HBM4EU science and policy for a healthy future

HORIZON 2020 Programme
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# Background paper to the conference on "Human biomonitoring in Europe – science and policy for healthy citizens"

## 1 Introduction

This paper sets the scene for discussions at the conference on Human Biomonitoring in Europe – science and policy for healthy citizens**,** 28 September 2018, Vienna, Austria.

This high-level Stakeholder Conference, held under the auspices of the Austrian Presidency and the European Commission, will highlight the benefits of human biomonitoring (HBM) for policy making, present the first results of the European HBM4EU joint initiative and contribute to shaping the future of Human Biomonitoring in Europe.

☞ *Marike Kolossa-Gehring, German Environment Agency, will introduce the HBM4EU initiative at the conference.*

HBM measures environmental chemicals and their metabolites in the human body, usually through analyses of blood, urine, hair, breast milk or tissues, providing an aggregated measure of the level of exposure to chemicals through different exposure pathways. As such, HBM is an important tool for assessing exposures of the human population to chemicals, and in the case of harmful chemicals, estimating potential health risks[1].

## 2 Chemical safety as a social concern

The issue of chemical safety is a matter of public concern, with one in four European Union (EU) citizens "very concerned" about exposure to chemicals in their daily life[2]. As individuals with their own chemical body burdens, citizens have an interest in understanding human exposure to chemicals. At the same time, their purchasing decisions as consumers influence the marketability of products containing chemicals and can drive innovation to substitute hazardous substances with alternatives. As members of the electorate, citizens can exercise their vote and influence policy directions by calling for enhanced chemical safety.

Recognising the concern of citizens, in 2002 the EU agreed "*to achieve, by 2020, that chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment*"[3]. The EU's 7th Environmental Action Programme[4] from 2013 reiterates this objective and foresees action on a range of chemicals policies and calls for efforts to address key gaps in the evidence base on chemicals. In particular, HBM is identified as a tool that can serve the

[1] Ganzleben, C et al, 2017. Human biomonitoring as a tool to support chemicals regulation in the European Union. International journal of hygiene and environmental health. 220. 10.1016/j.ijheh.2017.01.007.
[2] European Commission, 2017, Special Eurobarometer 456, Chemical safety, Summary
[3] United Nations, 2002 United Nations, 2002. A/CONF.199/L.1 - Draft plan of implementation of the World Summit on Sustainable Development, United Nations
[4] EU, 2013, Decision No 1386/2013/EU of the European Parliament and of the Council of 20 November 2013 on a General Union Environment Action Programme to 2020 'Living well, within the limits of our planet'. Official Journal of the European Union L. 354/171.

chemicals agenda by providing "*authorities with a more comprehensive view of actual exposure of the population to pollutants, especially sensitive groups such as children, and can provide better evidence for guiding appropriate responses*".

Yet we continue to face limitations in our current understanding of chemical risks to human health, with gaps in toxicity and exposure data for a large number of emerging substances used in consumer products. In addition, the characteristics and effects of long-term and low-dose exposure to mixtures of chemicals remain poorly understood[5].

☞ *Kestutis Sadauskas, Directorate General for the Environment, European Commission, will provide a presentation on a strategic approach to chemicals in Europe.*

# 3 Applying HBM results in chemical policy making

HBM evidence can be used to prioritise substances, exposure routes and vulnerable groups for targeted policy measures to reduce exposure, to evaluate the effectiveness of policy measures, and to promote more comprehensive health impact assessments of policy options[6].

☞ *Sabine Juelicher, Directorate General for Health and Food Safety, European Commission, will talk about the role of HBM to support evidence-based, targeted risk management measures and further improve food safety.*

A number of concrete examples of how HBM results can be used as evidence to support a number of key steps in the regulatory process are considered below.

## 3.1 Prioritising substances for policy measures

The German HBM Commission derives HBM values based on toxicological and epidemiological data, with the aim of interpreting HBM data in terms of the health impact of the exposure levels identified[7]. HBM I value represents the concentration of a substance in human biological material below which, based on the current state of knowledge, there is no risk of adverse health effects. The HBM II value describes the concentration of a substance in human biological material above which adverse health effects are possible and where there is an acute need for the reduction of exposure. Assessing HBM data against these values can therefore inform processes to prioritise substances for policy action.

HBM4EU will establish HBM values for all HBM4EU priority substances. Thus far, HBM values for DEHP and for Hexamoll® DINCH® have been developed.

HBM4EU has also developed a scoping paper for an indicator on chemical exposure in the European population.

[5] EEA-JRC, 2013. Environment and human health, Joint EEA-JRC Report. European Environment Agency Report No 5/2013, Copenhagen, Denmark; Prüss-Ustün A et al, 2011, Knowns and unknowns on burden of disease due to chemicals: a systematic review, Environ Health, 10:9

[6] Joas R, et al, 2012. Harmonised human biomonitoring in Europe: activities towards an EU HBM framework. Int J Hyg Environ Health. 215(2):172-5

[7] Umwelt Bundesamt, 2016. German Human Biomontioring Commission; Schulz, C et al, 2007, The German Human Biomonitoring Commission, Int J Hyg Environ Health. 210(3-4):373-82

## 3.2 Informing chemical risk assessment

In chemicals risk assessment frameworks, the default approach is to assess external intake, often from single routes of exposure. This approach includes various uncertainties and often overestimates the real uptake via one exposure route. At the same time, actual exposure may be underestimated since exposure routes that fall under separate legislative frameworks may not be accounted for in the assessment.

A 2015 review of the application of HBM to human exposure assessment for food safety identified potential added value, and argued that the application of HBM data to risk assessment can help to reduce the uncertainty inherent in assessing exposure[8]. In a 2017 report on chemical risk assessment, the US National Academies of Sciences, Engineering and Medicine described HBM as an essential tool enabling advances in exposure science and epidemiology[9].

☞*Anna-Maria Andersson, Copenhagen University Hospital, Denmark will present an example of the use of HBM data used for the risk management of phthalates under REACH.*

☞ *Michael Bader, BASF SE, Germany will talk about the added value of HBM for exposure analysis and risk assessment at work.*

HBM4EU has produced a report on current practice with HBM in risk assessment. The report identifies HBM as a tool to survey the real-life body burden of humans resulting from 'total' exposure to chemicals via different routes, which may be controlled under distinct legislative frameworks. The report presents examples of the advanced use of HBM and provides recommendations for the better inclusion of HBM in human risk assessment and health impact assessment.
With a particular focus on occupational exposure, HBM4EU has documented access to existing occupational HBM data and launched a survey on exposure to chromate VI in the occupational setting.

## 3.3 Identifying exposure pathways

HBM data on internal exposure, together with information on individual behaviours, diet and lifestyle, can be combined with data on substances in the environment and or in food and feed to identify the most important exposure pathways as a basis for controlling emissions at source.

Using modelling tools, HBM4EU matches internal exposure with external environmental sources to identify the most likely exposure pathways.

☞*Marco Martuzzi, WHO European Centre for Environment and Health, will talk about the role that HBM data can play in responding to local contamination.*

HBM4EU has produced a report on the optimal methodology for exposure reconstruction from HBM data and started work to refine PBTK/D models.

[8] Choi, J., Mørck T.A. and Knudsen, L., 2015. Review of the state of the art of human biomonitoring for chemical substances and its application to human exposure assessment for food safety. EFSA Supporting Publications. 12(2), 2397-8325

[9] US National Academies of Sciences, Engineering, and Medicine, 2017, Using 21st Century Science to Improve Risk-Related Evaluations. USA, Washington, DC: The National Academies Press.

In addition, HBM4EU partners have teamed up with members of the regulatory community from the DG SANTE, the European Safety Authority and the European Chemical Agency in developing HBM4EU activities to monitor a number of pesticides in humans. The aim is to complement the monitoring of these substances in food and feed under the Multiannual Community Control Programme for 2018, 2019 and 2020 (Commission Implementing Regulation (EU) 2017/660).

## 3.4 Understanding health impacts and linking to health surveys

In order to justify chemicals policies, it is increasing necessary to provide evidence of the mechanism through which human exposure to chemicals leads to impacts on health.

Under HBM4EU, we are combining health information with the results of human biomonitoring in order to inform our understanding of exposure-response relationships.

We will assess the potential health impacts of chemical exposures in different age groups and across genders, taking into account other factors such as socio-economic status, lifestyle, diet and environmental conditions. We will generate and assess the evidence for a causal link between chemicals and health impacts and identify the most suitable markers of such effects.

We will also the investigate the effects of exposure to mixtures of chemicals, and will use cutting edge technologies to search for emerging substances in human matrices that may serve as early warnings of future concern.

HBM4EU has produced a report on the opportunities for and obstacles to combining HBM and health studies, including an overview of the availability of health studies with biological samples to establish causal links between exposures and health, as well as the availability of administrative registers. The report also includes guidelines for combining HBM and health studies.

In terms of establishing mechanistic links between adverse health outcomes in the human population and exposures to priority chemical stressors, a principle tool is the use of Adverse Outcome Pathways (AOP). As a first step, HBM4EU developed an approach to allow for the systematic documentation of AOPs, with the aim of validating AOPs.

Regarding effect biomarkers, HBM4EU partners established criteria for the prioritisation of biomarkers of effect, and then applied these criteria to the identification of effect biomarkers for 1st list of HBM4EU priority substances.

The list of HBM4EU priority substances that are the subject of research under HBM4EU includes a number of chemicals that are either recognised or suspected to show endocrine disrupting properties, including bisphenols, phthalates, per-and poly fluorinated compounds, and several flame retardants. Scoping documents are available for each substance group, with further information on hazards, exposure and legislative status, as well as relevant HBM4EU activities.

## 3.5 Evaluating policy effectiveness

Information on exposure patterns and time trends in exposure can be used to assess whether restrictions have actually resulted in reduced health risks for the European population or for specific sub groups, such as workers.

As an example of the application of HBM to evaluating policy impacts, the Global Monitoring Plan of the Stockholm Convention on persistent organic assesses long-term trends in the levels of POPs present in humans[10]. In 2013, the WHO/UNEP Human Milk Survey provided results that indicate success in eliminating certain POP pesticides from human milk, linked to implementation of the Stockholm Convention on Persistent Organic Pollutants[11].

*☞Katarina Magulova, Secretariat of the Basel, Rotterdam, and Stockholm Convention, will talk about the role of HBM data in supporting the implementation of international chemicals conventions.*

## 3.6 Understanding human exposure to chemical mixtures

As mentioned above, as important knowledge gaps in chemical risk governance is the risks to human health from exposure to chemical mixtures[12].

In HBM4EU work is underway to develop a database of HBM data on mixtures and a statistical plan for data analysis[13]. Evidence of actual human exposure to mixtures will enable a comprehensive and integrated assessment of the cumulative effects of different chemicals, taking into account different routes and sources of exposure.

HBM4EU is collaborating with other EU research framework projects[14] to address different aspects of the impacts of mixtures on human health and the environment, including also research activities, at the European Food Safety Authority and the Joint Research Centre.

These projects have collaborated to produce a joint position paper on the risk assessment and risk management of mixtures at EU level entitled "Preventing risks for people and environment from hazardous chemical mixtures". In addition, scientists collaborated with EU institutions to produce a joint paper entitled "Current EU research activities on combined exposure to multiple chemicals"[15].

*☞Carl-Gustaf Bornehag, Karlstad University, Sweden, will present a novel approach for the risk assessment of chemical mixtures using HBM.*

## 3.7 Flagging exposure to emerging substances

Emerging substances are a key concern for the regulatory community. Over the past 20 years, the diversity of chemicals on the market has grown exponentially. HBM can signal human exposure to emerging chemicals.

[10] UNEP, 2016. Global Monitoring Plan on Persistent Organic Pollutants
[11] UNEP, 2013. UNEP/POPS/COP.6/INF/33, Results of the global survey on concentrations in human milk of persistent organic pollutants by the United Nations Environment Programme and the World Health Organization. United Nations Environment Programme
[12] European Commission, 2012. Communication from the Commission to the Council, The combination effects of chemicals Chemical mixtures, /* COM/2012/0252 final */
[13] Vlaanderen, J et al, 2017, HBM4EU Deliverable 15.3 HBM mixture database description and proposed statistical analysis plan
[14] Namely EDC-MIXRISK, EUROMIX, EU-TOXRISK and SOLUTIONS
[15] Bopp, S., et al., 2018, Current EU research activities on combined exposure to multiple chemicals", Env. Int. 120

HBM4EU has produced a prioritised list of emerging substances, and has identified new analytical screening methods and statistical tools that can identify emerging chemicals based on their physicochemical properties or their biological actions.

# 4 Producing legitimate and credible knowledge

It is a principle objective of HBM4EU to generate results that meet the knowledge needs of EU policy makers. To be used as a basis for policy making, HBM4EU results must be accepted as legitimate and credible by a broad range of different interest groups.

Engagement with stakeholders, including non-governmental organisations representing environmental, health and consumer priorities, as well as trade unions and industry, is crucial to the success and sustainability of the HBM4EU project. Established in 2017, the Stakeholder Forum is the formal channel for stakeholder input to the HBM4EU project and its members are invited to provide strategic input to key HBM4EU processes.

The selection of substances that are the subject of research activities under HBM4EU represents a critical step. In order to secure the legitimacy, credibility and societal relevance of our work, HBM4EU partners consulted policy makers, scientists and stakeholders when developing and implementing the Strategy for the prioritisation of substances for monitoring and research activities.

From 2017 to 2018, HBM4EU partners implemented an extensive consultation process as part of the strategy for the prioritisation of chemicals. The process is fully documented in a report and on the HBM4EU website with the aim of achieving full accountability of the process and making it transparent to external interested parties.

In parallel to the prioritisation process, we have also established a Rapid Response Mechanism. This online mechanism allows policy makers to efficiently channel new and urgent needs for information to the HBM4EU partners.

Key decisions on the HBM4EU strategic approach are taken by the HBM4EU Management Board must then be approved by our Governing Board, a body that includes representatives from all partners countries, as well as the European Environment Agency (EEA), the European Food Safety Authority (EFSA) and the European Chemicals Agency (ECHA). HBM4EU also benefits from input from an A0dvisory Board, consisting of international, high-level experts in the field of HBM, human health and environment from across the world.

The involvement of citizens is critical important in ensuring the legitimacy and credibility of the HBM4EU project. With the explicit aim of understanding public concern regarding chemicals and capturing the perspectives of non-experts when prioritising chemicals for research, HBM4EU has thus far undertaken two outreach activities with European citizens: an online questionnaire and a focus group with members of the general public.

HBM4EU is developing a process for the joint interpretation of HBM results between regulators, scientists and stakeholders. The aim of this process is to promote consensus regarding the meaning of results and their translation into targeted policy measures.

The HBM4EU Strategy for the communication and dissemination of HBM4EU results identifies end users and sets out approaches for open dialogues with different users to understand their knowledge needs. In terms of communicating with the public, HBM4EU has produced non-technical leaflets on the project in multiple languages and one-page sheets on HBM4EU priority substances,

describing chemical safety issues for each substance. A short video explains the project goals in non-technical and accessible language.

☞*Catherine Ganzleben, European Environment Agency, Copenhagen, will explain how HBM4EU results are communicated to end users.*

# 5 A European network and harmonised procedures

National Hubs have been established in each country to coordinate activities, so creating a robust HBM Platform at pan-European level.

Technical guidelines and protocols to support the implementation of harmonized, high quality and cost-effective surveys have been produced, including harmonised materials for communication with participants and obtaining their consent. HBM4EU identified criteria for the prioritisation of biomarkers and produced a list of biomarkers, matrices and analytical methods for the 1st list of HBM4EU priority substances. Candidate laboratories that can undertake analysis on these substances have been identified and a quality assurance/quality control scheme has been developed.

☞*Argelia Castaño, Instituto de Salud Carlos III, Spain, will present the progress made towards building an European platform for HBM surveys.*

HBM4EU runs a targeted training programme that builds capacities and serves to reinforce efforts to harmonise approaches to HBM across countries.

The Data Management Plan describes the data management life cycle for all datasets collected, processed and generated under the project. The Data Policy describes the data management procedures to be followed by the consortium. In order to ensure a harmonised approach to data analysis, HBM4EU has developed a statistical analysis plan, including statistical plans for the evaluation of time trends, geographic comparisons, evaluation of exposure determinants, a strategy for the calculation of EU reference values, and a plan for conducting uncertainty analysis.

All human biomonitoring data generated under the project will be made available to policy makers and metadata will be accessible via the EC's Information Platform for Chemical Monitoring (IPCHEM). Existing data used under HBM4EU may also be made available via IPCHEM to the extent possible, while respecting all ethics and legal restrictions that might apply.

☞*Greet Schoeters, Flemish Institute for Technological Research (VITO), Belgium, will present the work on collecting and analysing EU wide HBM data and making them available in IPCHEM.*

# 6 The future of HBM in Europe

Looking forward, there is clearly potential to further develop the use of HBM results in support of both risk assessment and risk management in chemicals regulation. Indicators of success have been developed to enable HBM4EU partners to track progress towards this goal.

The 2013 7th Environmental Action Programme calls for the development by 2018 of a Union Strategy for a non-toxic environment that addresses key areas of concern in chemical safety.

A recent letter to the European Commission from the environment ministers of nine EU member states and Norway expressed serious concern about delays to several chemicals policy initiatives, including:

- The strategic approach to pharmaceuticals in the environment;
- The non-toxic environment strategy;
- The integrated product policy framework; and
- The strategy on endocrine disruptors.

The EU Council has also reiterated its concerns over the pace at which the executive is moving forward with these policy measures[16].

☞ *Robert Barouki, French National Institute of Health and Medical Research (INSERM), Paris, will present scenarios for a sustainable next generation HBM.*

☞ *This will be followed by a high-level panel discussion the future of HBM in Europe, involving:*

- Hans Bruyninckx, Executive Director of the European Environment Agency, Copenhagen
- Lilian Busse, Head of Division Environmental Health and Protection of Ecosystems of the German Environment Agency, Berlin
- Bjørn Hansen, Executive Director of the European Chemicals Agency, Helsinki
- Anne Paoletti, Scientific Director for Biology and Health, Directorate General for Research and Innovation, French Research Ministry, Paris
- Kateřina Šebková, Director of the National Centre for Toxic Compounds and Stockholm Convention Regional Centre, Brno
- Hans Verhagen, Senior Scientific Adviser, European Food Safety Authority, Parma

Readers please note that this document is intended to be read online and includes multiple hyperlinks, including links to key results produced under HBM4EU.

All these results are available for download from the HBM4EU website at www.HBM4EU.eu

[16] Council of the European Union, 2018, Council conclusions on Delivering on the EU Action Plan for the Circular Economy