



HBM4EU

POLICY BRIEF

JULY 2022



European Human Biomonitoring Initiative

Emerging Chemicals

This policy brief summarizes the adverse human health effects of emerging chemicals, their main exposure pathways for humans, and how human biomonitoring (HBM) of emerging chemicals could be of value in the development of EU policies.

Emerging chemicals or chemicals of emerging concern (CECs) are either novel chemicals (recently developed

substitutes for substances currently subject to regulation or that have been banned); or chemicals which have been present in the environment-food-human nexus for a period of time, but for which a “new concern” has been identified, such as new analytical performances, recently identified toxicological evidence or evolution of regulatory dispositions.

KEY MESSAGES

- An ambitious open access EU database of known substances to be addressed as CECs was elaborated, including more than 70,000 parent-compounds and more than 300,000 metabolites. This is a new resource for the scaled-up deployment and implementation of suspect screening analyses and associated support to policy capacity.
- A competent and harmonised EU network for suspect and non-targeted screening approaches dedicated to emerging chemicals in human fluids and tissues was established. This allows for more data generated in the environment-food-human nexus communities, in support of harmonized approaches and comparable data for improved support to policy.
- Several proofs of concept were conducted to illustrate the effective application of these new screening approaches and their potential for supporting policy through a contribution to early warning, mixture assessment, and prioritization. This led to the first candidates of exposure markers and real-life mixtures to be deeply considered in risk assessment.

BACKGROUND: HBM4EU

The European Human Biomonitoring Initiative, HBM4EU, running from 2017 to June 2022, is a joint effort of 28 countries, the European Environment Agency and the European Commission, and co-funded under Horizon 2020. The main aim of the initiative is to coordinate and advance human biomonitoring in Europe. HBM4EU has provided a wealth of improved evidence of the actual exposure of citizens to chemicals and their possible health effects. Human biomonitoring allows us to measure our exposure

to chemicals by measuring either the substances themselves, their metabolites or markers of subsequent health effects in body fluids or tissues. Information on human exposure can be linked to data on sources and epidemiological surveys to inform research, prevention, and policy with the objective of addressing knowledge gaps and promoting innovative approaches. If you would like to read more about the project itself, please visit the HBM4EU [website](#).

HBM4EU RESULTS

To further support current and future HBM studies, HBM4EU has produced a variety of publicly available groundwork materials for a harmonised approach, to study planning and conduct in Europe, available in the [HBM4EU online library](#).

The main results for CECs are:

- Approximately 12 EU laboratories from 8 countries were involved in suspect and non-targeted screening activities applied to human samples.
- Overall, more than 3,000 human samples were analysed, and several hundreds of exposure markers detected associated to emerging hazardous chemicals, among which, several dozens were structurally identified.
- Chemicals included in 51 publicly available databases related to CECs were collected and aggregated into a single quality assured/quality controlled consolidated and open-access database ([CECScreen](#)), to be used as a comprehensive list of compounds to be monitored by suspect screening approaches.
- An open access software (Haloseeker (v2.0) for non-targeted screening (NTS) of halogenated markers of exposure through high resolution MS chemical profiles, acting as a user-friendly facilitating resource for implementing NTS.
- The first interlaboratory study, with a total number of 155 human urine and 60 human blood samples from cohorts/biobanks analysed including general and occupationally-exposed populations with suspect screening methods in four European laboratories from France, Germany, Belgium and Austria before the HBM4EU-related harmonization work. Pesticides, plasticizers and PFASs were examples of markers with high detection frequencies (e.g. N,N-Diethyl-3-methylbenzamide (DEET) or 2-Hydroxybenzothiazole), showing their widespread presence in populations of various European countries.
- Several suspect screening proof-of-concept studies were conducted, leading to around 600 human urine/blood samples analyzed by individual partners. Around 200 markers were identified out of the 1200 detected. This included halogenated substance-related markers.
- A harmonized large-scale study (SPECIMEn) of the general population (adult-child pairs) living either nearby (<250 m) or further away (>500 m) from agricultural fields (e.g. orchards) was organised. Samples were collected for winter/spring time periods from five countries. Five laboratories analysed 2,000 human urine samples and, established a preliminary list of 45 exposure markers.
- Several non-targeted screening proof-of-concept studies analysing around 100 human milk and placenta samples. Around 30 exposure markers were identified out of the 300 detected.
- A framework for quality assured/quality controlled laboratories which consolidated and harmonized the development/application of suspect and non-targeted screening in HBM.
- Existing or newly collected European HBM data on substitutes of already regulated chemicals of the following substance groups: PFAS, bisphenols, phthalates, DINCH and organophosphorous substances (policy briefs available [here](#)).

EXPOSURE & HEALTH EFFECTS

Chemicals of Emerging Concern (CECs) impacts on human health cannot be listed as CECs do not refer to a specific substance group or have a grouping rationale based on a particular toxicological characteristic or common physico-chemical properties.

INPUT TO POLICY PROCESSES AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability and the Zero-Pollution Action Plan. These are available in the [HBM4EU Science to Policy section](#).

Existing EU policies cover regulations on chemicals, consumer products, the environment and occupational exposure.

CECs are mostly monitored in environmental matrices and compartments, especially water for which several structured initiatives, networks and organization exist ([Norman network, 2019](#)). Consideration of CECs in the chemical food safety area is also gaining in maturity.

Substance of potential concern may undergo substance evaluation as part of REACH ([Regulation \(EC\) No 1907/2006](#)).

Regarding environmental legislation, the [Water Framework Directive](#) establishes a watch list of substances for which Union-wide monitoring data are gathered for the purpose

of supporting prioritisation exercises. This may include substances of toxicological concern which are discharged in the environment-food-human continuum but are rarely or not measured. The second watch list was outlined in [Commission Implementing Decision 2018/840/EU](#).

The Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) released a position paper in 2018 on "[Emerging Issues and the Role of the SCHEER](#)". The SCHEER highlighted that identifying emerging issues early can raise awareness, thereby allowing the authorities to take appropriate and timely action to ensure public safety and/or environmental protection.

The Ministry of I&M/RWS (The Netherlands) and the OVAM (Flanders) have commissioned an inventory on the awareness and policy on emerging contaminants in Europe. This inventory aims to compile available knowledge and experience related to legislation, governance and policy.

POLICY QUESTIONS

1 Is there an early warning system for the presence of hazardous chemicals in EU population?

The answers to the policy questions below are summarised. For more details, please see the Substance Reports available on the [substance specific page](#) of the HBM4EU website.

To identify new emerging substances, five European laboratories have joined forces and are applying their suspect screening capabilities to analyse 160 human urine/blood samples from various cohorts. A predefined list of suspect markers was used for which the expected detected signal characteristics have been inventoried within a MS reference laboratory. Based on this list, dozens of markers were identified from various substance groups including those for pesticides, plasticisers, UV-filters, and PFAS. Several were detected with high frequencies which demonstrates their widespread presence in the populations of various EU countries.

More information is available in [D16.3 Report on generated HBM data and global framework for emerging chemicals](#) and to [D16.5 Global framework for emerging chemicals](#).

2 Does the work of HBM4EU support the REACH process to identify substances of potential concern?

HBM4EU has successfully built the framework and capacities for generating comprehensive suspect lists and linked tandem mass spectral databases. Chemicals included in 51 publicly available databases related to CECs were collected and aggregated into a single quality assured/quality controlled (QA/QC) consolidated database ([CECScreen](#)). To facilitate prioritisation for confirmation efforts and reduce the amount of chemicals to be considered further, metadata related to physicochemical properties, environmental fate and toxicity was included for the compounds in the CECs inventory.

3 What strategies were developed to identify yet unknown compounds of toxic concern in human biological matrices?

Three approaches were considered. A data driven approach: capacity on acquisition of high-resolution mass spectrometric data within the consortium was inventoried and brought together. The workflow for harmonisation and QA/QC consolidation of the necessary reference MS data is laid down in [AD16.4 "Annotation framework"](#).

A chemically driven approach, which highlights crucial methodological questions of non-targeted analysis workflows including sample preparation, data acquisition, data mining and expert reviewing and proposes guidelines to implement NTA in Human Biomonitoring research ([D16.2 Workflow for screening emerging chemicals](#)).

A biology driven approach, that combines suspect and non-targeted methodologies with effect directed analyses (EDA). An overview of bioassays for analysing human samples and EDA approaches has been published ([AD16.3 Direct effect-based approaches applied to the screening of emerging substances](#)).

KNOWLEDGE GAPS

At the policy level, the main challenge is to develop an early warning system to rapidly pass these chemicals through a biomonitoring program and further risk assessment process.

At the scientific level, the main challenge associated with CECs is the development of new methodological strategies to rapidly document exposure and the related health impacts, as well as to detect and prioritise these chemicals based on relevant and well-integrated exposure and toxicological data.

CECs are not well addressed in existing HBM programmes in part due to a lack of effective analytical methods to detect and quantify many such markers of exposure of various nature simultaneously. The subsequent lack of exposure data results in uncertainty regarding the actual burden of those substances on the human population.

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