HBM4EU science and policy for a healthy future

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HBM4EU

POLICY BRIEF

JUNE 2022

European Human Biomonitoring Initiative

PFAS

This policy brief summarizes the adverse human health effects of Per- and Polyfluoroalkyl substances (PFASs), their main exposure pathways for humans, and how human biomonitoring of PFASs could be of value in the development of EU policy.

PFASs are a large group of man-made chemicals extensively used in a wide number of industrial and consumer applications. PFASs are persistent in the environment and tend to bioaccumulate in food chains. Many PFASs are shown to be toxic to human health.

KEY MESSAGES

- **HBM4EU aligned studies[1] (2014-2021) have generated baseline levels of internal exposure to 12 PFASs for European teenagers (1957 samples; age: 12-18 years).**
- **14.26% of the European teenagers tested exceed the internal serum level of 6.9 µg/L PFASs, EFSA's[2] guideline value for a tolerable weekly intake of 4.4 ng/kg. The maximum exceedance from individual studies was 23.8%. Highest median values are observed in studies conducted in Northern and Western Europe.**
- **PFASs data from 17 HBM-studies can already be consulted in the online European HBM dashboard.**

Current exposure exceeds the EFSA Guidance values for PFASs in some parts of the EU population.

- **PFASs concentrations are in general higher in men with a trend on participants with higher educational level having higher exposure levels. In some studies, higher levels of PFASs were observed with increasing age.**
- **From the HBM4EU data collections, a decreasing trend for PFOA and PFOS concentrations can be derived, while this is not the case for other PFASs.**

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 Comission, 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 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 prokect itself, please visit the HMB4EU website.

1 The HBM4EU Aligned Studies are a survey aimed at collecting HBM samples and data as harmonised as possible from (national) studies to derive current internal exposure data representative for the European population/citizens across a geographic spread.

2 EFSA: European Food Safety Authority

HBM4EU RESULTS

HBM4EU laid the foundations for a European HBM **platform to monitor human exposure to priority chemicals (including PFASs) and related health effects in a harmonised and quality-controlled way**. A Quality Assurance/Quality Control Programme was implemented in order to establish a European database of candidate laboratories that are equally qualified for exposure biomarker analysis.

As part of the HBM4EU aligned studies, biomarkers of exposure to 12 PFASs were measured in teenagers (12-18 years). Around **14% of the European teenagers tested exceed** the internal serum level of 6.9 µg/l PFASs, which corresponds to the EFSA guideline value for a tolerable weekly intake of 4.4 ng/kg. The maximum exceedance from individual studies has been 23.8%. Highest median values are observed in studies conducted in Northern and Western Europe.

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. Different **research protocols have been developed to further analyse the PFASs data**, including European exposure levels, exposure distributions, geographical comparisons, exposure determinants, exposure-effect associations (BMI and metabolism, sexual maturation, asthma and allergy), and exposure-effect biomarker – health effect path analysis (sexual maturation and metabolism) (D10.10 Statistical analysis plan for the co-funded studies of WP8). More results are expected to be published in the course of 2022.

An inventory of available effect biomarkers for PFASs and novel biomarkers was created including cholesterol and adiponectin for metabolic disturbances, thyroid hormones for endocrine disturbances, reproductive hormones and kisspeptin for infertility and sexual maturation, and immune and inflammatory markers for asthma. Relevant mechanistic and adverse outcome pathway (AOP) information related to effects on metabolism, birth outcomes and immune system were provided to cover knowledge gaps.

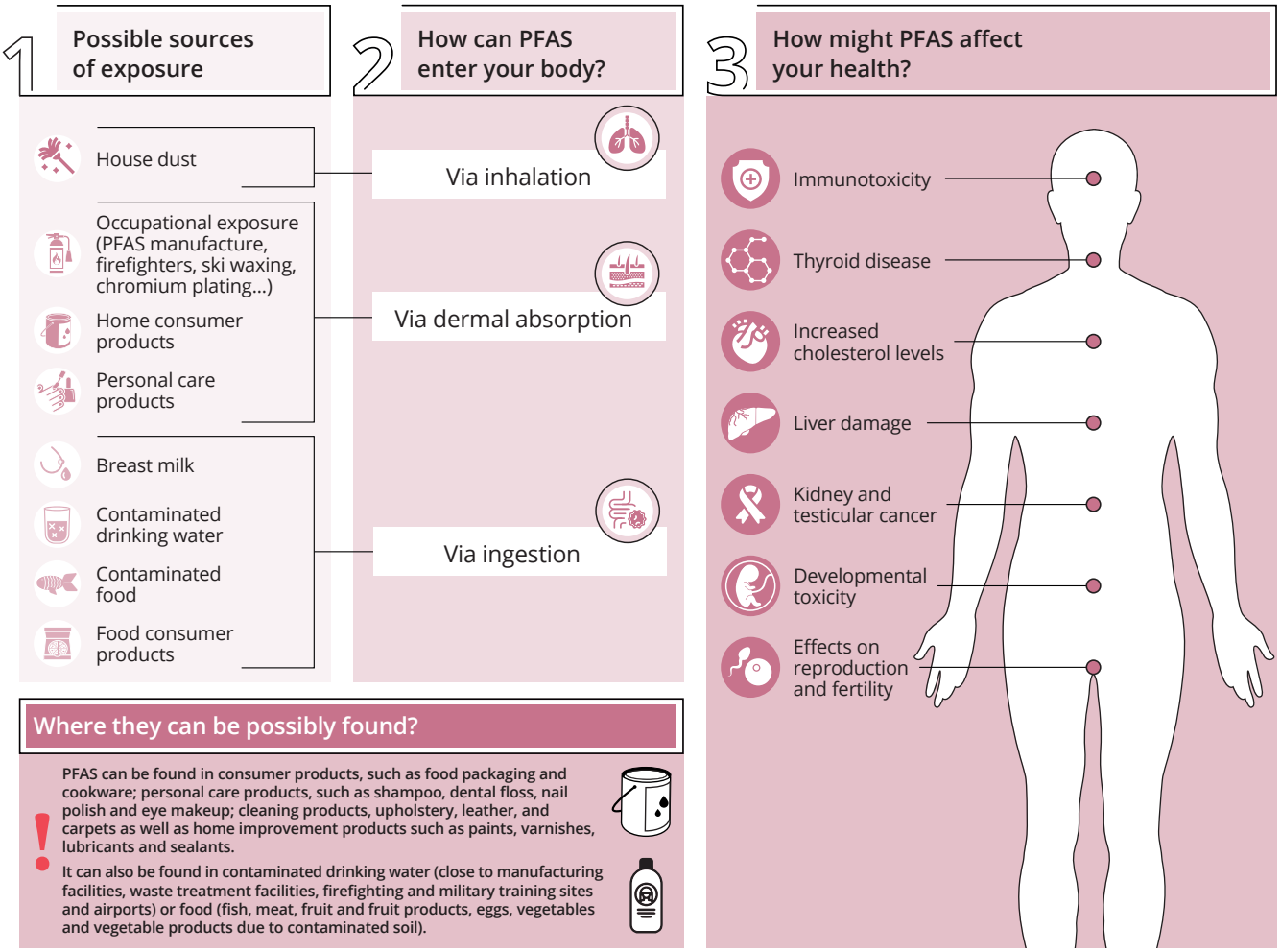
The **mixture risk assessment of PFASs** takes three approaches for comparison, the Relative Potency Factor (RPF) approach, the Hazard Index (HI) approach, and the sum value approach of the European Food Safety Agency (EFSA). The risk assessment of mixtures goes beyond the single substance assessment, which is usually applied and reflects more the actual exposure of people. All three approaches confirmed the conclusion drawn in the recent EFSA scientific opinion which postulates a risk at current exposure concentrations.

EXPOSURE & HEALTH EFFECTS

For the general population, the main route of exposure to PFASs sis through food and the consumption of contaminated drinking water. Within the HBM4EU data collections, diet was found to be an important exposure determinant of PFASs. Higher serum levels of PFNA and PFOS were associated with higher consumption of fish and seafood (increase in serum levels by 20 and 21%, respectively) and higher consumption of eggs (increase in serum levels by 14 and 11%, respectively). Additionally, higher exposure to PFOS was linked to higher consumption of offal (increase in exposure by 14%) and consumption of local food (increase in exposure by 40%). For other food items (meat, fast food, drinking water, milk), no or weak associations with individual PFASs were found. Other main exposure determinants in HBM4EU data collections were attribution to a certain cohort as well as sex and education.

Figure 1 gives an overview of the main sources of exposure, exposure pathways and health effects associated with PFASs exposure.

Figure 1. Overview of sources, pathways and health effects associated with PFASs



INPUT TO POLICY PROCESSES AND RELEVANT POLICY MEASURES

HBM4EU results have contributed to consultations for the Chemicals' Strategy for Sustainability, the Zero-Pollution Action Plan, as well as ECHA and EFSA consultations. These are available in the HBM4EU Science to Policy section.

Various PFASs such as PFOA, HFPO-DA, PFBS, PFNA, PFDA, PFTeDA, PFTrDA, PFU(n)DA and PFHxS, are included in the substances of very high concern (SVHC) List under the REACH Regulation, due to their PBT or vPvB[3] properties. Some PFASs have a harmonised EU classification and labelling under the CLP regulation, as toxic to reproduction, the liver and as suspected carcinogens.

Due to the serious concerns related to the widespread use and contamination with PFASs a **set of actions to address PFASs with a group approach, under legislation on water, sustainable products, food, industrial emissions, and waste has been proposed in the European Chemicals' Strategy for Sustainability** and in the accompanying document on PFASs. Specific PFASs are regulated by several legislations and cross-regulation activities. These cover i) implementation of international conventions, actions and agreements, and wider chemicals legislation; ii) consumer products; iii) occupational exposure, and iv) the environment (e.g., emissions to air and water). These regulations are to be adapted and tightened.

A REACH restriction to limit the risks to the environment and human health from the manufacture and use of all per- and polyfluoroalkyl substances (PFASs) for all uses, except those which are deemed as essential is to be expected in 2023.

3 PBT: persistent, bioaccumulative, toxic | vPvB: very persistent, very bioaccumulative

POLICY QUESTIONS

1 What is the current exposure of the EU population to PFASs and do they exceed health-based Guidance Values[4] (external and internal HBM guidance values), where available?

HBM4EU aligned studies (2014-2021) have generated baseline levels of internal PFASs concentrations for teenagers (12-18 years). Samples were collected in 9 sampling sites (Norway, Sweden, Slovakia, Slovenia, Greece, Spain, Germany, France, Belgium).

The indicator developed under HBM4EU shows that current internal exposure in teenagers exceed the guidance values for the sum of the 4 PFASs. The indicator, based on internal exposure data from European teenagers, shows that combined exposure to PFOS, PFOA, PFNA and PFHxS of teenagers in the EU exceeds the EFSA health-based guidance value in a fraction of the participants. Exceedances in the different studies and locations ranges from 1.34% up to 23.78% of the participants with an extent of exceedance (P95/6.9 µg/L) varying from 0.74 - 1.78. The studies conducted in Western and Northern Europe had the most teenagers exceeding the guidance value.

The median concentrations in the different European studies are within the same range, e.g., P50 values for PFOA range from 0.76 to 4.8 µg/L, PFNA levels from 0.28 to 0.86 µg/L and PfHxS from 0.18 to 1.61 µg/L. **PFOS remains the dominant congener**; P50 values range from 1.67 µg/L to 8.06 µg/L. These levels support the ones reported in the recent EFSA opinion on the risks to human health related to the presence of perfluoroalkyl substances in food.

2 Is exposure driven by diet, consumer exposure, occupation, or environmental contamination?

Regarding exposure determinants in the HBM4EU data collections, besides cohort, sex and education, diet was an important determinant of PFASs. Higher serum levels of PFNA and PFOS were associated with higher consumption of fish and seafood (increase in serum levels by 20 and 21%, respectively) and higher consumption of eggs (increase in serum levels by 14 and 11%, respectively). Additionally, higher exposure to PFOS was linked to higher consumption of offal (increase in exposure by 14%) and consumption of local food (increase in exposure by 40%). For other food items (meat, fast food, drinking water, milk), no or weak associations with individual PFASs were found.

Regarding occupational exposure, a study to investigate PFASs exposure in chromate plating facilities was carried out. In total 155 plasma samples of workers are analysed from five studies. Results will be available before June 2022.

3 Which areas and environmental media in Europe are contaminated with PFASs?

PFASs accumulate in the environment and have been found to contaminate surface-, ground- and drinking water and accumulate in plants. **PFASs production sites, fire training areas, airports and waste disposal facilities as well as sewage treatment plants can lead to contamination of the environment, which in turn leads to exposure of people living in these areas.** Currently, there are several hotspots known in different countries (e.g., Germany, Sweden, Italy, Spain, The Netherlands, Belgium, Denmark and Austria). It can be assumed that hot spots exist in most European countries. **HBM4EU is developing a guidance document on how to deal with Human Biomonitoring, health risk assessment and risk communication in (PFASs) hotspots.**

4 For substances that exceed the health-based guidance values, health effects cannot be excluded.

4 Can differences in PFASs profiles be observed in different population groups and time periods?

Geographical differences in internal exposure can be observed in the HBM4EU aligned studies for PFOS, PFOA, PFNA, PFHxS and their sum. Highest median values are observed in studies conducted in Northern and Western Europe.

To study differences in PFASs profiles in different time periods, analysis of time trend studies is needed, which are **currently not available at European level.** So far, time trend data are available for the sum Σ(PFOA + PFNA + PFHxS + PFOS) only for Germany. When comparing the PFASs levels in **plasma samples of young adults from the German Environment Specimen Bank** in the period from 2007 to 2019, a clear decrease can be seen. While the maximum P95 (P50) value for the sum of the 4 PFASs was 28.87 (13,82) µg/L in 2007, in 2019 it is only 8.28 (4,59) µg/L. Data from two mother- child studies in Vienna/Austria also showed a decline in the P50 values for the sum of the 4 PFASs from 4.3 µg/l in 2010 to 2.2 µg/L in 2019.

Datasets are also available for individual PFASs in other countries: Norway, Germany, Belgium, Spain, Slovakia, Denmark and Czechia.

5 What are the PFASs levels and health effects in vulnerable population groups?

Analyses of epidemiological data from cohort studies performed within the HBM4EU consortium shows associations of higher maternal PFASs levels with an increased propensity for infections in the children up to age 4 and the frequency of use antibiotics until adolescent age. Associations with poorer cardiovascular risk profile based on higher cholesterol and lipid profile, higher fasting blood glucose, BMI and blood pressure, higher body weight, BMI-score and waist circumference at age 9, among boys were found. **PFASs mixture was associated with an increase in triglyceride and insulin levels and decrease in HDL cholesterol** and with a modest interaction of endogenous hormones. Further, **prenatal PFASs exposure could be associated with reproductive disorders** such as preeclampsia and pregnancy hypertension, delay of menarche and abnormal menstruation/length, reduction of birth weight, length, and change in gestational length, decreases in semen quality and sperm count. One study showed correlations with the anogenital distance in girls and a risk of cerebral palsy in boys.

6 Are there differences in exposure of the EU population to regulated and non-regulated PFASs? Have restrictions led to a reduction in exposure?

To date PFOS and PFOA are still the substances occurring in the highest concentrations in blood in Europe, however other PFASs compounds are also detected in many human samples. Alternative PFASs compounds have lower exposure levels compared to regulated PFASs compounds. However, due to a large proportion of non-detects for alternative PFASs compounds and a big difference in absolute values of the limit of quantification (LOQs) reached across studies there is a need for lowering the LOQ in the chemical analysis. HBM indicators display HBM levels for regulated and not yet regulated PFASs.

The EFSA opinion on PFOS and PFOA in food, states that generally after the year 2000, the concentrations in serum/plasma of PFOS, PFOA and in some studies PFHxS have decreased, while the concentrations of PFNA, PFDA and PFUnDA have increased.

7 Has restriction of PFOS according to the POP Regulation led to a reduction in exposure?

The effectiveness evaluation under the **Stockholm Convention concluded that PFOS levels seem to be gradually declining.** The data collections in HBM4EU also demonstrate the decrease of PFASs within the observed period.

8 What is the impact of a pending 2016 ECHA decision to restrict the manufacturing, marketing and use of PFOA under REACH?

Although in some individual EU countries, decreasing time trends of PFOA have been described the **HBM4EU aligned studies still show that a fraction of the teenagers in Europe exceed guidance values for PFOA and that substitute PFASs are detected.** It is of utmost importance to avoid regrettable substitutions.

KNOWLEDGE GAPS

Data on health impacts of different PFASs are available for a comparatively small number of PFASs, of which especially PFOS and PFOA are well researched. There is **a need for human-relevant hazard and HBM data**, and there are also gaps for the majority of the 4,000 PFAS currently used related to uses, exposure patterns and toxicity.

There is a gap of Human Biomonitoring data for PFASs **other than those addressed in the risk assessment** (specifically those which are used/formed in high volumes as a result of substituting legacy PFASs). There is **a need to measure the total organic fluorine content in humans** in order to assess the magnitude of the so far unknown or not yet assessable contribution of PFASs in humans. Furthermore, non-target analytical methods could be used to identify new relevant substances.

To support the science-based grouping of PFASs, a better understanding of the modes of action of different PFASs is needed. Further studying relative potencies of PFAS for mixture risk assessment would be of added value.

There is also **a need to better coordinate EU regulations in different areas**, e. g. food and drinking water, as well as food contact material and environmental regulations to strengthen overarching risk management and avoid further contaminations with PFASs.

Human biomonitoring in hotspots highlights the **urgent need to develop PFASs minimising measures at all levels, including in the human body.** This seems essential to ensure the protection of vulnerable groups, specifically pregnant and breastfeeding women in hotspots.

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