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Instituto_Nacional de Saúde Doutor Ricardo Jorge

ESTABLISHING HUMAN BIOMONITORING PROGRAM IN THE EUROPEAN UNION - THE PORTUGUESE PERSPECTIVE

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Toxi-Latin 2023: III Congresso Latino-Americano De Toxicologia Ambiental, Experimental e Nanomateriais- 26-30/09/2023 - Belo Horizonte (MG), Brasil

The National Institute of Health Doutor Ricardo Jorge (Instituto Nacional de Saúde Doutor Ricardo Jorge, INSA)

- Funded in **1899** by the medical doctor **Ricardo Jorge** (Porto, 1858 – Lisboa, 1939), as a laboratory arm of portuguese health system
- Triple mission: state laboratory, national reference laboratory and national health observatory.
- With headquarters in Lisbon, also has centres in **Porto** (Centro de Saúde Pública Doutor Gonçalves Ferreira) and in **Águas de Moura** (Centro de Estudos de Vectores e Doenças Infecciosas Doutor Francisco Cambournac).

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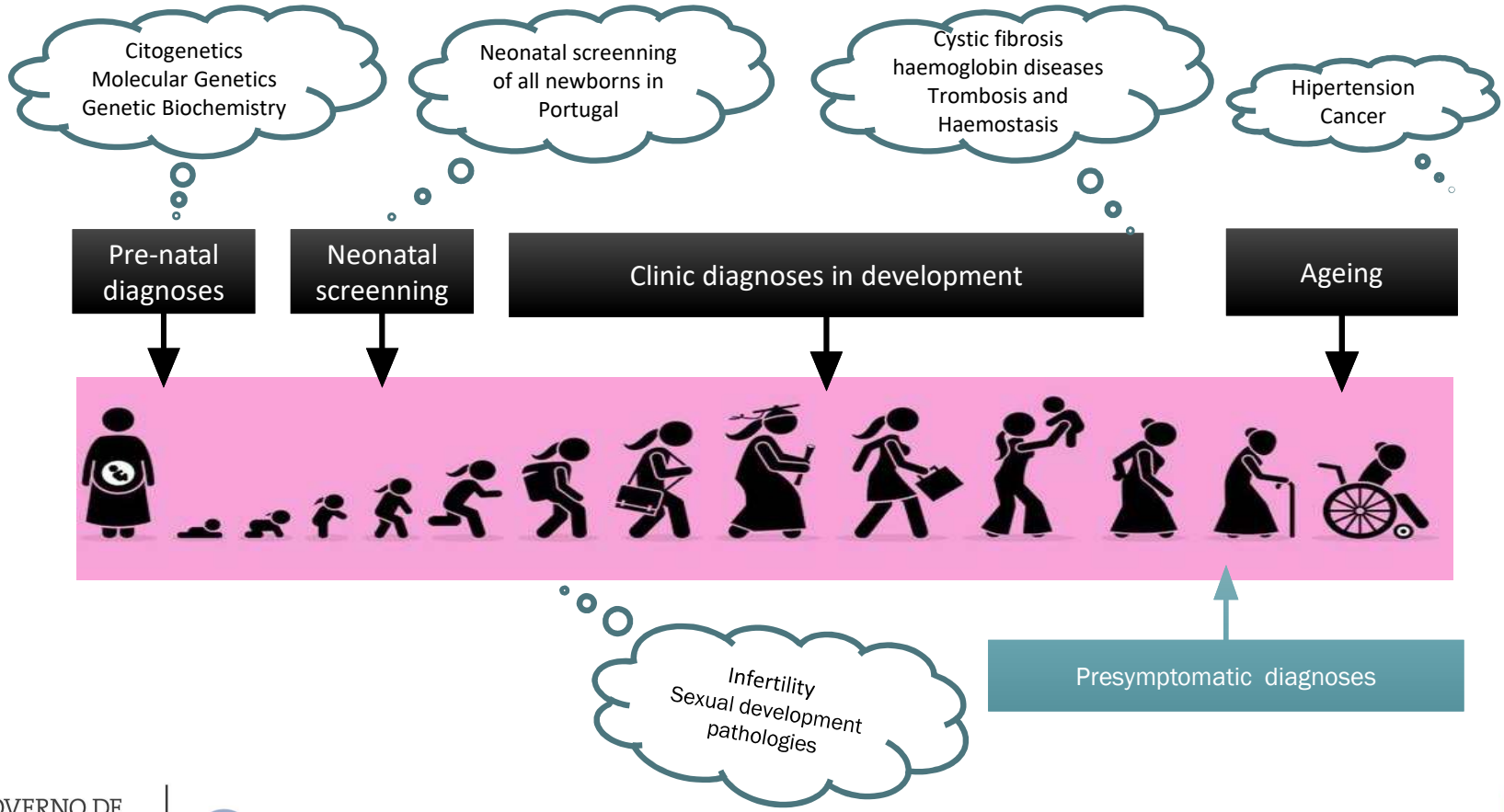
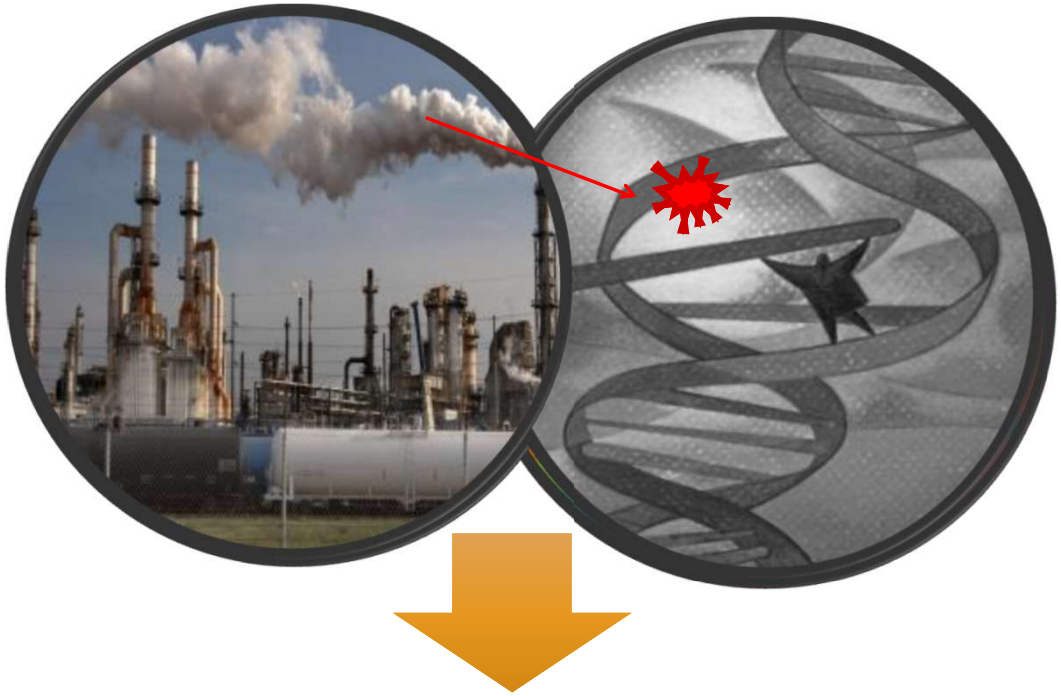
Human Genetics Department



Genetic Toxicology Research Group

Environment GENOME



Since 1996, investigates the adverse effects on our genome upon exposure to physical, chemical or biological stressors

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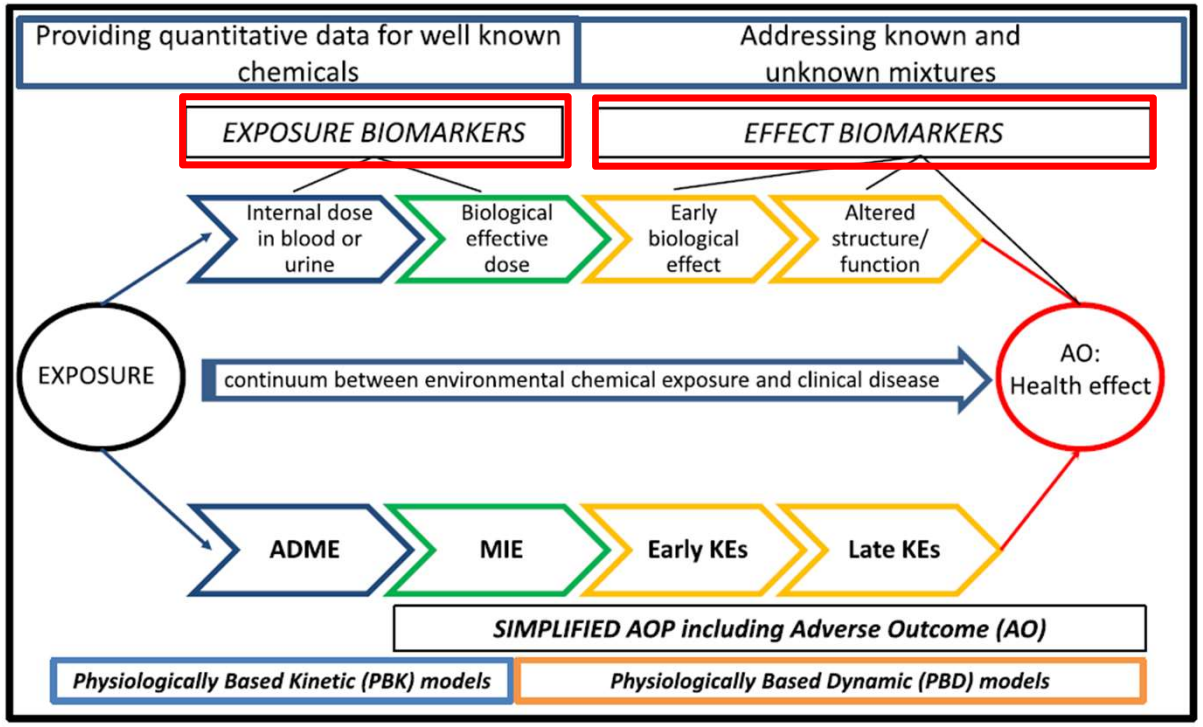
HBM as source of realistic exposure and effect data

Human biomonitoring (HBM) Is the direct measurement of people's exposure to substances, by measuring the substances, their metabolites or their effects in human matrices, such as blood or urine.



Zare Jeddi et al., 2021. Environment International 146 (2021) 106257

The importance of HBM

HBM can help to improve chemical policies in five major key areas:

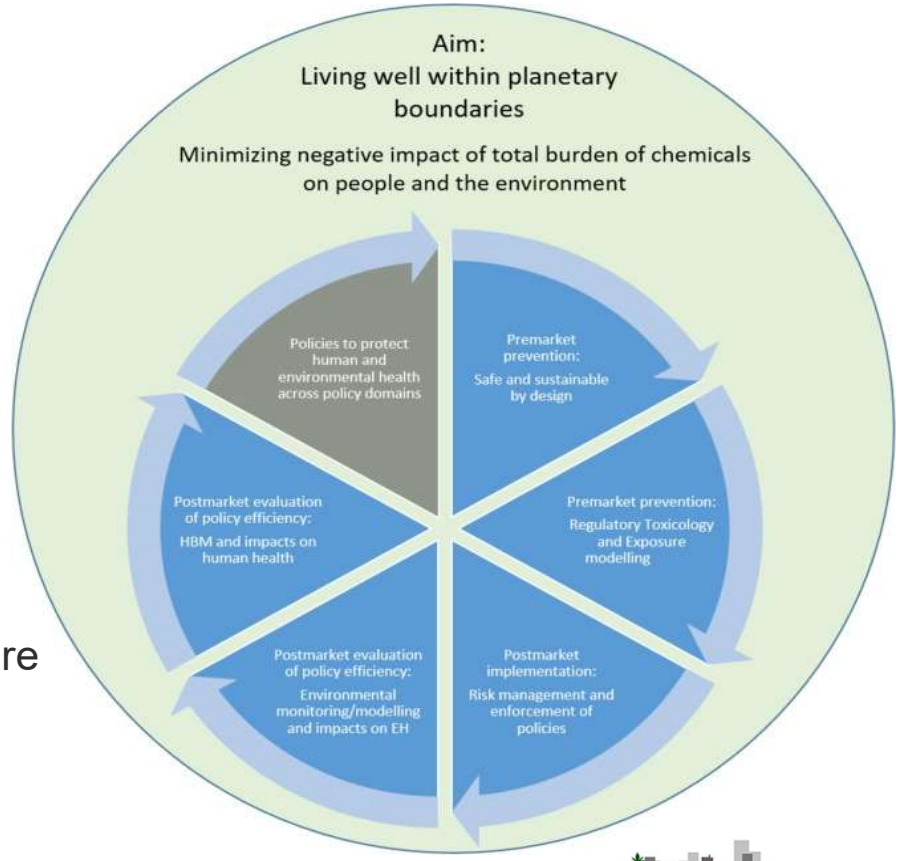
(1) assessing internal and aggregate exposure in different target populations

(2) assessing exposure to chemicals across life stages

(3) assessing combined exposure to multiple chemicals (mixtures)

(4) bridging regulatory silos on aggregate exposure and

(5) enhancing the effectiveness of risk management measures



Zare Jeddi, Hopft, Louro et al. 2022. Environment International (168) 107476

HBM – recognising the data gaps

- **HBM programs have been established by some countries:**
  - **Health Canada,** leads a number of HBM activities in general and targeted populations within Canada - https://health-infobase.canada.ca/biomonitoring/
  - US National Health and Nutrition Examination Survey (NHANES), coordinated by CDC - https://www.cdc.gov/nchs/nhanes/index.htm
  - **In Europe,** some countries are good examples of using HBM programs:
    - Flemish human biomonitoring program (Belgium) - https://omgeving.vlaanderen.be/en/flemish-human-biomonitoring-program
    - The German Environmental Surveys (GerES) - https://www.umweltbundesamt.de/en/topics/health/commissions-working-groups/human-biomonitoring-commission-hbm-commission

- **In Portugal, data on HBM relies on few targeted research studies published in scientific literature.**
- **Different approaches to HBM are undertaken by several EU countries, leading to inequalities at the level of available data and consequent policies.**

The HBM4EU project- Human Biomonitoring for Europe

General objective:

❖ To understand human exposure to chemicals and resulting health impacts and communicate with policy makers to ensure that the results are exploited in the design of new chemicals policies and the evaluation of existing measures

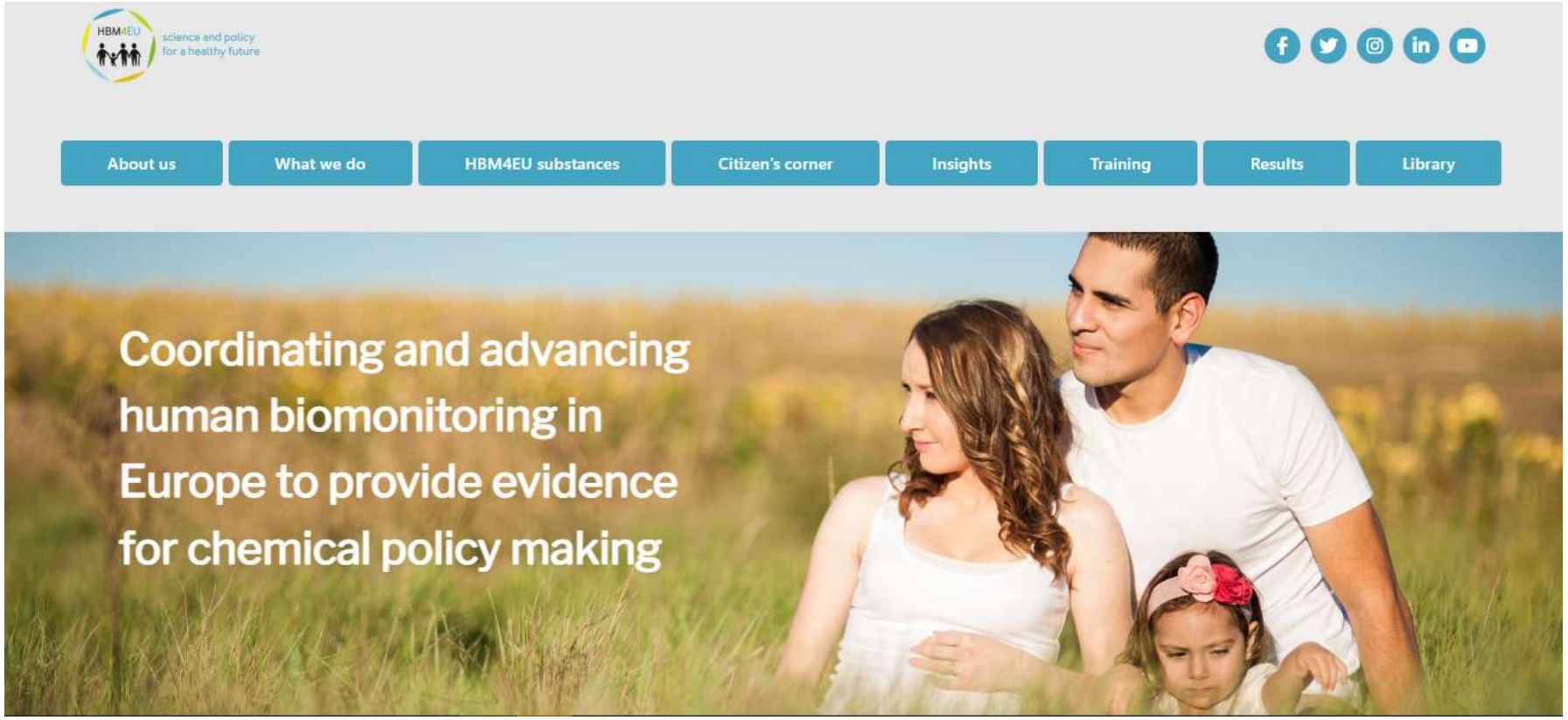
Gaps to be filled:

❖ Generate data on exposure to single substances and to combinations of chemical substances

❖ Produce evidence-based knowledge on the link between external exposure via different routes, internal levels and human health

❖ This knowledge is essential to inform and implement effective policy-making to protect the EU population from the impacts of chemical exposure on health

The HBM4EU project



HBM4EU work

PILLAR 1: SCIENCE TO POLICY

- Prioritization and input to the annual work plan
- Translation of results into policy
- Sustainability and capacity

PILLAR 2: EUROPEAN HBM PLATFORM

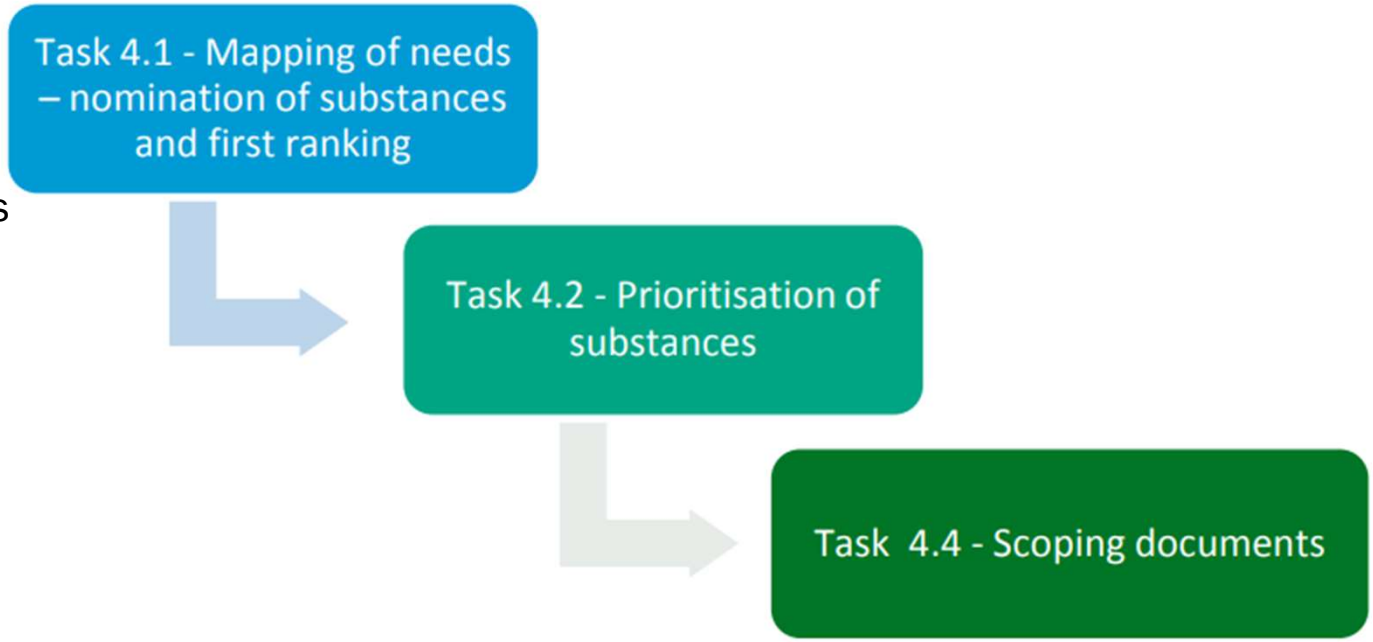
- Survey design and fieldwork
- Targeted fieldwork surveys and alignment at EU level
- Laboratory analysis and quality
- Data management and analysis

PILLAR 3: EXPOSURE AND HEALTH

- Linking HBM, health surveys and registers
- From HBM to exposure
- Establishing exposure health relationships
- Effect Biomarkers
- Mixtures, HBM and human health risks
- Emerging Chemicals

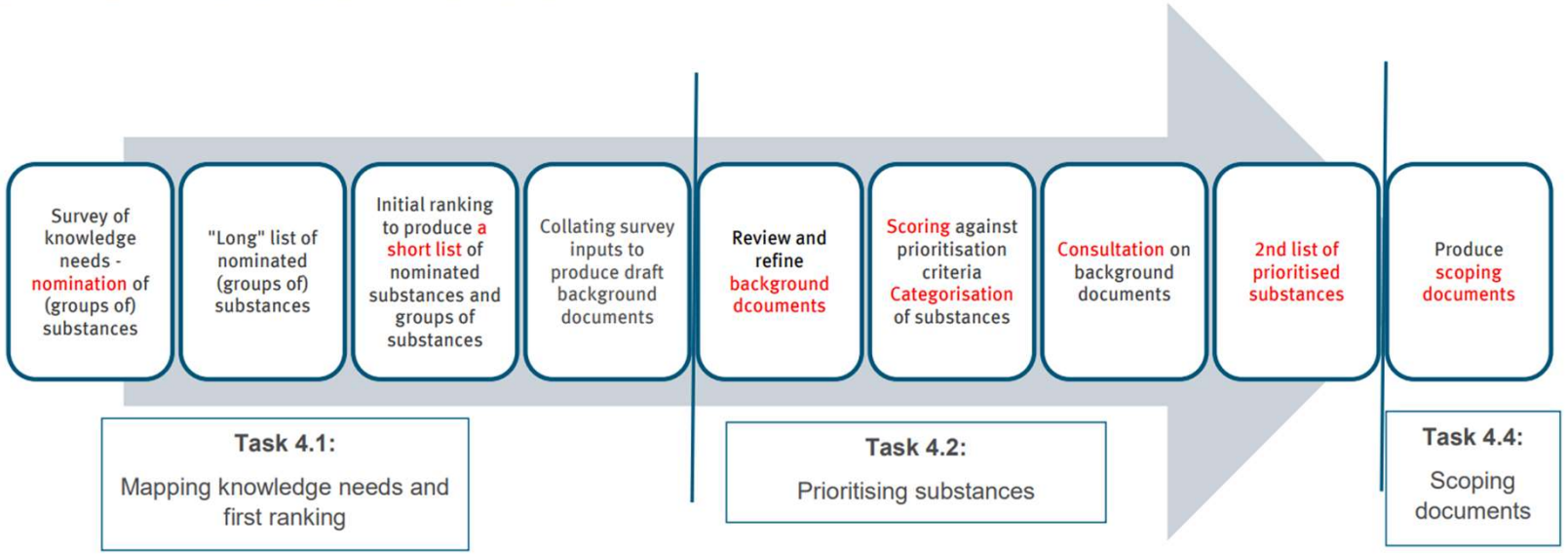
HBM4EU Strategy for the prioritisation of substances

policy makers
stakeholders
scientists



https://www.hbm4eu.eu/wp-content/uploads/2017/03/HBM4EU_D4.3_Prioritisation_strategy_criteria-1.pdf

HBM4EU Strategy for the prioritisation of substances



https://www.hbm4eu.eu/wp-content/uploads/2017/03/HBM4EU_D4.3_Prioritisation_strategy_criteria-1.pdf

HBM4EU Priority substances lists

1st List of Priority Substances
Phthalates/Hexamoll® DINCH
Bisphenols
Per-/polyfluorinated compounds
Flame retardants
Cadmium and chromium
Polycyclic aromatic hydrocarbons (PAHs)
(concerning air pollution)
Aniline family (aniline and e.g. MOCA)
Chemical mixtures

2nd List of Priority Substances
Arsenic & its compounds
Acrylamide
Aprotic solvents
Diisocyanates
Lead & its compounds
Mercury & its organic compounds
Mycotoxins
Pesticides, including Pyrethroids
UV filters - Benzophenones

Deliverable Report D4.8 https://www.hbm4eu.eu/work-packages/deliverable-4-8-third-list-of-hbm4eu-priority-substances/

HBM4EU Priority substances lists

3rd List of Priority Substances

Mercury*
Trace/heavy metals (e.g.: Al, Co, Mn, Cd*, Pb, Cu, Zn, Ni, Cr*, W, natural U, Bi, Beryllium, manganese, nickel, arsenic, lithium, vanadium, antimony);
Metals in batteries: cobalt (Co), Nickel, (Ni), Lithium (Li). Nanoforms of Co and Ni
Aluminium and manganese: occupational
Acrylamide *
Per- and polyfluoroalkyl substances (PFASs) *
Flame retardants: Brominated flame retardants, Organophosphate flame retardants, Flame retardants (including TDCPP, TBBPA) (DBDPE, Decabromo-diphenyl ethane) *
Plant protection products and biocides, with focus on glyphosate, pyrethroides, carbamate, dithiocarbamates, organophosphates *
Fungicides: includes SDHI fungicides (boscalid, bixafen, fluxapyroxad); Azoles (imazalil, ipconazole, metconazole, penconazole, prochloraz, tebuconazole, tetraconazole); Dithiocarbamates; Famoxadone and Dimoxystrobin; Isothiazolinones (CIT/MIT, BIT), Triazole derivative metabolites (TDM)
Phthalates and substitutes, FCM phthalate substitutes, DEHTP (Bis(2-ethylhexyl) terephthalate) *
Industrial solvents (e.g. BTEX metabolites, dry cleaning solvents, paint solvents) *
Persistent Organic Pollutants of Increasing Concern such as Dechloranes, Chlorinated paraffins and Chloronaphtalene, Dioxins and PCB
Synthetic fragrances (OTNE-Tetramethyl acetyloctahydronaphthalene, Galaxolide, Lysmeral/Lilial Polycyclic musks, Lyral, Hydroxycitronellal , Isoeugenol)
UV filters (salicylates, cinnamates and benzophenones) *
Chemical Mixtures (including contaminants e.g. Mycotoxins and plant contaminants, and air pollutants with EDC properties) *
Medical substances: occupational
Polycyclic aromatic hydrocarbons (PAHs) **
Bisphenols (BADGE/DGEBA, Bisphenol-A-diglycidylether / Diglycidylether of Bisphenol A, and Tetrabromo-bisphenol A (TBBPA); 3-1 Tetrabromobisphenol A) *
Emerging substances of concern, unknowns, non-targeted screening *
Substances with potential to bioaccumulate in air-breathing organisms
Nanomaterials, nanoplastics, nano titanium dioxide
Mycotoxins, in particular Ochratoxin A (CAS 303-47-9). Emerging and endocrine active mycotoxins. *
Endocrine disruptors**
Styrene**
MOAH Mineral oil aromatic hydrocarbons**
Pyrazoles**

* Some substances/groups have already been prioritised or partially addressed (for groups) in HBM4EU.

Deliverable Report D4.8
https://www.hbm4eu.eu/work-packages/deliverable-4-8-third-list-of-hbm4eu-priority-substances/

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HBM4EU portuguese participation

- **General population aligned studies** – based on National Health survey with specimens collection
- **Focused Occupational studies** – exposure of workers to Cr(VI), Ewaste, Diisocyanates

- Development of harmonised study designs
- Standard Operating Procedures to use throughout EU
- Laboratory analysis and quality assurance – setting up of HBM laboratory network
- Measuring exposure and effect biomarkers
- Effect biomarkers implementation in human biomonitoring
- Mixtures Risk Assessment – case studies
- Improving Risk Assessment by using HBM
- Data analysis and Data sharing according FAIR principles

HBM4EU portuguese participation- Development of harmonised study designs

Hexavalent Chromium exposure


Environmental Research 177 (2019) 108583

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Environmental Research

journal homepage: www.elsevier.com/locate/envres

Setting up a collaborative European human biological monitoring study on occupational exposure to hexavalent chromium

Tiina Santonen[a,*], Alessandro Alimonti[b], Beatrice Bocca[b], Radu Corneliu Duca[c], Karen S. Galea[d], Lode Godderis[e,f], Thomas Göen[f], Bruno Gomes[g], Ogier Hanser[h], Ivo Iavicoli[i], Beata Janasik[j], Kate Jones[k], Mirja Kiilunen[a], Holger M. Koch[l], Elizabeth Leese[k], Veruscka Leso[i], Henriqueta Louro[g], Sophie Ndaw[h], Simo P. Porras[a], Alain Robert[h], Flavia Ruggieri[b], Paul T.J. Scheepers[m], Maria J. Silva[g], Susana Viegas[n], Wojciech Wasowicz[j], Argelia Castano[o], Ovnair Sepai[p]

Electronic waste exposure

International Journal of Environmental Research and Public Health

MDPI

Study Protocol

HBM4EU Occupational Biomonitoring Study on e-Waste—Study Protocol

Paul T. J. Scheepers [1,*], Radu Corneliu Duca [2,3], Karen S. Galea [4], Lode Godderis [3,5], Emilie Hardy [2], Lisbeth E. Knudsen [6], Elizabeth Leese [7], Henriqueta Louro [8,9], Selma Mahiout [10], Sophie Ndaw [11], Katrien Poels [3], Simo P. Porras [10], Maria J. Silva [8,9], Ana Maria Tavares [8], Jelle Verdonck [3], Susana Viegas [12,13], Tiina Santonen [10] and HBM4EU e-Waste Study Team [†]

Diisocyanates exposure

International Journal of Environmental Research and Public Health

MDPI

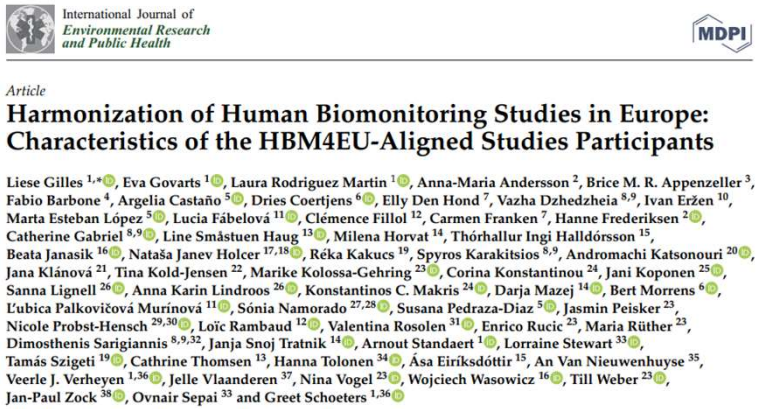
Study Protocol

HBM4EU Diisocyanates Study—Research Protocol for a Collaborative European Human Biological Monitoring Study on Occupational Exposure

Kate Jones [1,*], Karen S. Galea [2], Bernice Scholten [3], Marika Loikala [4], Simo P. Porras [4], Radia Bousoumah [5], Sophie Ndaw [5], Elizabeth Leese [1], Henriqueta Louro [6,7], Maria João Silva [6,7], Susana Viegas [8,9], Lode Godderis [10,11], Jelle Verdonck [10], Katrien Poels [10], Thomas Göen [12], Radu-Corneliu Duca [10,13], Tiina Santonen [4] and HBM4EU Diisocyanates Study Team [†]

HBM4EU portuguese participation - Development of harmonised study designs

General Population aligned studies



International Journal of *Environmental Research and Public Health*

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Article

Harmonization of Human Biomonitoring Studies in Europe: Characteristics of the HBM4EU-Aligned Studies Participants

Liese Gilles [1,*], Eva Govarts [1], Laura Rodriguez Martin [1], Anna-Maria Andersson [2], Brice M. R. Appenzeller [3], Fabio Barbone [4], Argelia Castaño [5], Dries Coertjens [6], Elly Den Hond [7], Vazha Dzhedzheia [8,9], Ivan Eržen [10], Marta Esteban López [5], Lucia Fábelová [11], Clémence Fillol [12], Carmen Franken [7], Hanne Frederiksen [2], Catherine Gabriel [8,9], Line Småstuen Haug [13], Milena Horvat [14], Thórhallur Ingi Halldórsson [15], Beata Janasik [16], Nataša Janev Holcer [17,18], Réka Kakucs [19], Spyros Karakitsios [8,9], Andromachi Katsonouri [20], Jana Klánová [21], Tina Kold-Jensen [22], Marike Kolossa-Gehring [23], Corina Konstantinou [24], Jani Koponen [25], Sanna Lignell [26], Anna Karin Lindroos [26], Konstantinos C. Makris [24], Darja Mazej [14], Bert Morrens [6], Ľubica Palkovičová Murínová [11], Sónia Namorado [27,28], Susana Pedraza-Diaz [5], Jasmin Peisker [23], Nicole Probst-Hensch [29,30], Loïc Rambaud [12], Valentina Rosolen [31], Enrico Rucic [23], Maria Rüther [23], Dimosthenis Sarigiannis [8,9,32], Janja Snoj Tratnik [14], Arnout Standaert [1], Lorraine Stewart [33], Tamás Szigeti [19], Cathrine Thomsen [13], Hanna Tolonen [34], Ása Eiríksdóttir [15], An Van Nieuwenhuyse [35], Veerle J. Verheyen [1,36], Jelle Vlaanderen [37], Nina Vogel [23], Wojciech Wasowicz [16], Till Weber [23], Jan-Paul Zock [38], Ovnair Sepai [33] and Greet Schoeters [1,36]

toxics

MDPI

Article

Trends of Exposure to Acrylamide as Measured by Urinary Biomarkers Levels within the HBM4EU Biomonitoring Aligned Studies (2000–2021)

Michael Poteser [1,*], Federica Laguzzi [2], Thomas Schettgen [3], Nina Vogel [4], Till Weber [4], Aline Murawski [4], Phillipp Schmidt [4], Maria Rüther [4], Marike Kolossa-Gehring [4], Sónia Namorado [5], An Van Nieuwenhuyse [6], Brice Appenzeller [7], Edda Dufthaksdóttir [8], Kristín Olafsdóttir [9], Line Småstuen Haug [10], Cathrine Thomsen [10], Fabio Barbone [11], Valentina Rosolen [12], Loïc Rambaud [13], Margaux Riou [13], Thomas Göen [14], Stefanie Nübler [14], Moritz Schäfer [14], Karin H. A. Zarrabi [14], Liese Gilles [15], Laura Rodriguez Martin [15], Greet Schoeters [15], Ovnair Sepai [16], Eva Govarts [15] and Hanns Moshammer [1,17]

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HBM4EU portuguese participation - Development of harmonised study designs

General Population aligned studies

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Harmonized human biomonitoring in European children, teenagers and adults: EU-wide exposure data of 11 chemical substance groups from the HBM4EU Aligned Studies (2014–2021)

Eva Govarts [a,*,1], Liese Gilles [a,1], Laura Rodriguez Martin [a], Tiina Santonen [b], Petra Apel [c], Paula Alvito [d,e], Elena Anastasi [f], Helle Raun Andersen [g], Anna-Maria Andersson [h], Lenka Andryskova [i], Jean-Philippe Antignac [j], Brice Appenzeller [k], Fabio Barbone [l], Zohar Barnett-Itzhaki [m], Robert Barouki [n], Tamar Berman [o], Wieneke Bil [p], Teresa Borges [q], Jurgen Buekers [r], Ana Cañas-Portilla [s], Adrian Covaci [t], Zsofia Csako [u], Elly Den Hond [p], Darina Dvorakova [v], Lucia Fabelova [w], Tony Fletcher [x], Hanne Frederiksen [h], Catherine Gabriel [y,z], Catherine Ganzleben [aa], Thomas Göen [ab], Thorhallur I. Halldorsson [ac], Line S. Haug [ad], Milena Horvat [ae], Pasi Huuskonen [b], Medea Imboden [af,ag], Marta Jagodic Hudobivnik [ae], Beata Janasik [ah], Natasa Janev Holcer [ai,aj], Spyros Karakitsios [y,z], Andromachi Katsonouri [f], Jana Klanova [i], Venetia Kokaraki [ak], Tina Kold Jensen [al], Jani Koponen [am], Michelle Laeremans [s], Federica Laguzzi [an], Rosa Lange [c], Nora Lemke [c], Sanna Lignell [ao], Anna Karin Lindroos [ap], Joana Lobo Vicente [aa], Mirjam Luijten [p], Konstantinos C. Makris [aq], Darja Mazej [ae], Lisa Melymuk [i], Matthieu Meslin [ar], Hans Mol [as], Parisa Montazeri [at,au,av], Aline Murawski [f], Sónia Namorado [aw], Lars Niemann [ax], Stefanie Nübler [ay], Baltazar Nunes [az], Kristin Olafsdottir [ba], Lubica Palkovicova Murinova [w], Nafsika Papaioannou [bb,c], Susana Pedraza-Diaz [s], Pavel Piler [i], Veronika Plichta [ay], Michael Poteser [az], Nicole Probst-Hensch [af,ag], Loïc Rambaud [bc], Elke Rauscher-Gabernig [ay], Katarina Rausova [w], Sylvie Remy [d], Margaux Riou [bd], Valentina Rosolen [be], Christophe Rousselle [bf], Maria Rüther [c], Denis Sarigiannis [y,z,bc], Maria J. Silva [bd], Zdenka Šlejkovec [ae], Janja Snoj Tratnik [ae], Anja Stajnko [ae], Tamas Szigeti [u], José V. Tarazona [be], Cathrine Thomsen [bd], Ziga Tkalec [ae], Hanna Tolonen [am], Tomas Trnovec [w], Maria Uhl [bg], An Van Nieuwenhuyse [bh], Elsa Vasco [d], Veerle J. Verheyen [a], Susana Viegas [bh], Anne Marie Vinggaard [bi], Nina Vogel [c], Katrin Vorkamp [bj], Wojciech Wasowicz [ab], Till Weber [c], Sona Wimmerova [w], Marjolijn Woutersen [p], Philipp Zimmermann [c], Martin Zvonar [i], Holger Koch [bk], Marike Kolossa-Gehring [c], Marta Esteban López [s], Argelia Castaño [s], Lorraine Stewart [x], Ovnair Sepai [x], Greet Schoeters [a,x,bl]

Govarts E et al. Int J Hyg Environ Health. 2023 Apr;249:114119. https://doi.org/10.1016/j.ijheh.2023.114119

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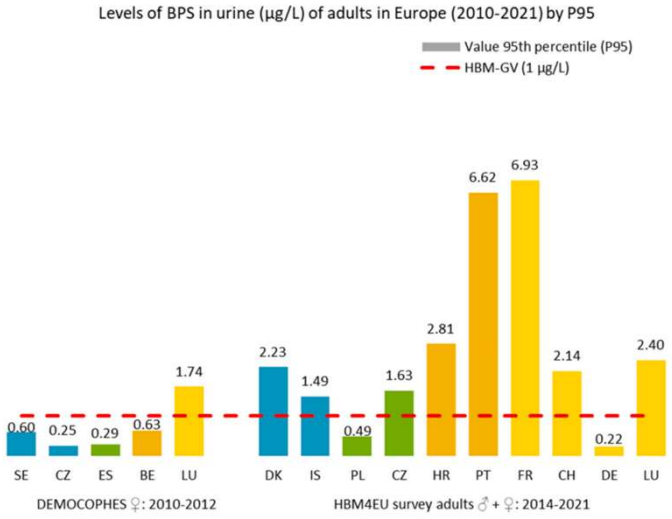
HBM4EU results support the Chemicals' Strategy for Sustainability and the Zero-Pollution Action Plan

Joana Lobo Vicente [a,*], Catherine Ganzleben [a], Roser Gasol [a], Ian Marnane [a], Liese Gilles [b], Jurgen Buekers [b], Jos Bessems [b], Ann Colles [b], Antje Gerofke [c], Madlen David [c], Robert Barouki [d], Maria Uhl [e], Ovnair Sepai [g], Ilse Loots [h], Ann Crabbé [h], Dries Coertjens [b], Marike Kolossa-Gehring [e], Greet Schoeters [b,c]

Lobo Vicente et al. 2023. Int J Hyg Environ Health https://doi.org/10.1016/j.ijheh.2023.114111



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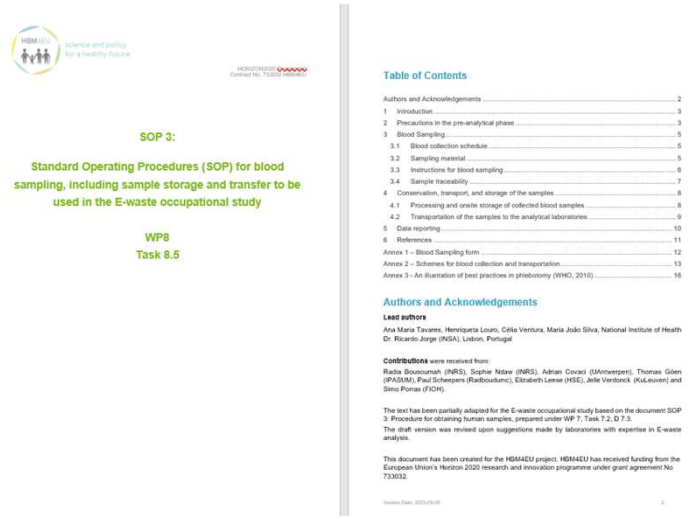
HBM4EU portuguese participation- Standard Operating Procedures development an



SOP 3:

Standard Operating Procedures (SOP) for blood sampling, including sample storage and transfer to be used in the E-waste occupational study

WP8
Task 8.5

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Authors and Acknowledgements

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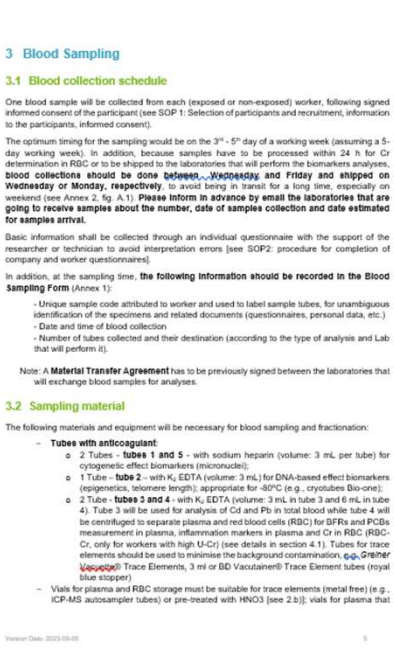
Radia Bousoumah (INRS), Sophie Ndaw (INRS), Adrian Covaci (UAntwerpen), Thomas Göen (IPASUM), Paul Scheepers (Radboudumc), Elizabeth Leese (HSE), Jelle Verdonck (KuLeuven) and Sino Porras (PDH).

The text has been partially adapted for the E-waste occupational study based on the document SOP 3: Procedure for obtaining human samples, prepared under WP 7, Task 7.2, D 7.3.
The draft version was revised upon suggestions made by laboratories with expertise in E-waste analysis.

This document has been created for the HBM4EU project. HBM4EU has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733032.



3 Blood Sampling

3.1 Blood collection schedule

One blood sample will be collected from each (exposed or non-exposed) worker, following signed informed consent of the participant (see SOP 1: Selection of participants and recruitment, information to the participants, informed consent).

The optimum timing for the sampling would be on the 3rd - 5th day of a working week (assuming a 5-day working week). In addition, because samples have to be processed within 24 h for Cr determination in RBC or to be shipped to the laboratories that will perform the biomarkers analyses, **blood collections should be done between Wednesday and Friday and shipped on Wednesday or Monday, respectively**, to avoid being in transit for a long time, especially on weekend (see Annex 2, fig. A.1). **Please inform in advance by email the laboratories that are going to receive samples about the number, date of samples collection and date estimated for samples arrival.**

Basic information shall be collected through an individual questionnaire with the support of the researcher or technician to avoid interpretation errors [see SOP2: procedure for completion of company and worker questionnaires].

In addition, at the sampling time, **the following information should be recorded in the Blood Sampling Form** (Annex 1):

- Unique sample code attributed to worker and used to label sample tubes, for unambiguous identification of the specimens and related documents (questionnaires, personal data, etc.)
- Date and time of blood collection
- Number of tubes collected and their destination (according to the type of analysis and Lab that will perform it).

Note: A **Material Transfer Agreement** has to be previously signed between the laboratories that will exchange blood samples for analyses.

3.2 Sampling material

The following materials and equipment will be necessary for blood sampling and fractionation:

- **Tubes with anticoagulant**:
  - 2 Tubes - **tubes 1 and 5** - with sodium heparin (volume: 3 mL per tube) for cytogenetic effect biomarkers (micronuclei);
  - 1 Tube – **tube 2** – with K_2 EDTA (volume: 3 mL) for DNA-based effect biomarkers (epigenetics, telomere length); appropriate for -80°C (e.g., cryotubes Bio-one);
  - 2 Tube - **tubes 3 and 4** - with K_2 EDTA (volume: 3 mL in tube 3 and 6 mL in tube 4). Tube 3 will be used for analysis of Cd and Pb in total blood while tube 4 will be centrifuged to separate plasma and red blood cells (RBC) for BFRs and PCBs measurement in plasma, inflammation markers in plasma and Cr in RBC (RBC-Cr, only for workers with high U-Cr) (see details in section 4.1). Tubes for trace elements should be used to minimise the background contamination, e.g. Greiner Vacuette® Trace Elements, 3 ml or BD Vacutainer® Trace Element tubes (royal blue stopper)
- Vials for plasma and RBC storage must be suitable for trace elements (metal free) (e.g., ICP-MS autosampler tubes) or pre-treated with HNO3 [see 2.b)]; vials for plasma that will be used for BFRs and PCBs determination should be first rinsed with hexane [see 4.1)]
- Regular phlebotomy syringe with a stainless-steel needle; the use of a silicone-coated needle or butterfly is recommended (e.g. Sarstedt 21G for metal analysis ref. 85.1162.600); the vacutainer system can be optionally used
- powder-free disposable gloves
- 70% alcohol swabs for skin disinfection
- Labels
- Garrottes/tourniquets
- Adhesive bandages or tapes
- Container for disposal of used needles after venepuncture
- Bench centrifuge, refrigerated
- Pipettes for collecting the plasma and buffy coat
- NaCl solution (0.9%)
- Refrigerator for samples storage at +4°C
- Dry ice
- Freezer samples for storage at -80°C
- Containers appropriate for blood samples shipment (at + 4°C and -80°C)

3.3 Instructions for blood sampling

The collection of blood samples requires a clean, quiet and confined space, the availability of sterile material for blood collection and staff trained in phlebotomy knowing the special precautions related to the handling of biological material, according to each country rules.

Blood sampling must only be done by personnel trained in phlebotomy techniques. In general, the blood is collected by venous puncture and manipulated under sterile conditions. The trained personnel shall be in charge of the procedure and shall use adequate personal protection equipment (lab coat and gloves). WHO (2010) provides the best practices on drawing blood and these should be followed (Annex 3). In general:

1. Keep the blood handling area clean and free of dust
2. Use only the supplies provided by the study responsible as detailed in Section 3.2; wear talc-free gloves
3. Prepare the 5 tubes and label them with the code number and other relevant information (date, time of collection)
4. Record relevant details in the record form (Annex 1 and Annex 2, fig. A.2);
5. Prepare the volunteer for phlebotomy;
6. Place the garrotte in the forearm and disinfect the collection site with 70% alcohol;
7. Collect approximately 18 mL (see table I) of venous blood by phlebotomy, loosen the garrotte and press a cotton ball with 70% alcohol against the puncture site;
8. Immediately distribute the blood from the syringe into the 5 labelled tubes, filling them to the mark to avoid the risk of haemolysis. **Tubes 3 and 4 should be the 1st tubes to be filled** to avoid contamination of phlebotomy needle when puncturing the rubber stopper of other tubes;
9. Invert each tube gently 8 times, in order to mix the sample with the anticoagulant. After mixing, keep tube 3 upright until further processing to avoid contact with stopper;
10. Check that the worker is okay and provide a plaster for puncture site as necessary.

- Preparation of SOPs
- Training

https://doi.org/10.3390/ijerph182412987

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HBM4EU portuguese participation- Measuring exposure biomarkers

Environmental Research 204 (2022) 111984

Contents lists available at ScienceDirect

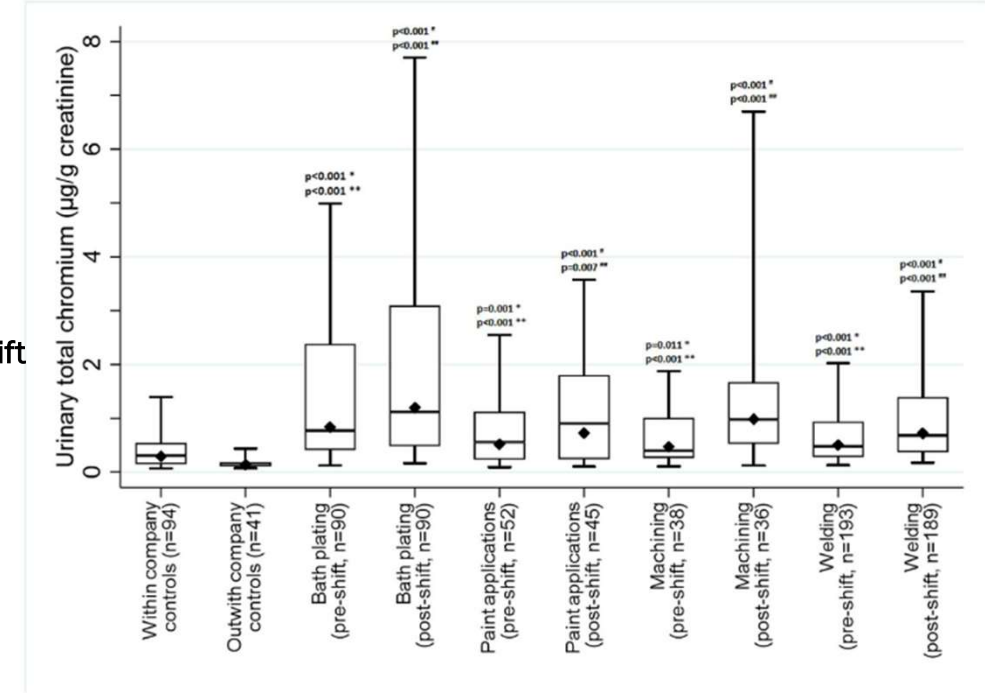
Environmental Research

journal homepage: www.elsevier.com/locate/envres

HBM4EU chromates study - Overall results and recommendations for the biomonitoring of occupational exposure to hexavalent chromium

Tiina Santonen [a,*], Simo P. Porras [a], Beatrice Bocca [b], Radia Bousoumah [c], Radu Corneliu Duca [d,e], Karen S. Galea [f], Lode Godderis [e,g], Thomas Göen [h], Emilie Hardy [d], Ivo Iavicoli [i], Beata Janasik [j], Kate Jones [k], Elizabeth Leese [k], Veruscka Leso [i], Henriqueta Louro [l,m], Nicole Majery [n], Sophie Ndaw [c], Hermínia Pinhal [l], Flavia Ruggieri [b], Maria J. Silva [l,m], An van Nieuwenhuyse [o,e], Jelle Verdonck [e], Susana Viegas [p], Wojciech Wasowicz [j], Ovnair Sepai [p], Paul T.J. Scheepers [q], HBM4EU chromates study team

- As compared to the control groups, all **worker groups showed significantly increased post-shift U–Cr levels**
- The highest exposure levels were observed in **chrome plating in baths.**
- N= 399 workers
- N= 209 controls



HBM4EU portuguese participation- Measuring effect biomarkers

toxics

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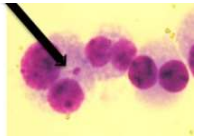
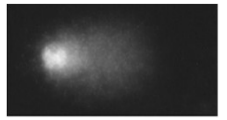
Article

HBM4EU Chromates Study—Genotoxicity and Oxidative Stress Biomarkers in Workers Exposed to Hexavalent Chromium

Ana Tavares [1], Kukka Aimonen [2], Sophie Ndaw [3], Aleksandra Fučić [4], Julia Catalán [2,5], Radu Corneliu Duca [6,7], Lode Godderis [6,8], Bruno C. Gomes [9], Beata Janasik [10], Carina Ladeira [11], Henriqueta Louro [1,9], Sónia Namorado [1], An Van Nieuwenhuyse [6,7], Hannu Norppa [2], Paul T. J. Scheepers [12], Célia Ventura [1,9], Jelle Verdonck [6], Susana Viegas [13,14], Wojciech Wasowicz [10], Tiina Santonen [2], Maria João Silva [1,9,*] and on behalf of the HBM4EU Chromates Study Team ‡





Increased genotoxicity:
- MN in lymphocytes,
- MN in reticulocytes
- comet assay data
- oxidative stress levels

in the exposed workers over the outwith company controls

Table 2. Results of genotoxicity biomarkers that were analyzed in the blood cells from workers that were exposed to Cr(VI) and the control groups (mean ± SD).

	MN PBL						MN RET		Comet Assay	
	n	MNBC (‰)	MN in BC (‰)	NPB (‰)	NBUD (‰)	CBPI	n	Micronucleated +CD71 Reticulocytes (‰)	n	Tail Intensity (%)
Total exposed Group	191	9.11 ± 6.08 *£	10.47 ± 7.19 *£	1.76 ± 2.92 £	0.57 ± 0.97 *	1.85 ± 0.26 *£	170	2.75 ± 1.92 £	74	6.34 ± 1.83 *£¥
Bath plating workers	39	12.56 ± 8.04 £	14.32 ± 9.64 £	3.02 ± 3.56 £	0.65 ± 0.98 £	1.72 ± 0.33 *	19	1.88 ± 1.14 *	12	7.36 ± 1.61 £¥
Chromate paint applicators	34	9.72 ± 6.36 £	10.82 ± 7.07 £	1.65 ± 2.98	0.40 ± 0.74 *¥	1.83 ± 0.24	33	2.03 ± 1.11 *	25	5.24 ± 1.26 *£
Welders	87	7.37 ± 4.78 *¥	8.55 ± 5.79 *¥	1.51 ± 2.89 £	0.60 ± 1.08 *	1.86 ± 0.23 £	90	3.40 ± 2.25 £¥	19	7.62 ± 1.92 £¥
Machining workers	12	8.04 ± 3.09	9.62 ± 4.01	0.63 ± 0.91 £	0.79 ± 0.99 *¥	2.00 ± 0.23 £	10	2.30 ± 1.34	5	5.04 ± 2.03 £
Other activities	19	9.60 ± 4.76 £	11.27 ± 5.97 £	1.17 ± 1.21	0.39 ± 0.74	1.98 ± 0.14 £	18	1.97 ± 0.72	13	6.12 ± 1.04 *£
Total control Group	93	10.47 ± 7.26	11.88 ± 8.19	1.77 ± 2.36	0.48 ± 0.88	1.83 ± 0.29	86	2.62 ± 2.16	43	4.59 ± 3.26
Within company	60	12.19 ± 7.58 £	13.68 ± 8.40 £	2.03 ± 2.36 £	0.65 ± 0.97 £	1.88 ± 0.30 £	50	3.13 ± 2.67 £	24	6.88 ± 2.44 £
Outwith company	33	7.33 ± 5.47 *	8.61 ± 6.77*	1.29 ± 2.30 *	0.18 ± 0.41 *	1.74 ± 0.24 *	36	1.92 ± 0.68 *	19	1.71 ± 1.18 *

MN PBL—cytokinesis-block micronucleus assay in peripheral blood lymphocytes; MNBC—frequency of micronucleated binucleated cells per 1000 binucleated cells; MN—micronuclei per 1000 binucleated cells; NPB—nucleoplasmic bridges per 1000 binucleated cells; NBUD—nuclear buds per 1000 binucleated cells CBPI—cytokinesis-block proliferation index; MN +CD71 RET—frequency of micronucleated +CD71 reticulocytes (per 1000 +CD71 reticulocytes); MN RET—micronucleus assay in reticulocytes; PBL—peripheral blood lymphocytes; * Significantly different from the within company controls; £ Significantly different from the outwith company controls; ¥ Significantly different from the total controls.

Tavares et al.. Toxics **2022**. 10. 483. DOI: 10.3390/toxics10080483

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HBM4EU portuguese participation- Correlating exposure and effect biomarkers

toxics

MDPI

Article

HBM4EU Chromates Study—Genotoxicity and Oxidative Stress Biomarkers in Workers Exposed to Hexavalent Chromium

Ana Tavares [1], Kukka Aimonen [2], Sophie Ndaw [3], Aleksandra Fučić [4], Julia Catalán [2,5], Radu Corneliu Duca [6,7], Lode Godderis [6,8], Bruno C. Gomes [9], Beata Janasik [10], Carina Ladeira [11], Henriqueta Louro [1,9], Sónia Namorado [1], An Van Nieuwenhuyse [6,7], Hannu Norppa [2], Paul T. J. Scheepers [12], Célia Ventura [1,9], Jelle Verdonck [6], Susana Viegas [13,14], Wojciech Wasowicz [10], Tiina Santonen [2], Maria João Silva [1,9,*] and on behalf of the HBM4EU Chromates Study Team [†]

- Different EBM correlate significantly with genotoxic Cr exposures in blood and urine

		MN PBL	Comet—Tail Intensity
Cr in plasma	n	279	112
	Corr. Coef	0.361	0.476
	p	<0.001	<0.001
Cr in red blood cells	n	279	112
	Corr. Coef	0.086	−0.216
	p	0.153	0.022
U-Cr (pre-shift)	n	260	100
	Corr. Coef	0.175	0.303
	p	0.005	0.002
U-Cr (post-shift)	n	252	98
	Corr. Coef	0.207	0.371
	p	0.001	<0.001

Strength of correlation according to the correlation coefficient (corr. Coef.) value: $0.1 \leq 0.2$ = poor; $0.2 \leq 0.5$ = fair; $0.5 \leq 0.7$ = moderate. U-Cr—concentration of Cr in urine; MDA—malondialdehyde; 8-OHdG—8-hydroxy-2′-deoxyguanosine; MN PBL—frequency of micronucleated binucleated cells per 1000 binucleated cells; MN RET—frequency of micronucleated reticulocytes per 1000 +CD71 reticulocytes.

Tavares et al.. Toxics **2022**. 10. 483. DOI: 10.3390/toxics10080483

HBM4EU portuguese participation- Mixtures Risk Assessment

toxics

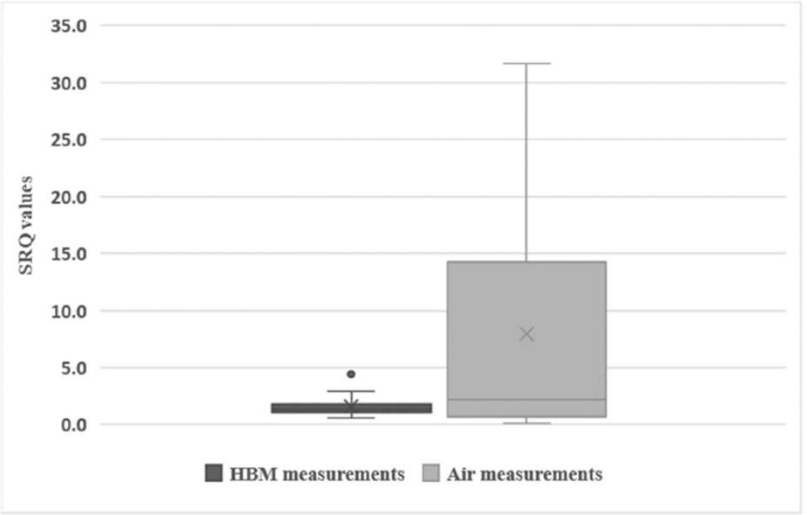
MDPI

Article

Occupational Exposure to Hexavalent Chromium, Nickel and PAHs: A Mixtures Risk Assessment Approach Based on Literature Exposure Data from European Countries

Ana Maria Tavares [1,2], Susana Viegas [3,4], Henriqueta Louro [1,2], Thomas Göen [5], Tiina Santonen [6], Mirjam Luijten [7], Andreas Kortenkamp [8] and Maria João Silva [1,2,*]

$$SRQ = \sum_{i=1}^{n} \frac{EL_i}{AL_i}$$



- Co-exposure to mixtures of Cr(VI), Ni and PAHs in waste incineration settings resulted in SRQ > 1.

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HBM4EU portuguese participation - Effect biomarkers implementation in HBM

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International Journal of Hygiene and Environmental Health

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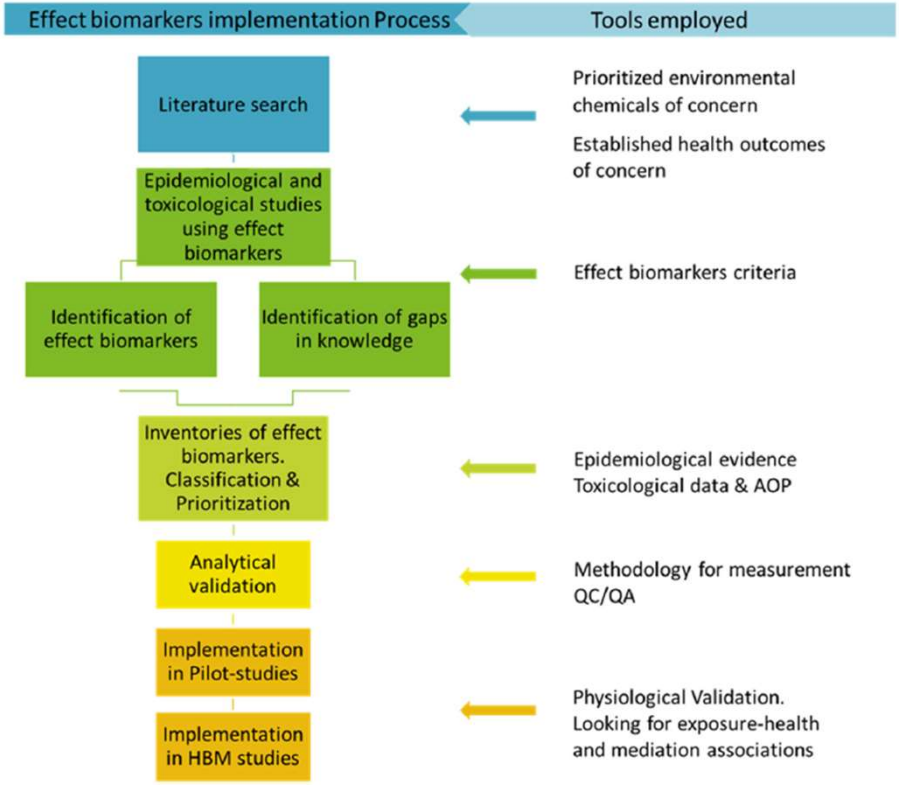
Implementation of effect biomarkers in human biomonitoring studies: A systematic approach synergizing toxicological and epidemiological knowledge

Andrea Rodríguez-Carrillo [a,b], Vicente Mustieles [a,b,c], Elena Salamanca-Fernández [a,b,*], Alicia Olivas-Martínez [a], Beatriz Suárez [a], Lola Bajard [d], Kirsten Baken [e], Ludek Blaha [d], Eva Cecilie Bonefeld-Jørgensen [f,g], Stephan Couderq [h], Shereen Cynthia D'Cruz [i], Jean-Baptiste Fini [h], Eva Govarts [e], Claudia Gundacker [j], Antonio F. Hernández [a,c,k], Marina Lacasaña [a,c,k], Federica Laguzzi [l], Birgitte Linderman [m], Manhai Long [f,g], Henriqueta Louro [n], Christiana Neophytou [o], Axel Oberemn [p], Sylvie Remy [e], Anna Kjerstine Rosenmai [q], Anne Thoustrup Saber [r], Greet Schoeters [e,s], Maria Joao Silva [n], Fatima Smagulova [i], Maria Uhl [t], Anne Marie Vinggaard [q], Ulla Vogel [q,r], Maria Wielsøe [f], Nicolás Olea [a,b,c], Mariana F. Fernández [a,b,c,*]



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HBM4EU portuguese participation – HBM for improved Risk Assessment

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Human biomonitoring in health risk assessment in Europe: Current practices and recommendations for the future

Henriqueta Louro[a,b], Milla Heinälä[c], Jos Bessems[d], Jurgen Buekers[d], Theo Vermeire[e], Marjolijn Woutersen[e], Jacqueline van Engelen[e], Teresa Borges[f], Christophe Rousselle[g], Eva Ougier[g], Paula Alvito[a,b], Carla Martins[a,b,i], Ricardo Assunção[a,b], Maria João Silva[a,b], Anjoeka Pronk[j], Bernice Schaddelee-Scholten[j], Maria Del Carmen Gonzalez[l], Mercedes de Alba[l], Argelia Castaño[l], Susana Viegas[k,l], Tatjana Humar-Juric[m], Lijana Kononenko[m], Alfonso Lampen[n], Anne Marie Vinggaard[o], Greet Schoeters[d], Marike Kolossa-Gehring[p], Tiina Santonen[q,*]

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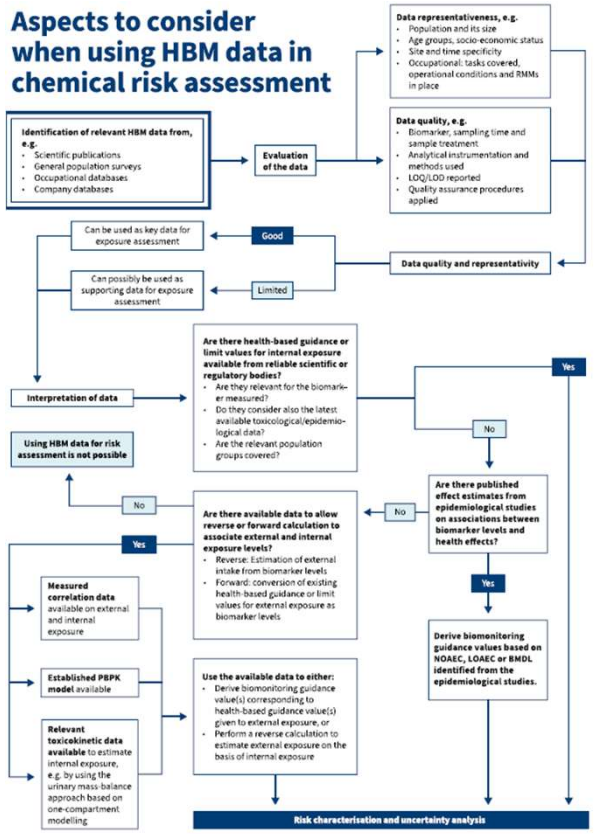
How to use human biomonitoring in chemical risk assessment: Methodological aspects, recommendations, and lessons learned from HBM4EU

Tiina Santonen[a,*], Selma Mahiout[a], Paula Alvito[b,c], Petra Apel[d], Jos Bessems[e], Wieneke Bil[f], Teresa Borges[g], Stephan Bose-O'Reilly[h], Jurgen Buekers[e], Ana Isabel Cañas Portilla[i], Argelia Castaño Calvo[j], Mercedes de Alba González[j], Noelia Domínguez-Morueco[j], Marta Esteban López[j], Ingrid Falnoga[k], Antje Gerofke[d], María del Carmen González Caballero[j], Milena Horvat[k], Pasi Huuskonen[a], Normunds Kadikis[a], Marike Kolossa-Gehring[d], Rosa Lange[d], Henriqueta Louro[b,c], Carla Martins[c,m], Matthieu Meslin[n], Lars Niemann[p], Susana Pedraza Díaz[j], Veronika Plichta[q], Simo P. Porras[a], Christophe Rousselle[g], Bernice Scholten[r], Maria João Silva[b,c], Zdenka Šlejkovec[s], Janja Snoj Tratnik[t], Agnes Šömen Joksić[u], Jose V. Tarazona[v,l], Maria Uhl[w], An Van Nieuwenhuyse[x], Susana Viegas[k,m], Anne Marie Vinggaard[o], Marjolijn Woutersen[r], Greet Schoeters[d,x]



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HBM4EU portuguese participation – HBM use in policy

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HBM4EU chromates study - Reflection and lessons learnt from designing and undertaking a collaborative European biomonitoring study on occupational exposure to hexavalent chromium

Karen S. Galea [a,*], Simo P. Porras [b], Susana Viegas [c,d,e], Beatrice Bocca [f], Radia Bousoumah [g], Radu Corneliu Duca [h,i], Lode Godderis [i,j], Ivo Iavicoli [k], Beata Janasik [l], Kate Jones [m], Lisbeth E. Knudsen [n], Elizabeth Leese [m], Veruscka Leso [k], Henriqueta Louro [o], Sophie Ndaw [g], Flavia Ruggieri [f], Ovnair Sepai [p], Paul T.J. Scheepers [q], Maria J. Silva [o], Wojciech Wasowicz [f], Tiina Santonen [b]

International Journal of Hygiene and Environmental Health 248 (2023) 114099

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International Journal of Hygiene and Environmental Health

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The HBM4EU chromates study – Outcomes and impacts on EU policies and occupational health practices

Tiina Santonen [a,*], Henriqueta Louro [b], Beatrice Bocca [c], Radia Bousoumah [d], Radu Corneliu Duca [e,f], Aleksandra Fucic [g], Karen S. Galea [h], Lode Godderis [f,i], Thomas Göen [j], Ivo Iavicoli [k], Beata Janasik [l], Kate Jones [m], Elizabeth Leese [m], Veruscka Leso [k], Sophie Ndaw [d], Katrien Poels [f], Simo P. Porras [a], Flavia Ruggieri [c], Maria J. Silva [b], An Van Nieuwenhuyse [e,f], Jelle Verdonck [f], Wojciech Wasowicz [i], Ana Tavares [b], Ovnair Sepai [n], Paul T.J. Scheepers [o], Susana Viegas [p,q]

Santonen, Louro et al., 2023. Int J Hyg Environ Health 248 (2023) 114099. https://doi.org/10.1016/j.ijheh.2022.114099

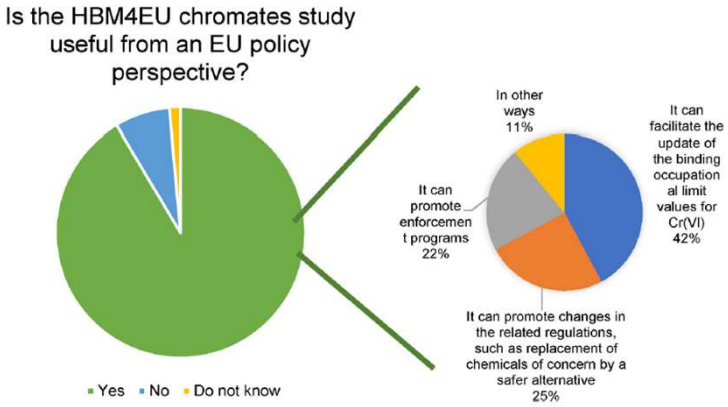

Fig. 3. Usefulness of the HBM4EU chromates study from the perspective of policy makers.

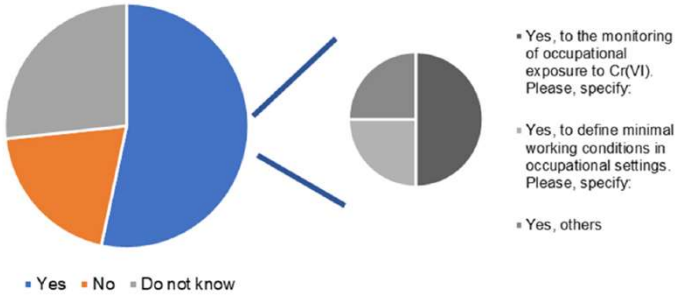

Fig. 4. Response to question: Planning to make new or update existing recommendations based on the findings of the HBM4EU chro

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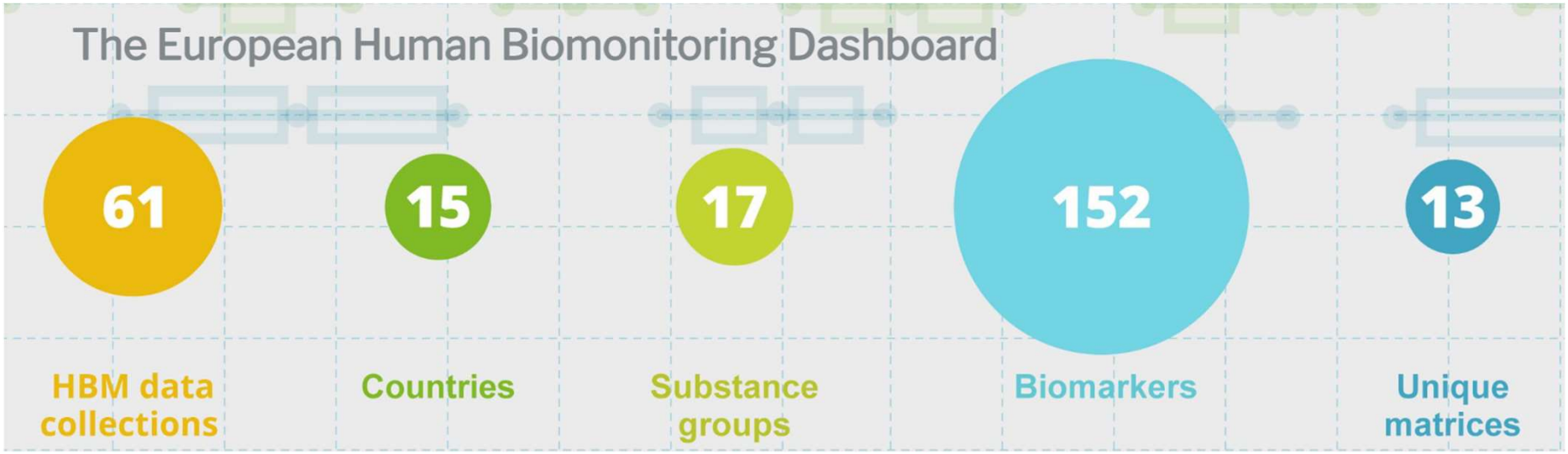
HBM4EU data FAIRness



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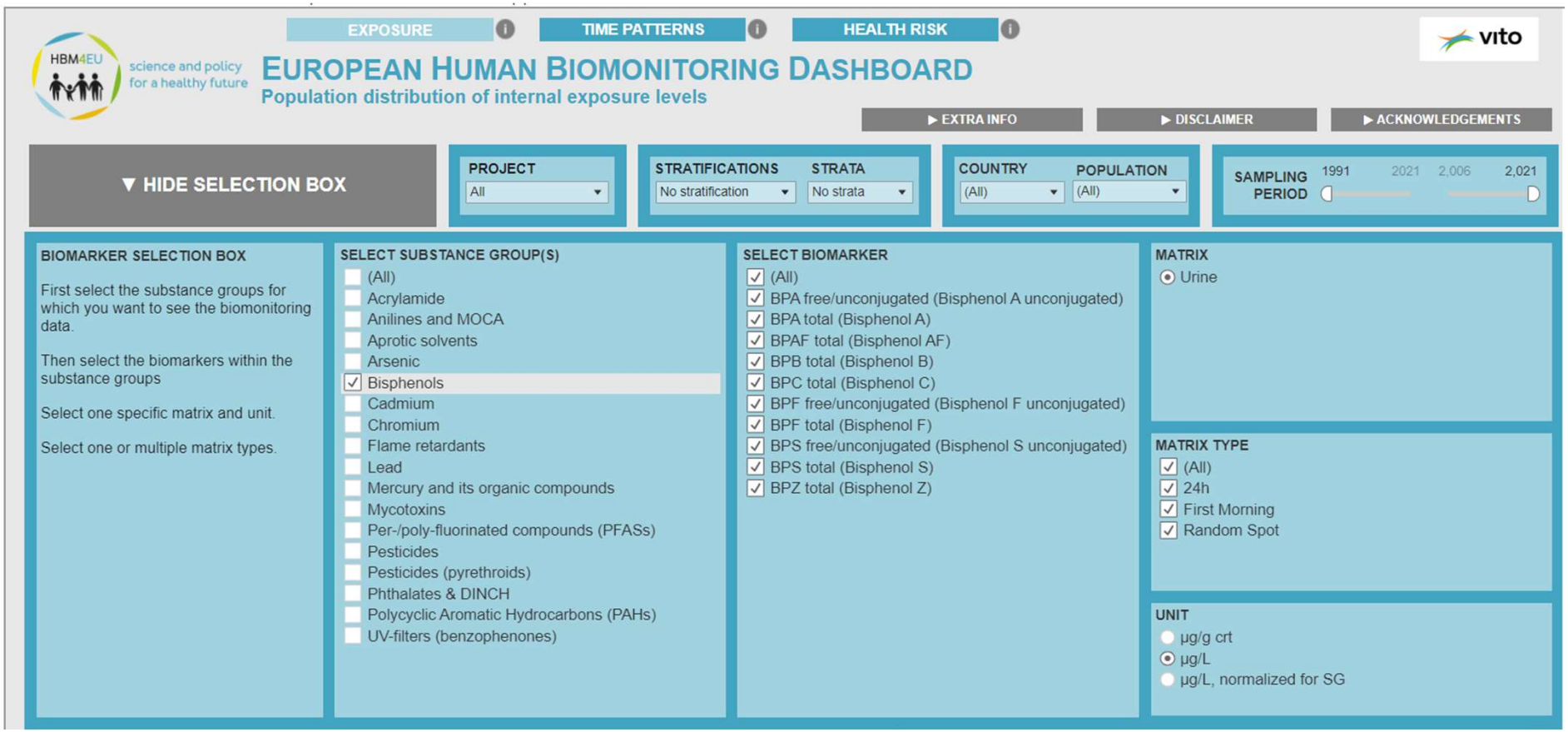

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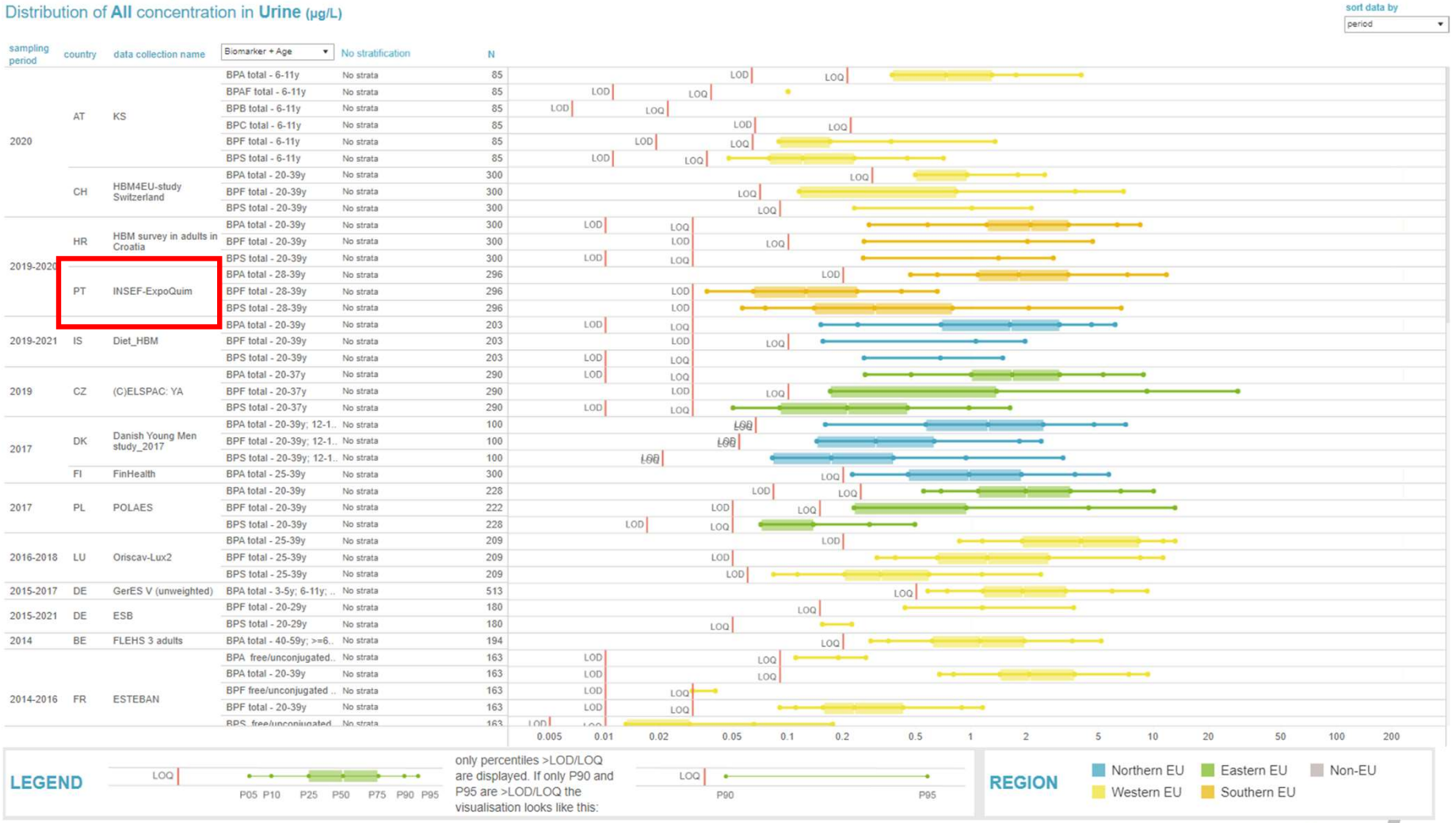

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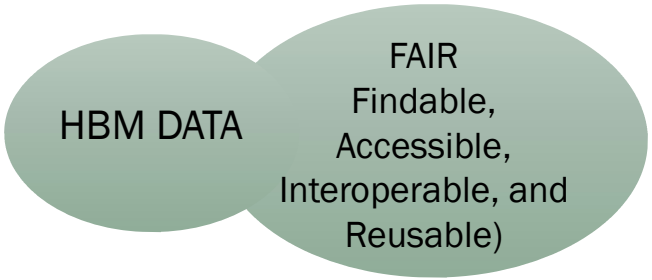
HBM and the FAIR principles



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A human biomonitoring (HBM) Global Registry Framework: Further advancement of HBM research following the FAIR principles

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FAIR environmental and health registry (FAIREHR)- supporting the science to policy interface and life science research, development and innovation

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TOXI LATIN 2023
DESAFIOS DA TOXICOLOGIA FRENTE AOS RISCOS AMBIENTAIS E À SAÚDE HUMANA
26 - 29 SETEMBRO
UFMG
BELO HORIZONTE
MINAS GERAIS - BRASIL

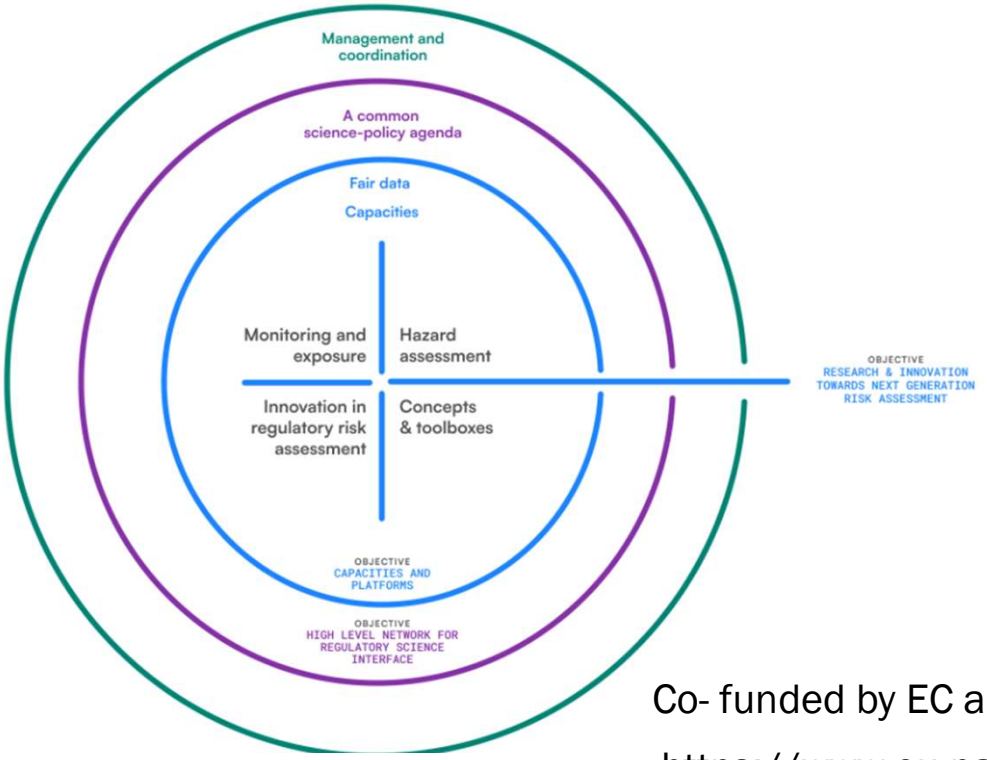
The way forward on HBM use in EU

- Science-Policy Interactions
- Networks, Partnership, Community – working together - Further enlarge established networks on HBM
- Infrastructure – EU Platform
- Guidelines for combining HBM and Health Examination studies
- Support from National Authorities in each country
- Take on board EU agencies such as ECHA,EFSA
- Co-funding by Public- Public partnership involving EC and national agencies

https://www.hbm4eu.eu/result/deliverables/
Deliverable Report D6.4 WP6 - Sustainability and Capacity building Deadline: February 2021

PARC

Partnership FOR THE Assessment OF Risks FROM Chemicals



The PARC programme has three main objectives:

1. Develop the scientific skills needed to address current and future challenges in chemical safety

2. Provide new data, methods and innovative tools to those responsible for assessing and managing the risks of chemical exposure

3. Strengthen the networks which bring together actors specialised in the different scientific fields contributing

Co- funded by EC and National Partners

https://www.eu-parc.eu/

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HBM in PARC – the portuguese participation

The overall goal of WP4 is to monitor chemicals guided by regulatory challenges both in humans and in the environment, observing different sources, chemical fates and exposure pathways. In support of a "one substance, one assessment approach", new and existing monitoring schemes will be combined and harmonised.

- Task 4.1: Further developing the human biomonitoring platform, generating new HBM data, and the network of qualified laboratories for **exposure biomarker** analysis created in HBM4EU

- Task 4.2: Better understanding the **presence of chemicals in the environment** via multiple sources and the resulting exposure of humans and ecosystems in an integrated way

- Task 4.3: Developing **robust, reliable and fit-for-purpose innovative tools and methods** to improve or renew existing monitoring schemes, especially to support the exposure assessment for particularly vulnerable sub-populations and the early warning detection of chemicals of emerging concern

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HBM in PARC – insights into upcoming work with the portuguese participation

- Further analysis of the data generated in HBM4EU
- General HBM survey
- Dedicated surveys to specific chemicals of concern
- Focused occupational studies
- **Preparation of a sustainable monitoring and surveillance system for Europe**

https://www.eu-parc.eu/

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HBM4EU
science and policy for a healthy future

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German Environment Agency (UBA)

PARC Partnership for the Assessment of Risks from Chemicals

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Questions?