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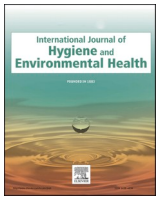

Special issue editorial: Key results of the european human biomonitoring initiative - HBM4EU

Human Biomonitoring (HBM) has increasingly become an established tool for the risk assessment of chemicals, chemical's safety, and for the steering of chemical policies in Europe, both at national level and worldwide for regulatory purposes. By monitoring internal human exposure, HBM is required to control the effectiveness of regulatory measures and to inform the general public as well as policy makers about the impacts of environmental pollutants and the use of synthetic chemicals on humans and the environment. HBM is important for achieving the goal of a sustainable and non-toxic environment for all by identifying areas with high risk of chemical exposure and by initiating, through science-to-policy approaches, targeted measures to reduce this exposure.

European citizens of all ages, as well as people worldwide, are exposed to a wide range of chemicals through their diet, their environment, the use of consumer products and at the workplace. Exposure to chemicals takes place through a variety of pathways and exposure routes, notably via dermal and oral uptake and by inhalation, with the combined exposure via all routes being the aggregate exposure. Knowledge about levels, co-exposures and extent of exposure are essential to inform effective policy-making to protect the European population from the impacts of exposure to hazardous chemicals on health.

Prior to the implementation of the European Human Biomonitoring Initiative (HBM4EU), a European Joint Programme, there was a clear lack of data on aggregate exposure to single substances and to combinations of chemical substances in the European population (highly exposed and vulnerable sub-groups) and on the actual distributions of exposure in different geographical European regions. Additionally, evidence-based knowledge on the link between external exposure via different routes, internal levels and human health was insufficient despite the productive long-standing national HBM programmes and the large number of Research and Development projects at national and European Union (EU) level. Furthermore, there have been significant limitations to the use of existing data as a basis for policy decisions at the EU level as they were not easily available and not collected according to harmonised protocols and might therefore not be comparable. The existing data were not representative of the European population and differences in the metadata characterising the datasets impede cross-dataset analyses.

At the beginning of this century, the European Commission which is responsible for chemicals policy, started a series of initiatives aiming at the development of a systematic, EU-wide HBM programme with harmonised methods, standards and study materials. First, in support of the Action 3 of the European Environment and Health Action Plan 2004–2010, an HBM Implementation Group was established to bring forward the development of a coherent approach to HBM in Europe in close cooperation with the Member States (Commission of the European Communities, 2003). In a second step, this approach was concretized in the first EU-co-funded project, Expert team to Support human BIOmonitoring on a European scale (ESBIO, 2009). Subsequently, the feasibility was piloted and further tested with the twin projects COPHES (Consortium to Perform Human Biomonitoring on a European Scale) and DEMOCOPHES (DEMOnstration of a study to Coordinate and Perform Human biomonitoring on a European Scale). While COPHES was working on the development of harmonised standards and setting up a framework for a coherent HBM in Europe (Joas et al., 2012; Schindler et al., 2014), DEMOCOPHES consisted in a feasibility study and generated the first HBM data for a limited number of substances in 1,844 children (5–11 years of age) and their mothers from 17 European countries (Den Hond et al., 2015). These results provided strong evidence for ubiquitous exposure of the European populations that were studied but also showed large differences between samples from different countries, thereby underlining the critical need for an EU-wide HBM study. These efforts ultimately led to the implementation of the large European Joint Programme, HBM4EU.

HBM4EU ran from 2017 to 2022 as a joint effort of 30 countries and 116 partner institutions from Europe and Israel with the aim to support and improve the EU's policies for chemicals, the environment and health. It was established as an innovative and unique type of large-scale, multi-national research programme operating at the science-to-policy interface. Importantly, national and EU level policy makers were included already early on in the planning phase of this demanding research programme. Policy needs, open policy and research relevant questions for altogether 18 prioritised substances and substance groups informed the setting up of this ambitious initiative. Important goals of HBM4EU were, besides the research output itself, a broad sharing of collected and produced data in accordance with the EU General Data Protection Regulation (2016/679) on the protection of natural persons with regard to the processing of personal data and a fast and easy access for policy makers and the scientific community to these results including the aggregated data sets, major conclusions, background information, and policy recommendations. A continuous and transparent dialogue between researchers and key actors in chemical regulation and policy-making at the EU level was maintained through an EU policy board. This board included representatives of different EU Departments and agencies such as the European Food Safety Authority (EFSA), the European Chemicals Agency (ECHA) and was led by the European Environmental Agency (EEA) which was also a partner of HBM4EU. In this way, HBM4EU ensured that policy makers gave input to the work plan development, kept track of the progress and were prepared and

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mobilised for optimal use of the research results to shape their policies and decisions.

The overarching objectives of HBM4EU were to:

i) harmonise procedures and tools for HBM at EU level,
ii) provide and, where missing, generate internal exposure data and link these data to aggregate external exposure and the relevant exposure pathways and sources,
iii) develop novel methods to identify human internal exposure to environmental and occupational chemicals and provide evidence for causal links with human health effects,
iv) provide policy-makers and the general public with science-based knowledge on the health risks associated with chemicals exposure, and
v) improve chemical risk assessment and policies in the EU through the effective use of HBM data.

To reach these objectives, the research activities were organized into clusters under three main pillars: 1) Science to Policy, which ensured the translation of results into policy, 2) European HBM Platform, which covered all components of HBM studies, and 3) Exposure and Health, which dealt with the research of innovative methods to determine the relation between exposure and health. By setting such a broad scope that emphasized involving and linking together different communities in the research process, HBM4EU ensured that the results of the initiative were relevant and useful to those most affected by exposures to hazardous chemicals.

This special issue contains the first comprehensive set of results from central activities of HBM4EU and reflects the complementarity of the HBM4EU components. However, it can only provide a glimpse of the extensive and intense work done collaboratively to further developing national HBM programmes in Europe and establishing HBM at a European level. Among the major outcomes of the project, we would like to highlight the importance of harmonisation of knowledge and protocols as a cornerstone for generating reliable scientific information on human exposure to hazardous chemicals in Europe to support the European environmental and health policy and the establishment of highly capable and EU-wide excellence networks.

The presented papers related to Pillar 1 "Science to policy" work expand on how HBM4EU results support current EU strategies, like the Chemicals Strategy for Sustainability and the Zero Pollution Action Plan (Lobo Vicente et al., 2023), and stress the importance of national awareness of HBM results for policy making (Ubong et al., 2023). They further elaborate on tools used to communicate with policy makers: indicators related to phthalates and DINCH exposure are presented as an example (Gerofke et al., 2023) and HBM guidance values for priority substances under the HBM4EU Initiative demonstrate how internal exposure levels can be interpreted concerning their potential health impact (Apel et al., 2023a,b). In addition, the use of HBM in chemical risk assessment is highlighted and methodological aspects, recommendations and lessons learnt are derived from HBM4EU work (Santonen et al., 2023b).

As ethics and ethical approvals are indispensable prerequisites of many studies and especially investigations in which humans are involved, HBM4EU has emphasized the EU-wide implementation and coordination of an ethics framework – and shares experiences and reflections in one of the papers included in this issue (Knudsen et al., 2023).

Harmonisation of materials and methods and operating procedures are essential for the preparation and generation of EU-wide comparable studies and study results. A tailor-made Quality Assurance (QA) program for analytical laboratories was designed and ran to this end. Lessons learned are derived for many aspects of the initiative, but this special issue dedicates three articles specifically to this topic: While one describes the tools and materials developed for a harmonised HBM study design and draws lessons from the development process, including the success in the QA program (Pack et al., 2023), the second one focusses on the coordination of the analytical phase (Vorkamp et al., 2023) and the third one discusses major aspects of administrative and scientific governance and steering of this multi-scale endeavour at the science-policy interface (Kolossa-Gehring et al., 2023).

The results of HBM4EU significantly contribute to understanding the exposure of European populations to a wide range of hazardous chemicals and how these exposures may impact human health. An overview paper showcases the EU-wide exposure data of 11 chemical substance groups in children, teenagers and adults from the HBM4EU Aligned Studies (2014–2021) (Govarts et al., 2023). A series of papers presents additional in-depth analyses of the internal exposure of Europeans.

HBM4EU work was organised around the 18 priority substances and substance groups. The comprehensive research on the substances is presented for two exemplary priority substance groups, the phthalates and substitute plasticisers as well as per- and polyfluoroalkyl substances (PFAS).

The phthalates case study perfectly illustrates the complex exposure situation and its numerous impacts on health and suggests some directions for a chemical policy aiming at a Zero Pollution ambition. Indeed, the study covers: current exposure to phthalates and DINCH in European children and adolescents (Vogel et al., 2023b); time trends following up the success of EU regulation and identifying needs for further action (Vogel et al., 2023a); the assessment of cumulative risks from simultaneous phthalate exposure (Lange et al., 2022); health-based guidance values and indicators as tools for risk description and transfer of results to policy conclusions (Apel et al., 2023a,b).

For the second substance group of high societal, scientific and health concern, PFAS, the study gives a comprehensive overview of European citizens exposure and evidence for the necessity to strengthen the protection of human health. It covers the exposure levels and determinants of variability in exposure in European teenagers (Richterová et al., 2023) a mixture risk assessment (following different methodological approaches) (Bil et al., 2023) and an overview of the PFAS results generated by all Work Packages (Uhl et al., 2023).

Further HBM results from the EU-wide HBM4EU Aligned Studies on the priority substances arsenic (Buekers et al., 2023), cadmium (Snoj Tratnik et al., 2022), and flame retardants in the general population and exposure determinants complement the picture of human internal exposure (van der Schyff et al., 2023).

The importance of HBM as a tool for the investigation of exposure at the workplace in a multi country setting was demonstrated by HBM4EU. Even though some companies may use HBM routinely, data are scarcely accessible. The HBM4EU chromates study underlines the need and use of an extension of occupational HBM studies to improve the protection of workers in the occupational setting in Europe and for collecting harmonised and comparable data (Santonen et al., 2023a).

In order to expand the HBM toolbox with new methods and findings concerning the relation of exposure and health, HBM4EU sought to explore different paths. One of them was the identification of relevant effect biomarkers, which is why a systematic approach to their implementation in HBM studies is explored in a dedicated article (Rodríguez-Carrillo et al., 2023). This Special Issue also elaborates on options to include more extensive health information in HBM studies (Tolonen et al., 2022).

New analytical and interpretation methods address the real-life simultaneous co-exposures to numerous chemicals which do not physiologically belong to the human body and how to deal with these very complex datasets. This special issue looks into the exposure and effects to mixtures of phthalates, PFAS, and pesticides as well as science-based recommendations for mixture risk assessment (Luijten et al., 2023; Ottenbros et al., 2023).

HBM4EU's key strengths include its interdisciplinary nature, which allows for a more comprehensive understanding of the complex interactions between exposures to hazardous chemicals and human health, and its multi-scale approach to exposure science, which provides

a more complete picture of how environmental exposures impact human health.

Even with all the success in HBM4EU and its legacy, the urgent need in our fast-paced and everchanging world for evaluation and regulation of newly emerging products and chemical use applications, need to be further developed and adapted. HBM4EU, with its systematic establishment of interlinked science-and-policy networks in the field of environmental health and chemical policies spanning national to European to international levels, can now serve as a beacon for a new generation of EU co-funded research partnerships.

HBM4EU's work is being continued in the new Partnership for the Assessment of Risks from Chemicals (PARC), as the next European project operating at the science-policy interface, building on the structures, networks and experiences of HBM4EU. PARC has a larger scope since it also covers exposure and effects of chemicals in the environment and puts an extensive focus on further development of hazard and risk assessment (Marx-Stoelting et al., 2023). Thus, PARC will be the next step towards a sustainable EU-wide HBM, an across-silo risk assessment of chemicals, a support for the European Green Deal and consequently for the protection of humans and the environment in Europe. It is highly expected by the scientific community and by citizens that a long-term sustainable HBM framework will be established in Europe in support of policy making and of environment and health research.

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Marike Kolossa-Gehring
Head of Section II 1.2 Toxicology, Health Related Environmental Monitoring, German Environment Agency, Corrensplatz 1, 14195, Berlin, Germany

Greet Schoeters
Environment and Health, Dept of Biomedical Sciences & Toxicological Centre, University of Antwerp, Belgium

Argelia Castaño
National Center for Environmental Health, Instituto de Salud Carlos III, 28220, Majadahonda, Madrid, Spain

Robert Barouki
Unité UMR-S 1124 T3S Inserm-Université Paris Cité, 45 rue des Saints Pères, 75270, Paris, France
France Service de Biochimie Métabolomique et Protéomique, Hôpital Necker Enfants Malades, 149 rue de Sèvres, 75015, Paris, France

Douglas Haines
Health Canada (retired), Ottawa, Canada

Alexandra Polcher
Ramboll, Werinherstraße 79, Gebäude 32a, 81541, München, Germany

Philipp Weise*
Section II 1.2 Toxicology, Health Related Environmental Monitoring, German Environment Agency, Corrensplatz 1, 14195, Berlin, Germany

* Corresponding author.
E-mail address: Philipp.Weise@uba.de (P. Weise).