HBM4EU

science and policy
for a healthy future

HBM4EU
PFAS

Science to support policy

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Based on work presented already by

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„What Europe is all about“: The HBM4EU network

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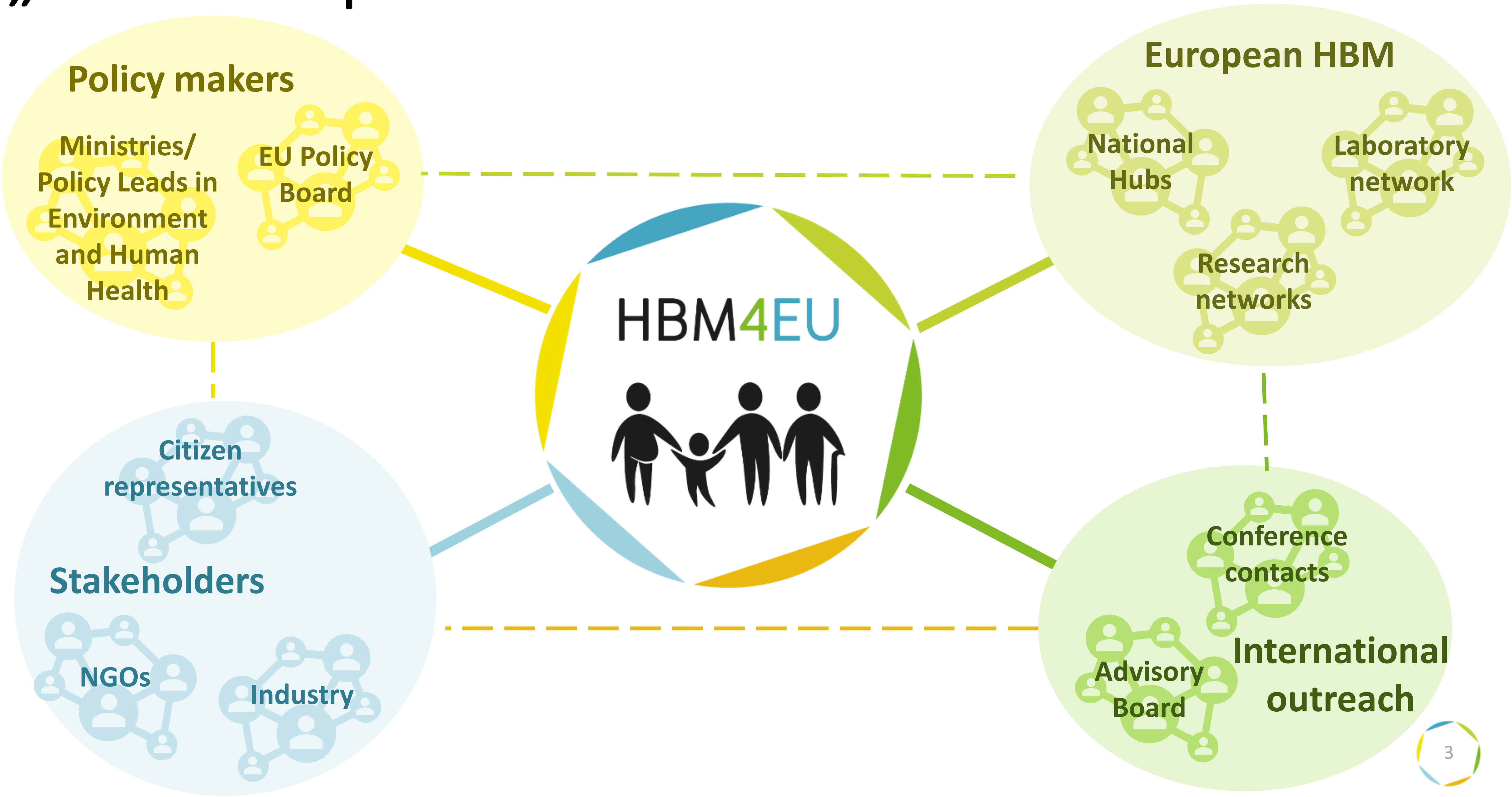


„What Europe is all about“: The HBM4EU network

Provided policy makers with a fast and easy access to results and data

Delivered answers to open policy-relevant questions on national and EU level

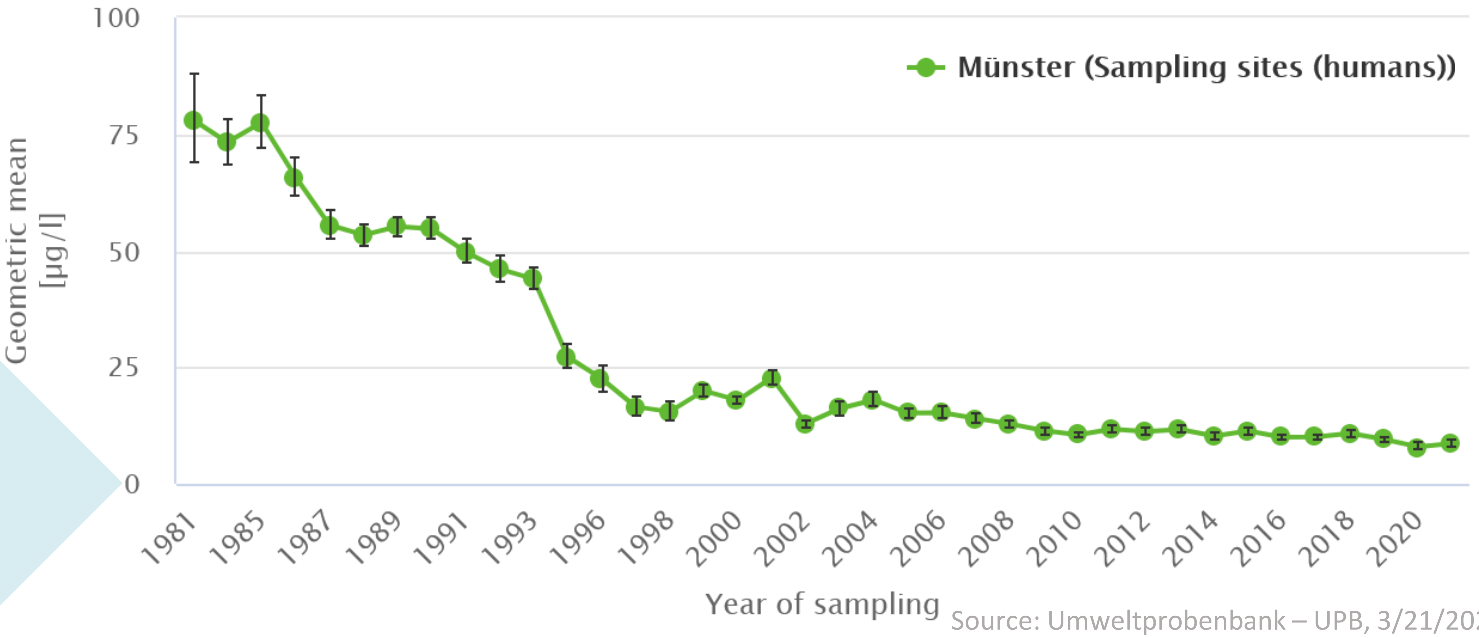
HBM4EU has bridged the gap between science and policy!

18 substances and substance groups prioritised in HBM4EU

Group	Colour	CMYK	RGB	Hex
Aniline family	Dark Green	C20 M0 Y15 K59	R84 G105 B86	#546959
Bisphenols	Medium Green	C57 M0 Y14 K22	R85 G198 B170	#55c6aa
Cadmium and chromium VI	Light Green	C19 M0 Y21 K21	R162 G201 B159	#a2c99f
Chemical mixtures	Dark Blue	C62 M32 Y0 K47	R51 G91 B134	#335b86
Emerging substances	Medium Blue	C54 M6 Y0 K24	R88 G182 B193	#58b6c1
Flame retardants	Light Blue	C24 M13 Y0 K6	R181 G208 B239	#b5d0ef
Polycyclic Aromatic Hydrocarbons (PAHs)	Dark Purple	C54 M90 Y25 K14	R128 G50 B106	#80326a
Per-/poly-fluorinated compounds	Medium Purple	C20 M64 Y26 K4	R200 G114 B140	#c8728c
Phthalates and Hexamoll® DINCH	Light Purple	C34 M40 Y11 K8	R171 G151 B180	#ab97b4
Acrylamide	Dark Red	C24 M95 Y54 K19	R167 G37 B70	#a72546
Aprotic solvents	Medium Red	C0 M87 Y63 K0	R232 G60 B74	#e83c4a
Arsenic	Light Red	C0 M55 Y60 K0	R255 G115 B101	#ff7365
Diisocyanates	Dark Orange	C0 M58 Y96 K8	R0 G0 B0	#eb6209
Lead	Medium Orange	C0 M49 Y100 K0	R243 G148 B0	#f39400
Mercury	Light Orange	C0 M25 Y100 K0	R253 G195 B0	#fdc300
Mycotoxins	Dark Brown	C543 M62 Y71 K562	R85 G58 B40	#553a28
Pesticides	Medium Brown	C38 M42 Y53 K28	R139 G119 B99	#8b7763
Benzophenones	Light Brown	C27 M40 Y41 K9	R184 G150 B137	#b89689

From national studies to European co-operation

Germany as an example for partner countries with national (HBM) programmes



Source: Umweltprobenbank – UPB, 3/21/2022

Knowledge and data existed on *national level*, but were not systematically and reliably made available for *EU policy processes*

From national studies to European co-operation

HBM4EU developed not just a system, but laid the foundations for active sharing of HBM data in Europe

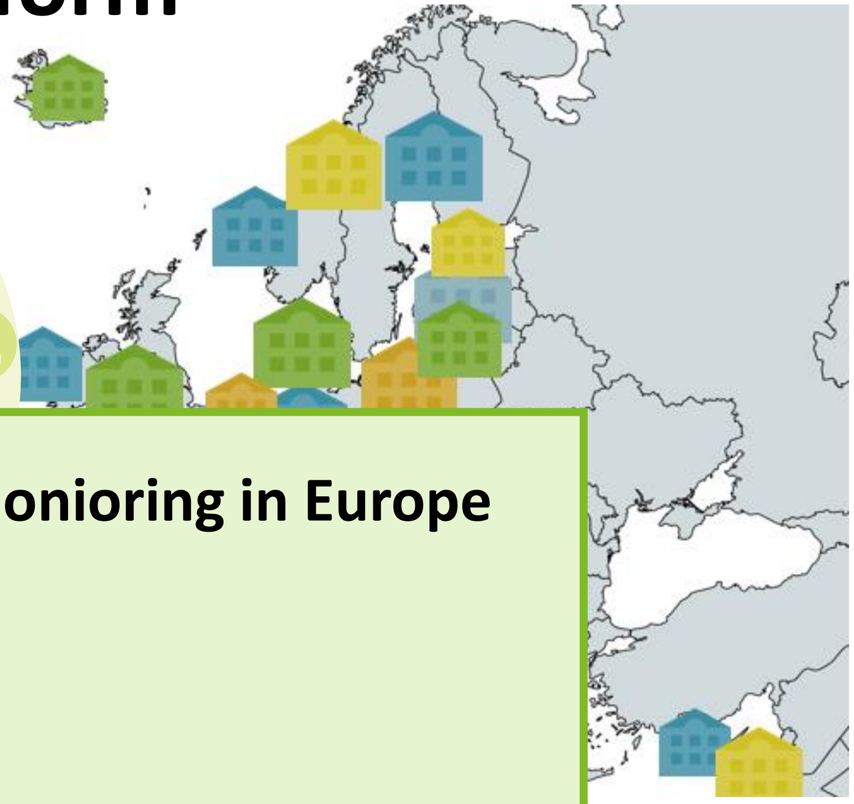
- Based on national commitment and agreements between countries
- Reliable and accessible data to inform policy makers and public

The HBM4EU network: The HBM platform

European HBM platform

Laboratory network

National Hubs



Big step towards harmonsation of human biomonioring in Europe

- ✓ Knowledge Exchange,
- ✓ Highest quality standards,
- ✓ Collaboration
- ✓ Capacity Building

166 laboratories:
45% of them HBM4EU qualified

Number of qualified labs for	Number of biomarkers
At least 1 biomarker	74
<5 biomarkers	26
5-10 biomarkers	23
11-20 biomarkers	10
>20 biomarkers	15

Study materials

Templates, SOPs, Guidelines and Questionnaires, Communication Materials

Existing and new HBM studies and data

HBM4EU aligned studies
25 studies, 21 countries

- Align existing and planned HBM studies: 2014-2021
- Samples available
- General population, no hot spots

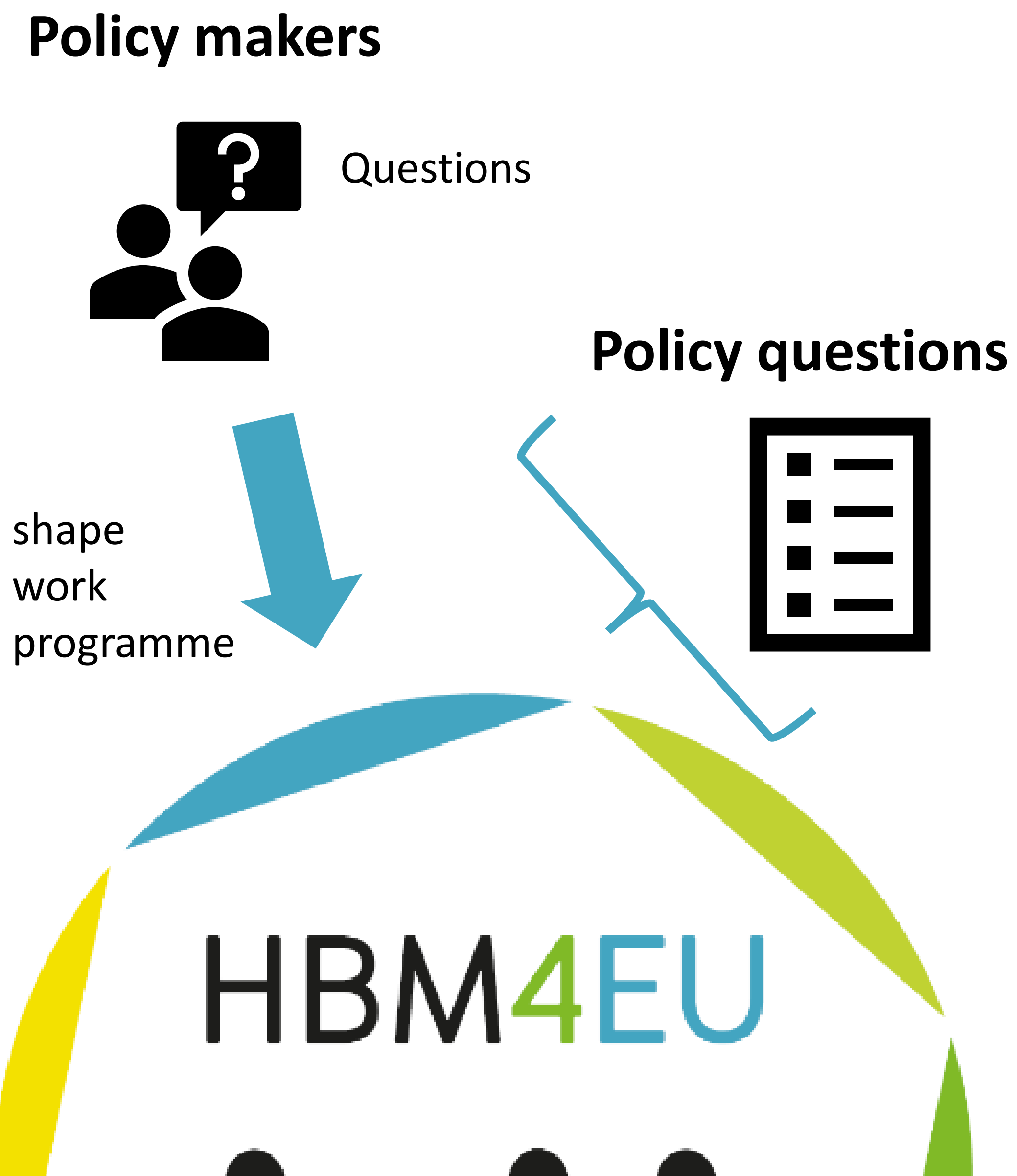
The HBM4EU Aligned studies

Children 6-11 years	Teenagers 12-19 years	Adults 20-39 years
		
14 countries	11 countries	12 countries
3431 participants	2950 participants	3716 participants
Phthalates, DINCH, FR, pesticides, acrylamide	Phthalates, DINCH, PFAS, arsenic species, UV-filters	Cd, Bisphenols, PAH, UV-filters, Mycotoxins, Acrylamide, pesticides
Collection period 2014-2021	Collection period 2014-2021	Collection period 2014-2021

Northern Europe   Eastern Europe   Southern Europe   Western Europe

Gilles et al. Harmonization of Human Biomonitoring Studies in Europe: Characteristics of the HBM4EU-Aligned Studies Participants. Int J Environ Res Public Health. 2022 doi: 10.3390/ijerph19116787.

PFAS in HBM4EU: Relevant policy questions



Selected example questions:

1. What is the current exposure of the EU population to PFAS and do they exceed Guidance values (reference and HBM values), where available?
2. Are there differences in exposure of the EU population to regulated and alternative PFAS compounds?
3. How can mixture effects of environmental and human PFAS mixtures present to date be estimated?
4. Paraphrased: What is the impact of existing regulations on PFAS exposure and is there a need for further regulations on PFAS?
5. Is exposure driven by diet, consumer exposure, occupation or environmental contamination?

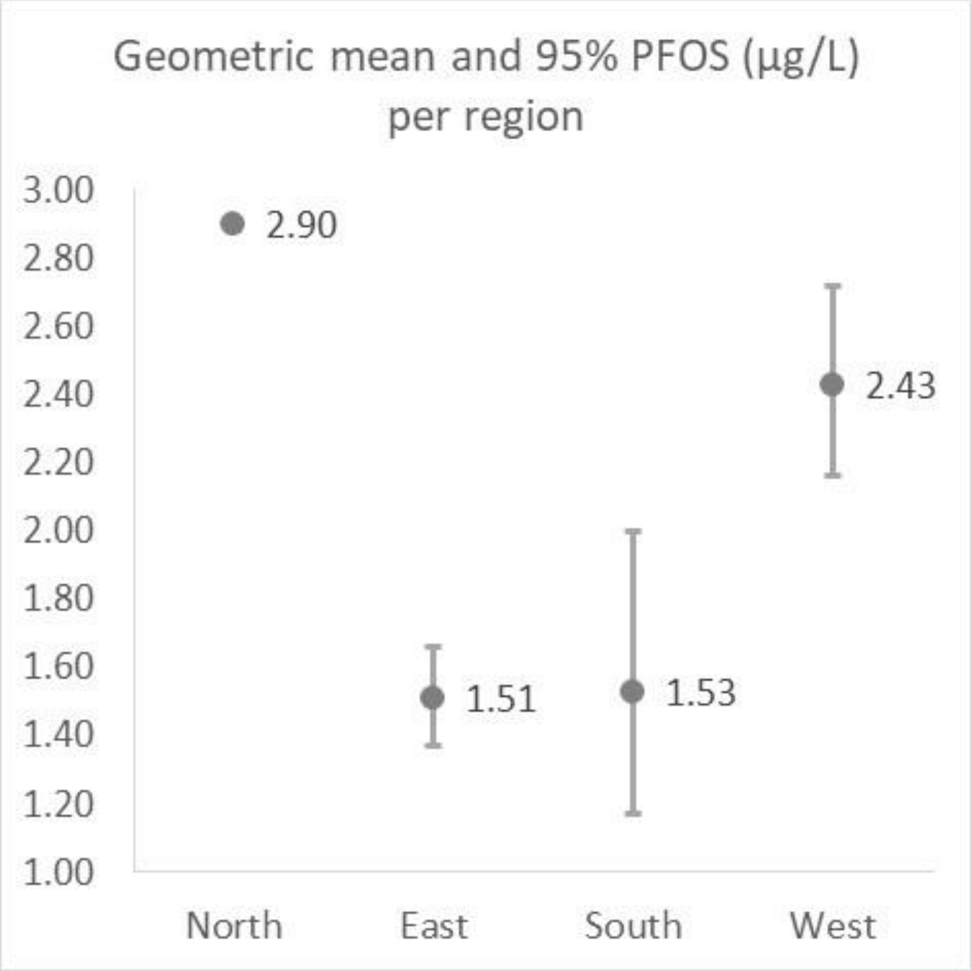
PFAS in HBM4EU: Relevant policy questions

HBM4EU partners

Consortium work provided answers, some of which are shown as examples in the following!

Geographical differences

Includes data from 8-9 EU countries:
NO, SE, SK, ES, Sl, EL, FR, DE and BE
Survey procedure used to estimate variance



Northern and Western Europe

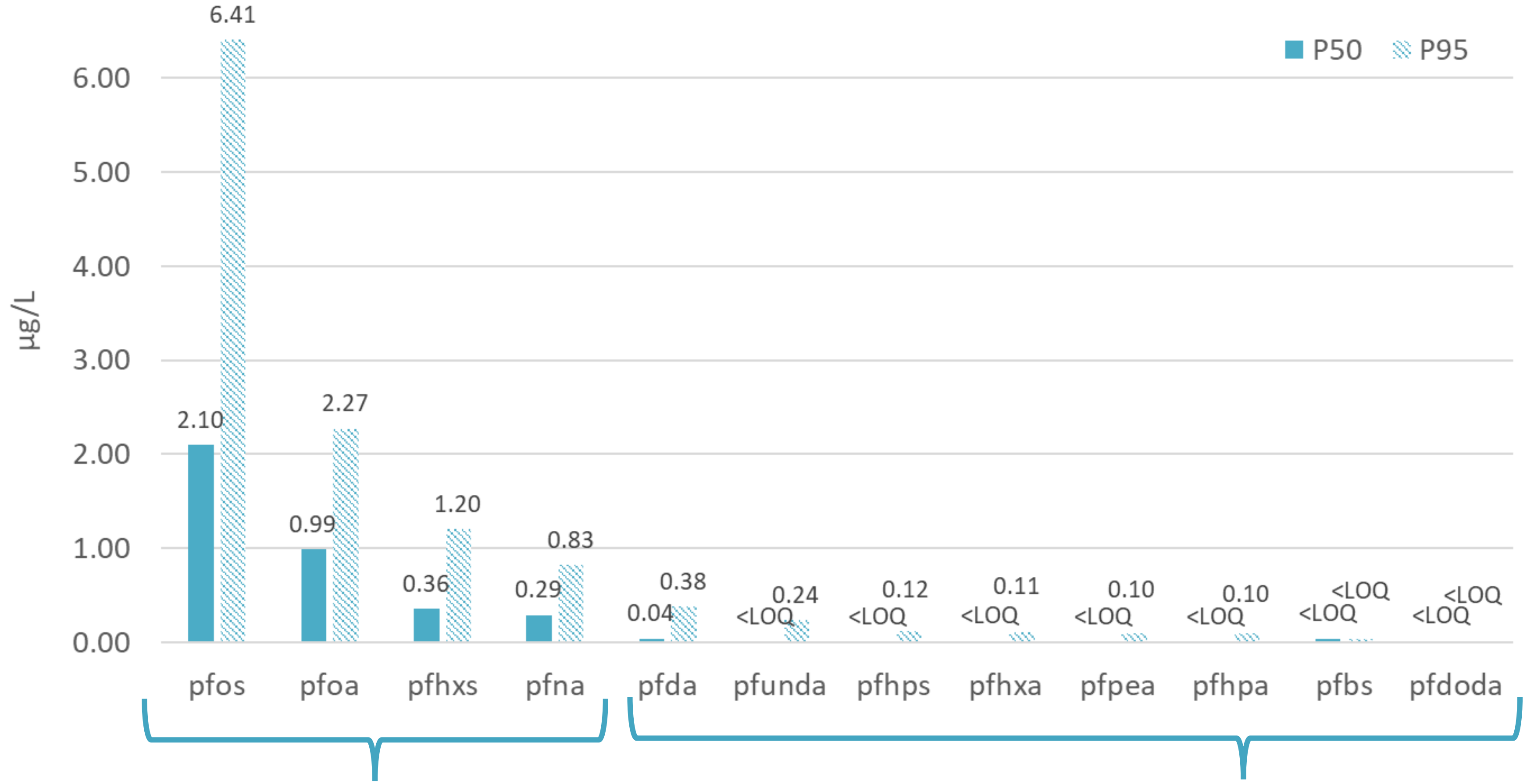
significantly higher values ($p<0.05$)*

Southern and Eastern Europe

PFOS as example, similar results for PFOA, PFNA and PFHxS!

*Adjusted for sex of the participant and highest educational level of the household

Exposure difference in regulated and non-regulated PFAS compounds in teenagers



Data is expressed in µg/L. For values below LOQ the lowest LOQ value is plotted on the graph. Includes data from 7-9 EU countries: NO, SE, SK, ES, SI, EL, FR, DE and BE

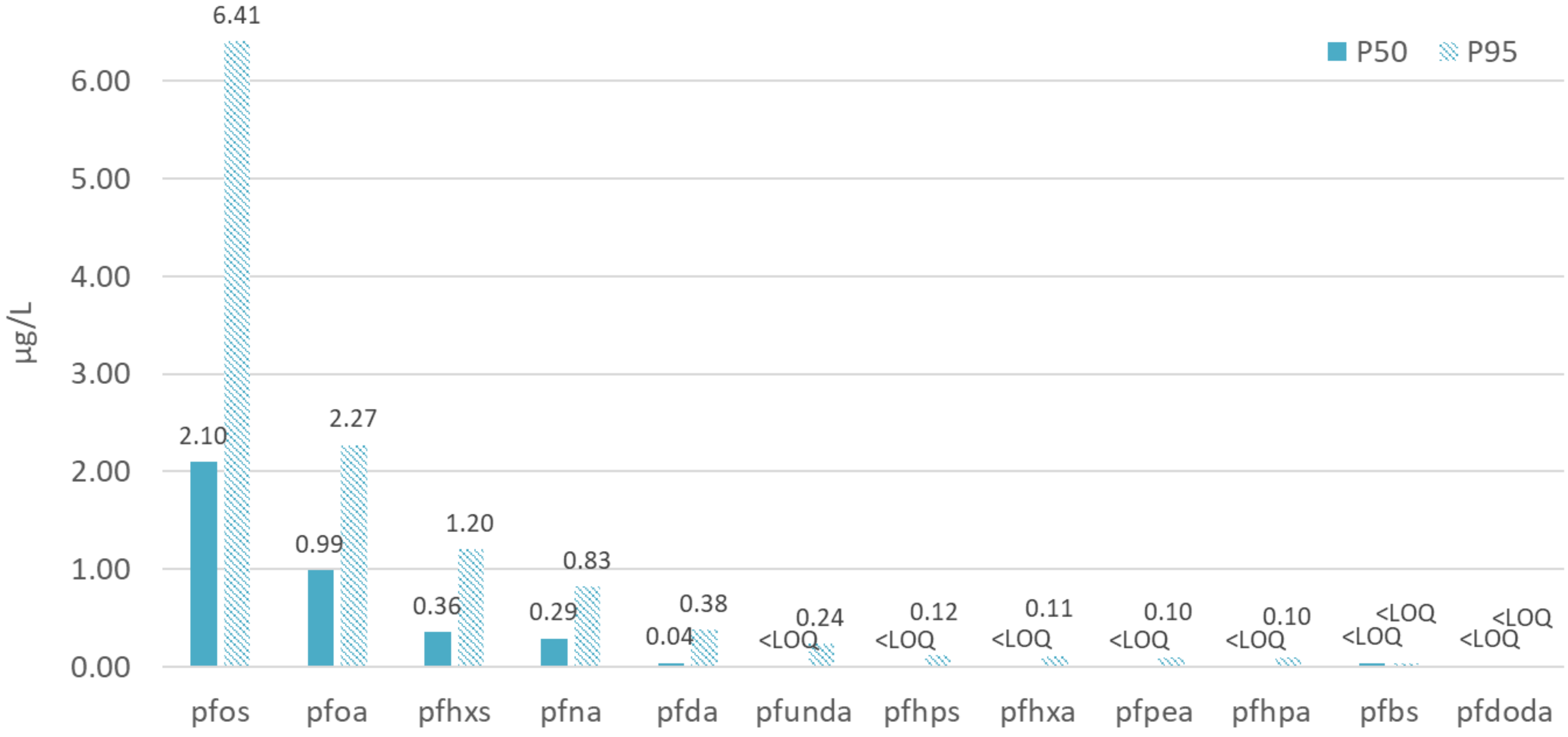
Alternative PFAS compounds have lower exposure levels compared to **regulated PFAS** compounds

Large proportion of non-detects for **alternative PFAS** compounds

POLICY QUESTION:

2. Are there differences in exposure of the EU population to regulated and alternative PFAS compounds?

Exposure difference in regulated and non-regulated PFAS compounds in teenagers



Data is expressed in µg/L. For values below LOQ the lowest LOQ value is plotted on the graph. Includes data from 7-9 EU countries: NO, SE, SK, ES, SI, EL, FR, DE and BE

POLICY QUESTION:

2. Are there differences in exposure of the EU population to regulated and alternative PFAS compounds?

However: big difference in absolute values of LOQs reached across studies

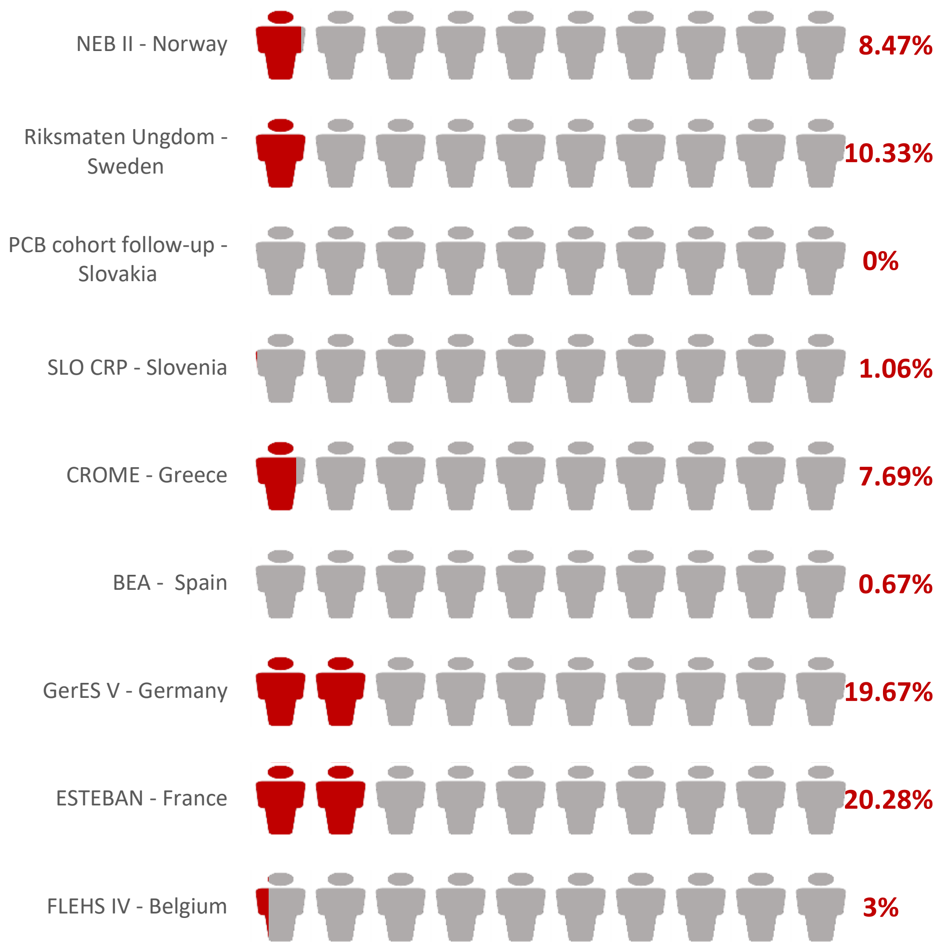
→ Lowering the LOQ is important for mixture risk assessment!

Health risks: single substance

PFOA as example

PFOS between 1-18% above HBM-I!

Share of European teenagers with PFOA levels exceeding HBM-I value: 2 µg/L



The German HBM Commission derives on the basis of toxicological and epidemiological studies the HBM-I value. It is defined as the concentration of a substance in human biological material at and below which no risk of adverse health effects is to be expected and consequently there is no need for action/intervention.

Between 0-20% above HBM-I value for PFOA (2 µg/L)

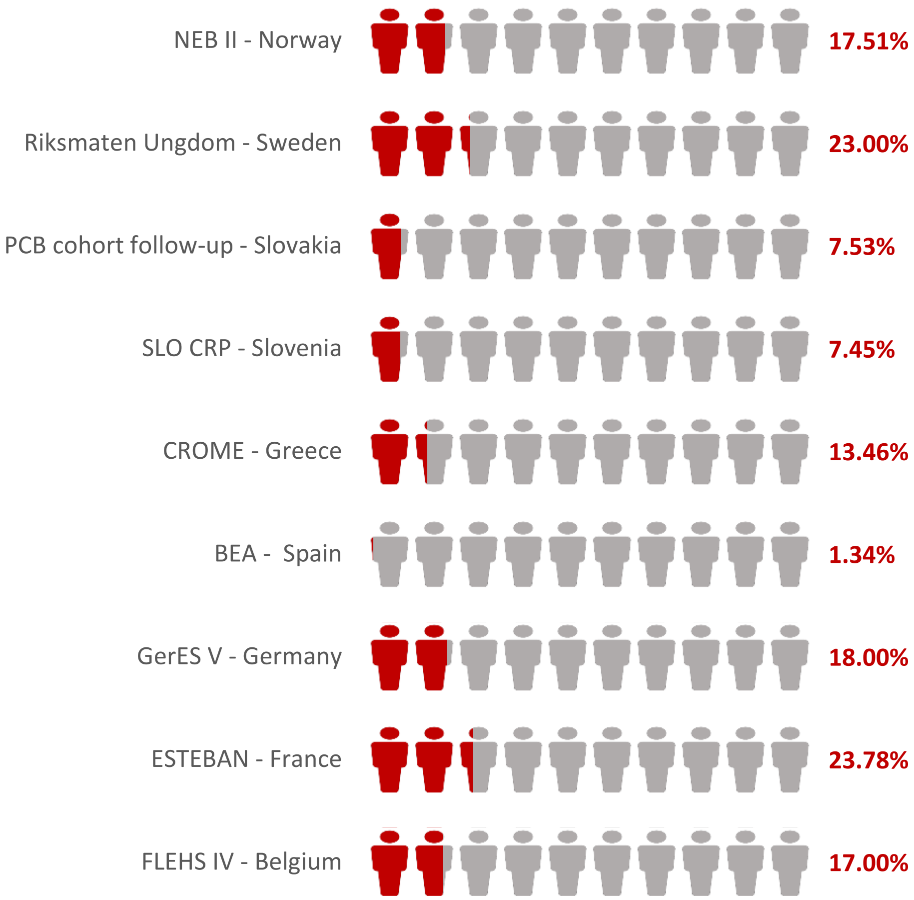
- ✓ **Northern Europe**: Norway = 8% & Sweden = 10%
- ✓ **Western Europe**: France = 20%, Germany = 20% & Belgium = 3%
- ✓ **Eastern Europe**: Slovakia = 0%
- ✓ **Southern Europe**: Spain = 1%, Slovenia = 1% & Greece = 8%

Health risks: combined exposure

Comparison with Health-Based Guidance values: EFSA opinion 2020 value*

**Derived for mothers -> approximation for teenagers*

Share of European teenagers with combined exposure levels to **PFOA + PFNA + PFHxS + PFOS** exceeding EFSA based value: 6.9 µg/L



- Between 1-24% above EFSA opinion value for sum (PFOA, PFOS, PFNA, PFHxS) (6.9 µg/L*)

✓ **Northern Europe**: Norway = 18% & Sweden = 23%

✓ **Western Europe**: France = 24%, Germany = 18% & Belgium = 17%

✓ **Eastern Europe**: Slovakia = 8%

✓ *Southern Europe*: Spain = 1%, Slovenia = 7% & Greece = 13%

In 2020, the European Food Safety Authority (EFSA) set a new safety threshold for intake as sum of the four PFAS of 4.4 ng/kg body weight per week, which is corresponding to an internal blood level of 6.9 µg/L. These guidance values were based on serum levels in females aged 35 years old and effects on immunity of their newborns.

Main Messages concerning EU wide internal exposure levels

The HBM4EU aligned studies have generated baseline levels of internal PFAS exposure in serum/plasma of European teenagers, 12-18 years of age, for the period 2014-2021:

- ✓ There is a statistically significant **geographical difference** in exposure levels for **the legacy PFAS compounds (PFOS, PFOA, PFNA, PFHxS)**, with higher average concentrations in Northern and Western Europe.
- ✓ Risk of adverse health effects cannot be excluded. All studies have study participants that exceed the guidance values based on the **EFSA opinion 2020**, exceedances vary from **1-24%** with an overall exceedance of 14%.
- ✓ Detection frequency is strongly varying between studies for **alternative PFAS compounds**, however strongly dependent on the LOQs reached in the labs

  → lower LOQs crucial for mixture risk assessment

Sum/mixture of PFAS has to be taken into account!

Three approaches for PFAS group risk assessment based on HBM data from HBM4EU Aligned Studies

1) Group Tolerable Weekly Intake (TWI) by EFSA may be interpreted as:

- Safe exposure limit of **17.5 ng/mL** in 1-y old children (PoD)
- Safe exposure limit of **6.9 ng/mL** for women of child-bearing age

2) Hazard index (HI) approach for HBM data

New

- Uses epidemiological studies, where adverse effects are associated with internal exposure to PFASs
- Either a given effect on immunotoxicity or on birth weight reductions birth weight (EFSA, 2020)

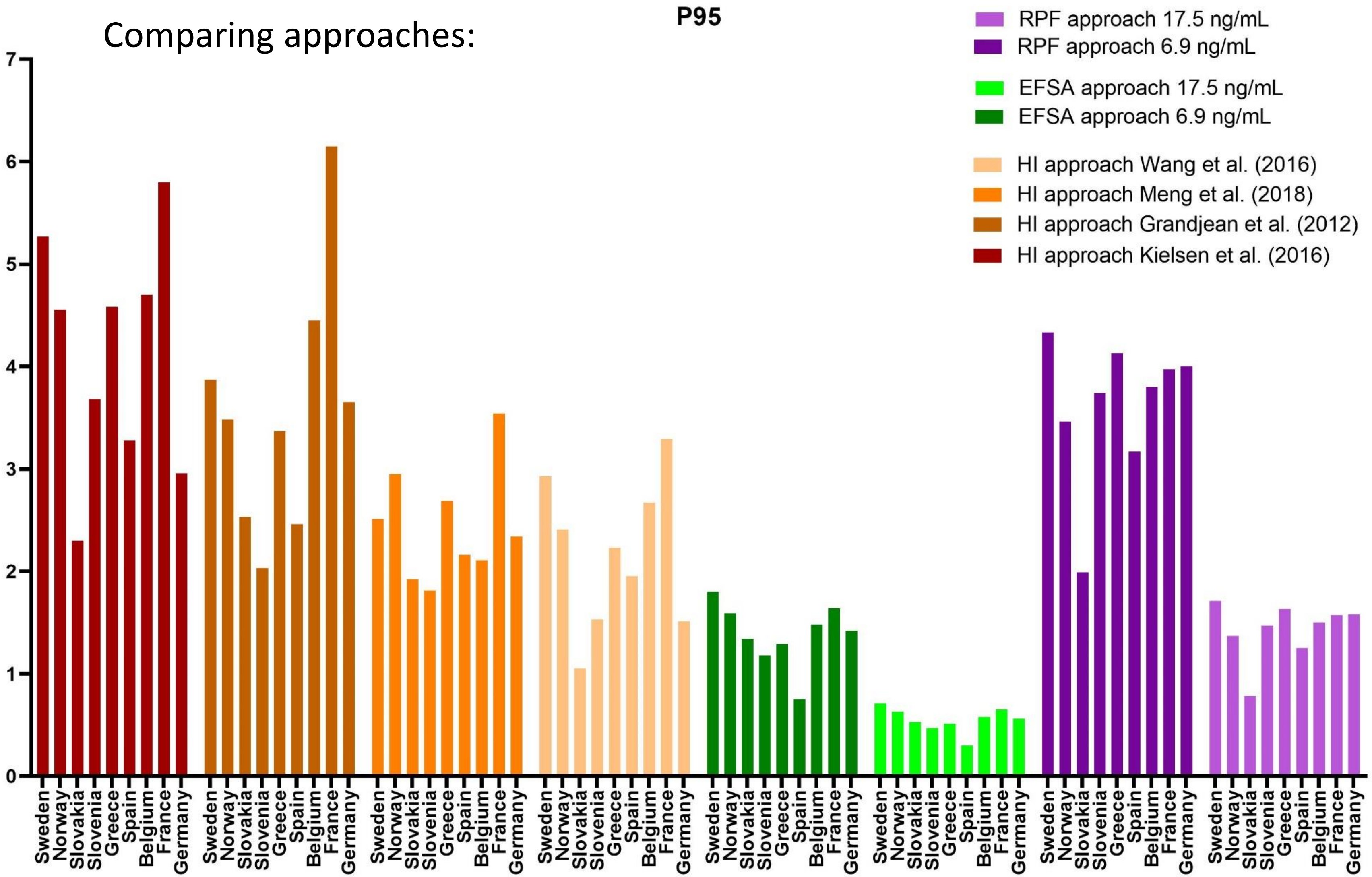
3) Relative potency factor (RPF) approach for HBM data

New

- Builds on assumption of dose addition, and derive RPFs based on internal exposure and liver toxicity in animal studies, index compound
- To be complemented with EFSA TWI

Risk characterization ratios based on **P95 mixture exposure** and values <LOQ set at zero

Comparing approaches:



Considering any of 3 approaches: Risk of adverse health effects due to PFAS exposure in parts of HBM4EU study population!

HI approach: highest risk estimates (6.2 for immune effects) in French study

RPF approach: highest estimates (4.33) in Swedish study population;

Sum value: highest RCR 1.8 in Swedish study population

Uncertainties of the approaches have to be considered

Assessment of 3 approaches

	Hazard Index approach	Sum value approach	RPF method
Advantages	• more than four PFASs • human data only (advantage compared to the RPF methodology)	• Straight forward (HBM GV of the 'EFSA-4' directly compared to recent European mixture exposure of the same compounds) • Relies on human data • summing exposure to the EFSA-4 per individual	• more than four PFASs • summing PEQ per individual • differential potencies of the different PFASs is taken into account
Challenges	• Due to positive correlation between different PFASs in epidemiological studies: likely to result in overestimation of risk • More conservative (combined exposure not assessed at individual level, only at population level)	• only four substances included • assumed equipotency of PFASs at the internal level, which may not be the case	• Uncertainty: extrapolation of the RPFs based on liver toxicity in experimental animals

Policy questions & answers via PFAS case study

Policy Question:

1. What is the **current exposure** of the EU population to PFAS and do they exceed Guidance values (reference and HBM values), where available?

Results of all three approaches indicate risk in (some parts of) the HBM4EU population, thereby confirming the results from EFSA (2020) opinion on PFAS in foods

Policy Question:

3. How can **mixture effects** of environmental and human PFAS mixtures present to date be estimated?

Various approaches available and developed, i.e. the sum value approach, hazard index approach, relative potency factor approach

Policy Question:

4. Paraphrased: What is the **impact of existing regulations** on PFAS exposure and is there a need for further regulations on PFAS?

Mixture risk assessment based on HBM data supports the need for risk management measures, and thereby supports the need for an EU-wide restriction on PFAS

Main Messages concerning PFAS mixture risk assessment

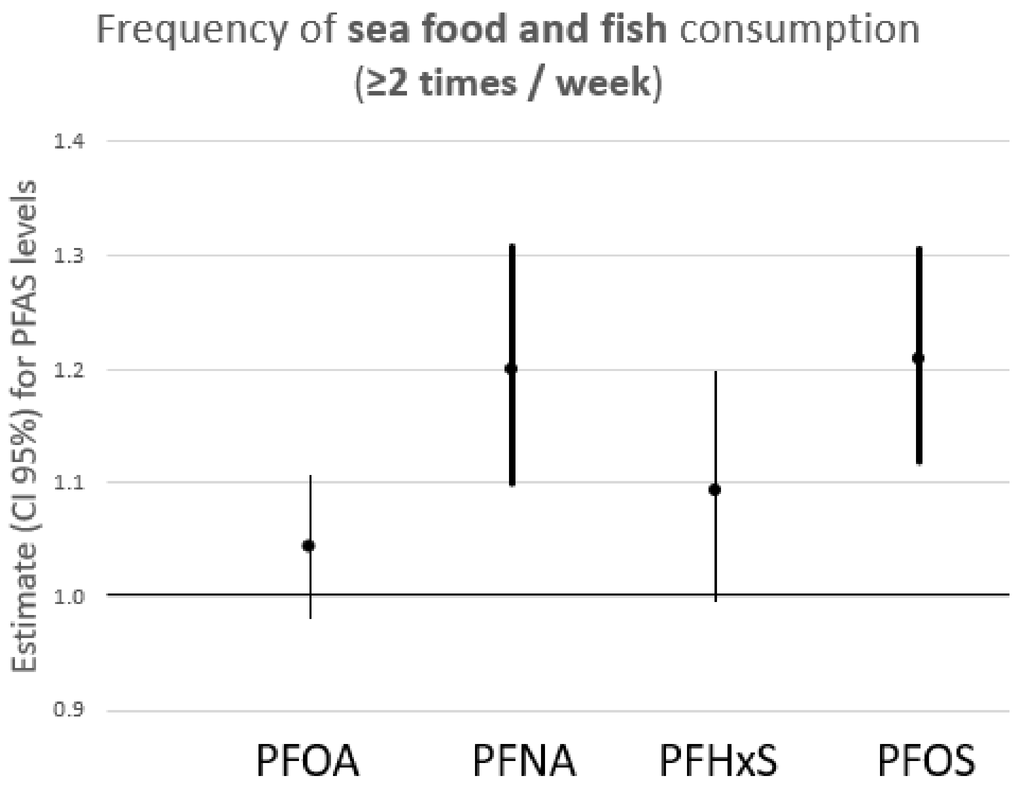
- Human biomonitoring data is a **valuable, empirical, measure for aggregate, combined exposure** to PFAS
- It is needed to **incorporate aggregate, combined exposure to PFAS** in risk assessment
- **Several methodologies for PFAS are available** to incorporate human biomonitoring data in risk assessment
- These methodologies **support the need for risk management measures**
- **Further refining and extending quantitative mixture risk assessment** for ‘forever chemicals’ is recommended and possible

Explanatory factors/determinants for the observed PFAS exposure levels

Variables (available in at least 7 out of 9 cohorts):

- frequency of food consumption (sea food, fish, meat, offal, milk, eggs, fast food, local food)
- water (water source at home, type of drinking water)
- renovation at home

Fixed factors in regression models: cohort, sex and education level of the household



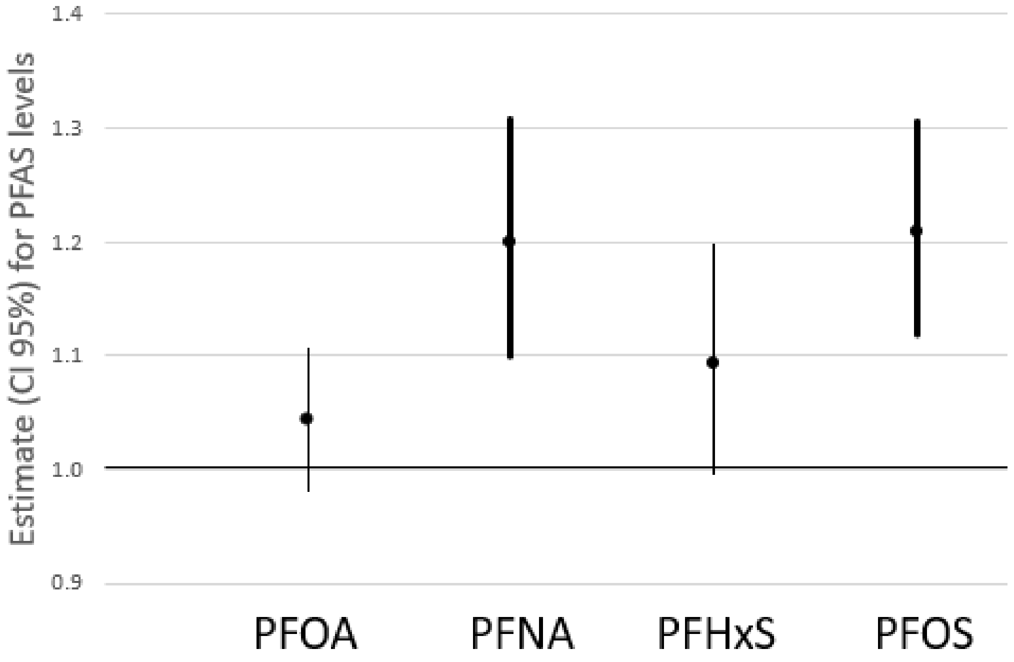
Higher consumption of **fish and sea food**:
- increased **PFNA** levels by 20% (95% CI: 10-31%)
- increased **PFOS** levels by 21% (95% CI: 12-31%)

Explanatory factors/determinants for observed PFAS exposure levels

Policy Question:

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

Frequency of **sea food and fish** consumption (**≥2 times / week**)



Higher consumption of **fish and sea food**:
- increased **PFNA** levels by 20% (95% CI: 10-31%)
- increased **PFOS** levels by 21% (95% CI: 12-31%)

Sea food and fish consumption just one determinant, others are

For PFNA and PFOS:
- higher **consumption of eggs** (increase in exposure by 14 % and 11 %, respectively)

For PFOS:
- higher **consumption of offal** (increase in exposure by 14 %)
- higher **consumption of local food** (increase in exposure by 40 %)

Other food items - no or weak associations with serum PFAS levels

Effects of diet!

Overall conclusion & messages

- ✓ Human Biomonitoring delivers **internal exposure** data from multiple sources and pathways
- ✓ **Regulation PFAS**: results support the PFAS group restriction under REACH, as blood serum mixture data indicates that the HBM4EU population is at risk of developing detrimental effects upon exposure to PFAS.
- ✓ **Analytical methods:** it is crucial to lower LOQs to further improve future interpretation and risk assessment.
- ✓ **Exposure trends:** follow-up exposure levels is needed to closely monitor the effects of regulatory measures over time (PARC).
- ✓ European-wide analyses of **PFAS concentrations in relevant food items** are needed.
- ✓ **Origin of food** could be an important parameter determining PFAS exposure from diet.

HBM4EU Dashboard

LEGEND

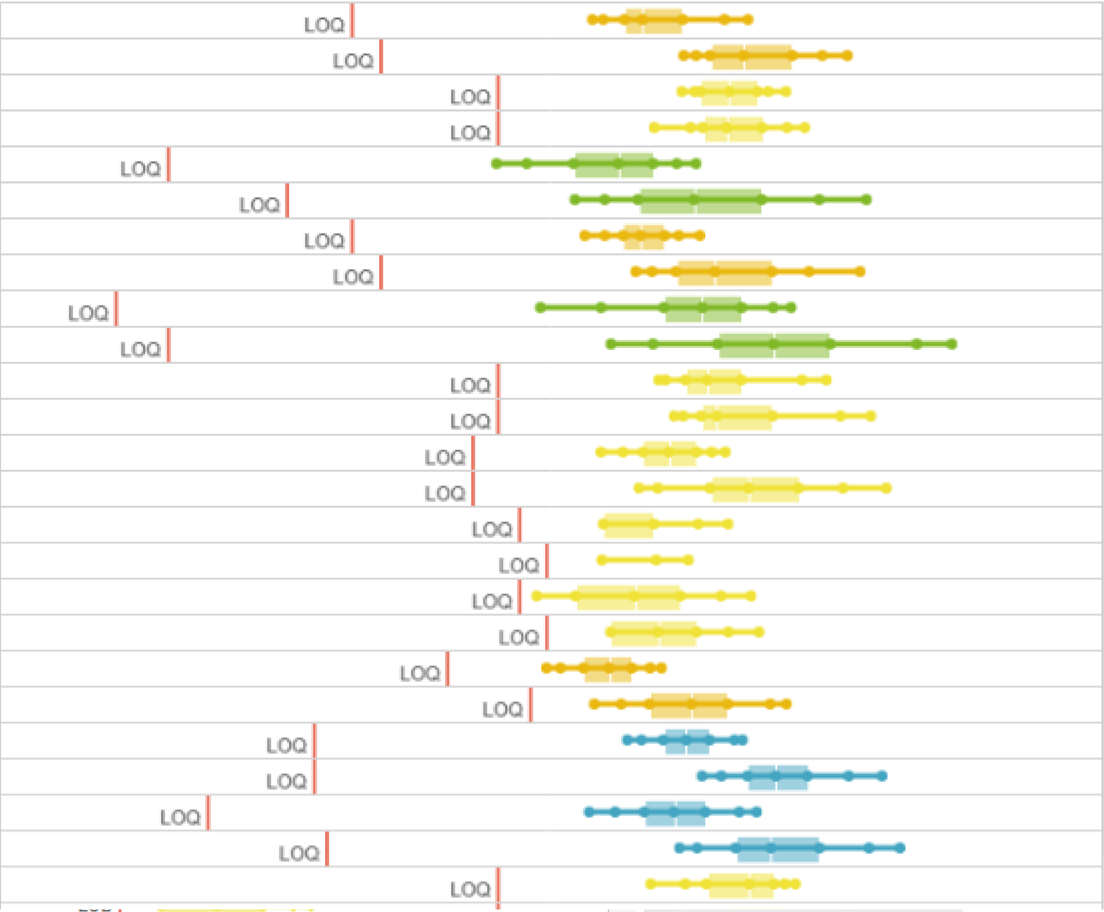
only percentiles >LOD/LOQ are displayed. If only P90 and P95 are >LOD/LOQ the visualisation looks like this:

REGION: Northern EU, Eastern EU, Western EU, Southern EU

Distribution of **Alle** concentration in **Blood** (µg/L)

sort data by: period

sampling period	country	data collection name	Biomarker + Age	No stratification	N
2020-2021	GR	CROME	PFOA - 12-18y	No strata	52
			PFOS - 12-18y	No strata	52
2019	DE	ESB_2019	PFOA - 20-39y	No strata	20
			PFOS - 20-39y	No strata	20
2019-2020	SK	PCB cohort follow-up	PFOA - 15-17y	No strata	292
			PFOS - 15-17y	No strata	292
2018	SI	SLO CRP	PFOA - 12-15y	No strata	94
			PFOS - 12-15y	No strata	94
2018-2019	CZ	CzechHBM-AE_2018	PFOA - 20-39y; 40-59y;..	No strata	395
			PFOS - 20-39y; 40-59y;..	No strata	395
2017	DE	ESB_2017	PFOA - 20-39y	No strata	20
			PFOS - 20-39y	No strata	20
2017-2018	BE	FLEHS IV	PFOA - 13-16y	No strata	300
			PFOS - 13-16y	No strata	300
2017-2019	AT	NEWDA_Child	PFOA - <1y	No strata	128
			PFOS - <1y	No strata	136
		NEWDA_Mother	PFOA - 20-39y; 40-59y;..	No strata	136
			PFOS - 20-39y; 40-59y;..	No strata	136
2017-2018	ES	BEA	PFOA - 13-17y	No strata	299
			PFOS - 13-17y	No strata	299
2016-2017	NO	NEBII	PFOA - 12-14y	No strata	177
			PFOS - 12-14y	No strata	177
	SE	Riksmaten	PFOA - 12-17y	No strata	300
			PFOS - 12-17y	No strata	300
2015	DE	ESB_2015	PFOA - 20-39y	No strata	20



2003-2004 BE FLEHS 1 adolescents

HBM4EU Dashboard

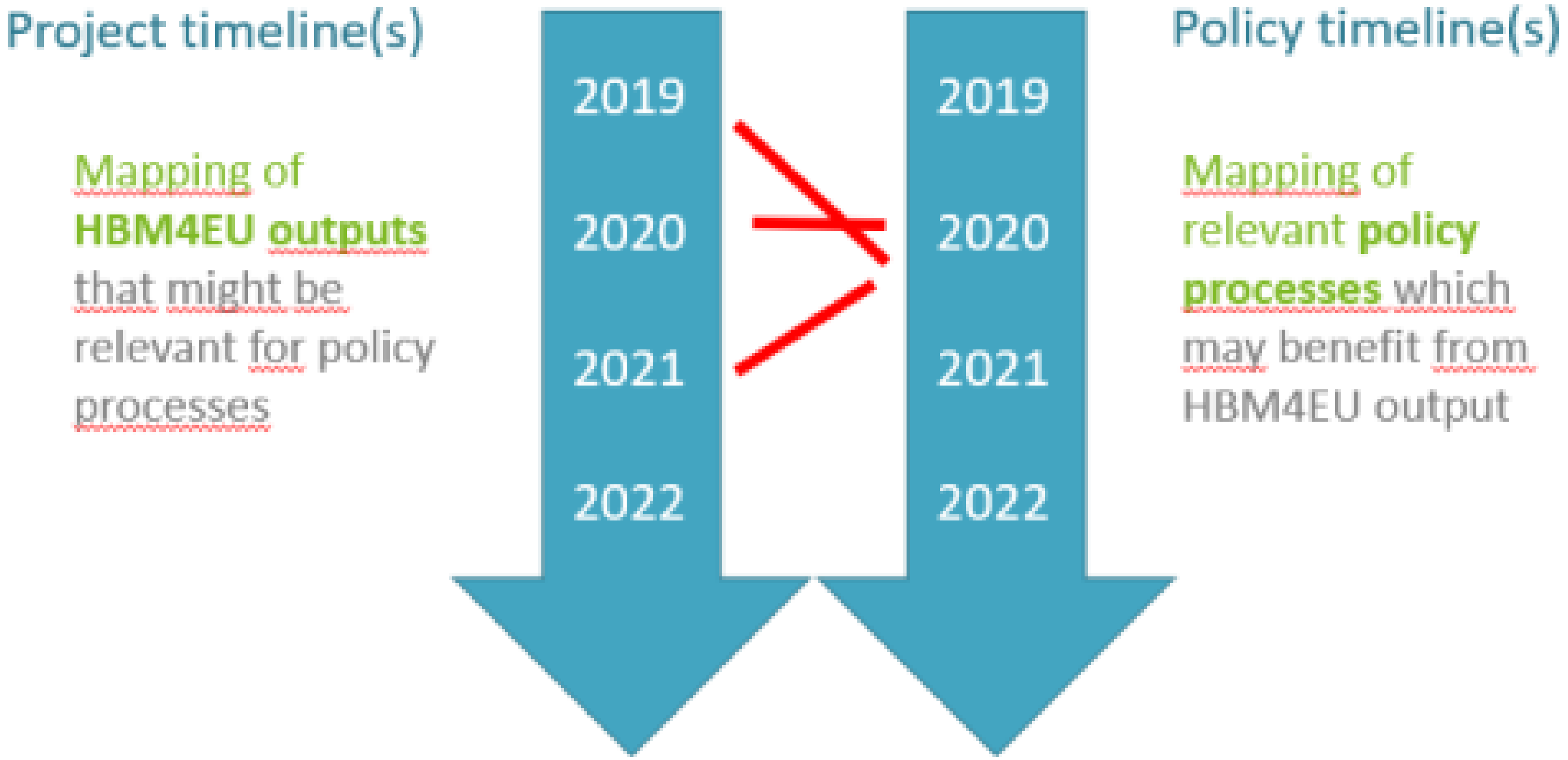
FAIR data:
making data Findable, Accessible, Interoperable and Reusable

Via IPCHEM
https//ipchem.jrc.ec.europa.eu/

Via European HBM dashboard
https://www.hbm4eu.eu/eu-hbm-dashboard/

„Timelines of Opportunity“ identified for PFAS

Useful and possible to ‘align’ project timeline with the policy’s agenda?



From Deliverable AD5.9 Timelines of opportunity: How HBM4EU can support chemicals management policy needs

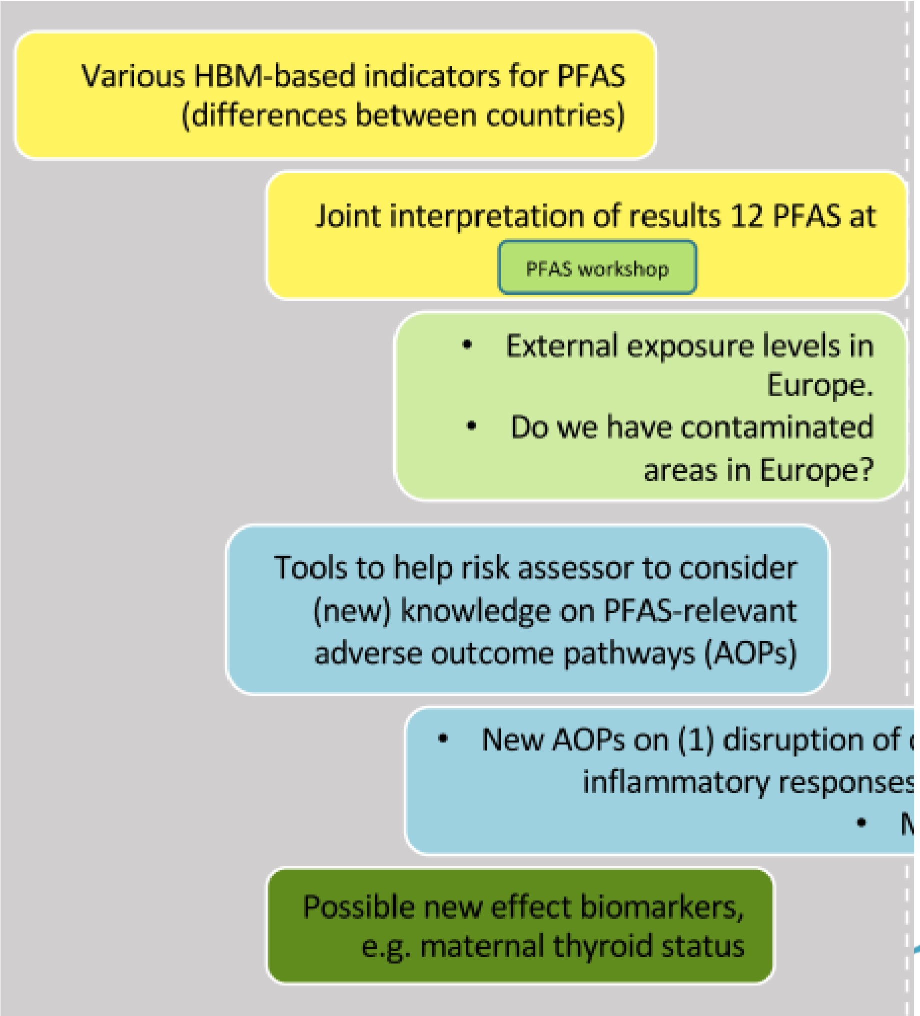
„Timelines of Opportunity“ identified for PFAS

WINDOWS OF OPPORTUNITIES (FOR THE PFAS CASE)

Examples:

- **restriction intention for all PFAS** (except for essential uses), announced by the Netherlands at the Council of Ministers of the Environment (December 2019)
- **Public consultation (early 2020) on EFSA’s draft scientific opinion** (CONTAM panel) on the risks to human health related to the presence of PFAS in food
- **Preparatory study work** (2019) for restrictions of PFAS in firefighting foam and in textiles (TULAC), commissioned by DG ENV (‘pre Annex XV dossiers’)

Timeline envisioned within HBM4EU (excerpt for 2020):



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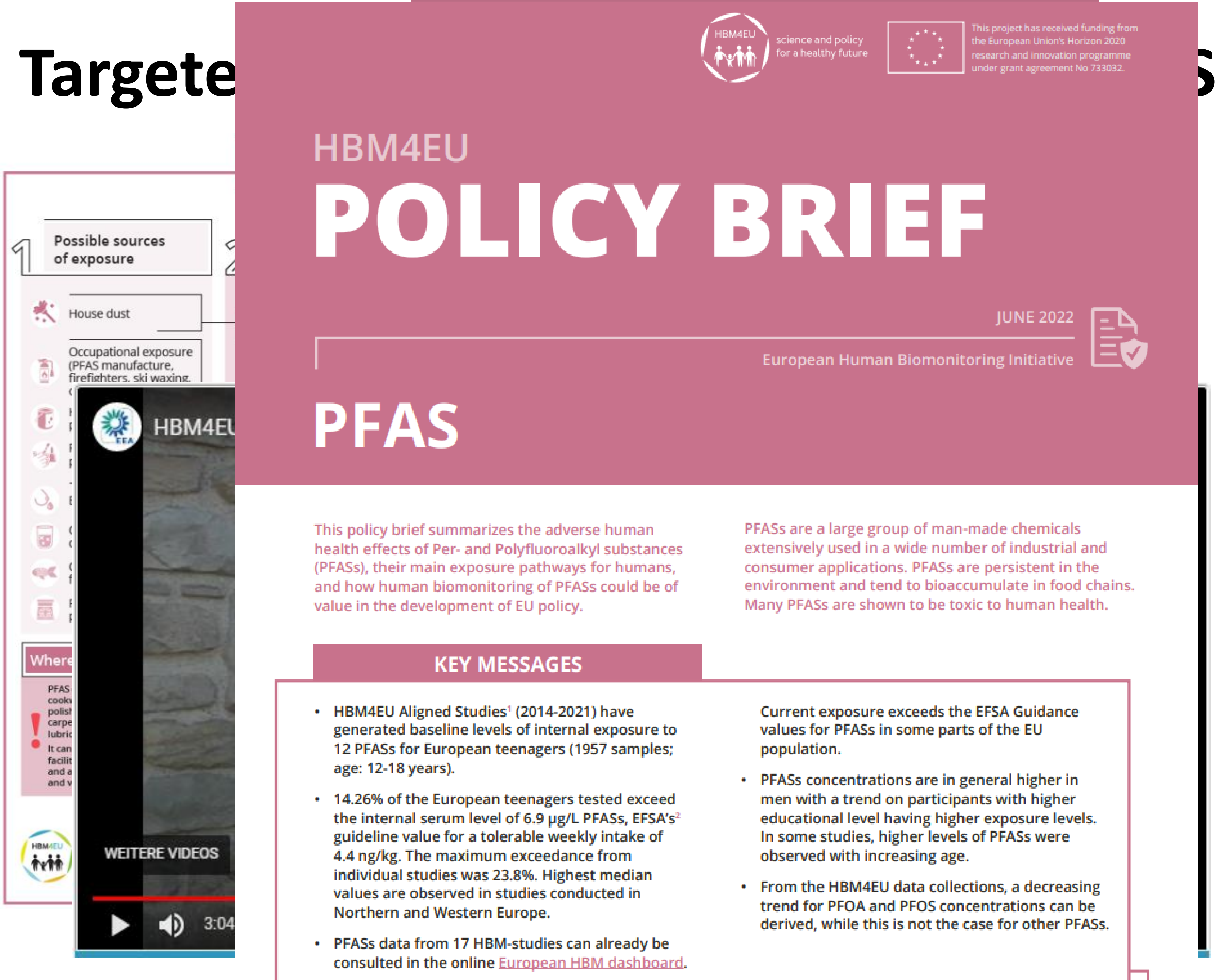

Infographics

Fact Sheets

Videos

Policy Briefs

… reports, publications and other results on the

HBM4EU Website

www.hbm4eu.eu

HBM4EU

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for a healthy future

@hbm4eu

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Lubica Murinova – SZU

Wieneke Bil – RIVM

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