i-HBM WORKING GROUP

International Human Biomonitoring (i-HBM) Working Group – Three Year Planning Report 2021-2024

Drafted by:
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Mission:

The i-HBM Working Group aims to promote the use of population-level human biomonitoring data to inform public health decision-making by developing harmonized resources to facilitate the interpretation of human biomonitoring data in a health risk context.

Audience:

The primary audience for this group's efforts is biomonitoring programs and data users including chemical regulators, risk managers and environmental health researchers.

Organization:

- Chair and co-chair
- Secretariat
- Steering Committee (6 members + chair, co-chair, secretariat)
- Committees: Web Resource, Outreach
- Members

Background/Context:

In order to characterize population exposures to environmental chemicals, many jurisdictions conduct human biomonitoring (HBM) activities. The capacity to interpret these data at the population level is gradually improving with the development of human biomonitoring guidance values. There are two broad categories of these values, reference values and risk-based values. Reference values allow for the comparison of new HBM data to an existing value from a national HBM program such as the Canadian Health Measures Survey (CHMS), National Health and Nutrition Examination Survey (NHANES), Korean National Environmental. Health Survey (KoNEHS), German Environmental Survey (GerES), etc. Risk-based values provide a concentration for a chemical above which current evidence suggests there is an increased risk for adverse health effects in a population. These values allow for the interpretation of population level HBM data in a health risk context. Derivation of risk-based values requires either an epidemiological study (e.g. lead action level) or an established risk assessment value (e.g. ADI, TDI, RfD).

HBM data users (e.g. biomonitoring programs, regulators and risk managers) are primarily interested in understanding how current exposures to a given chemical compare to some health- or risk-based benchmarks, such as established risk assessment values (e.g., ADI, TDI, RfD, TRV). There are a number of values that have been derived from external risk assessment values including Biomonitoring Equivalents (BEs) and the German Human Biomonitoring Commission's HBM values. **While more and more of these values are being developed, there remains a lack of harmonization in approaches for using these values to interpret population level HBM data.** The i-HBM working group was founded to foster international collaboration to increase the

use of HBM data in regulatory decision making, harmonize approaches for interpreting population level HBM data, and facilitate interpretation in easy to understand and readily available tools and tutorials.

First Meeting:

The launch occurred at the ISES 2020 annual meeting (virtual) and generated significant international interest and currently includes over 50 members. The first meeting of the Working Group was held virtually on November 25, 2020 with 41 attendees representing a range of biomonitoring programs from Europe, Asia and North America.

The meeting provided an opportunity to present and discuss the mission, terms of reference and proposed plan for forming a steering committee in 2021. The i-HBM dashboard (also called the *Guidance Value Database and Comparison Tool)* was presented to the working group. The database and tool were created as a repository for currently available human biomonitoring guidance values and to facilitate understanding of how they may be used as screening tools to interpret population-level human biomonitoring data.

This meeting provided the chance to connect with international colleagues and discuss the direction, format and goals of the i-HBM working group. It also provided an opportunity to solicit feedback on the mission and the database and comparison tool. The mission statement has been updated and feedback has been incorporated into the tool.

Next steps for the working group include finalizing the mission and three-year plan along with establishing a steering committee to help guide the strategic direction and move the collaborative projects forward.

The i-HBM Working Group is in alignment with the newly developed *Health Canada: Framework for Science and Research Excellence*.

i-HBM Dashboard: https://biomonitoring.shinyapps.io/guidance/

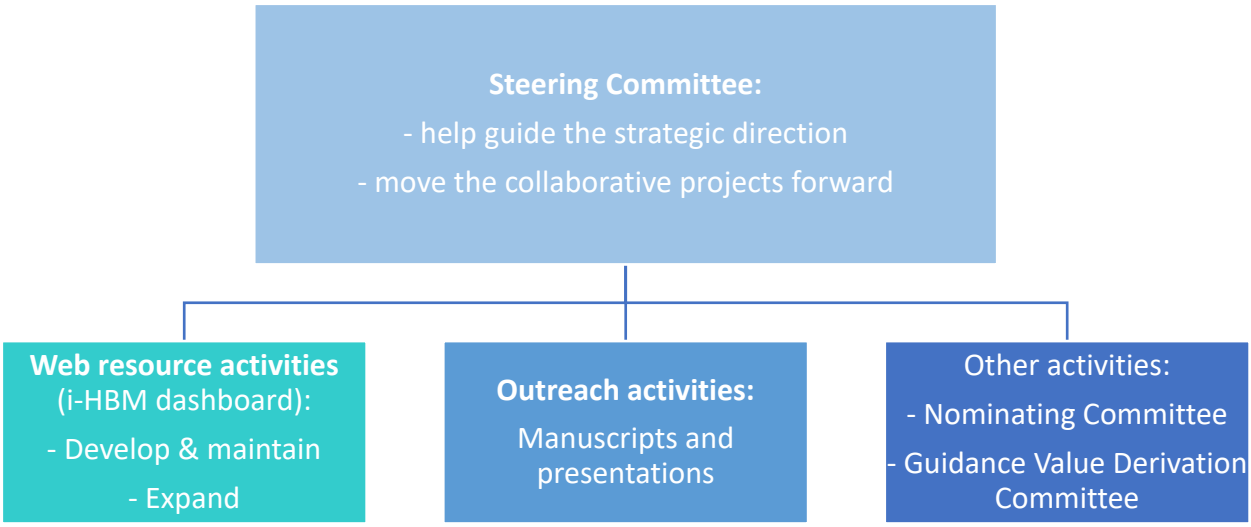
To facilitate the interpretation of human biomonitoring data, the i-HBM dashboard was developed as a comprehensive database of available interpretation values. This compilation of values will form the basis of the tool that will simplify the interpretation of HBM data in a public health risk context.

The objectives of the dashboard are:

- To be an open-access, curated database of human biomonitoring guidance values developed for use in interpreting human biomonitoring data for the general population
- To enable a user-friendly search for human biomonitoring guidance values for specific chemicals and/or biomarkers of exposure
- To assist users (risk assessors, risk managers and biomonitoring programs) with the interpretation of human biomonitoring data by allowing users to compare population-level data to the human biomonitoring guidance values and providing standardized outputs in the form of figures and descriptive text.

This dashboard will form the basis for the project work done over the next three years by the i-HBM working group.

i-HBM Proposed Plan and Projects (2021-2024):



1. **Steering Committee (SC)**

   Timeline: 2021-2022

   Lead: i-HBM working group chair

   Work description: Form committee with representation from biomonitoring programs and risk assessors or other data users from various international jurisdictions.

   Activities:
   a. Form committee (i-HBM working group chair)
   b. Meet twice per year
   c. Schedule and set agenda for i-HBM working group meetings
   d. Seek funding (if needed)
   e. Make assignments for projects
   f. Make recommendations for additional committees and membership

2. **i-HBM dashboard and tutorials**

   Timeline: 2021-2022

   Lead: Web Resource Committee – membership may include individuals familiar with the interpretation of biomonitoring in the context of risk-based values; may also include

individuals from the risk assessment community and those familiar with developing risk-based values

Work description: Update the existing i-HBM dashboard to include clearly defined objectives, expanded chemical-specific queries (e.g. comparison between existing HBM data from national programs and various guidance values, comparisons between new HBM data for a given population and existing HBM data from national programs and guidance values), refined interpretation guidance and tutorials to guide data users in the use of the dashboard.

Requirement: Resource(s) to work on the i-HBM dashboard with expertise in building, developing and designing databases in R; use of shinyapps; website development

Activities:

a. Review and provide input on i-HBM dashboard design features
b. Review and provide input on chemical-specific query outputs including graphs, tables and comparisons (Web Resource Committee)
c. Draft documents to serve as resources for data users to understand how to interpret the information in query outputs (Web Resource Committee)
    i. Tutorial 1: How to interpret HBM data using the i-HBM dashboard
    ii. Tutorial 2: What are the differences between the available human biomonitoring guidance values (e.g. BEs, HBMs)
    iii. Additional tutorials: differences in interpretation between chemicals with short and long half-lives, cancer vs non-cancer, BEs vs tissue-based guidance values
d. Review and comment on interpretation resources (i-HBM working group)

3. Outreach

Timeline: 2021-2023

Lead: Outreach Committee – membership may include experts who are able to commit to contributing to manuscript and presenting at targeted meetings/conferences

Work description: Conduct outreach to help educate and inform data users of the value of the i-HBM dashboard and how HBM data can/should be interpreted.

Activities:

a. Prepare manuscript for publication in scientific journal on the i-HBM dashboard and harmonizing the communication of HBM data interpretation
b. Prepare briefing documents and presentations
c. Conduct outreach (e.g. ISES, SRA, SOT)

4. Maintenance and Expansion

Timeline: 2022-2024

Lead: Web Resource Committee, Outreach Committee, others (Nominating Committee, Guidance Value Derivation Committee)

Work description: Maintenance and expansion of i-HBM dashboard and tutorials and outreach/engagement.

Activities:

a. Modify i-HBM dashboard output and resources to ensure aligned with users needs (Web Resource Committee)
b. Prepare additional manuscripts (Outreach Committee)
c. Identify chemicals for which new human biomonitoring guidance values need to be developed (Nominating Committee)
d. Develop new human biomonitoring guidance values (Form Guidance Value Derivation Committee)

Appendix I

Glossary ***require input and agreement from working group*

Biomonitoring Equivalents (BEs) – The concentration of a chemical or metabolite in a biological medium (blood, urine, human milk, etc.) consistent with defined exposure guidance values or toxicity criteria, including reference doses and reference concentrations (RfD and RfCs), minimal risk levels (MRLs) and tolerable daily intakes (TDIs). [Summit Toxicology; Health Canada]

Biomonitoring Guidance Values (BGVs) – Any guidance values established to allow interpretation of human biomonitoring values. This includes RV95, HBM-I, HBM-II and BEs.

Biomonitoring Guidance Values (BGVs) – This value represents the upper concentration of the substance or a metabolite of the substance in any appropriate biological medium corresponding to a certain percentile (generally 90 or 95 percentile) in a defined reference population. If background levels cannot be detected, the BGV may be equivalent to the detection limit of the biomonitoring method, which then is to be specified in the document. A value exceeding the BGV might help to identify the need for an expert consideration of the working conditions. Unlike BLVs, BGVs are not health-based and therefore do not set a limit between absence or presence of adverse health effects. [former EU Scientific Committee on Occupational Exposure Limits (SCOEL)]

Blood Screening Value – These values represent steady-state venous blood concentrations corresponding to an exposure at the reference dose or exposure guidance value. These values have been calculated for several volatile organic compounds (VOCs) using a single generic physiologically-based pharmacokinetic model and a limited number of physiological and chemical specific parameters. Where there is an exceedance, a more detailed evaluation may be required. This may include an investigation of exposure pathways, development and application of fully-developed PBPK models, and reviewing the underlying toxicological data, risk assessments, and other risk management strategies may be undertaken.

Epidemiology-Based Guidance Values – see *Tissue-Based Guidance Values*

Exposure Guidance Values – see *Risk Assessment Values*

External Dose-Based Risk Values – see *Risk Assessment Values*

HBM – Human biomonitoring

HBM-I – The concentration in human biological material of a substance at and below which, according to the knowledge and judgement of the German Human Biomonitoring Commission, there is no risk for adverse health effects and, consequently, no need for action. [German HBM Commission]

HBM-II – The concentration in human biological material of a substance at and above which, according to the knowledge and judgement of the German Human Biomonitoring Commission, there is an increased risk for adverse health effects and, consequently, an immediate need for exposure reduction measures. [German HBM Commission]

HBM guidance values (HBM-GVs) – Health-related guidance values referring to the internal body burden that can be compared directly with HBM data. These values are derived for both the general population and occupationally exposed adults. They are derived within HBM4EU for priority substances identified by the HBM4EU chemicals prioritization strategy based on existing needs to answer policy relevant questions as raised by national and EU policy makers. The strategy for deriving HBM-GVs is based on already existing approaches from the German HBM Commission, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) as well as from the US-based scientific consultant Summit Toxicology. [HBM4EU]

HBM-GVs for the general population (HBM-GV_{GenPop}) – The concentration of a substance or its specific metabolite(s) in human biological media (e.g. urine, blood, hair) at and below which, according to current knowledge, there is no risk of health impairment anticipated, and consequently no need for action. They are equivalent to the HBM-I values from the German Human Biomonitoring Commission. When they are estimates of chemicals' concentrations in biological matrices consistent with existing external exposure guidance values (toxicity reference values or TRVs), they correspond in this case to BEs. [HBM4EU]

HBM-GVs for occupationally exposed adults (HBM-GV_{Worker}) – A concentration of a substance or its relevant metabolite(s) in human biological media aiming to protect workers exposed to the respective substance regularly (each work day), and over the course of a working life from the adverse effects related to medium- and long-term exposure. Similar in definition to Biological Limit Values (BLVs). [HBM4EU]

Health-based biological limit values (BLVs) – Biological limit values (BLVs) are reference values for evaluating potential health risks in the practice of occupational health. A BLV is a guideline for the control of such risks and should not be used for other purposes. Due to biological variability, an individual's measurement may exceed the BLV without incurring an increased health risk. If, however, the biological levels persistently exceed the BLV, or if the majority of measurements obtained from a group of workers at the same workplace exceed the BLV, the cause of the excessive values must be investigated and proper action taken to reduce the exposure. Exposure equivalent to the BLV generally do not affect the health adversely, when attained regularly under workplace conditions, except in cases of hypersensitivity. In the first instance, BLVs represent the levels of determinants which are most likely to be observed in specimens collected from a worker exposed to the chemical in question exclusively by inhalation at the level of the occupational exposure limit (OEL). Exceptions are BLVs for substances for which the OELs serve as protection against non-systemic effects (e.g. irritation or respiratory disorders) or for substances which require biological monitoring due to other routes of absorption, in particular the skin. [French Agency for Food, Environmental and Occupational Health & Safety (ANSES); former EU Scientific Committee on Occupational Exposure Limits (SCOEL)]

Reference Values (RV95s) – The reference value for a chemical substance in human biological material (e.g., blood, urine) is derived according to a defined statistical method from a series of measuring results obtained. Samples to be used for this purpose have to be collected employing a defined group of the general population. In analogy with to the IUPAC guideline (Poulsen et al., 1997), the German HBM Commission and Health Canada use as reference value the 95th percentile of the measured pollutant concentration levels in the relevant matrix of the reference population.

To derive it, it is rounded off within the 95% confidence interval. In addition, when the database is appropriate and sufficient to do so, RV95s are defined for sub-groups (e.g., non-smokers, children, etc.). Wherever possible, RV95 are defined using data obtained for a suitable reference population, such as the population studied in the German Environmental Surveys (GerES). [German HBM Commission; Health Canada]

Risk Assessment Values – Exposure limits established to protect humans form developing adverse effects resulting from exposures to chemicals. There are several formal risk assessment values established by different regulatory agencies. These include acceptable daily intakes, tolerable daily intakes, reference doses, reference concentrations, etc. Each carries a slightly different definition. An example is: Acceptable Daily Intakes (ADIs) - Estimated maximum amount of an agent, expressed on a body mass basis, to which individuals in a (sub)population may be exposed daily over their lifetimes without appreciable health risk. Other examples include Tolerable Daily Intakes (TDIs) and oral Reference Doses (RfDs).

Risk-Based Values – also referred to as biomonitoring screening values, health risk-based values, risk-based biomonitoring evaluation values, risk assessment–based values (e.g. BEs, HBM-I)

Tissue-Based Guidance Value – These values are derived from a robust set of epidemiological studies establishing a quantitative relationship between biomonitoring levels in humans and an observed biological/toxicological response. Examples include the blood lead intervention level and the blood methylmercury guidance values, both established by Health Canada, and the human biomonitoring values for polychlorinated biphenyls in blood serum, established by the German Human Biomonitoring Commission. Exceeding these guidance values at the individual or population level indicates a need for medical follow-up, and for jurisdictions to identify and mitigate sources of exposure.

Toxicity Reference Value (TRV) – see *Risk Assessment Values*