



## EUROPEAN HUMAN BIOMONITORING INITIATIVE (HBM4EU) IMPACT LEAFLETS

### IMPROVED UNDERSTANDING OF THE NATURE AND LEVEL OF CHEMICAL EXPOSURE OF EU CITIZENS

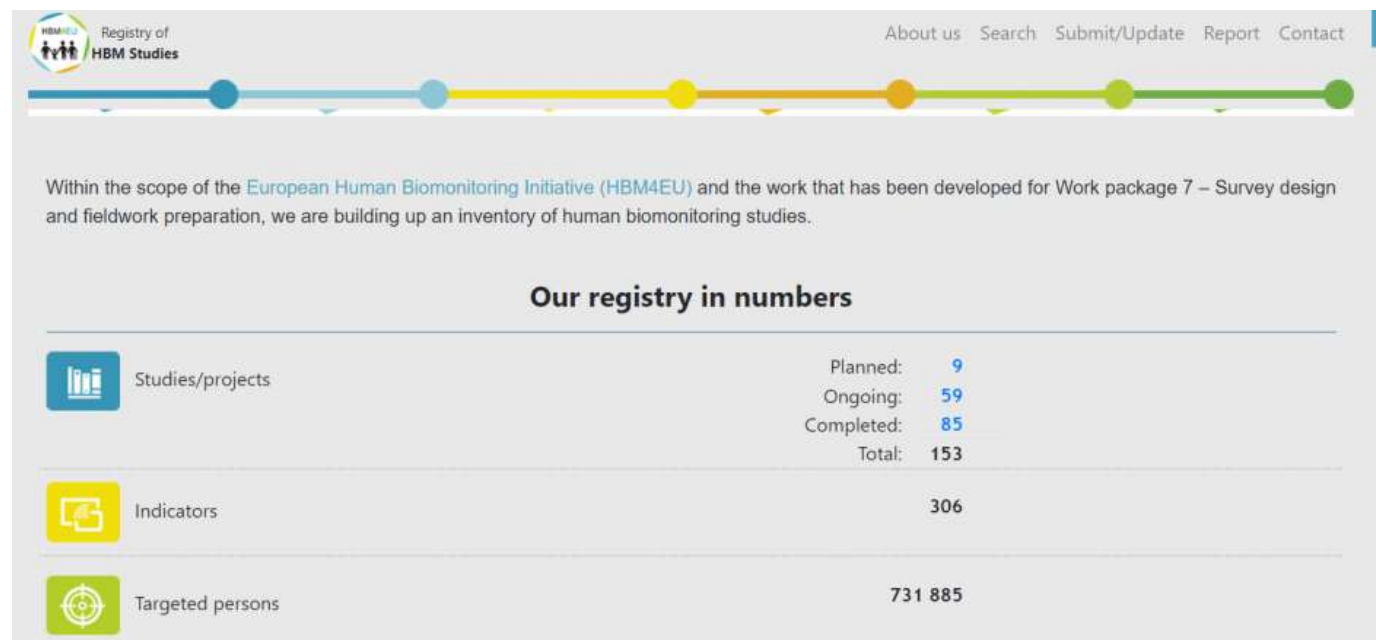
#### KEY IMPACTS

- Existing European HMB data were inventoried in a registry. Exposure distributions were calculated in a harmonised way and included in **IPChEM** and the **HBM dashboard**
- For the first time, European exposure values are calculated for a number of prioritised compounds
- New European HBM data (targeted and non-targeted) generated under HBM4EU increase our understanding of chemical exposure of EU citizens and allow to answer policy questions formulated in scoping documents
- Exposure reconstruction has been performed for 1st and 2nd set priority substance groups. They allow to calculate risk characterization ratios by dividing the external exposure estimate with the toxicological reference value (TRV) of the substance (TDIs, RfDs, slope factors)
- 19 HBM-GV developed for general population and 11 HBM-GV for occupational population
- Risk Assessment on the prioritized compounds is done
- Comparison with HBM-GVs, if available, shows that health risks cannot be excluded for many substances (e.g. PFAS, phthalates,...)

#### KEY FACTORS

##### Existing European HBM data made accessible

##### REGISTRY OF EXISTING STUDIES



Registry of HBM Studies

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Within the scope of the **European Human Biomonitoring Initiative (HBM4EU)** and the work that has been developed for Work package 7 – Survey design and fieldwork preparation, we are building up an inventory of human biomonitoring studies.

#### Our registry in numbers

|                  |            |         |
|------------------|------------|---------|
| Studies/projects | Planned:   | 9       |
|                  | Ongoing:   | 59      |
|                  | Completed: | 85      |
|                  | Total:     | 153     |
| Indicators       |            | 306     |
| Targeted persons |            | 731 885 |

Within the scope of HMB4EU an inventory of HBM studies was built containing 153 studies or projects (9 planned, 59 ongoing, 85 completed): <http://hbmjps.topick.pt/>.

Based on this inventory, information on existing HBM studies in Europe was collected and a metadata registry of HBM studies was integrated in IPCHEM.





## HBM4EU newly generated HBM data

HBM4EU also allowed to get a picture of the current (2014-2020) chemical exposure of the EU population and specific occupationally exposed populations through target screening of known chemicals and non-target screening/suspect screening for emerging unknown chemicals. These studies provided EU wide information on levels of internal exposure to HBM4EU prioritised chemicals in human samples.

### HBM4EU NEWLY GENERATED HBM DATA

| Chemical substance / Study | HBM4EU Aligned Studies |                   |                | DEMOCOPHES             |                     | SPECIMEn | HBM-MOM study | Occupational studies |                    |               |
|----------------------------|------------------------|-------------------|----------------|------------------------|---------------------|----------|---------------|----------------------|--------------------|---------------|
|                            | EU-wide children       | EU-wide teenagers | EU-wide adults | Time trends - children | Time trends - women |          |               | Chromate study       | Diisocyanate study | E-waste study |
| HBM targeted               | Phthalates             | X                 | X              |                        | X                   | X        |               |                      |                    | X             |
|                            | DINCH                  | X                 | X              |                        | X                   | X        |               |                      |                    |               |
|                            | PAH                    |                   |                | X                      | X                   | X        |               |                      |                    |               |
|                            | PFAS                   |                   | X              |                        |                     |          |               |                      | X                  |               |
|                            | Flame retardants       | X                 |                |                        | X                   | X        |               |                      |                    | X             |
|                            | Cadmium                |                   |                | X                      | X                   | X        |               |                      |                    | X             |
|                            | Bisphenols             |                   |                | X                      | X                   | X        |               |                      |                    |               |
|                            | Chromium VI            |                   |                |                        |                     |          |               |                      | X                  | X             |
|                            | UV-filters             |                   | X              | X                      |                     |          |               |                      |                    |               |
|                            | Glyphosate/AMPA        | X                 |                | X                      |                     |          |               |                      |                    |               |
|                            | TCPy/Pyrethroids       | X                 |                | X                      |                     |          |               |                      |                    |               |
|                            | Mycotoxins             |                   |                | X                      |                     |          |               |                      |                    |               |
|                            | Mercury                |                   |                |                        |                     |          |               | X                    |                    | X             |
|                            | Lead                   |                   |                |                        |                     |          |               |                      | X                  |               |
|                            | Diisocyanates          |                   |                |                        |                     |          |               |                      | X                  |               |
|                            | Acrylamide             | X                 |                | X                      |                     |          |               |                      |                    |               |
|                            | Arsenic species        |                   | X              |                        |                     |          |               |                      |                    |               |
| Effect biomarkers          | X                      | X                 |                |                        |                     |          |               | X                    | X                  | X             |
| Suspect screening          |                        |                   |                |                        |                     | X        |               |                      |                    |               |
| Non-targeted screening     |                        |                   |                |                        |                     | X        |               |                      |                    |               |

✓ New data from the HBM4EU Aligned Studies will be used for the derivation of European Exposure values.



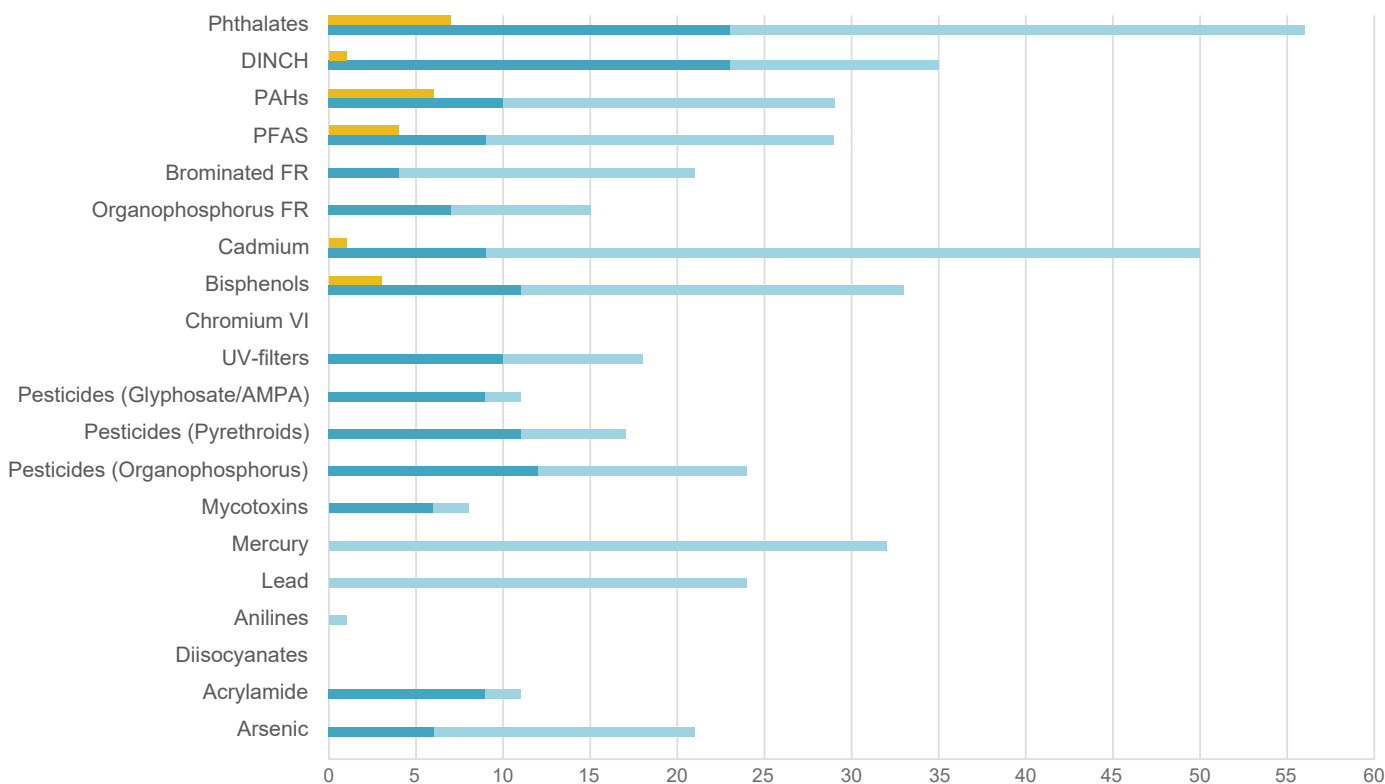


## Exposure distributions and European exposure values

HBM4EU developed a statistical analysis plan to calculate EU exposure values or exposure distributions to describe human chemical exposures in the EU population and to study more specific in-depth research questions such as identification of exposure determinants (sources), identifying vulnerable populations, impact of policy measures, etc.

### Number of datasets for which exposure distributions have been calculated (for existing studies)

■ European exposure values ■ # datasets for which exposure distributions are available ■ Number of new exposure distributions from Aligned studies



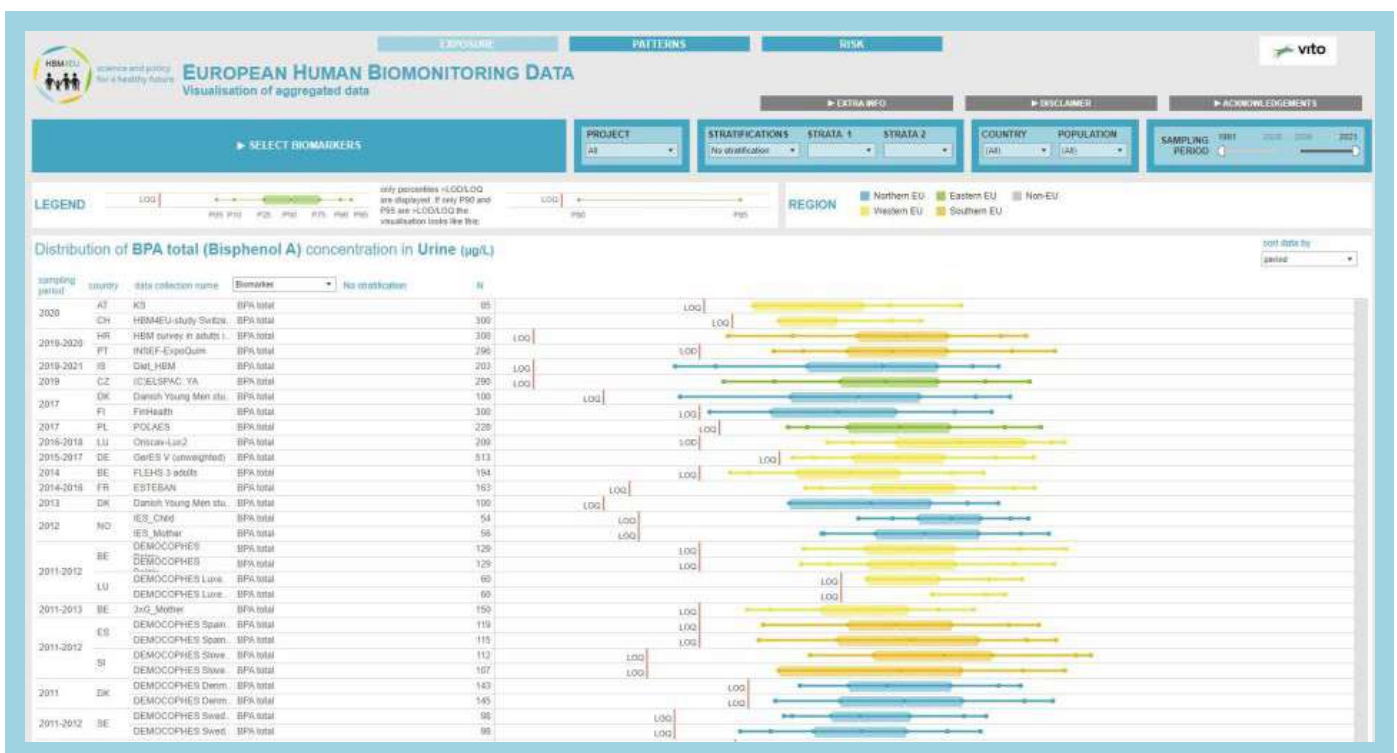
European exposure values (EEVs) were calculated on data from the HBM4EU Aligned Studies. EEVs are available for Cd, Bisphenols (BPA, BPS, and BPF) and PAHs (1-naphthol, 2-naphthol, 2-hydroxyfluorene, 1-hydroxyphenanthrene, 3-hydroxyphenanthrene, 1-hydroxypyrene) in adults, PFASs (PFOS, PFOA, PFNA, PFHxS) in teenagers and phthalates (BBzP, DiBP, DnBP, DEP, DiNP, DiDP, DEHP) and DINCH in children and teenagers (separate EEVs derived for children 6-11yrs, and teenagers 12-18 yrs). EEVs were only calculated when data from all 4 EU regions is available (North, East, South and West) and if the detection frequency is >60%





## Visualisation of HBM exposure data to stimulate use of data

- ✓ An online interactive dashboard is available to consult exposure levels (<https://www.hbm4eu.eu/eu-hbm-dashboard/>).
- ✓ The European HBM dashboard was launched March 30, 2021 and has reached 6.143 unique views after 1 year.
- ✓ At the beginning of the PARC project, the European HBM dashboard will be integrated in the PARC website.
- ✓ These data are used to calculate exposure distributions and to study more specific in depth research questions such as identification of exposure determinants (sources), identifying vulnerable populations, impact of policy measures, etc.





## Large scale screening of emerging chemicals in human samples

- In addition to classical targeted analysis, HBM4EU has developed a framework for large-scale screening of emerging chemicals applied to HBM studies.
- HBM4EU has:
  - built the basis of an EU network of partners with advanced capacities in the field of Suspect screening / Non targeted screening applied to human matrices;
  - developed and conducted several proof-of-concept studies illustrating the usefulness of these approaches.
- Overall, these efforts resulted in more than 3000 analysed samples and several 100s of detected exposure markers.
- PARC will extend the network and harmonisation between environment – food – HBM communities for the development of these innovative approaches.

The network developed resources and tools:

### CECSscreen open access EU database on chemicals of emerging concern:

- > 70.000 parent compounds
- > 300.000 simulated metabolites

### Haloseeker (v2.0):

- open access software for non-targeted screening (NTS) of halogenated markers of exposure through high resolution MS chemical profiles
- > user friendly facilitating resource for implementing NTS

### QA/QC and harmonization:

- a set of provisions and criteria for increased consistency and comparability of SS data generated from human matrices (major output of the Specimen Study (5 labs/countries involved))
- > basis for extension to environment-food-HBM continuum (PARC).

- facilitates large-scale detection of chemicals in exposome research
- coupled to mass spectrometry (MS) reference library to increase the confidence level with regard to the identity of the detected exposure markers during the annotation process.

## Real Case Applications

### 1. Non targeted screening studies:

- 100 human milk and placenta samples analyzed.
- 30 exposure markers identified out of 300 detected



### 2. Suspect screening studies:

- 600 human urine/blood samples analyzed by individual partners for multi-class suspect screening analyses.
- 200 markers identified out of 1200 detected (+ 2000 samples for Specimen study)

### 3. Non targeted screening/Effect-directed analysis studies:

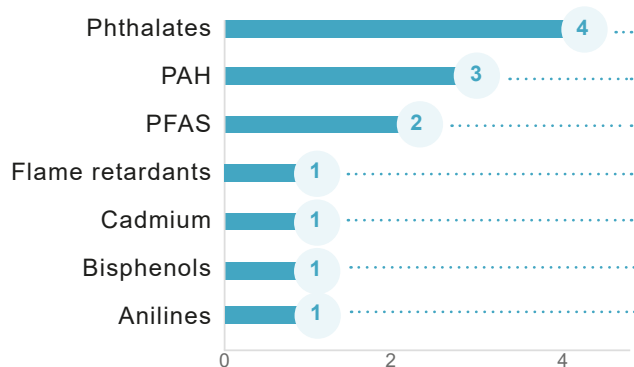
- proof-of-concept of chemical profiling coupled to effect directed analysis for revealing CECs of exposure and toxicological concern



## Exposure modelling

Number of priority chemicals for which integrated external and internal exposure models have been parameterized and validated

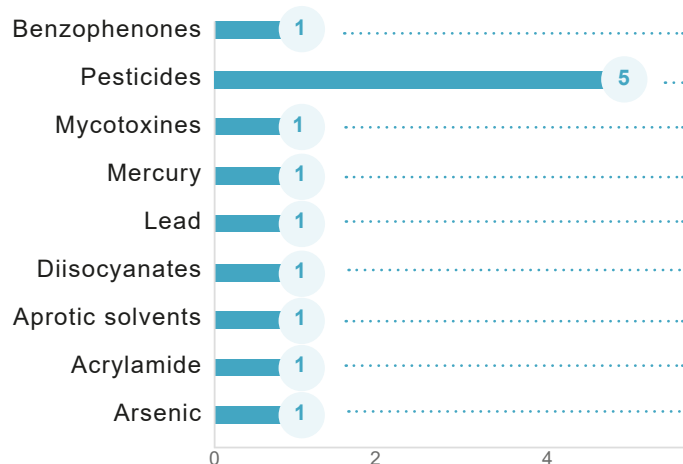
### 1<sup>st</sup> set of priority compounds



### Compounds addressed:

DEHP, DiNP, BBzP, DnBP, DINCH  
Pyrene, Benzo(a)pyrene  
PFOA, PFOS  
TCEP  
Cd  
BPA  
o-toluidine

### 2<sup>nd</sup> set of priority compounds



### Compounds addressed:

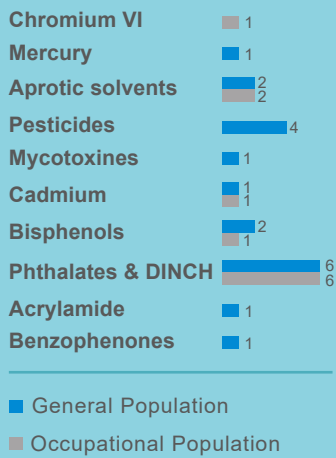
Benzophenones  
Cis-permethrin, Trans-permethrin, deltamethrin, chlorpyrifos, glyphosate  
DON  
Hg  
Pb  
MDI  
NMP  
acrylamide  
As

- Average external exposure is below the current regulatory safety thresholds for most of the assessed 1<sup>st</sup> set priority chemicals.
- Outliers are BBzP, PFOS and Cd, of which the daily intake is close to the tolerable daily or weekly intake and ortho-toluidine, of which the mean daily intake would result in a cancer risk on the order of 10<sup>-4</sup> i.e. a non-acceptable level on EU population level.



## Human Biomonitoring Guidance Values (HBM-GV)

HBM-GV derived by substance



- ✓ HBM-GV have been developed under HBM4EU to interpret HBM data in a health risk assessment context and their application to setting safe human exposure values was promoted.
- ✓ For the general population HBM-GV have been derived for DEHP, DINCH, DPHP, DnBP, BBzP, DiBP, BPA, BPS, Cd, NEP, NMP, DON, cyfluthrin (4-F-3-PBA) and deltametrin (cis-DBCA).
- ✓ For the general population a provisional HBM-GV has been derived for mercury, BP-3, acrylamide (AAMA), pyrethroids (3-PBA), chlorpyrifos (TCPy), mycotoxins (DON). The term provisional HBM-GV is used when a value has been derived within HBM4EU according to the approach by Apel et al. 2020 but a consultation hasn't been performed.
- ✓ For occupational population HBM-GV have been derived for DEHP, DINCH, DPHP, DnBP, BBzP, DiBP, BPS, Cd, DMAC, CrVI and DMF.

## Use of HBM data for risk assessment

- Within HBM4EU, risk assessment was performed using HBM data for HBM4EU's priority substances: anilines, cadmium/chromium, flame retardants, PFAS and mixtures of PFAS, phthalates bisphenols, UV-filter benzophenone-3, acrylamide, aprotic solvents, arsenic, diisocyanates, lead, mercury and its organic compounds, mycotoxins, pesticides and PAHs. These examples showed that HBM can be included in RA, and its inclusion generally benefits the RA.
- Up to date no external references (e.g. by EFSA or ECHA) were identified. First references are expected after the end of HBM4EU, since aligned studies and the HBM dashboard have only come recently available.

Links: <https://www.ncbi.nlm.nih.gov/pubmed/33045523>

