HBM4EU

science and policy
for a healthy future

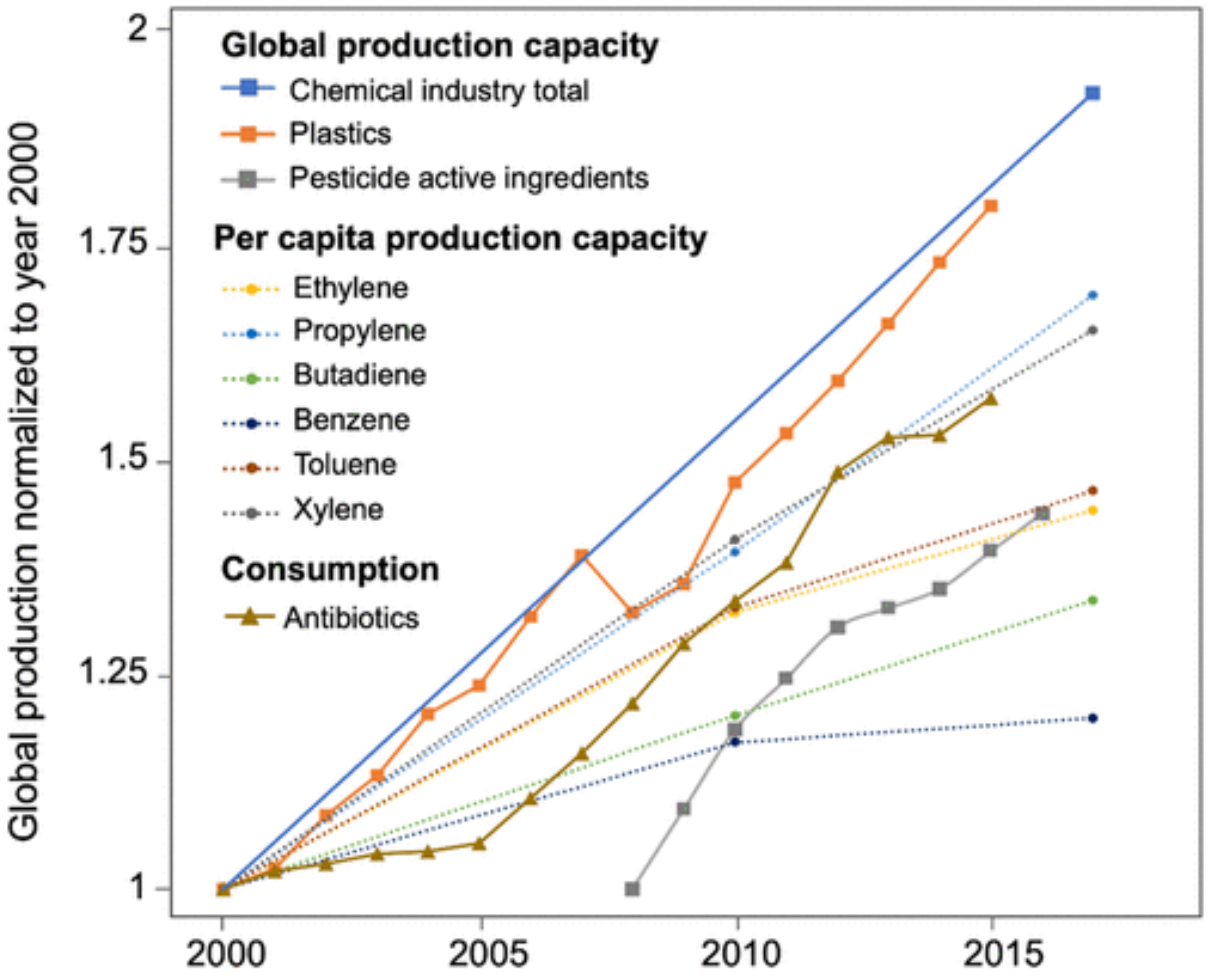
Human biomonitoring to support risk assessment and chemical policies in Europe: Results from HBM4EU

Greet Schoeters, VITO & University of Antwerp

ESTIV/ ACCST 23 June 2023

vito

Challenges for chemical risk assessment



Persson, Environ. Sci. Technol. 2022, 56, 3, 1510–1521

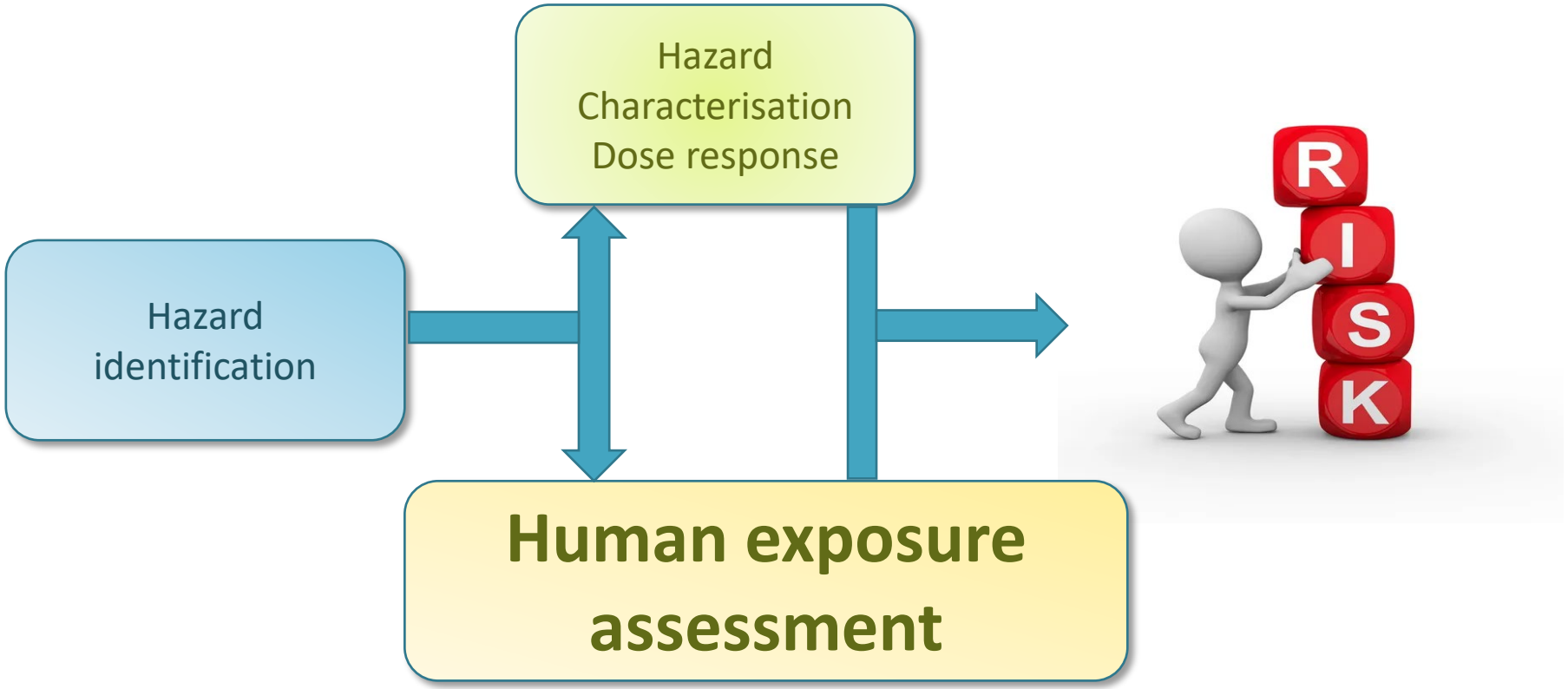
- More than 100 000 different chemicals on the market
- 4.7 trillion US dollars revenues in2021
- 302 million tonnes of chemicals consumed in the EU in 2020
- About 10% of chemicals consumed in EU are carcinogenic, mutagenic or reprotoxic (Eurostat 2020)

EU chemicals strategy for sustainability

By 2050, pollution is reduced to levels no longer considered harmful to health and natural ecosystems:

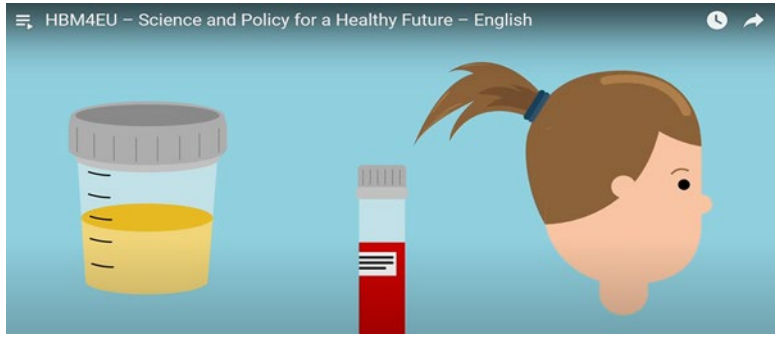
- Banning and restricting – except for essential uses
- Substituting with substances of less concern
- Tackling “cocktail effect”

Chemical Risk assessment



Adapted from Wittwehr et al, Comput Toxicol. 2020 doi: 10.1016/j.comtox.2019.100114.

Human biomonitoring



Measures chemicals
and their reaction products
directly in urine, blood,..

Integrates
exposures from inhalation,
ingestion, dermal uptake

Human biomonitoring makes pollution personal

HBM4EU

The European Human Biomonitoring Initiative – HBM4EU

5.5 years, extended (2017-2022), **European Joint Programme** under Horizon 2020

Total budget: **~ 74 million €**

30 countries (25 EU Member States, 3 associated countries, Switzerland) and the **European Environment Agency**

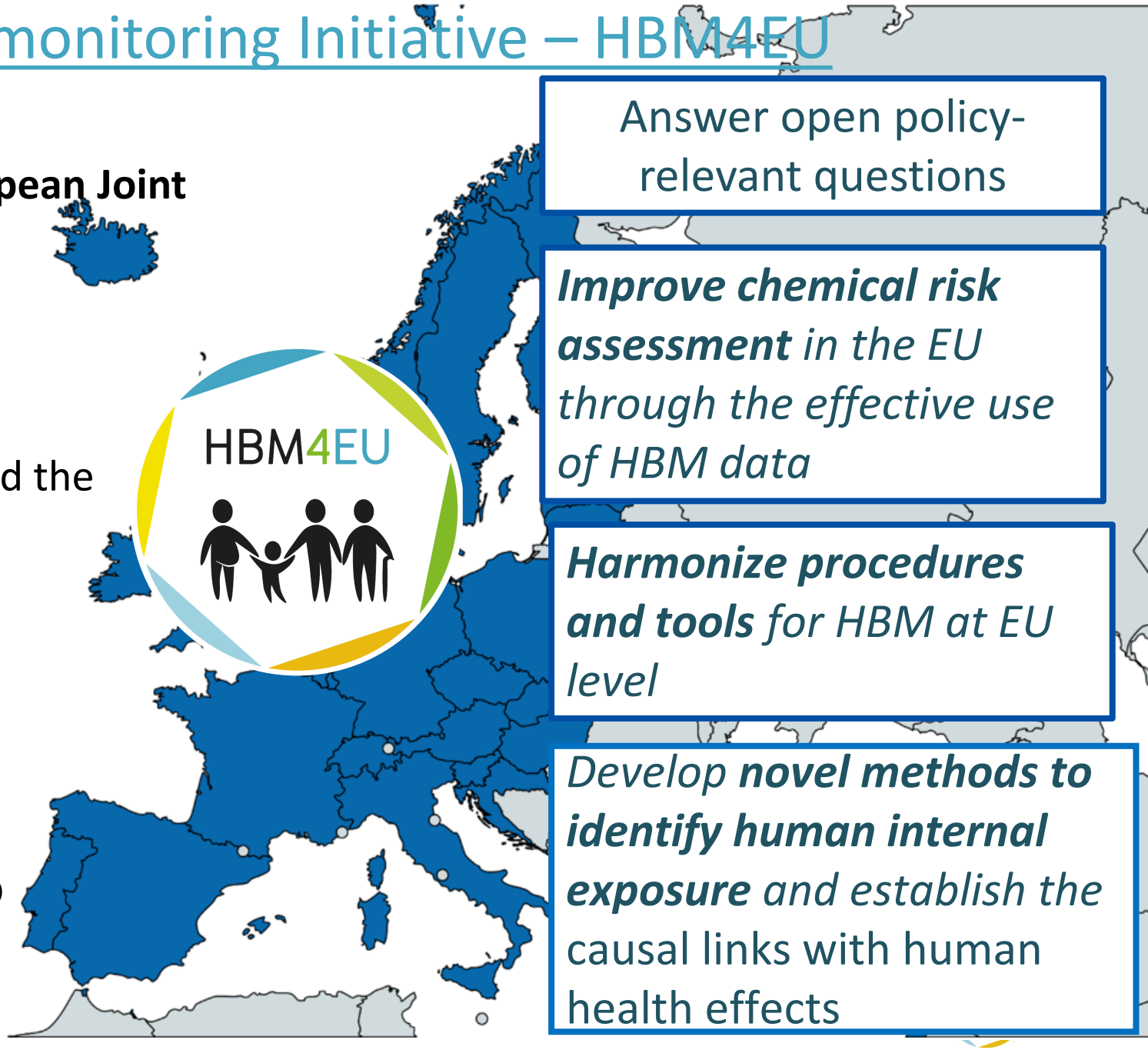
116 Partner organisations

Coordinated by the German Environment Agency (UBA)

Umwelt Bundesamt

vito

Co-coordinated by VITO



Answer open policy-relevant questions

Improve chemical risk assessment *in the EU through the effective use of HBM data*

Harmonize procedures and tools *for HBM at EU level*

Develop ***novel methods to identify human internal exposure*** *and establish the* causal links with human health effects

Ganzleben et al, Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2017.01.007.

The science policy nexus in HBM4EU

We started the dialogue with policy makers: national and at EU level

- What are the policy questions?
- What are the priorities?
- Input from policy context?
- Uptake in policies?

Clearly communicate science

Deliver at the right moment.

- Farm to fork-transition of farming and diet
- Sustainable chemical's strategy
- Zero pollution ambition

Lobo Vicente J; Int J Hyg Environ Health. 2023 doi: 10.1016/j.ijheh.2023

From Policy to science: prioritisation and capturing policy questions

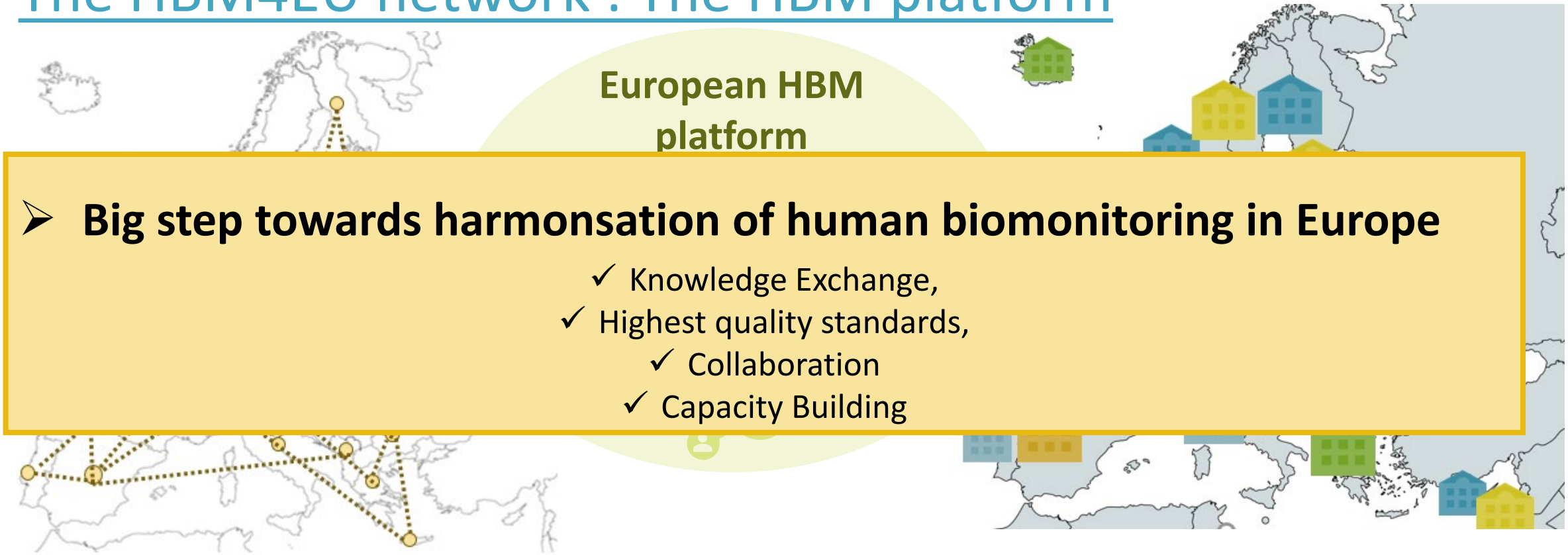
Phthalates/DINCH
Bisphenols
Per-/Polyfluorinated compounds
Flame Retardants
Cadmium & Chromium
PAHs and air pollutants
Anilin family: MOCA
Chemical mixtures
Emerging chemicals

Acrylamide
Aprotic solvents
Arsenic
Diisocyanites
Lead
Mercury
Mycotoxines
Pesticides
UV filters

- What is the current exposure of the EU population?
- Are exposures different between countries? Why?
- Are exposure levels above any health relevant health assessment values?
- Has European regulation an effect?
- Should the substance be subject to (further) regulation ?

Ougier et al, Int J Hyg Environ Health. 2021, doi:10.1016/j.ijheh.2021.113778.

The HBM4EU network : The HBM platform



European HBM platform

- **Big step towards harmonsation of human biomonitoring in Europe**
  - ✓ Knowledge Exchange,
  - ✓ Highest quality standards,
  - ✓ Collaboration
  - ✓ Capacity Building

166 laboratories: 45% of them HBM4EU qualified

152 biomarkers
9 chemical groups

Existing and new HBM studies and data

https://ipchem.jrc.ec.europa.eu/
https://www.hbm4eu.eu/eu-hbm-dashboard/

HBM4EU aligned studies: harmonization in 21 countries

Inclusion criteria

- ✓ General population
- ✓ Samples collected between 2014-2021

Exclusion criteria

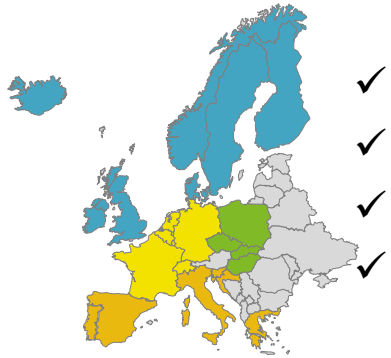
- !no hotspot areas
- ! Specific targeted populations e.g. patient groups

Domains for which reliable data are **needed:**

Age

- ✓ **Children (6-11y)**
- ✓ **Teenagers (12-19y)**
- ✓ **Adults (20-39y)**

Geographical coverage



- ✓ **North 21% → 2**
- ✓ **East 11% → 1**
- ✓ **South 28% → 3**
- ✓ **West 40% → 3/4**

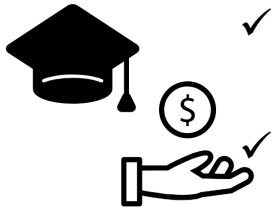
Sex

- ✓ **Male**
- ✓ **Female**

→ 50:50 ratio

Domains with minimal prevalence (10%):

SES socio-economic status



- ✓ Educational level (ISCED- classification from UNESCO)
- ✓ Level 0-6

Subject living environment

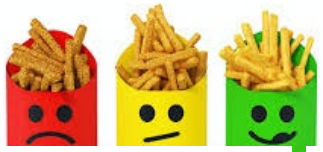
Inhabitants of

- ✓ Low
- ✓ Medium
- ✓ high density communities

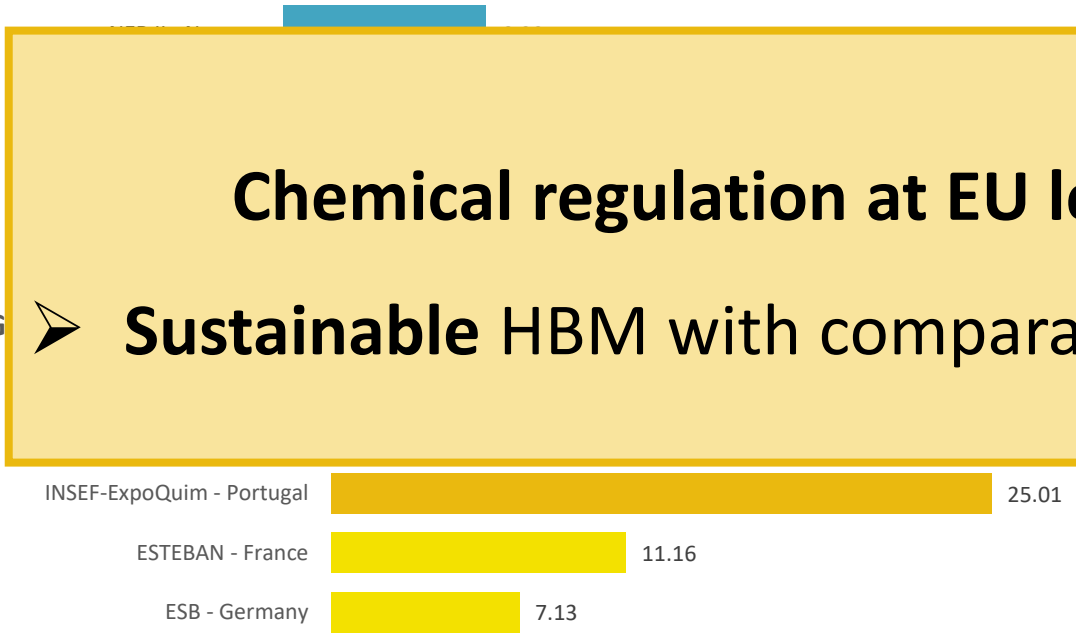
Gilles et al, Int J Environ Res Public Health. 2022, doi: 10.3390/ijerph19116787.

Geographical differences

Acrylamide biomarkers



GAMA in urine (µg/g crt) of children in Europe by mean value (P50)



PFOS+PFOA+PFHxS+PFNA

Geographical differences in exposure to PFOS in blood (µg/L) of teenagers in Europe (2014-2021) by median value (P50)

Chemical regulation at EU level but national implementation

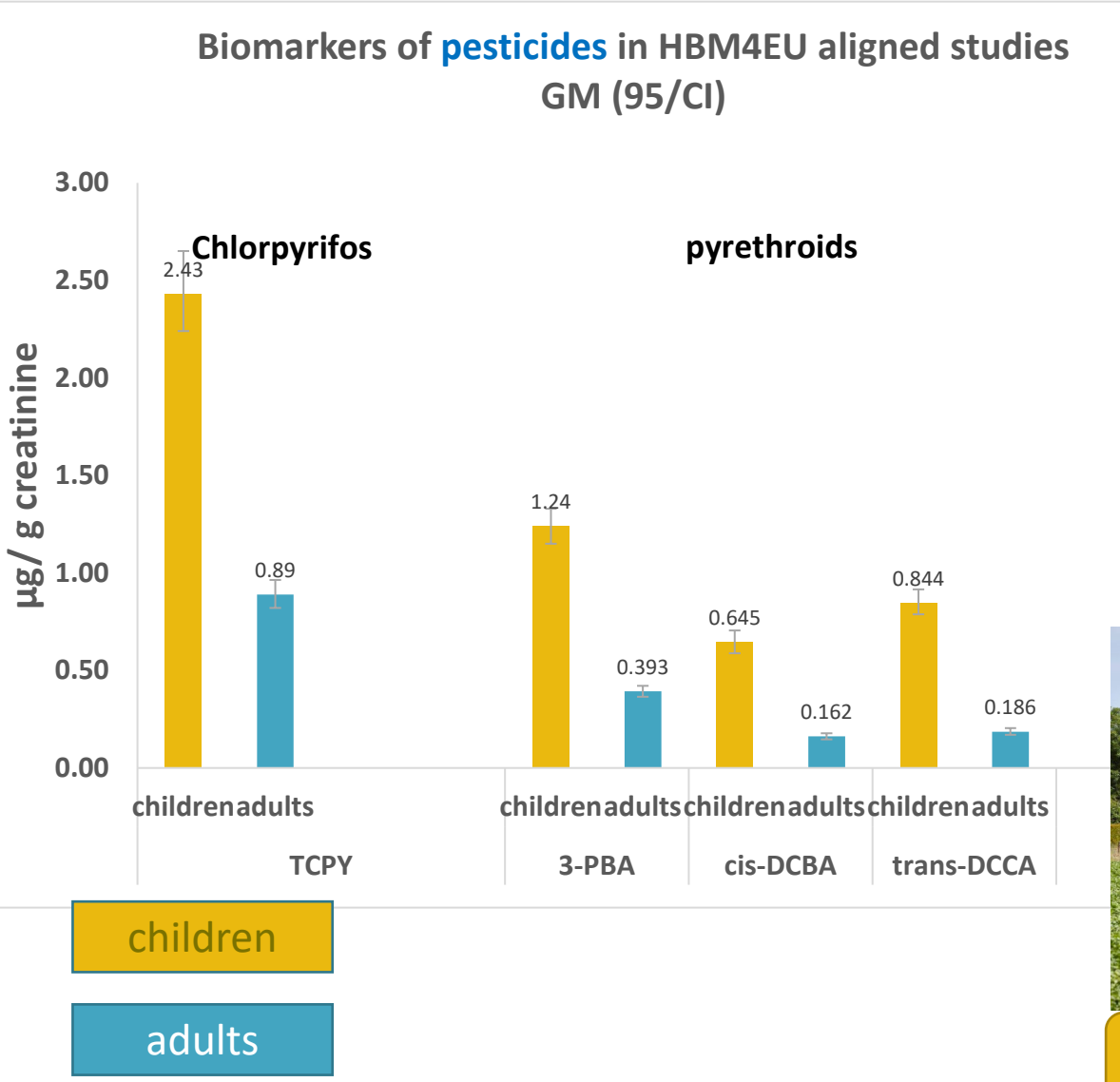
➢ **Sustainable** HBM with comparable data is necessary on European level!

North | East | West | South

Poteser et al, Toxics. 2022 doi: 10.3390/toxics10080443

Uhl et al, Int J Hyg Environ Health. 2023 doi:10.1016/j.ijheh.2023.114168.

Younger age groups have higher biomarker levels than older ages



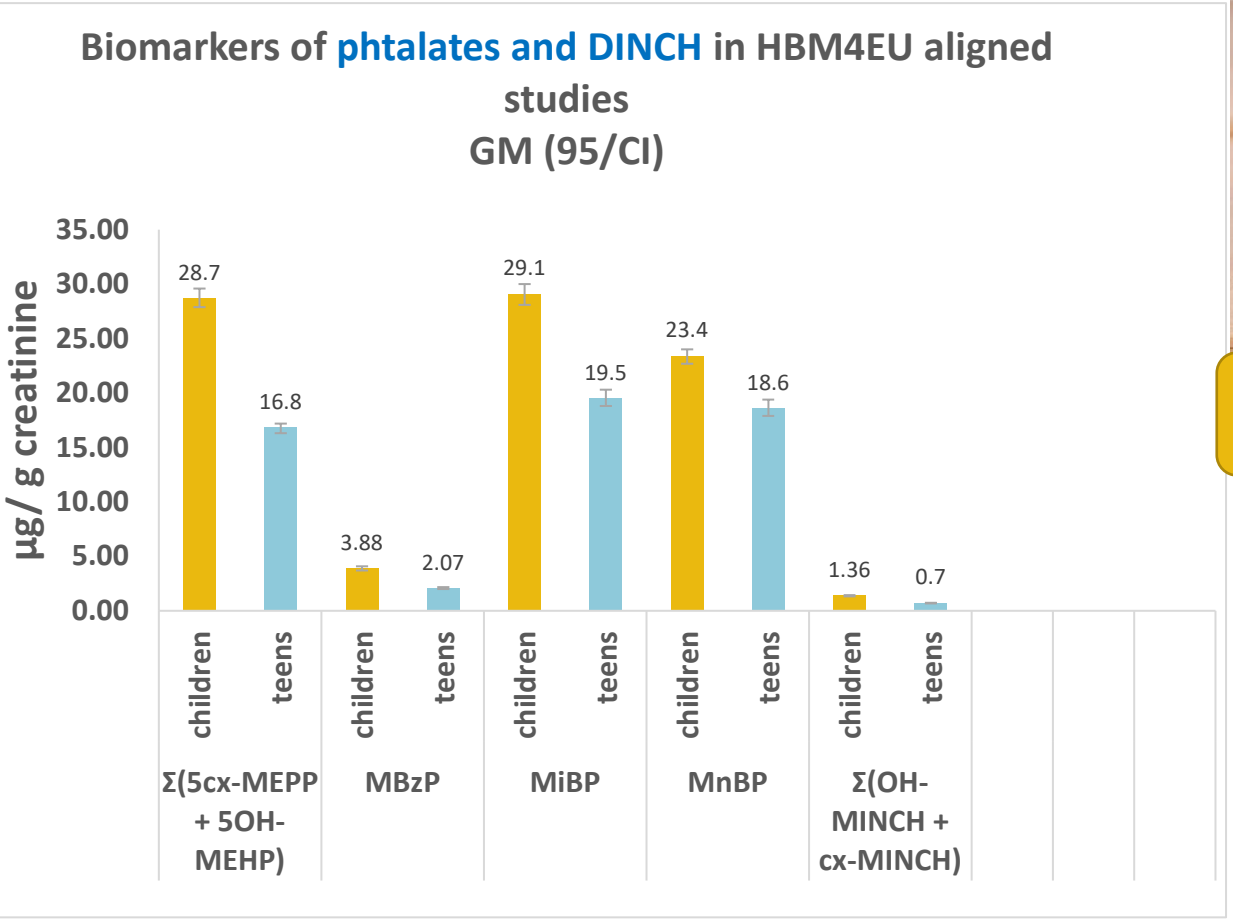
Higher intake of food per kg body weight

Higher inhalation rate

Tarazona et al, Toxics. 2022 doi: 10.3390/toxics10080451

Tarazona et al, Toxics 2022 doi: 10.3390/toxics10080451

Younger age groups have higher biomarker levels than older ages



children

teenagers

Vogel et al, Int J Hyg Environ Health. 2023 doi:10.1016/j.ijheh.2022.114101.

Higher exposure to dust
Different breathing zones

Playing behaviours
Hand to mouth contact

Higher body surface area to mass ratio

Protecting vulnerable ages: children & adolescents – transgenerational equity?

- **Aprotic solvents**
  - NMP highest in young children, NEP highest in adolescents
- **Acrylamide**
  - Levels are higher at younger ages
- **Benzophenones**

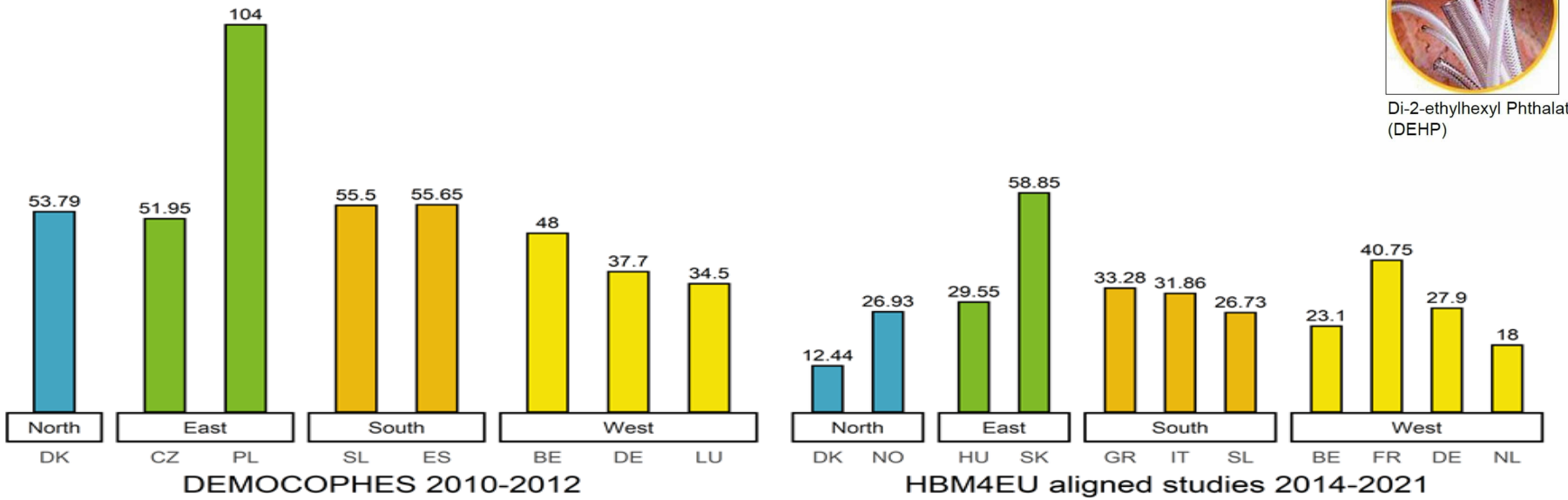
Protect children as they are often more exposed than older age groups

oxin

  - Children have higher levels than teenagers except MEP
- **Pyrethroids**
  - HBM levels (P50 and P95) are higher in children compared to adults for 3-PBA, cis-DBCA , cis and trans DCCA,
- **Chlorpyrifos**
  - Concern for health risk in some children populations with P95 higher than in adult studies

Changes over time

DiBP exposure of children P50 for the biomarker MiBP in µg/L.



Phthalates

Di-2-ethylhexyl Phthalate (DEHP)

Diethyl Phthalate (DEP)
Dibutyl Phthalate (DBP)

Di-2-ethylhexyl Phthalate (DEHP)
Butylbenzyl phthalate (BBzP)

Chemical regulation at EU level works to reduce exposure

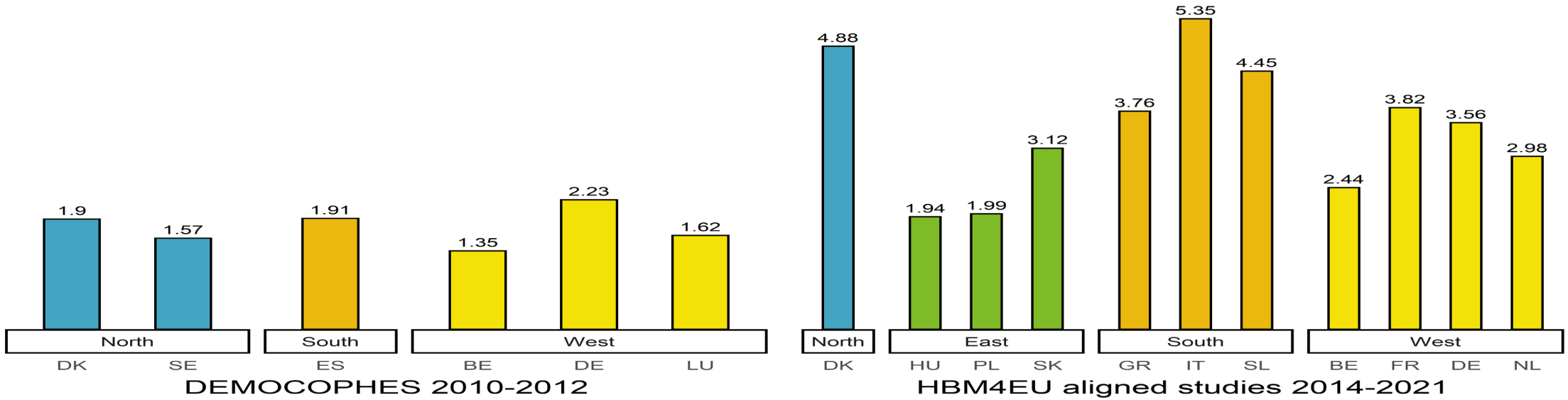
Phthalates, BPA, PFOS and PFOA

BUT!!!!

Gerofke et al, Int J Hyg Environ Health. 2023, doi: 10.1016/j.ijheh.2022

Changes over time

DINCH exposure of children, P50 for the biomarker ∑ (OH-MINCH + cx-MINCH) in µg/L

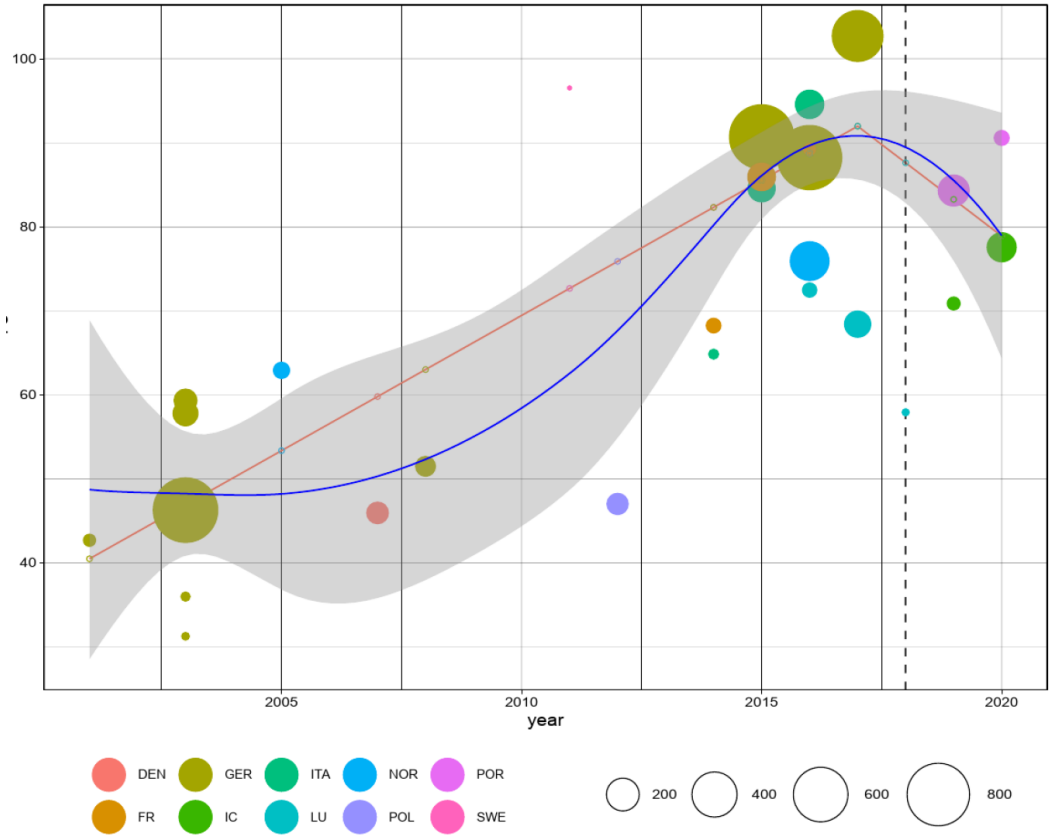


Subsitutes pop up !!!

Rapid update of TDI(ADI) is needed if new toxicological information becomes available

Gerofke et al, Int J Hyg Environ Health. 2023, doi: 10.1016/j.ijheh.2022

Acrylamide in adults, urinary metabolites measured over time



Time trend analysis based on harmonized published data (2000-2015) and HBM4EU studies (2015-2021) show:

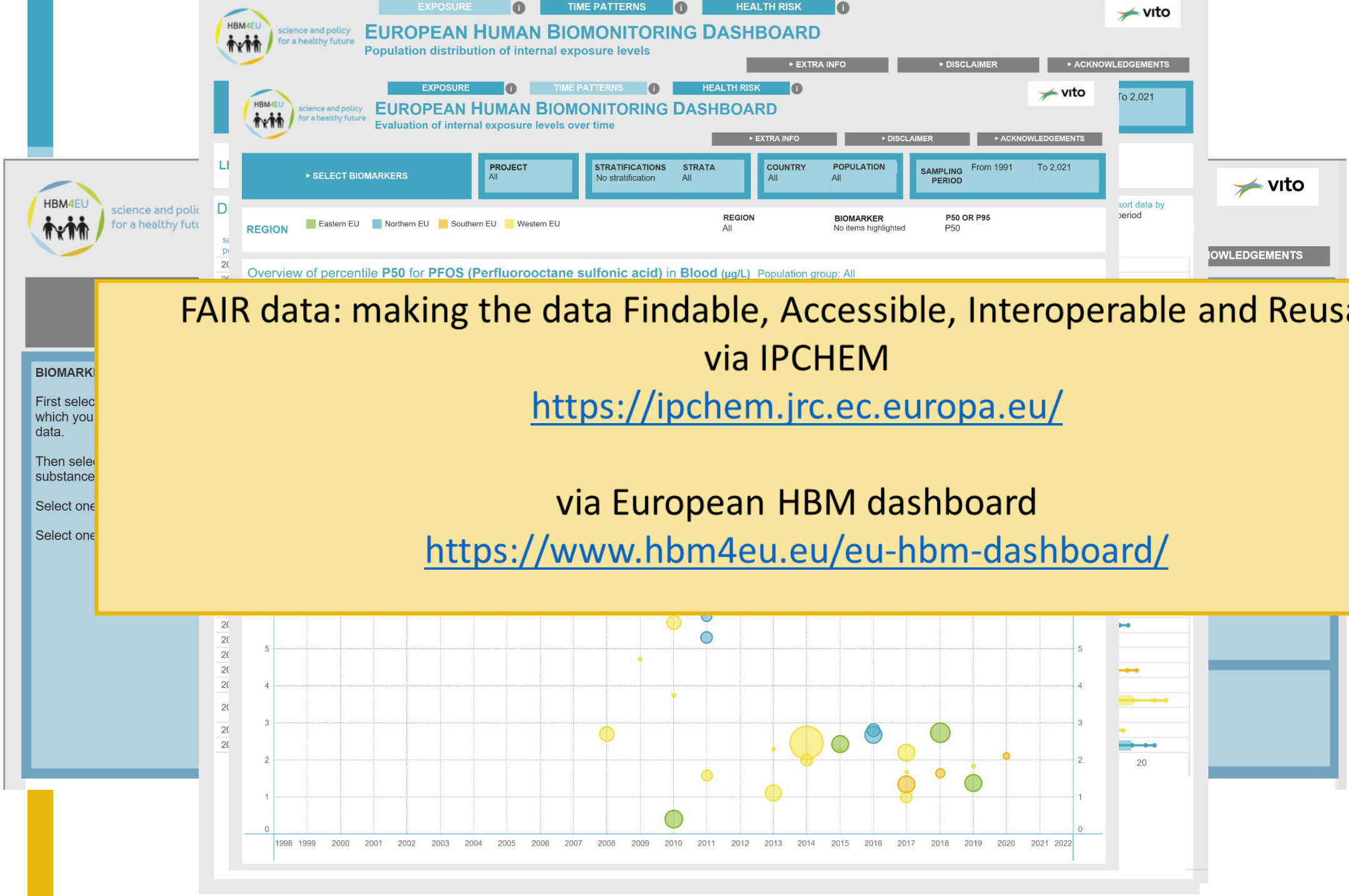
- An increasing of AAMA concentration over time from 2000 to 2017
- A decreasing of AAMA during 2018-2020

mitigation measures are not visible till 2017

BUT there is an indication of first slightly effect of the 2017 EU regulation mitigation measures only in ADULTS (no data on children)

AAMA: N-acetyl-S-(2-carbamoylethyl)-cysteine

Poteser etal, Toxics. 2022 doi: 10.3390/toxics10080481.



FAIR data: making the 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/

Risk quotients: fraction of the population at risk

- Comparison with health based guidance values
- Interpretation: adverse health effects cannot be excluded if health based guidance values are exceeded (based on current scientific knowledge)

  - 27 HBM-GVs derived in HBM4EU

  - Biomonitoring equivalents (Summit Toxicology)
  - HBM I (German HBM commission)

Apel et al. Strategy to derive human biomonitoring guidance values (HBM-GVs) for health risk assessment. Int J Hyg Environ Health. 2020. doi: 10.1016/j.ijheh.2020.113622.

HBM4EU data support current policy decisions

Share of European teenagers with chemical exposure levels (median) of PFASs with concerns for health.

Chemical substance	% population exceeding guidance value	
PFOA HBM-I: 2 µg/L	**7.66%**	
PFOS		
Σ(PFOA + PFNA + PFHxS + PFOS) EFSA opinion: 6.9 µg/L	**14.26%**	
Σ(PFOA + PFNA) EFSA opinion: 2 µg/L	**19.01%**	

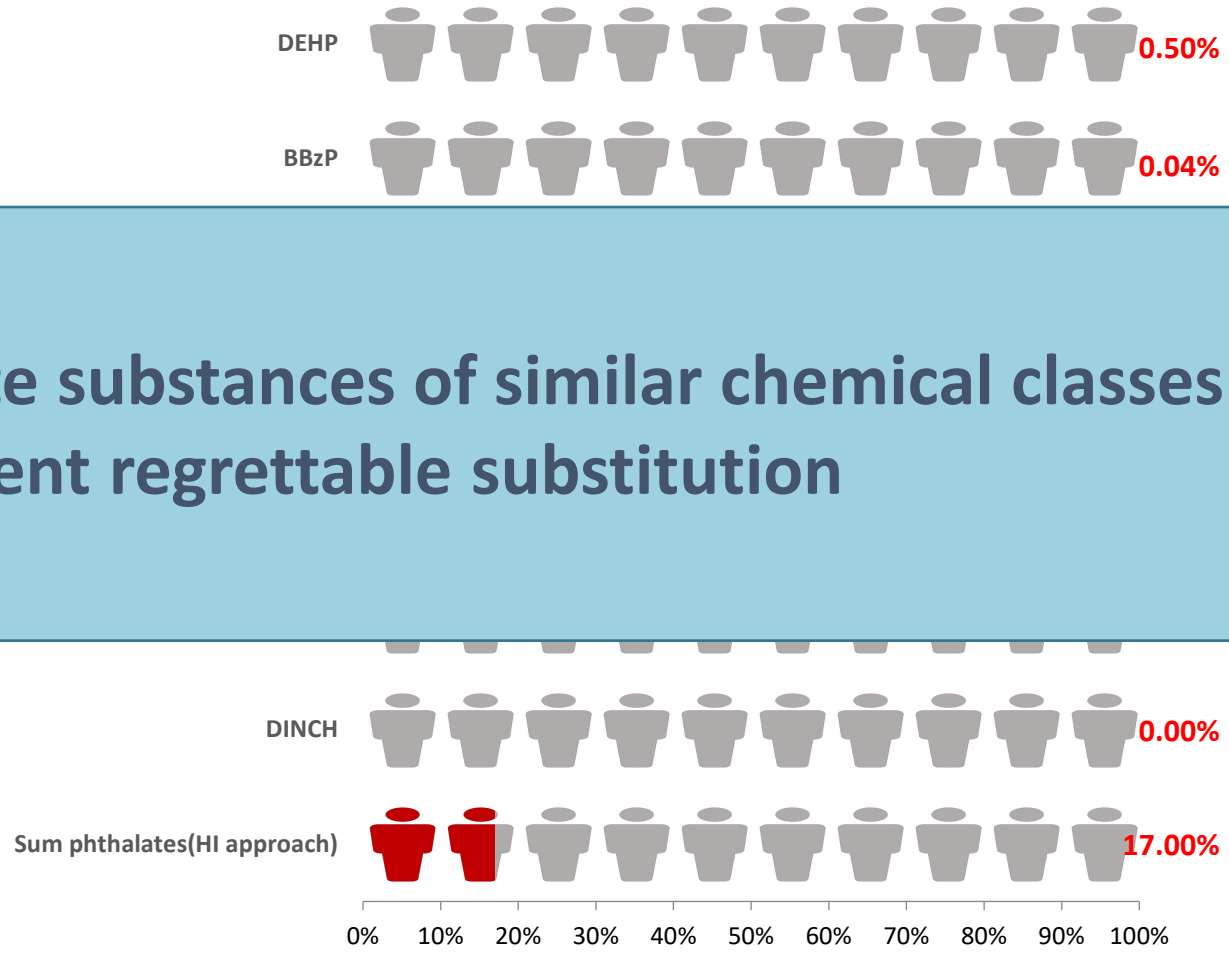
Results from HBM4EU: HBM-GV-exceedance shown by HBM4EU demonstrate necessity of regulatory actions!

Strong support for i.a. PFAS group restriction activities

The data presented are from teenagers 12-19 year collected across Norway, Sweden, Slovakia, Slovenia, Greece, Spain, Germany, France and Belgium. Values <LOD/LOQ are replaced by LOD/2 or LOQ/2. Sums are only calculated if one of the markers constituting the sum is detected for at least 60%.

Uhl et al, Int J Hyg Environ Health. 2023 doi: 10.1016/j.ijheh.2023.114168.

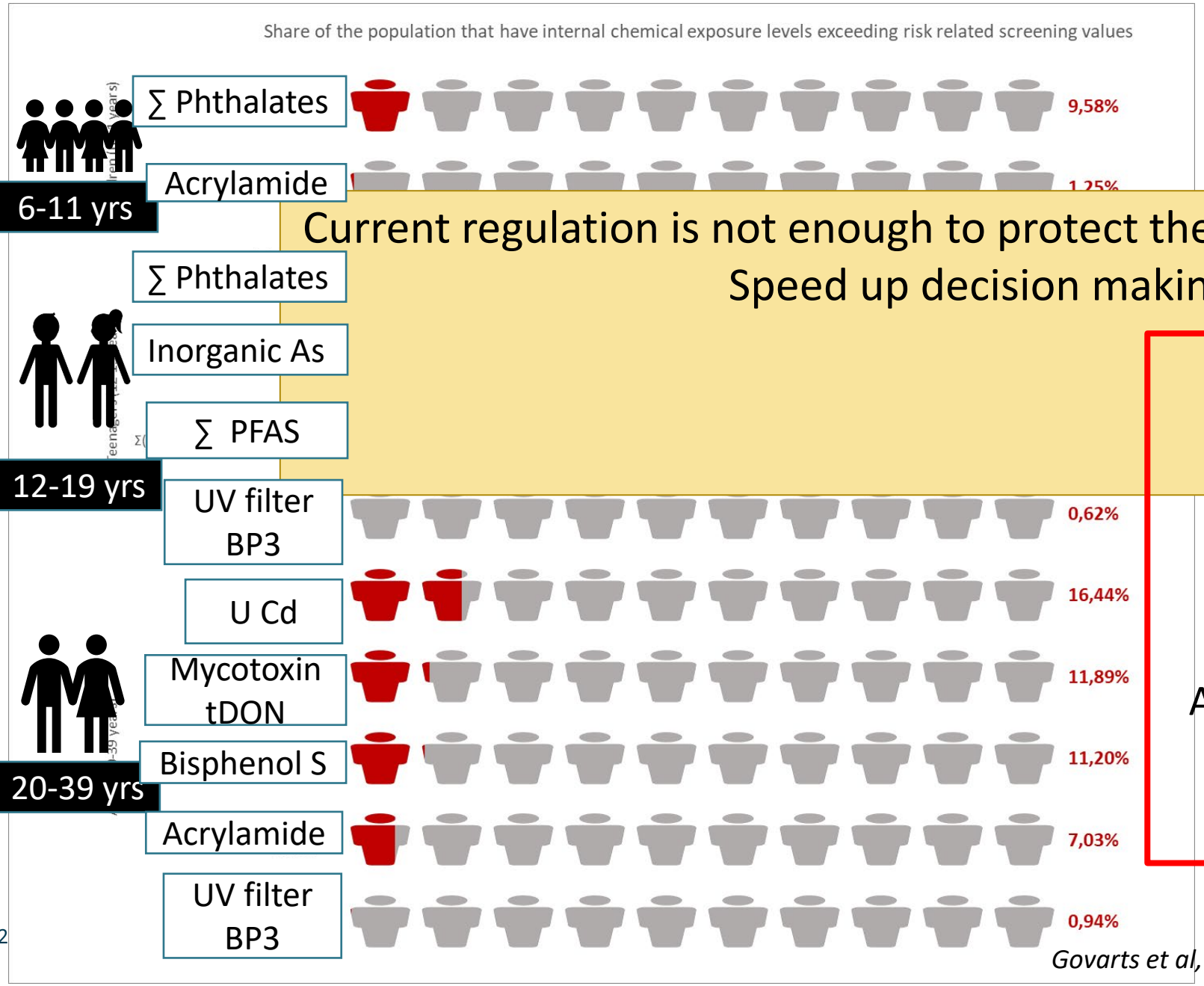
Fraction of children (HBM4EU aligned study) at risk from phthalate and DINCH



Regulate substances of similar chemical classes at group level to prevent regrettable substitution

Lange et al, Int J Hyg Environ Health. 2022 doi: 10.1016/j.ijheh.2022.114052.

Fraction of the HBM4EU aligned study population at risk



Current regulation is not enough to protect the population sufficiently
Speed up decision making

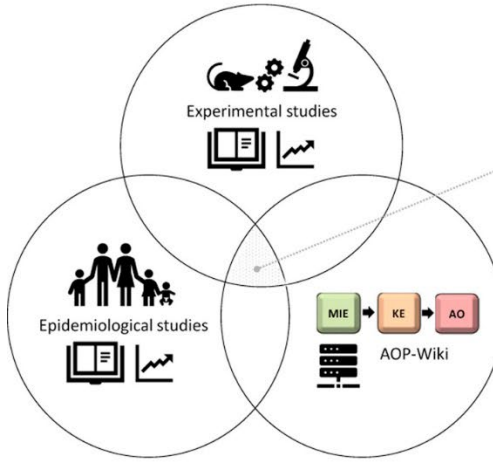
Exceedance of health based guidance values

↓

Adverse health outcomes cannot be excluded

Govarts et al, 2022, IJHEH, doi: 10.1016/j.ijheh.2023.114119

Exposure and health relationship in the aligned studies

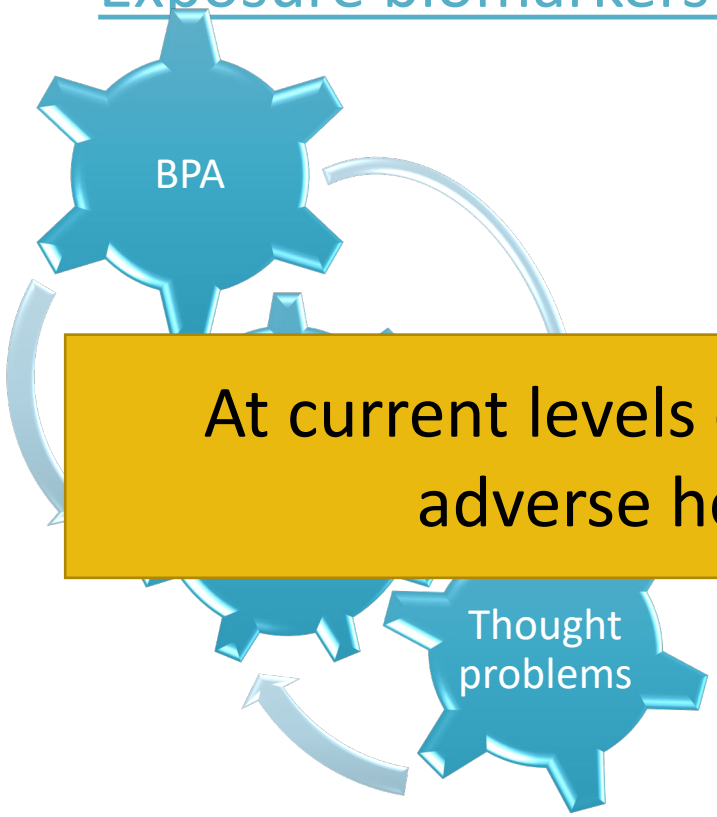


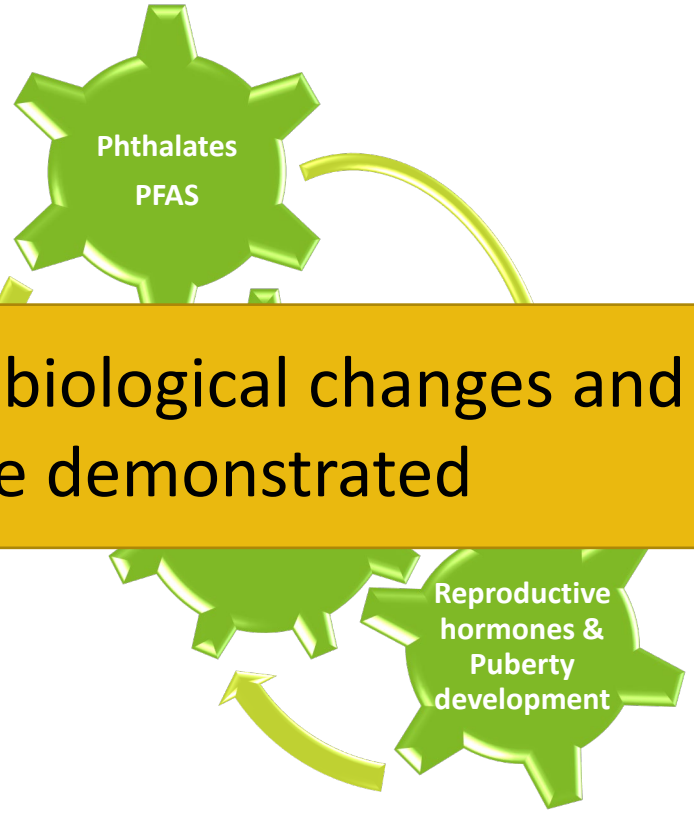
Exposure biomarker → Biochemical biomarker → Effect biomarker → Health outcome

		Molecular	Clinical	Health outcome
Flame retardants, Phthalates	Neurodevelopment	-TR Histone modification -BDNF methylation	- TSH, T3, T4 - LH, FSH - TT, E2 - SHBG - BDNF	- Neurobehaviour - Neuropsychological tests
Phthalates, PFAS	Sexual maturation	- ER, AR, PPARα, PPARγ Histone modification - Kisspeptin methylation	- LH, FSH - TT, E2 - SHBG - Kisspeptin - 8-OHdG	- Pubertal development - Sexual maturation
Phthalates, PFAS	Metabolism & BMI	- PPARα, PPARγ, GR, TR methylation - Kisspeptin methylation	- Glucose and insulin - TG, TC, HDL-C, LDL-C - Leptin, adiponectin - TSH, T3, T4 - Kisspeptin NEW - 8-OHdG	- BMI - Waist circumference - Body fat mass - Glucose intolerance - Diabetes - Hypertension

Baken et al, Environ Res. 2019 doi: 10.1016/j.envres.2019.05.013.
Rodríguez-Carrillo A., Int J Hyg Environ Health. 2023 doi: 10.1016/j.ijheh.2023

The causal chain:
Exposure biomarkers--- effect biomarkers --- health outcomes





At current levels of human exposure , biological changes and adverse health outcomes can be demonstrated

Mustieles et al, Environ Int. 2020 doi: 10.1016/j.envint.2020.105811.

Rodriguez-Carrillo A, Sci Total Environ. 2023 doi: 10.1016/j.scitotenv.2023.161668.

Regulatory actions needed – EU level

- **Bisphenols**
  - Regulate BPA substitutes and bisphenols as a group:
    - P95 of BPF is higher than P95 of BPA in 5 of 11 sampling sites (adults - aligned studies), median levels of urinary BPA substitutes are increasing in all European regions
- **PFAS**
  - PFAS as a group to further reduce exposure
  - Up to 23.8% of teenagers exceed the EFSA based guidance values for sum of 4 PFAS

UV filter
BP3

A sustainable **surveillance** HBM network for Europe is needed

- A sustainable network of QA/QC laboratories
- Harmonisation of materials and procedures
- Accessible and comparable HBM data

Research and follow up is needed

Develop early warning capacity

- Develop early warning capacity for chemicals of emerging concern
- Monitoring of internal exposure to substitutes (BPA, OPFRs) as levels are increasing
- Improve capacity for suspect and non-target screening
- Patterns in real life internal exposures
- Mixture exposures and effects

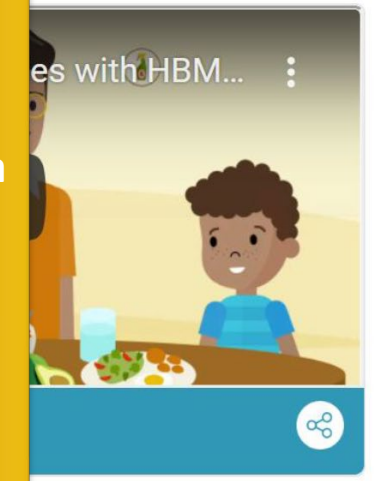
PARC

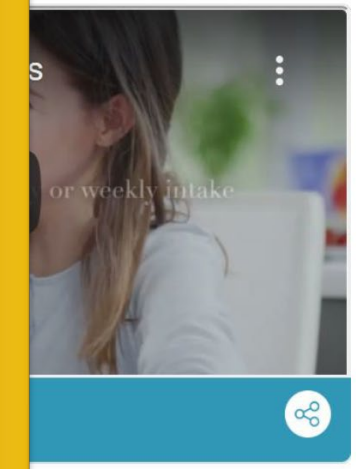
HBM4EU dissemination

Special Issue: Key results of the European Human Biomonitoring Initiative - HBM4EU Edited
by Marike KolossaGehring, Greet Schoeters, Douglas Haines, Argelia Castano, Robert Barouki, Alexandra Polcher, Philipp Weise
https://www.sciencedirect.com/journal/international-journal-of-hygiene-and-environmental-health/special-issue/109W6SHSZ74

Special Issue "Analysis of Human Biomonitoring Data and Risk Assessment of Human Exposure to Environmental Chemicals: What Do We Learn for Prevention?"
https://www.mdpi.com/journal/toxics/special_issues/Human_Biomonitoring_Europe

https://www.hbm4eu.eu/





greet.schoeters@uantwerpen.be

Thank you:

HBM4EU research partners

HBM4EU management board

HBM4EU policy board

National hubs

Stakeholders

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