resolution analytical tools for suspect and non-target screening is also being explored under the umbrella of HBM4EU in an advantageous way moving forward from direct exposure and effect analysis in humans to mixtures of chemicals.
- HBM4EU teamed up with four other EU funded research projects, i.e. EDC-MixRisk, EuroMix, EU-ToxRisk and SOLUTIONS to produce a joint position paper "[Preventing risks for people and environment from hazardous chemical mixtures](#)". The paper proposes 12 key actions and recommendations to improve risk assessment of chemical mixtures and was sent to the Director Generals of DG Environment, DG Research and Innovation and DG Health and Food Safety.

Understanding the health impacts of chemical exposure and promoting chemical safety

The roadmap sets the goal of promoting the highest standards of environmental and health protection globally. HBM4EU strongly supports enhanced efforts at European level to protect the population from the health impacts of exposure to chemicals.

- Under HBM4EU, we are combining health information with human biomonitoring data to understand exposure-response relationships for priority chemicals and mixtures. Health-related administrative registers include information on births and deaths, malformations, hospitalizations, medical prescriptions and the prevalence of diseases, such as cancer. Health register data on an individual level can be linked to health examination surveys and data from human biomonitoring studies to better understand causality.
- Understanding the impact of a chemical on population health requires comprehensive knowledge of the mechanisms by which a chemical exerts toxicity. Adverse Outcome Pathways (AOPs) provide a framework to integrate information from all levels of biological organization: from initiating events at the molecular level to the final adverse outcome on health at the level of the organism. Within HBM4EU we develop tools to link priority substances to critical AOP events, thereby gaining insight into possible health effects of chemicals. We focus on substances for which available toxicity data is very limited, such as emerging chemicals used to replace chemicals restricted on the basis of known hazards. We have also started developing quantitative AOPs which will enable us to connect substances at realistic exposure levels to putative health effects.
- In addition, HBM4EU is identifying biomarkers of effect, which can be used to measure molecular, cellular, biochemical, physiologic, behavioural, structural or other alterations in an organism driven

by chemical exposure. This allows us to complement exposure data with mechanistically based biomarkers of effects in relation to specific health problems and measure the impacts of chemicals in the human body. Biomarkers of effect are particularly useful not only to assess the risk of developing a given disease but also to minimize this risk through effective preventive interventions and to identify individuals who may be more susceptible to particular chemical compounds.

- HBM4EU has selected specific biomarkers of effect that will be investigated in human observational studies. This proof-of-principle can generate new knowledge on exposure health outcome associations and its underlying mechanisms at EU level.
- Developing QA/QC activities in order to increase the quality and comparability of HBM data used in risk assessment, modelling exposure pathways, or AOPs, by improving the analytical methodologies (e.g. reducing the LOQs) and extending the range of chemicals.

Delivering health and safety in the workplace

Occupational exposures to specific chemicals may, in many instances, be several times higher than environmental exposures experienced by the general population. Human biomonitoring provides a valuable tool for understanding human exposure to chemicals in the workplace and ensuring safety at work.

- HBM4EU is combining results from national occupational human biomonitoring surveys that have used harmonized study designs and methodologies to improve the usefulness of the information collected from occupational studies and deliver added value at EU level. Within HBM4EU, we are implementing three targeted occupational studies focusing on different priority substances.
- The first targeted occupational study was on chromium VI, focussing in companies performing surface treatment and stainless-steel welding. The main aims were to support recent regulatory measures (REACH and CMD) related to occupational exposure to Cr(VI) as well as creating representative EU-wide data on the occupational exposure to Cr(VI) in Europe. Sampling was done in France, Belgium, the UK, the Netherlands, Finland, Poland, Portugal, and Italy. Preliminary results showed that chrome platers have the highest urinary chromium levels, in some cases more than 10-times higher than levels measured in the control population. In other cases, pre-shift chromium levels were also higher than in controls. Although welders showed elevated levels, their levels were lower than chrome platers. Exhaled Breath Condensate (EBC) samples exhibited the same trend as seen in urinary chromium: chrome platers showed higher levels than welders, although welders also had elevated levels compared to the controls. Analysis of the results from the air samples and wipe samples (collected from the hands of workers) provide information on the exposure routes, which will be used to give recommendations for the minimization of the exposure at workplaces.
- The second occupational study will focus on diisocyanate exposure in the manufacturing and repair of large vehicles (non-booth spraying of e.g. boats/planes), the use of diisocyanate based hot-melt glues in different sectors, and construction sector, which includes different sources of diisocyanates exposure (floorings/screeds, insulation). Sampling will take place in 2020 with results available on 2021.
- The third occupational study will be in occupational exposures in E-waste handling. With the main aim being to support the sustainable processing of E-waste in Europe. By conducting a HBM study, we hope to contribute to awareness of potential hazards and stimulate good work practices that will lead to further improve protection of the worker's health from the risk of exposure to toxic components, including that of combined exposures. The study will include the assessment of exposure to several HBM4EU priority compounds, including metals (lead, inorganic mercury, cadmium, chromium), phthalates, and flame retardants. The study will be performed in Portugal,



Poland, Germany, Latvia, The Netherlands and in Luxembourg and probably in Belgium, Finland and UK.

Access to information and bridges between scientists and policy makers

The Roadmap recognises the need to adapt EU chemicals policies to reflect new scientific evidence, and to address gaps in the knowledge base.

- HBM4EU is explicitly producing new evidence to address knowledge needs identified by risk assessors and managers at European and national level, as well as by stakeholders at European level.
- Reflecting the priority to make information digitally available, biomonitoring data generated under HBM4EU will be available to policy makers, with metadata accessible via the Information Platform for Chemical Monitoring (IPCHEM). In compliance with the General Data Protection Regulation the publicly availability of human biomonitoring data at the individual level is restricted, with datasets available on request.
- HBM4EU partners have established an effective and open dialogue with actors involved in the policy process, in particular through exchanges with the European Food Safety Authority (EFSA), the European Chemicals Agency (ECHA), the European Environment Agency (EEA, also an HBM4EU partner) and relevant Directorate Generals (DGs), including DG Environment, SANTE, GROW and EMPL. These open exchanges have served to build trust and provide a forum for the joint interpretation of scientific evidence, facilitating the uptake of science in policy making.
- Elaborating an inventory of capacities and expertise of European laboratories and creating a network of analytical laboratories with proven utility for scientist and policy makers.
- In addition to exposure data, HBM4EU provides information on exposure pathways and possible health effects of priority substances and points to lack of sufficient knowledge when relevant.
- The HBM4EU ambassador has pointed out the relevance of HBM activities in different policy circles.