Human biomonitoring programmes: importance for protecting human health from negative impacts of chemicals

Technical summary

World Health Organization
European Region
Abstract
This publication summarizes key information on HBM: its objectives, the value of the information obtained through HBM surveys for making decisions on chemicals management to minimize negative health impacts, and challenges countries may face when implementing national HBM programmes. It also highlights the unique value of HBM for assessing prenatal exposure, building capacity, and preparing for emergencies related to environmental pollution. This publication is primarily aimed at public-health and health-care professionals, environmental protection and chemicals management experts, chemists, and students.

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Abbreviations

ADHD  attention deficit hyperactivity disorder
AMAP  Arctic Monitoring and Assessment Programme
BBLV  binding biological limit value
DALY  disability-adjusted life-year
DBzP  dibenzylpiperazine
DEHP  di(2-ethylhexyl) phthalate
DEMOCOPHES  Demonstration of a Study to Coordinate and Perform Human Biomonitoring on a European Scale
DEP  diethyl phthalate
DiBP  diisobutyl phthalate
DnBP  di-n-butyl phthalate
EDC  endocrine disrupting chemical
EU  European Union
GMP  Global Monitoring Plan
HBCD  hexabromocyclododecane
HBM  human biomonitoring
HBM4EU  European Human Biomonitoring Initiative
IQ  intelligence quotient
NHANES  National Health and Nutrition Examination Survey
PARC  European Partnership for the Assessment of Risks from Chemicals
PBDEs  polybrominated diphenyl ethers
PFAS  per- and polyfluoroalkyl substances
PFC  perfluorinated compound
PFOA  perfluorooctanoic acid
PFOS  perfluorooctane sulfonate
POP  persistent organic pollutant
REACH  Registration, Evaluation, Authorisation and Restriction of Chemicals
UNEP  United Nations Environment Programme
UV  ultraviolet

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Introduction

Human biomonitoring (HBM) is a reliable instrument for assessing human exposure to chemicals from different sources, by different pathways, and during certain periods of life through direct measurement of concentrations of chemical pollutants or their metabolites in human fluids and tissues (1,2).

HBM was first introduced in 1934 to investigate exposures to chemicals in workplaces. Since then, it has become an integral tool for assessing human exposures in many contexts. It is used in activities ranging from scientific studies to large national programmes. National HBM programmes exist within many countries and at national, regional and global levels. Some programmes have a long history, and some are relatively new; for example, HBM programmes have been running in the United States of America since 1976 (3), in Germany since the early 1980s (4) and at the European Union level since 2010 (5). See Annex 1 for a summary of the history of HBM.

Chemicals and their health effects

Chemicals in the environment

Every day throughout our lives, we are exposed to many chemicals, including hazardous chemicals in air, water, soil, food and consumer products. The total number of industrial chemicals in commerce globally is estimated to be 40 000 to 60 000; of these, 6000 account for more than 99% of the total volume (6). By August 2019, the European Union (EU) under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation had registered 22 600 chemicals. Global chemical production is projected to double by 2030 and triple by 2050, with production shifting to low- and middle-income countries (7).

Exposure to chemicals changed in the 21st century, and continues to increase in complexity due to developments in the production, trade and use of chemicals; rapid invention and promotion of new products; growing exposure to chemical mixtures; and continuous releases of persistent and bioaccumulating chemicals. As the production and use of chemicals, including toxic chemicals, are projected to increase, associated risks to human health are also expected to grow (7). To address this, regulatory decisions and measures based on scientific research and reliable assessments of population exposures to chemicals are urgently needed.

Hazardous chemicals and their mixtures are a matter of concern for human health

According to the latest estimates, 2 million lives and 53 million disability-adjusted life-years (DALYs) were lost globally in 2019 due to exposures to selected chemicals (8). Exposure to lead alone is estimated to account for 21.7 million DALYs worldwide due to long-term effects on health, including 30% of the global burden of idiopathic intellectual disability, 4.6% of the global burden of cardiovascular diseases and 3% of the global burden of chronic kidney diseases (9).

1 Throughout this publication, the term “environment” includes the ambient environment, consumer products and food.
HBM for chemical exposure and health risk assessment

What information can be obtained from HBM?

HBM surveys generate the data needed for exposure and risk assessment, including data on:

- internal dose/body burden of hazardous chemicals in entire populations, specific subpopulations and individuals (see Box 1);

- intrauterine (fetal) exposures (if pregnant women are involved in the HBM survey) and early-life (newborn) exposures (see Box 2);

- aggregated uptake of a given chemical through all exposure pathways (inhalation, oral and dermal) and from all sources (food, consumer products, drinking-water, air, etc.);

- simultaneous exposure to many chemicals and chemical mixtures; and

- time and spatial trends of population exposures (see Box 3).

Box 1. Internal dose assessment

There are two main approaches to assess body burden:

- environmental modelling based on knowledge of chemical toxicokinetics, chemical levels in environmental media, and issues such as people’s nutrition status, health and lifestyle; and

- measurement of chemicals directly in biological samples through HBM.

Data resulting from another approach (HBM) are often the most relevant metric for health-risk assessment, especially for bioaccumulating and/or persistent chemicals (10).

Box 2. Intrauterine exposure assessment

Mercury exposure in the womb can result from a mother’s consumption of contaminated foods. It can adversely affect a baby’s growing and developing brain and nervous system later in life. Characterizing prenatal exposure to mercury using analysis of maternal hair samples provides information for evaluating the health risks of mercury and planning risk-reduction measures at population and individual levels (11).

Box 3. Evaluation of time and spatial trends

HBM surveys conducted in the framework of the Global Monitoring Plan (GMP) of the United Nations Environment Programme (UNEP) and WHO yielded estimates that levels of the majority of regulated persistent organic pollutants (POPs) are decreasing over time in human milk and/or blood. Some of the newer POPs, such as polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD), showed an increase over time followed by a recent decrease, demonstrating the effectiveness of restrictions and banning of production and use of these chemicals (12).

HBM surveys conducted in Canada confirmed that concentrations of methylparaben and propylparaben in urine in the Canadian population aged 3–79 years significantly decreased in 2012–2013 and 2018–2019, by 46% and 58% respectively (13,14).

HBM surveys also revealed that concentrations of specific pesticides are higher among populations of southern Europe than northern Europe. Conversely, exposure to some perfluorinated compounds (PFCs) is higher in northern Europe (15,16). This knowledge creates opportunities for governments to take measures to ensure that all residents are protected from exposure to hazardous chemicals.
What evaluations and conclusions can be based on HBM results?

HBM data create a scientific basis for:

• identifying highly exposed subpopulations (for example, residents in contaminated areas);

• defining priority chemicals of public health concern (see Box 4);

• deriving reference values for exposure assessment;

• revealing priority fields and areas for urgent actions;

• identifying sources of chemicals such as consumer choices, nutrition, exposure-related behaviour (if accompanied by questionnaires and/or interviews) (see Box 5);

• assessing risks for public health and individuals;

• identifying health determinants (if accompanied by medical investigations);

• linking HBM results and potential health disorders; and

• supporting risk assessment in emergency situations.

Box 4.
Priority chemicals of public health concern

HBM is useful for identifying emerging chemicals and thus raising awareness about emerging risks. For example, in Belgium, HBM contributed to the definition of pyrethroids, herbicides, parabens, acrylamide/glycidamide, nitrosamine and nitrate (both smoke flavouring), and PFCs as emerging chemicals. These are newly identified hazards to which new, unexpected and significant exposure may occur (17).

Box 5.
Identification of sources of chemicals

Evaluation of the exposure to phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children (6–11 years old) used urine samples from 98 mother–child pairs living in either a rural or an urban area. A questionnaire allowed for the investigation of potential predictors of exposures. The study found an association of paraben concentrations with use of cosmetics and personal care products (18).

Why is this information critical for sound chemicals management?

HBM results are critical for the justification of risk-reduction measures. Evaluations and conclusions from HBM surveys contribute to:

• identification of targeted actions to protect populations from the negative impacts of chemicals;

• decision-making on management of the most hazardous chemicals (restriction, prohibition) (see Box 6);

• evaluation of the success or failure of regulations and voluntary risk-reduction measures (see Box 7);

• transparency in the development of government policies and thus increased public trust;

• justification of international actions to reduce emissions and releases of global pollutants and the transboundary impacts of chemicals; and

• prioritization of measures to reduce the health-care costs associated with conditions and diseases attributable to chemicals.
Box 6. Phthalates regulation policy based on results of HBM

Nine regulations aimed at reducing exposure to reprotoxic phthalates were adopted in the EU between 1999 and 2020. HBM demonstrated that all policy actions and risk-reduction measures led to decreases in human exposure to phthalates: time-trend analyses showed rapidly declining metabolite concentrations (19).

Box 7. Evaluation of effectiveness of risk-reduction measures using HBM

The reduction of blood lead levels in the population of the United States is a result of the withdrawal of lead from gasoline and paints, a decision taken based in HBM results. The second campaign of the National Health and Nutrition Examination Survey (NHANES) demonstrated that lead exposure in the population decreased from 16 µg/dL to less than 10 µg/dL four years after the introduction of unleaded gasoline to the market. The reduction was much greater than expected, prompting the United States Environmental Protection Agency to accelerate total elimination of lead from gasoline. As a result, in 2013/2014, less than 1% of children had a blood lead level exceeding 5 µg/dL (20).

Box 8. Building laboratory capacities for mercury HBM

In the framework of a UNEP/WHO project to develop a global plan for mercury monitoring, a number of actions were taken to build national laboratory and HBM capacities. These included trainings for national coordinators and laboratory analysts, interlaboratory comparisons for the determination of mercury in blood and urine, various troubleshooting initiatives, and the organization of working spaces within reference laboratories for staff to conduct analyses of mercury under the supervision of experienced specialists (21).

Other benefits of HBM

Addressing the needs of the most vulnerable – leaving no one behind

HBM results create a scientific basis for protecting the health of the most vulnerable population groups. Commonly, young children have higher concentrations of most chemical pollutants per kilogram of body weight compared to older age groups. This holds true for a number of modern pesticides and plastic constituents. Young children are especially vulnerable to developing adverse health effects later in life when exposed in early years. HBM enables the measurement of concentrations of chemicals or their metabolites in subpopulations such as young children, pregnant mothers and older people. HBM data can also supply information according to population-specific characteristics such as socio-economic status, allowing for the identification of more highly exposed subpopulations that may require targeted protection measures.

Building capacity

The implementation of national HBM programmes involves capacity-building, as HBM is a complex process with several stages/phases that require multidisciplinary expertise. HBM surveys can involve scientists, risk assessors and managers, epidemiologists, toxicologists, laboratory specialists, lawyers, and journalists, among others. In addition to trainings and other opportunities to exchange knowledge and expertise, HBM requires laboratory capacities (see Box 8).

Communicating with the public and addressing communities’ needs

HBM is a powerful tool for facilitating communication with the general public. Studies are done through personal contact with study participants, and the results and their toxicological interpretation lead to recommendations for exposure reduction. These recommendations are then spread via media, announcements and public health services or through targeted information tools such as social media, videos and policy briefs.
HBM may also be conducted in response to health concerns in a community resulting from the discovery of environmental contamination or a disease cluster with a possible chemical exposure origin. These studies are often conducted with involvement and support of local communities and authorities. Examples include HBM studies with people living in the vicinity of industrially contaminated sites, for example, sites recently discovered to be contaminated with per- and polyfluoroalkyl substances (PFAS) around Europe (22). In hot spots where exposures are high, communities often participate directly and may provide input on study design and recruitment of participants.

HBM surveys also offer possibilities for local authorities to interact directly with the public, raising awareness and generating public dialogue with citizens and authorities sharing responsibility for the environment protection. Citizens receive concrete information on the concentrations of hazardous chemicals in their bodies and are informed of potential exposure sources and of ways to reduce them.

**Implementing HBM programmes and reporting on international agreements**
The Stockholm Convention on POPs and the Minamata Convention on Mercury oblige Parties to monitor exposure to regulated chemicals, including through the use of HBM, and to assess the effectiveness of the implementation of the agreements based on HBM results (23,24). The GMP was the first global initiative to develop and apply a harmonized approach to HBM in the context of POPs. It demonstrated the value of a harmonized approach, which was further developed in the framework of other regional and EU projects (12). See Annex 2 for more information.

**Gathering new knowledge**
HBM surveys have resulted in new knowledge on chemicals, their sources, human exposures, effective protection measures and the fate of chemicals in the environment. For example, HBM is an essential part of birth cohort studies around the world to investigate environmental and social health determinants (see Box 9).

**Box 9. New knowledge on health determinants and origin of diseases**
In Europe, 12 cohorts related to environmental exposure from around 100 ongoing investigations are addressing several aspects: genetic and biological factors, psychological/social environments, medical care and medications, and lifestyle and environmental parameters (25).

The German Environment Agency has commissioned the conceptual work for a birth cohort study (100 000 to 200 000 parent–child pairs) to investigate environmental health problems in children (26). To characterize epidemiological signatures of disease in young children in Japan, the Japanese Environment and Children Study began recruitment in January 2011. Approximately 100 000 expecting mothers were recruited over a three-year period, and the study plans to follow participating children until they reach 13 years of age (27).

**Preparing for emergencies**
A regular HBM programme prepares authorities to implement effective interventions in response to environmental disasters and health concerns related to chemical exposures (see Box 10).

**Box 10. PFAS in humans and the environment**
HBM has detected a range of PFAS in the blood of European citizens. Though the levels for the most prevalent, studied and regulated PFAS – perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) – are decreasing, levels of newer PFAS are increasing. In some areas, concentrations of PFOA and PFOS in the most exposed citizens were above proposed benchmark levels for adverse effects in humans. Specific needs for population protection were considered to protect highly exposed populations, for example, monitoring of PFOA and PFOS in drinking-water (28).
Policy support for HBM

As mentioned above, the value of HBM for exposure assessment has been recognized in two multilateral environmental agreements: the Stockholm Convention on POPs and the Minamata Convention on Mercury (23,24). In the WHO European Region, policies and actions on environment and health have been shaped by ministerial conferences and their outcome documents:

- the 2004 Budapest Declaration on Environment and Health, which focused on the theme “The future for our children” (28);
- the 2010 Parma Declaration on Environment and Health, which set clear targets to reduce the adverse health impacts of environmental threats (29); and
- the 2017 Ostrava Declaration on Environment and Health, which stressed the need to strengthen national capacities for coordination, monitoring and implementation (30).

These declarations highlight the need to protect vulnerable populations such as pregnant women and children from exposures to hazardous chemicals, and recommend implementation of HBM. Countries are encouraged to conduct HBM surveys to:

- detect and measure population exposures
- monitor spatial or temporal differences in population exposures
- evaluate the efficacy of public health actions to reduce exposures.

The WHO Chemicals Road Map also encourages governments and other stakeholders to integrate health and environmental monitoring and surveillance systems for chemicals (31).

Legal basis for HBM

Only a few countries in the Region have a legal basis to perform HBM; hence follow up and further harmonization depend heavily on research initiatives and are not ensured. In the EU, HBM is only required by law to control occupational exposures to specific chemical agents for which a binding biological limit value (BBLV) exists (Directive 98/24/EC). Currently, only one BBLV (for blood lead level) is given under EU occupational safety and health legislation (32). Independently, Member States apply biological limit values as a health surveillance tool to assess individual or population exposures or health risks.

The first international occupational studies applying HBM were conducted in the framework of the European Human Biomonitoring Initiative (HBM4EU); these indicated higher chromium biomarker levels in chromium platers than in surface-treatment workers and welders. The data of genotoxicity biomarkers also evidenced that controls recruited within companies (for example, office workers) displayed levels of genotoxic damage much higher than those of controls recruited outside companies (33).

Cost of HBM surveys and health costs of inaction

Setting up a national HBM programme requires capacities for recruiting and informing study participants, measuring chemicals or their metabolites in analytical laboratories, analysing data, and implementing reporting and communication initiatives, as well as all relevant financial support. The costs depend on a survey objective and scale (see Box 11). Overall, the following points are important to consider.

- HBM programmes can be costly. Most are government funded, and all require long-term and sustainable funding.
- HBM complements, but does not replace, environmental and food monitoring systems, both of which are commonly prescribed by legislation.
Careful study design and labour-intensive logistics are required for recruitment of participants. In some countries, these efforts can be combined with already-established population studies such as health examination surveys or nutritional surveys.

Biomarker analysis of chemical exposures requires specialized laboratories.

Box 11. Cost of sample analysis

Projects such as Demonstration of a Study to Coordinate and Perform Human Biomonitoring on a European Scale (DEMOCOPHES) and HBM4EU have demonstrated that sample analysis can be organized and distributed among European laboratories with high-quality results. Prices in 2019 for biomarker analysis of groups of PFCs, bisphenols and phthalates averaged between €80 and €250 per sample and per substance group. From 200 to 300 samples are recommended for robust statistics (34).

However, HBM costs are minor compared to savings from health gains and other economic benefits associated with preventing human exposures to chemicals. Savings due to prevention of diseases and protection of human health are always greater than the costs of HBM programmes. Below are several examples.

- In 2015, the health costs in the EU of the median annual disease attributable to exposure to endocrine disrupting chemicals (EDCs) were estimated at €163 billion (1.28% of the EU’s gross domestic product) (35). The calculation for exposure to EDCs is based on HBM data and on the evidence of EDCs’ causation of intelligence quotient (IQ) loss and associated intellectual disability, autism, attention deficit hyperactivity disorder (ADHD), endometriosis, fibroids, childhood obesity, adult obesity, adult diabetes, cryptorchidism, male infertility, and mortality associated with reduced testosterone (36). These estimates represent only those EDCs with the highest probability of causation. A broader analysis would have produced greater estimates of burden of disease and costs.

- Exposure to organophosphate pesticides is associated with IQ loss, mental retardation and ADHD. Internal levels as determined by HBM of organophosphate exposures in EU populations were associated with 13.0 million (sensitivity analysis: 4.2 million to 17.1 million) lost IQ points per year and 59 300 (sensitivity analysis: 16 500 to 84 400) cases of intellectual disability, at an annual cost of €146 billion (sensitivity analysis: €46.8 billion to €194.0 billion) (35).

- Phthalates may contribute substantially to male reproductive disorders and diseases, with annual associated costs of nearly €15 billion in the EU. These estimates are based on phthalate metabolite measurements from the pan-European DEMOCOPHES study. Data were collected on EDCs including di(2-ethylhexyl) phthalate (DEHP), dibenzylpiperazine (DBzP), di-n-butyl phthalate (DnBP) and diisobutyl phthalate (DiBP), for which there were sufficient epidemiological studies showing the highest probability of causation (36).

- Based on the methylmercury measurements in hair of mothers from 17 European countries who participated in the DEMOCOPHES study (2012–2013), it was estimated that the total annual benefit of exposure prevention within the EU is more than 600 000 IQ points per year, corresponding to a total economic benefit of between €8 billion and €9 billion per year (37).

Scientific and ethical principles of HBM

All research with humans must be carried out in ways that show respect and concern for the rights and welfare of individual participants and the communities in which research is carried out, ensuring that risks are minimized and are reasonable in light of the importance of the research. Research must also be sensitive to issues of justice and fairness. The main criteria for inviting groups, communities and individuals to participate in research must be scientific, and not compromised social or economic position or ease of manipulation (38,39).
In the ethics of research involving human subjects, distributive justice requires the equitable distribution of both the burdens and the benefits of participation in research. Differences in distribution are justifiable only if they are based on morally relevant distinctions between people. When vulnerable individuals and groups are considered for recruitment in research, researchers and research ethics committees must ensure that specific protections are in place to safeguard their rights and welfare. The personal and health information of study participants must also be managed in compliance with ethical principles and relevant national regulations (38,39).

Challenges of HBM

Despite the exceptional value of HBM for exposure and risk assessment and for regulatory decisions, the following challenges still limit its use.

- HBM should be accompanied by the collection of environmental and behavioural data to identify exposure factors.
- HBM is relatively time-consuming and expensive, especially if a large number of chemicals are analysed.
- The number of samples needs to be large enough to obtain a reliable picture of population exposure (especially to chemicals with a short lifetime in the body).
- The relationship between human chemical exposures and adverse health outcomes is complex. Most diseases are multifactorial, and chemicals are often one of the risk factors. Quantification of risks based on population studies is difficult and only possible for a limited number of chemicals.
- Current chemical regulations are based on single-substance assessments and authorizations. HBM measures real multiple exposures in the body, which are related to mixture effects. This complicates communication about risks and risk-reduction measures.
- Communication of individual HBM results is sensitive as it concerns personal health.

The following key challenges can also create barriers to using HBM in regulatory decisions.

- The presentation of HBM data is not harmonized (that is, not consistently structured or aligned), the quality of the data is unclear (quality assurance/quality control for chemical analysis is lacking) and contextual information (metadata) is missing.
- Coverage of regulatory enforcement by legislation is insufficient, and gaps persist in aligned and connected legal frameworks that require the use of HBM.
- A limited number of countries run long-term, consistent programmes that allow for the regular use of HBM in a regulatory context.
- Availability of HBM data on time and in full is limited.
- Methodologies at the science–data–policy interface need improvement and harmonization.

Producing and gathering scientific knowledge and applying harmonized approaches can support countries in addressing these challenges. Further cooperation on HBM to facilitate the establishment of national monitoring programmes is a priority in the WHO European Region and globally.

HBM results in support of regulatory decisions

HBM results from the GMP (12), the DEMOCOPHES study (40), comparisons of European national study results with the United States’ NHANES (3) and, more recently, HBM4EU (41), have all shown large country-to-country variability in internal exposure of populations across age groups and for all biomarkers. For example, HBM4EU showed that biomarker levels of PFCs are higher in teenagers of northern European countries, while biomarkers of the organophosphate pesticide chlorpyrifos and of the pyrethroids cypermethrin, cyfluthrin and permethrin are higher in children and adults of southern European countries (15). These data offer
authorities evidence on which to base targeted control of potential sources and other preventive measures.

Results from DEMOCOPHES and HBM4EU also indicated that people in Europe are co-exposed to at least five phthalates: DEHP, DnBP, DiBP, DBzP and DEP (40,41). This information triggered the European Chemicals Agency to assess the risk of the phthalate mixture and, as a result these phthalates were further restricted in the EU. Eight years later, the HBM4EU aligned studies showed a clear reduction in the exposure to these restricted low molecular-weight phthalates, but an increased presence of unrestricted substitute plasticizers.

Inequity in exposure is also related to social status and wealth. HBM4EU showed that low molecular-weight phthalates that are no longer used in newly manufactured products in Europe are still detected and present at higher levels in teenagers of less educated households. Lower educational attainment was associated with higher concentrations of metabolites of polycyclic aromatic hydrocarbons (PAHs) in adults, which may be related to tobacco smoking and living in more polluted areas. These adults also exhibited higher levels of acrylamide and the mycotoxin deoxynivalenol. Such results can justify regulatory decisions to support the adoption of healthy lifestyles in particular emphasis with at-risk population groups. In contrast, teenagers from more educated households had higher levels of PFCs. These results were also seen in additional studies focused on other POPs. This may relate to more fish and meat consumption in these households, and could justify public education on changing eating habits (41).

Several hazardous chemicals are more concentrated in younger individuals: HBM4EU demonstrated this for biomarkers of acrylamide, ultraviolet (UV) filters (benzophenones), phthalates and pesticides (41). Children are not only more vulnerable than adults to these chemicals, they are also often more exposed to them; hence the recurring call at ministerial conferences to better protect our children.

HBM experience globally and in the WHO European Region

Global HBM surveys on POPs conducted in 1987–1992, and since 2007 have been carried out in a uniform manner globally. The global monitoring of exposure builds on existing HBM activities carried out nationally and regionally. WHO surveys performed mainly in Europe and North America in 1987–1989 and 1992–1993 exclusively focused on three POP groups (polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins and dibenzofurans). In 2001–2003, a larger global survey was implemented, covering the 12 POPs initially listed in the Stockholm Convention. Following the ratification of the Convention, WHO and the UNEP have organized surveys on a regular basis. These studies significantly enlarged the geographical scope, providing representative results for all regions of the globe. Currently, the survey covers the 30 POPs listed in the Convention. The programme assists national and regional capacity-building by supporting technical/analytical capability to detect POPs in humans.

- In Europe, programmes using HBM to regularly follow up on chemical exposures exist in several countries, for example, Germany (since 1977/1985), Czechia (since 1994), Flanders (since 2002) and Slovenia (since 2007). Spain started a programme with recruitment in 2009, and a French cross-sectional survey started in 2014. Longitudinal large-scale birth cohorts have been established in Denmark, France, Norway and Spain, some with an HBM component.

- In the framework of the DEMOCOPHES study (2010–2012), 17 countries collected comparable HBM data from mothers and their children and measured cadmium, mercury, specific phthalates and cotinine (5).

- HBM4EU (2017–2022) aligned national programmes and complemented regional studies. It included 30 countries and 117 partner institutions, and targeted 3 age groups: children (6–11 years), teenagers (12–19 years) and adults (20–39 years). Internal exposure was assessed through analyses of samples collected between 2014 and 2021 for phthalates and di-(iso-nonyl)-cyclohexane-1,2-dicarboxylate (substitute DINCH), brominated and
organophosphorus flame retardants, PFAS, cadmium, bisphenols, PAHs, arsenic species, pesticides, mycotoxins, acrylamide and UV filters (benzophenones). The European Partnership for the Assessment of Risks from Chemicals (PARC) was built on the achievements of HBM4EU and, as part of the initiative, will promote HBM and the use of its results for chemical risk assessment in participating countries (42).

The network of the Arctic Monitoring and Assessment Programme (AMAP) was established to assess the implications and impacts of pollution on the health of Arctic residents. It uses HBM to monitor concentrations of contaminants in maternal blood and breast milk in the eight circumpolar nations, and assesses spatial and temporal patterns/trends and potential health effects at present and future levels. Research on a broad range of health effects is carried out within the framework of AMAP, including neurodevelopmental disorders, cardiovascular diseases, metabolic and immune dysfunctions, obesity, and diabetes (43).

Canada, Japan, South Korea and the United States (the largest experience globally) have also established national HBM programmes to follow up on chemical exposures among their populations either by cross-sectional programmes or by longitudinal birth cohorts.

**HBM in low-resource countries: considerations**

Implementing HBM in low-resource countries can be challenging due to lack of relevant expertise, inadequate laboratory capacities and the high costs of HBM. However, the following initial considerations for promoting the establishment of a national HBM programme can be considered (44).

- The first step in setting up an HBM programme in a resource-limited country is to secure the support of policy-makers by demonstrating its benefits for disease prevention and relevance to the country. It is important to emphasize that national HBM programmes can be cost-effective health investments, as the potential gains for human health through prevention of disease from exposures to chemicals outweigh the costs of HBM surveys.
- Priorities of the HBM programme should be aligned with national needs to provide a broader scope of significance.
- Participating in multi-country, especially global, initiatives provides stronger political incentives and opportunities for capacity-building and cost- and data-sharing. It also yields stronger impact and ensures greater overall sustainability of the programme.
- Engaging the health sector and educating citizens promotes individual and community action, and can push policy-makers to commit to act.
- Global knowledge and experience should provide a scientific basis and support the development and implementation of HBM programmes in low-resource countries.
References


Annex 1. History of human biomonitoring (HBM)

The following timeline presents key developments and achievements in the history of HBM (1–3).

- 1933 – Measurement of workers' exposure to lead
- 1936 – Measurement of workers' exposure to benzene metabolites
- 1976 – United States of America's National Health and Nutrition Examination Survey (NHANES)
- 1980 – Demonstration of effectiveness of a risk-reduction policy: NHANES data confirm decreased blood lead levels since 1976 in parallel to withdrawal of lead in gasoline in the United States
- 1985 – German Environment Survey
- 2004 – European Environment and Health Action Plan confirms “developing a coherent approach to biological monitoring”
- 2007 – WHO/United Nations Environment Programme (UNEP) Global Monitoring Plan (GMP) for monitoring persistent organic pollutants (POPs); Canadian Health Measures Survey
- 2010 – European Union (EU) Demonstration of a Study to Coordinate and Perform Human Biomonitoring on a European Scale (COPHES/DEMOCOPHES) project
- 2016 – EU European Human Biomonitoring Initiative (HBM4EU)
- 2018 – WHO protocol and standard operating procedures for assessment of prenatal exposure to mercury
- 2024–2025 (planned) – WHO guidance on HBM

References
Annex 2. HBM in multilateral environmental agreements

The Stockholm Convention on POPs aims to protect people and the environment from the harmful effects of these substances, which can remain intact for decades once exposure has taken place (1). Article 16 of the Stockholm Convention requires the Conference of the Parties to evaluate periodically whether the Convention is an effective tool in achieving its objective collecting comparable and consistent monitoring data on the presence of POPs in the environment and in humans. Twelve POPs were initially listed in the Convention. Nineteen additional chemicals have been listed in the annexes of the Convention since, bringing the total number of regulated POPs to 31.

Of the 53 countries in the WHO European Region, 52% have participated in various rounds of the human milk survey to date. Only two countries (8% of the Region) took part in the most recent round. Very little data are available for several of the POPs in breast milk listed after 2009. To follow up on these substances over time, it is important to start monitoring these substances now. In addition, it is critical to monitor possible substitution chemicals that have POP-like characteristics. Current results indicate that POPs regulated in source regions decades ago have significantly decreased, but are still present at low levels that have not changed since the previous GMP report in 2015. Some are still of concern in some regions.

The Minamata Convention on Mercury, which entered into force in August 2017, sets guidelines for limiting human exposure to mercury (2). Article 22 calls for Parties to monitor mercury in the environment as well as in vulnerable populations as a way of assessing the Convention’s effectiveness (3). In addition, Article 19 encourages Parties to develop and improve modelling and geographically representative monitoring of levels of mercury and mercury compounds in vulnerable populations and in environmental media. HBM in high-risk and/or representative populations can be used to track changes in exposure over time and space, and thus represents a powerful and potentially cost-effective tool to gauge progress.

Accepted biomarkers of mercury exposure include hair (for methylmercury), urine (for inorganic mercury) and blood (mostly for methylmercury but potentially also inorganic mercury). Hair and urine samples are particularly suitable as they provide information on the two main forms of mercury, and their collection is non-invasive and relatively inexpensive (sampling and analyses can be done for US$ 50 or less per item). In addition to the surveillance of the general population, tracking occupational exposure is required as several of the Convention’s articles target specific sectors such as artisanal small gold mining.

References
The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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