EUROPEAN HUMAN BIOMONITORING INITIATIVE (HBM4EU) INDICATOR LEAFLETS

USE OF HBM FOR RISK ASSESSMENT

Indicator 2.3 Number of references to HBM4EU related HBM data in risk assessment

SPECIFIC GOAL 1: Developing a common methodology for the interpretation and use of HBM data in policy making

RESPONSIBLE: Finnish Institute of Occupational Health (FIOH), Finland **WORK PACKAGE:** 5 (VITO)

KEY MESSAGES

- Although in the past few years HBM4EU has provided good examples on the use of HBM data in chemical risk assessment (RA), there is still quite some work to improve its use in regulatory RA.
- Work has been done to understand the key obstacles for the use of HBM data in regulatory RA, and a journal article based on the lessons learned in HBM4EU is being prepared to provide guidance.
- The use of new HBM4EU generated HBM data in RA has been reported by HBM4EU partners for the HBM4EU priority substances. Also external references (e.g. by EFSA and ECHA) are expected in the future, as the HBM4EU dashboard is now available, and more and more of the new HBM4EU aligned study data will be published.

WHY

HBM is an essential tool to survey the **internal aggregate exposure of humans** resulting from different exposure sources and via different routes of uptake (lung, skin, digestive tract).

Inclusion of HBM data **could therefore improve human health risk assessment** for both the general population and workers by providing **more accurate human exposure data**.

However, inclusion of HBM data in RA has been done but is not yet common practice.

It is necessary to provide strong anchoring of HBM in RA practices with the overall objective to minimize the human health impact of the use of hazardous substances.

Results

1. Review of the use of human biomonitoring data in chemicals risk assessment before HBM4EU. *Deliverable D5.1 converted to paper (Louro et al., 2019).*

GLOBAL ASSESSMENT SCHEMES

RA scheme	HBM recognized as an exposure assessment tool?	Specific guidance available for the use of HBM in RA?	Examples on the use of HBM exist?
WHO	YES	YES	YES
FAO/WHO JECFA	YES	NO	NO

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EUROPEAN ASSESSMENT SCHEMES

RA scheme	HBM recognized as an exposure assessment tool?	Specific guidance available for the use of HBM in RA?	Examples on the use of HBM exist?
REACH (ECHA Risk Assessment Committee RAC)	YES	Limited*	YES
Food Safety (EFSA CONTAM, PPR)	YES	YES	YES
Plant protection products regulation (PPP, EFSA)	YES	NO	HBM has been used for monitoring worker exposure
Biocidal products regulation (ECHA Risk Assessment Committee RAC)	YES	NO	NO
Occupational Safety and Health (EU-OSHA, DG Employment, ECHA RAC)	YES	NO	YES
Cosmetics regulation (SCCS)	NO	NO	YES

IPCS = International programme on Chemical Safety, JECFA = Joint expert committee on food additives, REACH = Registration, Evaluation and Authorization of Chemicals, RAC = ECHA Committee for risk assessment, SCCS = Scientific committee on customer safety, CONTAM = EFSA Panel on Contaminants in the Food Chain, PPR = EFSA Panel on Plant Protection Products and their Residues
*REACH guidance R8 mentions the possibility to derive DNELs based on biomarker levels, but no further guidance available

2. Examples of priority substances/groups for which HBM has been used in risk assessment

Restriction under REACH

Restriction of 4 Phthalates (DEHP, BBP, DBP, DiBP) in toys & childcare articles. The exposure assessment relied mostly on the urinary HBM data generated by the EU-wide DEMOCOPHES project. – *Dossier submitted by ECHA/Danish Authorities, 2016.* RAC opinion 2017, https://echa.europa.eu/fi/registry-of-restriction-intentions/-/dislist/details/0b0236e1806e7a36

Restriction of BPA in Thermal papers. The original dossier used modelled exposure data only (since HBM data were not available). Later the risk assessment was refined with HBM data. Confirming especially risk for workers (cashiers) and more specifically for the unborn child exposed in utero to BPA contained in thermal-paper handled by his/her mother. – *Dossier submitted by French Authorities, May 2014.* RAC opinion,2015:https://echa.europa.eu/fi/registry-of-restriction-intentions/-/dislist/details/0b0236e18051ba62

Restriction of PFOA Although the dossier included human HBM data for general population and workers, the restriction decision was mostly based on PBT properties. – *Dossier submitted by Norway and Germany, 2014.* RAC opinion 2015, https://echa.europa.eu/fi/registry-of-restriction-intentions/-/dislist/details/0b0236e180518e69

Proposed Restriction of PFHxS The restriction proposal include a section on human exposure, with information on exposure pathways and reference to HBM data. – *Dossier submitted by Norway, 2019.* No RAC opinion available yet

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Authorization under REACH examples

Authorization of MOCA (Aniline derivative) in polyurethane industry. Biomonitoring data were used for a more accurate exposure assessment and risk characterization.

Authorization of DBP used as an absorption solvent in a closed system in the manufacture of maleic anhydride.

Authorization on formulation of recycled soft PVC containing DEHP in compounds and dry-blends.

3. Major obstacles to use of HBM in RA identified in Louro et al., 2019

- Lack of HBM guidance values or biomonitoring equivalents
- Limited toxicokinetic information to support the interpretation of HBM data
- Lack of legal enforcement in the occupational health and safety (OSH) field

4. References to HBM4EU related HBM data in risk assessment

- The use of HBM4EU related HBM data in RA has been reported for HBM4EU prioritised substance groups in deliverables 5.1, 5.5, 5.8 and 5.11.
- Currently, RA manuscripts (some using data from aligned studies) are under preparation for: mercury and its organic compounds, bisphenols, 2 x pesticides mixtures (pyrethroids, chlorpyriphos), flame retardants (OPFRs), PFAS mixture, chromium VI, O-toluidine, mycotoxins, and phtalates.
- Up to date no external references (e.g. by EFSA or ECHA) were identified. First references are expected in 2022, since aligned studies and the HBM dashboard are now available.

WORK CONCLUDED

- Under the scope of HBM4EU, the state-of-the-art of HBM use in chemicals RA have been reviewed (with a special focus in Europe). See Deliverable 5.1; Louro et al.
- A set of scientifically sound health-based biological limit/guidance values was developed (see D5.2, AD 5.5, D5.6, D5.9, AD5.10, D5.14, D5.15)
- A survey was conducted under HBM4EU that identified hurdles and challenges faced by regulators
- Within HBM4EU, RA was performed using HBM data for a set of compound groups on HBM4EU's list of priority substances: anilines, cadmium/chromium, flame retardants, PAHs, PFAS and mixtures of PFAS, phthalates bisphenols, UV-filter benzophenone-3, Acrylamide, Aprotic solvents, Arsenic, diisocyanates, Flame retardants, Lead, Mercury and its organic compounds, Mycotoxins, Pesticides and PAHs (Deliverable 5.5., 5.8 and 5.11). These examples showed that HBM can be included in RA, and its inclusion generally benefits the RA
- Prepare guidance, on EU level, applicable to different regulatory schemes on the use of HBM in RA to further develop the integration of HBM in regulatory RA (manuscript in preparation)

FUTURE PERSPECTIVES

- Further refine scientific methodology/approaches for the setting of health based HBM values
- Continue research efforts for the development of approaches to integrate existing HBM data and in vitro, in silico and HTP screening data in combination with computational modelling (PBTK) to generate more reliable toxicokinetic information and to provide linkages between AOPs and human internal exposure levels
- Reinforce the capabilities of HBM and start discussions with regulators on better anchoring HBM as a tool in the various horizontal and vertical EU legislative RA frameworks. This is critical to increase the frequency of use of HBM data and improve the quality of regulatory RA by realistic, EU-specific exposure information (see e.g. AD5.10)

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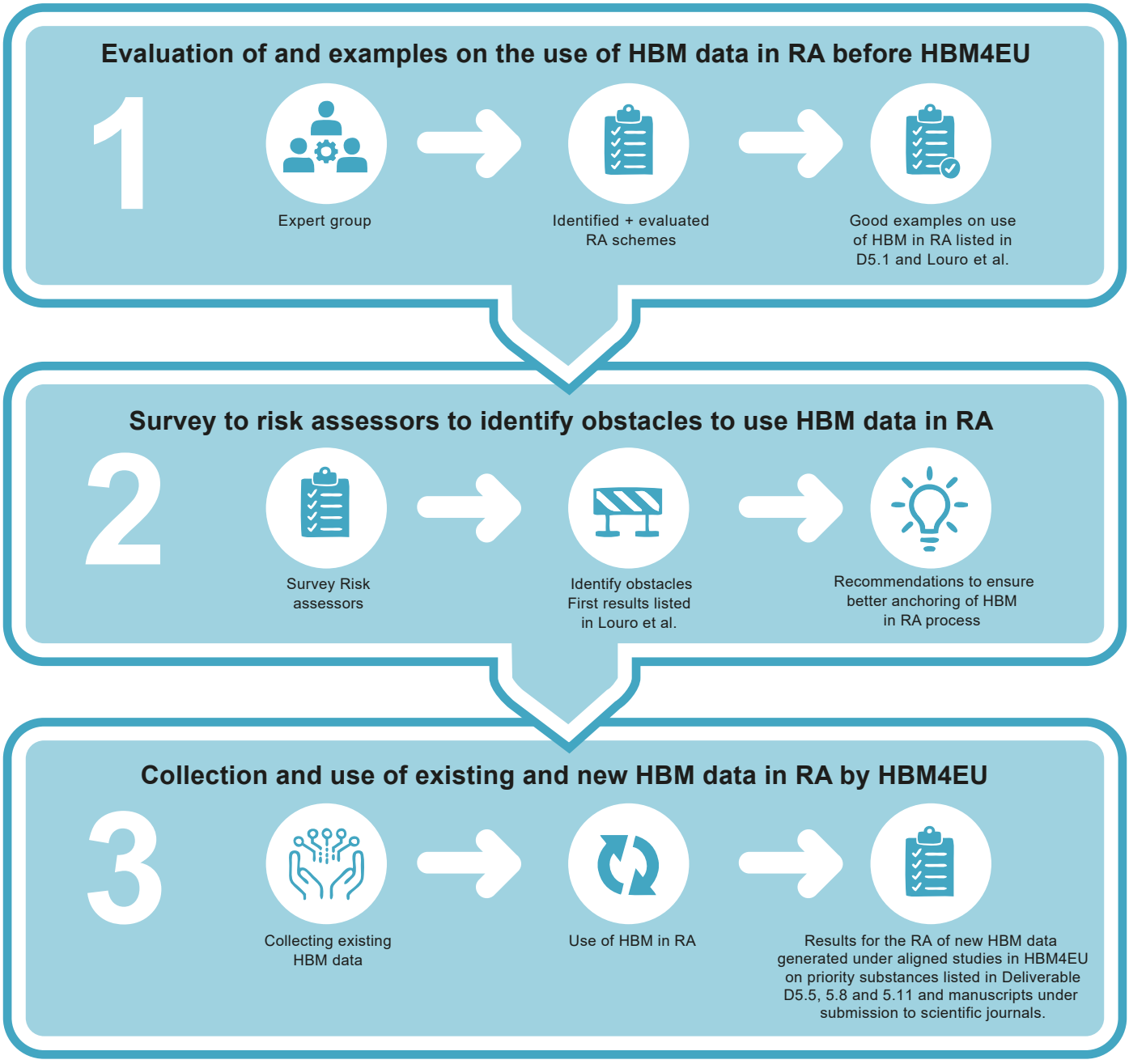
Methodology



Louro et al. 2019. Human biomonitoring in Health Risk Assessment in Europe: current practices and recommendations for the future. International Journal of Hygiene and Environmental Health 222 (2019) 727–737.
https://doi.org/10.1016/j.ijheh.2019.05.009 D5.1. Louro et al. (online)
https://doi.org/10.3390/toxics10050228
https://doi.org/10.3390/toxics10050234
https://doi.org/10.3390/toxics10050217

HBM4EU deliverables

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