

For our environment

Umwelt 
Bundesamt

HBM4IRE

HBM in support of regulatory actions and policy making

Marika Kolossa-Gehring & team

Section II 1.2 Toxicology, Health Related Environmental Monitoring

Human Bio Monitoring

Since 1970 in Germany...



Internal exposure



Identification of sources



Reduction measures

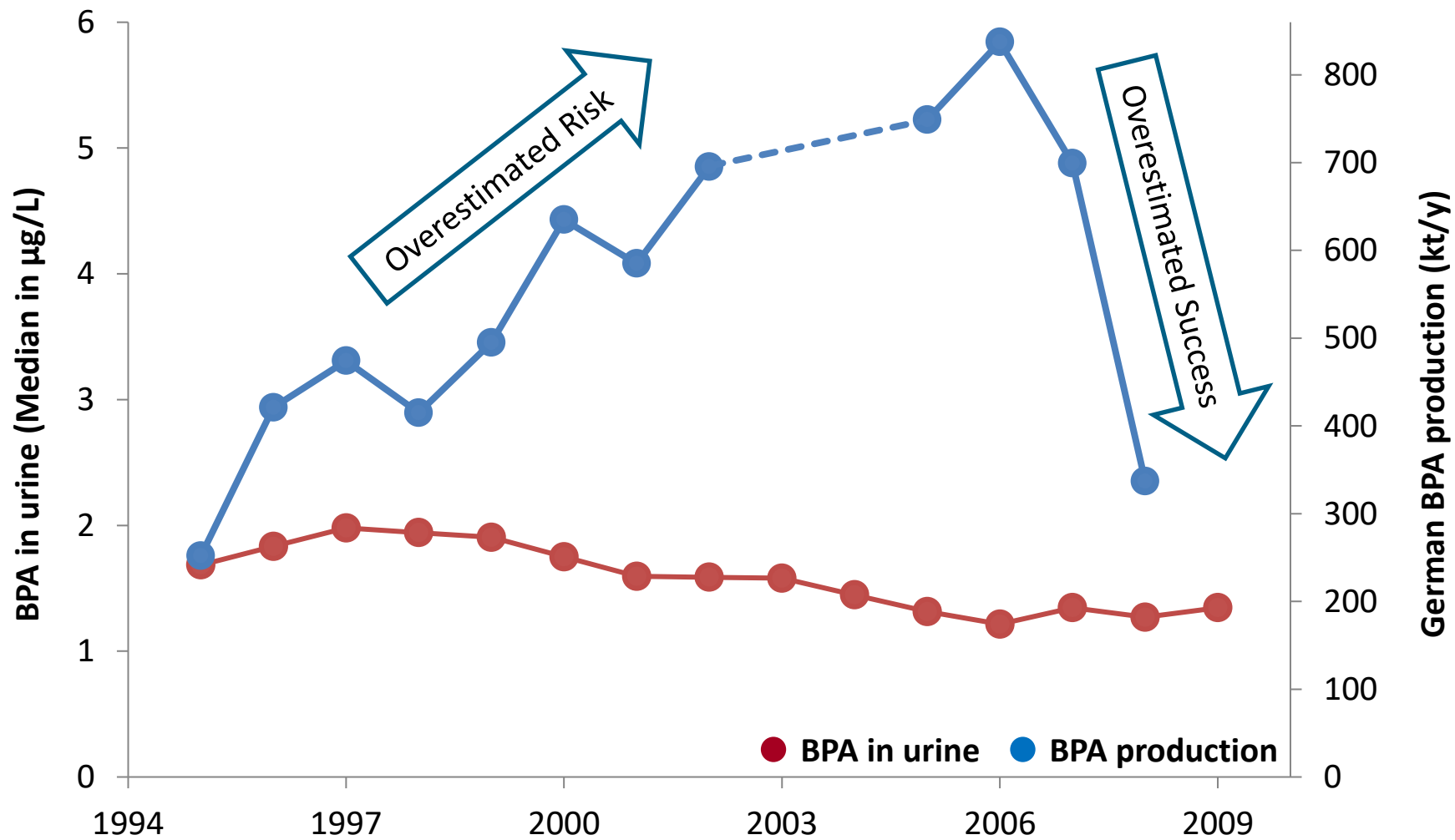


Policy recommendations



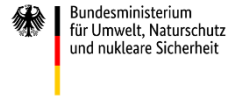
Control of success

The use of HBM: Bisphenol A - time trend (ESB)



Data from the German Environmental Specimen Bank

The German HBM system

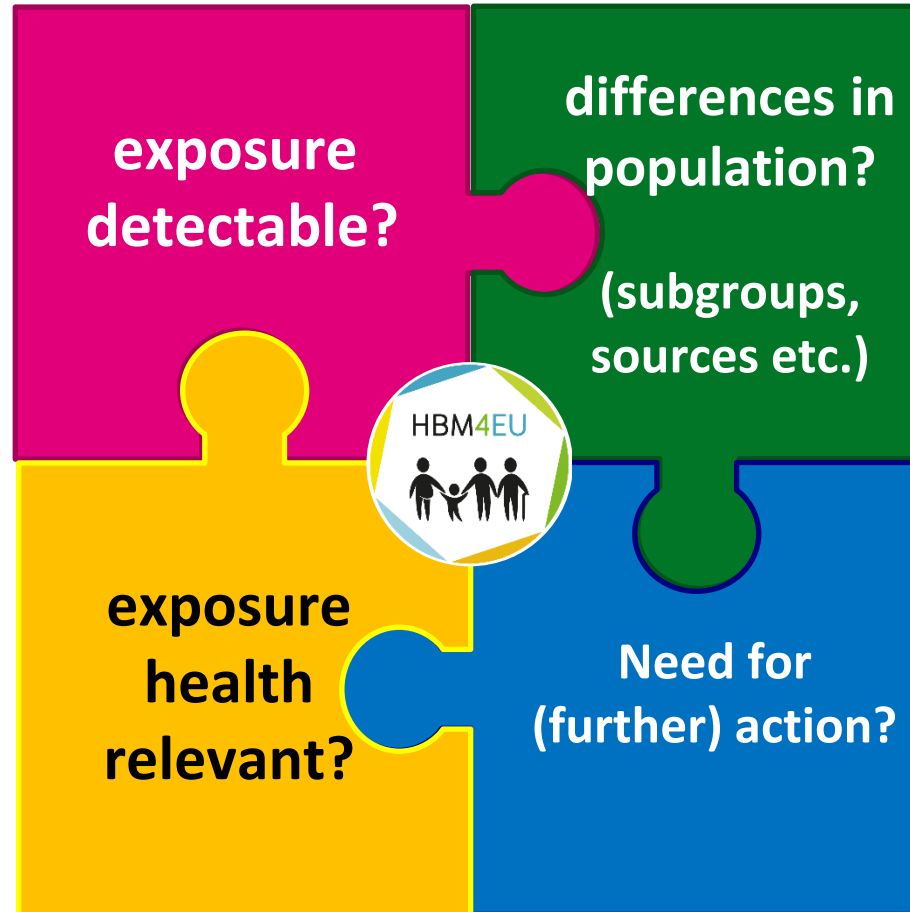


Co-operation for the further development of HBM

- new methods of analysis for health relevant substances



Human Biomonitoring Commission at UBA
- toxicologically derived HBM-values



German Environmental Survey (GerES)

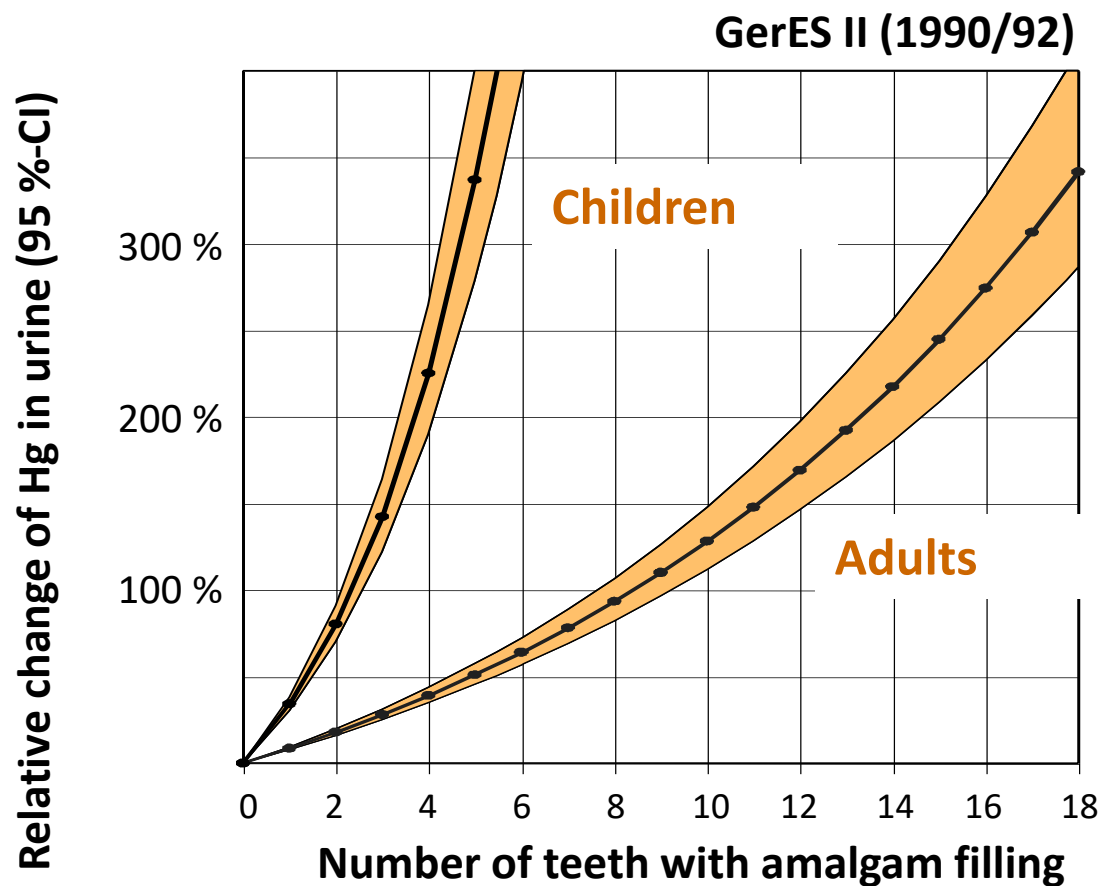
- population-representative HBM
- ambient monitoring
- interviews



German Environmental Specimen Bank (UPB)

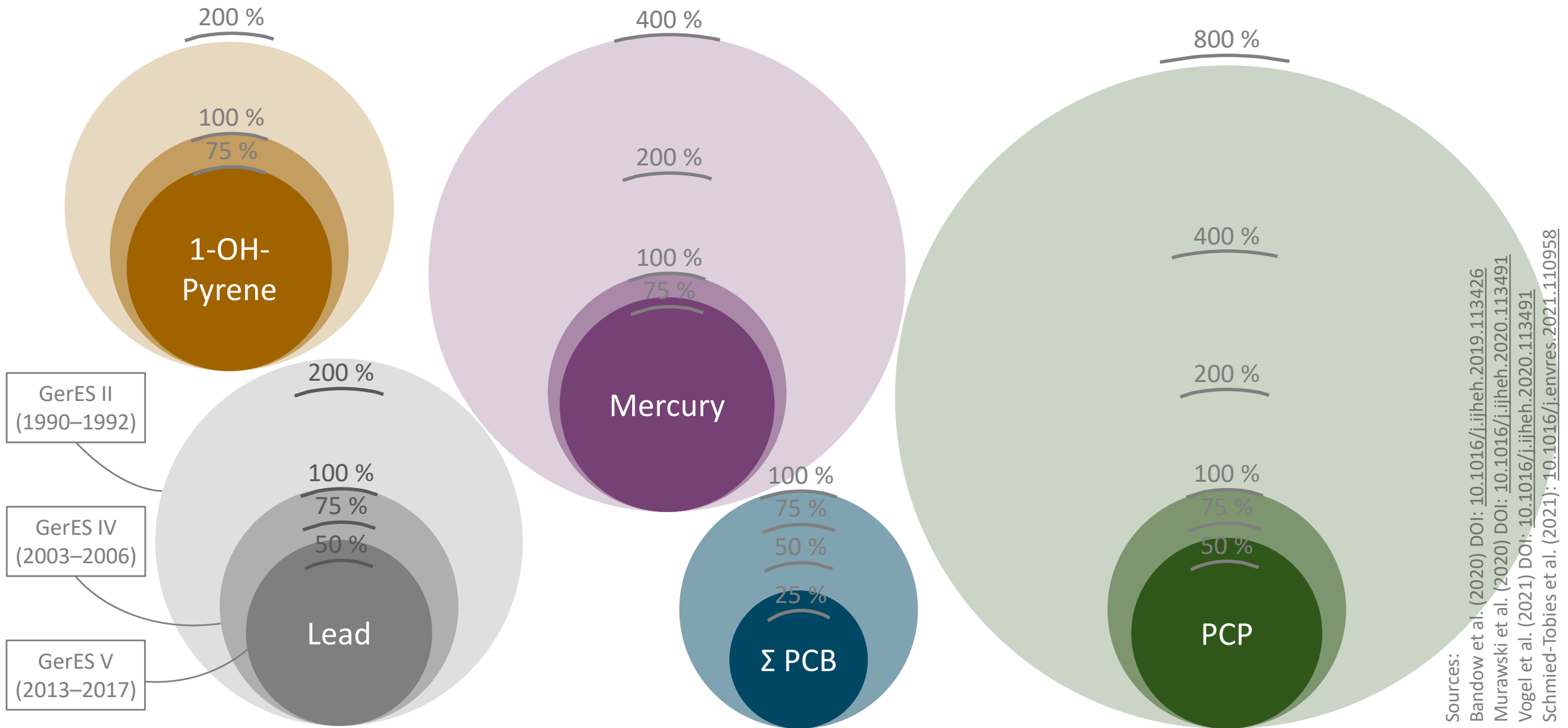
- retrospective monitoring
- time trends
(background exposure)

Protecting children's health: amalgam fillings and mercury in urine



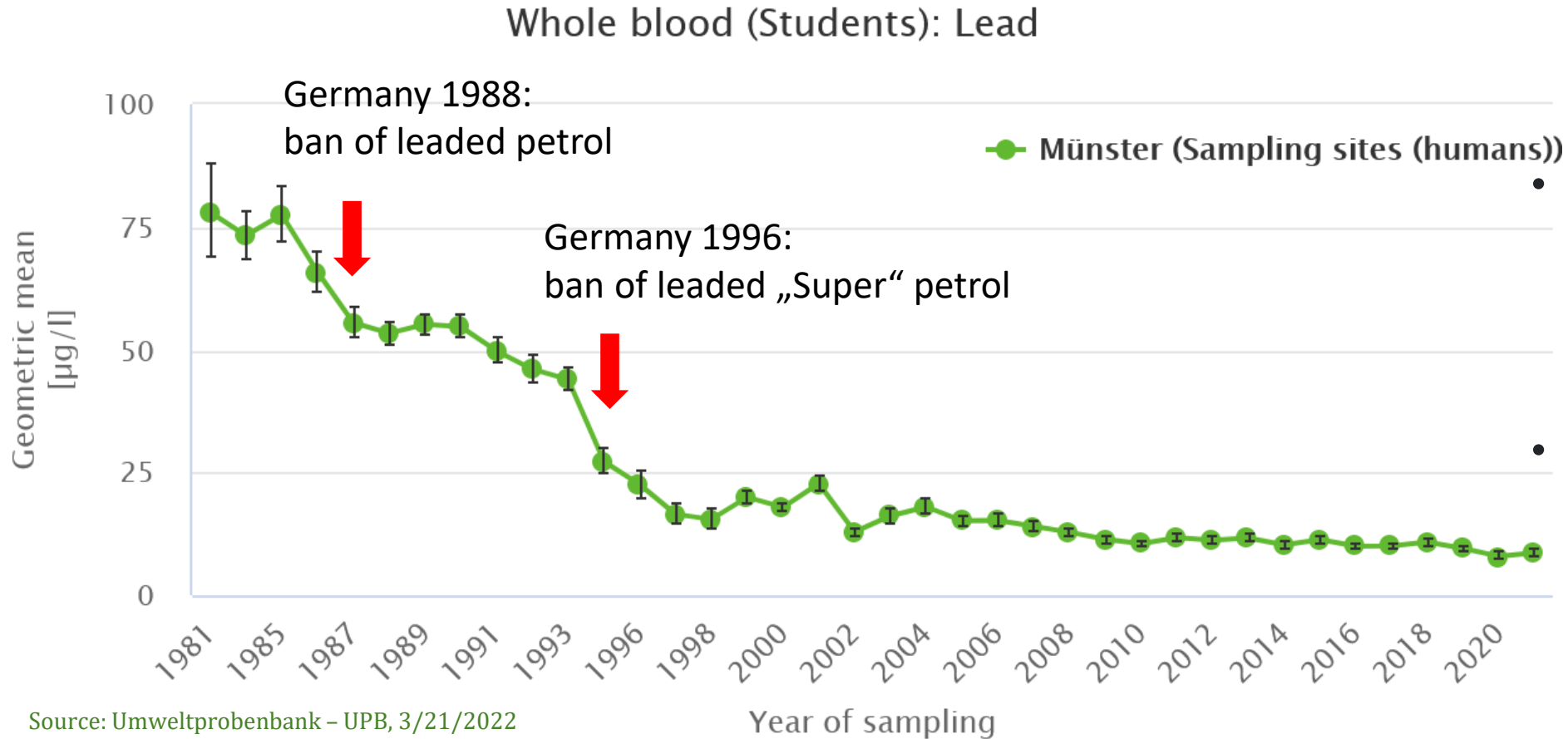
Official recommendation of the Federal Health Agency (1992):
The use of amalgam fillings for children under 6 years should be carefully assessed.

Declining exposure to „classic“ pollutants – regulations are effective!



Sources:
Bandow et al. (2020) DOI: [10.1016/j.ijheh.2019.113426](https://doi.org/10.1016/j.ijheh.2019.113426)
Murawski et al. (2020) DOI: [10.1016/j.ijheh.2020.113491](https://doi.org/10.1016/j.ijheh.2020.113491)
Vogel et al. (2021) DOI: [10.1016/j.ijheh.2020.113491](https://doi.org/10.1016/j.ijheh.2020.113491)
Schmied-Tobies et al. (2021): [10.1016/j.envres.2021.110958](https://doi.org/10.1016/j.envres.2021.110958)

The use of HBM: Lead – a time trend (ESB)



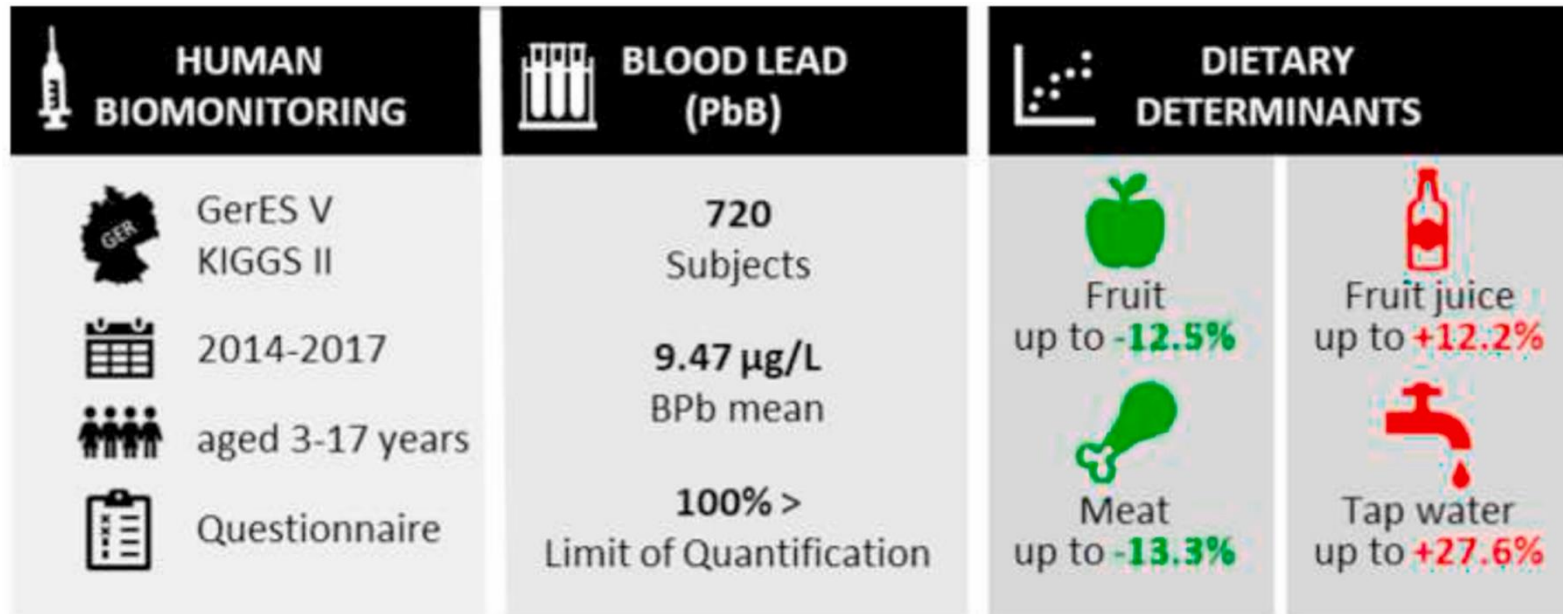
Source: Umweltprobenbank - UPB, 3/21/2022

- Mean body burden of >70 µg/L in 1981 was **reduced** within 26 years by about **83%** (levels < 15 µg/L in 2008!)
- In the past few years: exposure to lead constantly low: 2018 mean ~ 10 µg/L.

➡ HBM data allowed to check the effectiveness of a policy measure!

So is lead not an issue anymore?

Current data from GerES V:



From Hahn et al. (2022) <https://doi.org/10.1016/j.envpol.2021.118699>



Lead is still an issue: tap water, meat and fruit juice being the main dietary determinants of exposure.

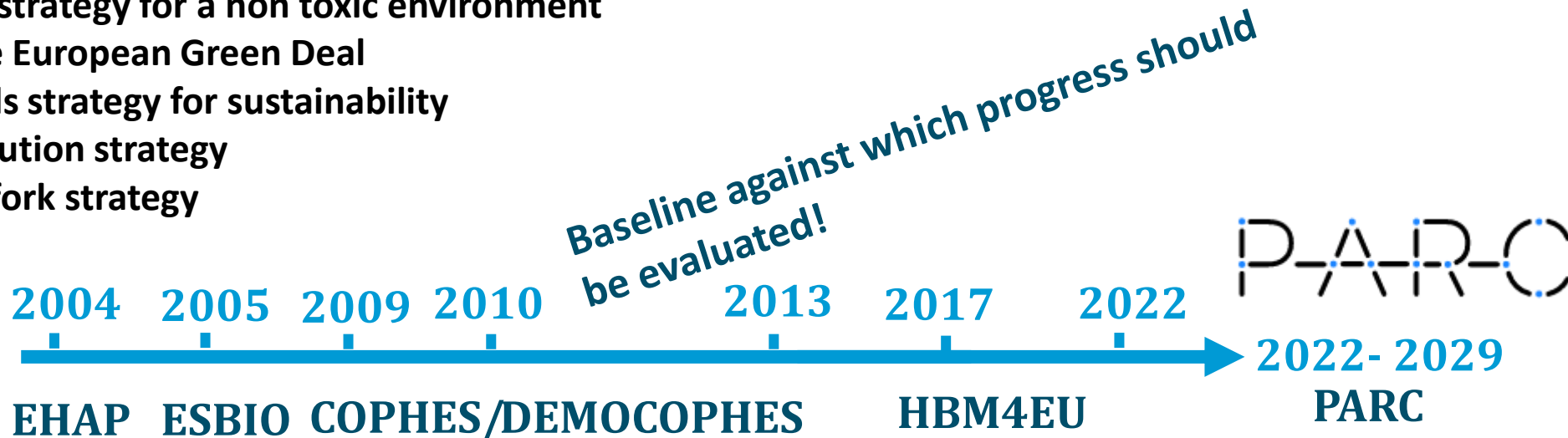
International Agency for Research on Cancer has classified lead with its inorganic compounds as a “possible human carcinogen” (group 2 A; IARC, 2006).

HBM commission: HBM-value for lead suspended

- no „safe“ concentration at and below which, according to the current knowledge and assessment by the HBM Commission, there is no risk of adverse health effects, and, consequently, no need for action

Why human biomonitoring in Europe?

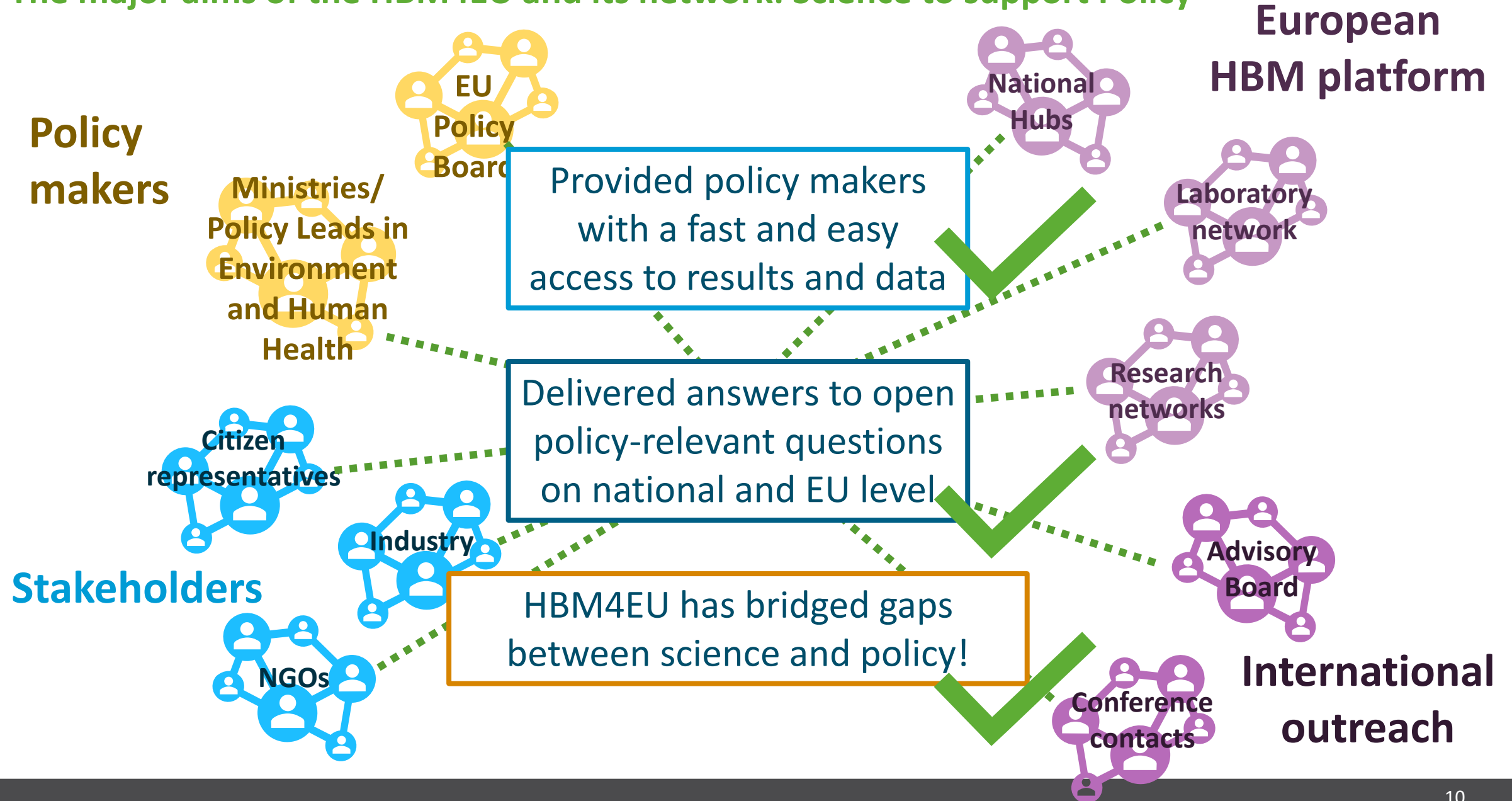
- EU Environment and Health Action Plan (EHAP), *Action 3: A coherent HBM for Europe*
- 7th Environmental Action Programme (2013): Living well, within the limits of our planet
- 2018 EU strategy for a non toxic environment
- 2020 The European Green Deal
- Chemicals strategy for sustainability
- Zero pollution strategy
- Farm to fork strategy



Push for indicators:
Need to monitor ongoing trends in exposure!



The major aims of the HBM4EU and its network: Science to support Policy



The European Human Biomonitoring Initiative (HBM4EU)

European HBM platform

Laboratory network

National Hubs

Big step towards harmonisation of HBM in Europe



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



Harmonised procedures, methods & data

and data

166 labor
45% of th

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

Templates, SOPs, Guidelines and Questionnaires, Communication Materials



HBM4EU aligned studies 25 studies, 21 countries

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

HBM4EU results: Cadmium

Determinants of exposure
(HBM4EU Aligned studies):
POOLED ANALYSIS

Cd in urine ($\mu\text{g/g crt}$)	Coeff (95% CI), BASIC MODEL
<i>n</i>	2475 (9 groups)
<i>overall p-value</i>	<0.001
Age (years)	1.03 (1.02-1.04)**
Sex (F vs. M)	1.33 (1.26-1.40)**
Smoking (yes vs. no)	1.25 (1.17-1.33)**
Isced - low	1.00
Isced - medium	0.86 (0.76-0.97)*
Isced - high	0.86 (0.76-0.96)*
Sampling year	0.96 (0.93-1.00)*

$p < 0.10$, * $p < 0.05$, ** $p < 0.01$

Mixed models, country as a random effect
(additionally adjusted for **crt**, **sample type**,
sampling season)

Adding potential dietary exposure sources to the basic model:

Vegetarian diet → 36 % increase in urine Cd

Cropland → 0.3 % increase in urine Cd per each % of cropland

Phosphorus fertilizer → 68 % increase in urine Cd per increase 1 t/km²

(All statistically significant, $p=0.001$, 0.030 and <0.001 respectively)

- Main determinant: used to be smoking, now **vegetarian diet!**
- Connection to phosphate fertilisers
- **Cadmium cancerogenic**

HBM results show, that exposure to chemicals must be reduced at the source, especially when looking at future paths for human diet!

Tratnik et al. 2022

Bisphenols used in polymerisation (e.g. epoxies)

Bisphenol A (BPA)

Toxic to reproduction

Skin sensitising

Endocrine disrupting

CoRAP/SVHC/some uses restricted

Bisphenol S (BPS)

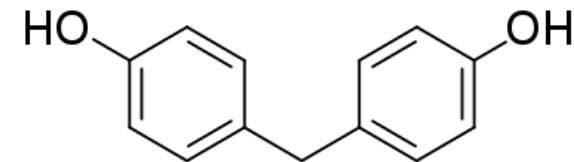
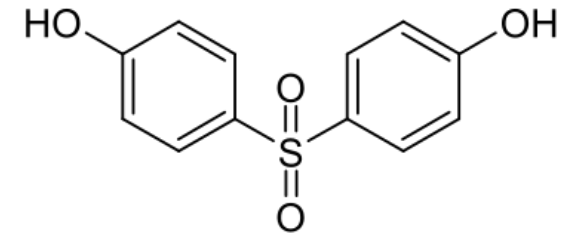
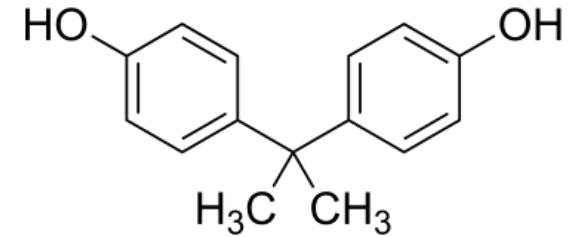
Toxic to reproduction

Endocrine disrupting

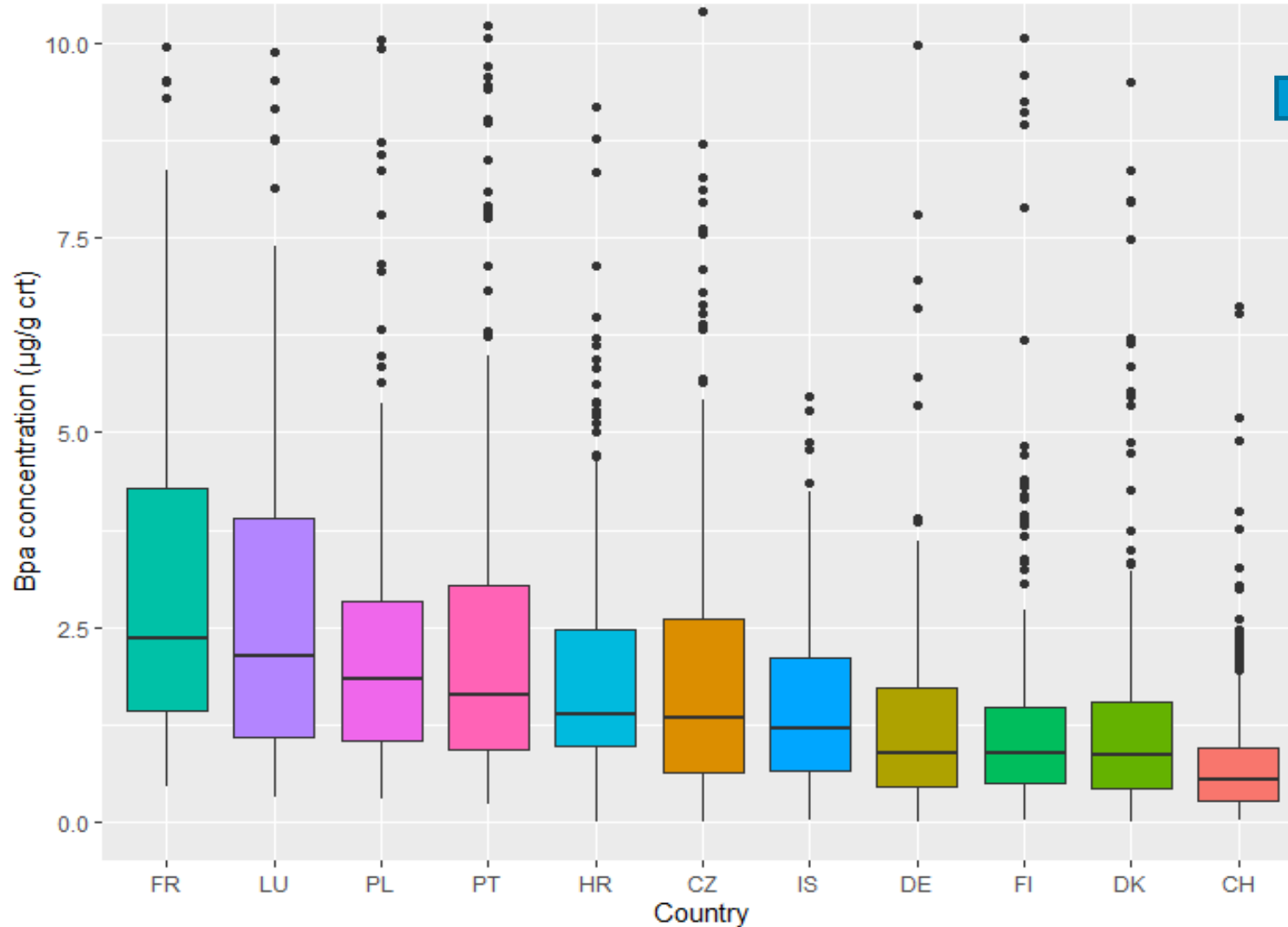
CoRAP/SVHC

Bisphenol F (BPF)

Considered skin sensitizing



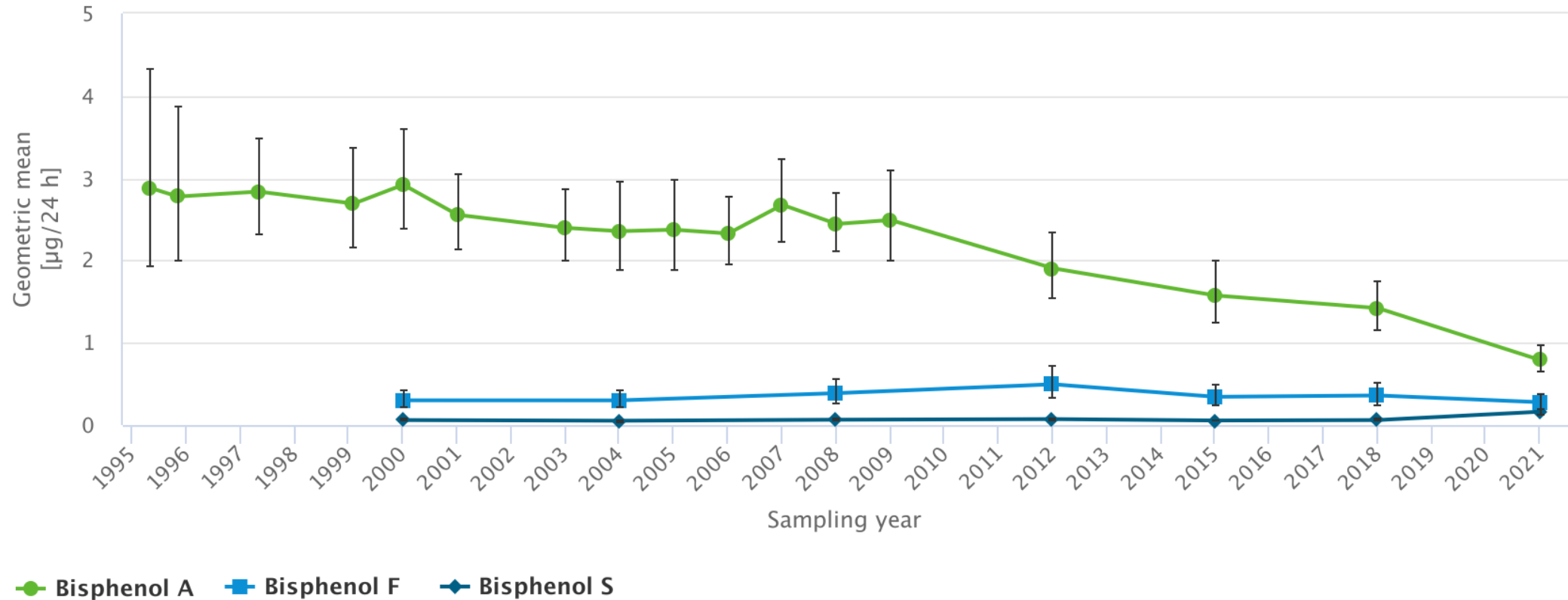
HBM4EU results: Bisphenol A - an exception or an indication of a systematic problem?



- Differences in Europe
- The new „EFSA-Opinion“: tolerable daily intake reduced by a factor of **20.000 (!)**
-> **0,2 ng/KG bw per day**

The previously established assessment system underestimated adverse effects by several orders of magnitude!

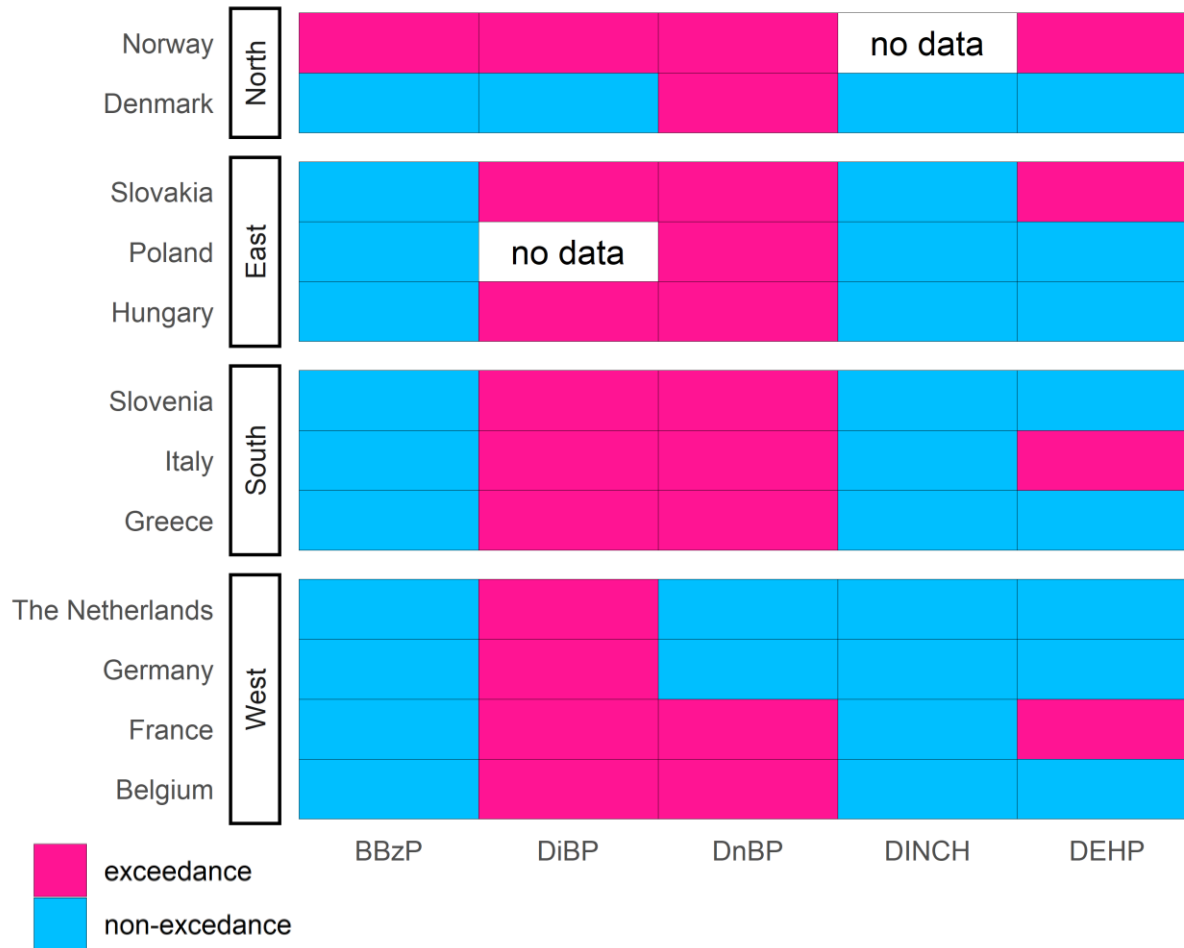
Bisphenols: regrettable Substitution



Values > LOQ:	<u>2000</u>	<u>2008</u>	<u>2021</u>
BPA	100%	98%	71%
BPS	20%	21%	60%
BPF	43%	41%	28%

Human Biomonitoring underlines need to act

Aligned Studies data: Phthalates in children (6-12 yrs)

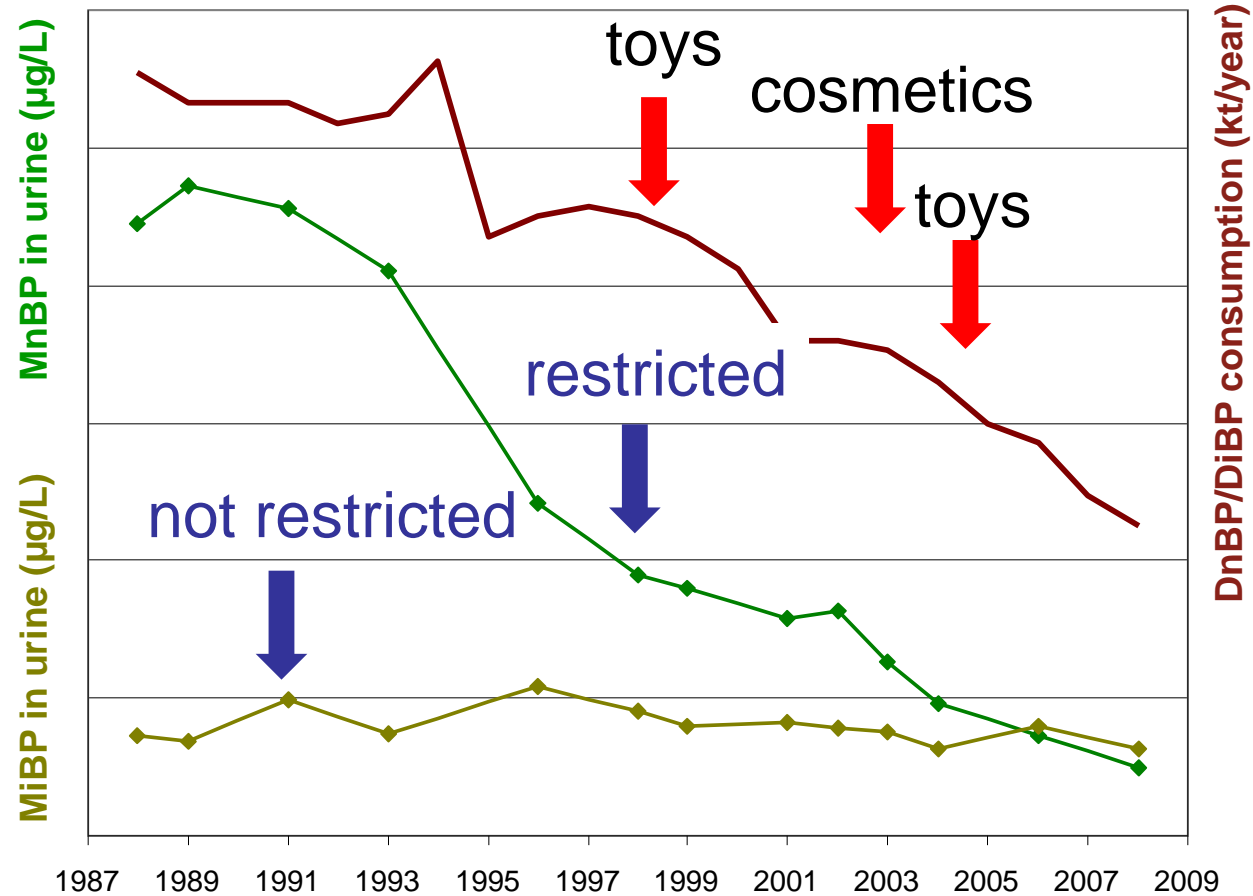


HBM4EU provides evidence:

People in Europe are still so highly **exposed** that **they are not safe** from health impacts caused by chemicals exposure



HBM – best exposure data available DnBP/DiBP consumption and MnBP, MiBP in urine: 1988 - 2008



- data from **ESB** (Munster, n=60/year, analysed by Koch/Göen University Erlangen), median;
- annual **consumption** of Σ DnBP and DiBP in Western Europe.

Phthalates: Infographic

1 Possible sources of exposure

Plastic tableware containing phthalates

Toys

Personal care products

Fabrics

Medical devices

Air & dust contaminated released from consumer products

2 How can phthalates enter your body?

Via ingestion

Via dermal absorption

3 How might phthalates affect your health?

- Attention deficit disorder, hyperactivity disorder
- Hormonal changes that can lead to health effects
- Asthma
- Insulin resistance
- Obesity
- Infertility

4 How can you reduce your exposure to phthalates?

- Do not microwave plastic utensils containing phthalates
- Prefer glassware to store food and beverages
- Read product labels and choose to use phthalate-free products
- Clean and air your home regularly to remove dust
- Choose fresh products rather than prepacked and processed food and drinks

The full infographics on phthalates and more substances at:

www.hbm4eu.eu



science and policy for a healthy future



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

The European Union has taken action to reduce phthalates known to cause risks including several phthalates in all articles, prohibiting the use in articles, and setting legal limits for certain phthalates in materials in direct contact with food.

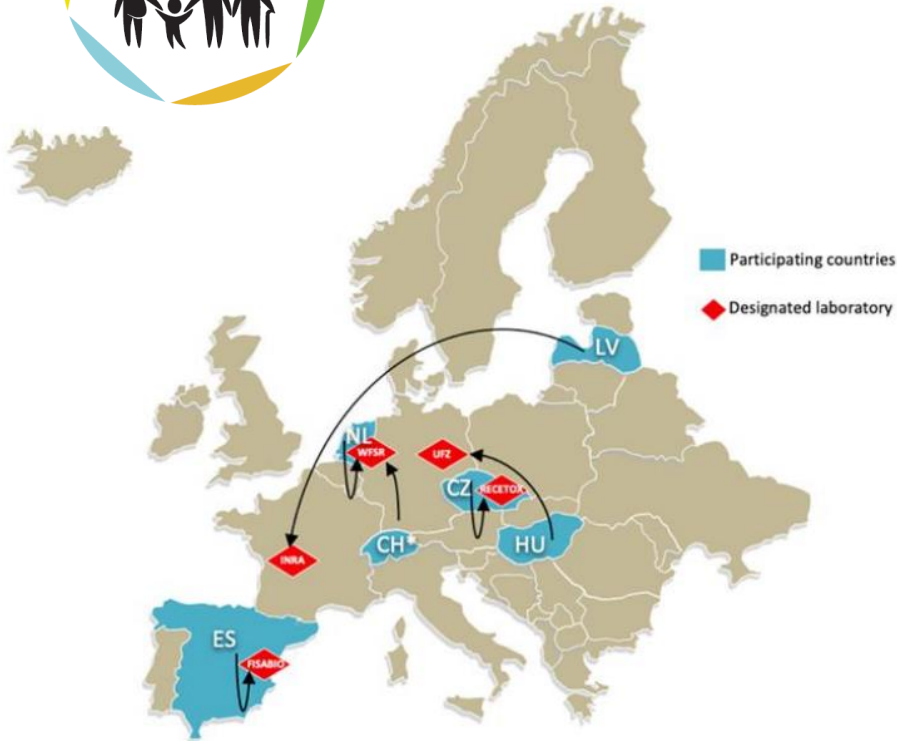
For more information on how the European Commission is helping citizens read the [HBM4EU Phthalates Factsheet](#).

Children are more sensitive to phthalates exposure, especially during early growth.

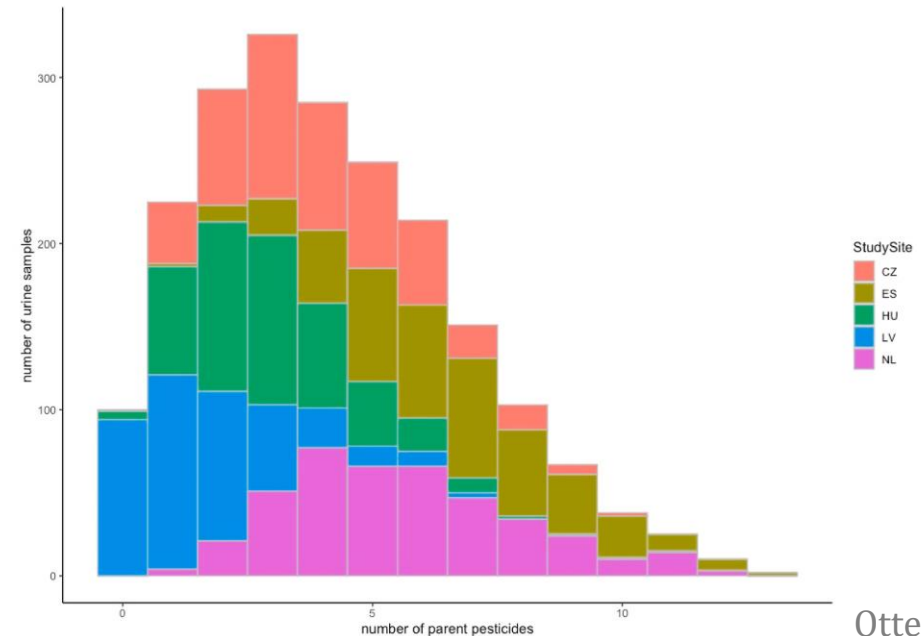
Multimethods and suspect screening



SPECIMEn study



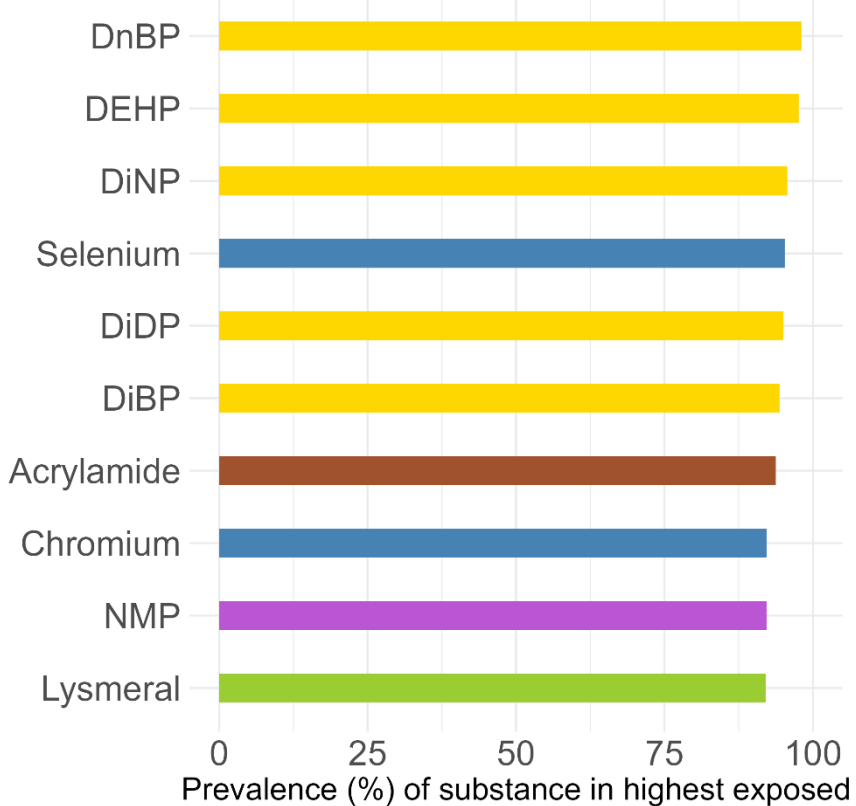
- 29 pesticides were identified at high levels of confidence in samples across all countries
- Mixtures: med. 3, max 13 pesticides per sample
- Examples:
Acetamiprid, Boscalid, Chlorpyrifos, Fludioxonil, Fluvalinate, Triclosan



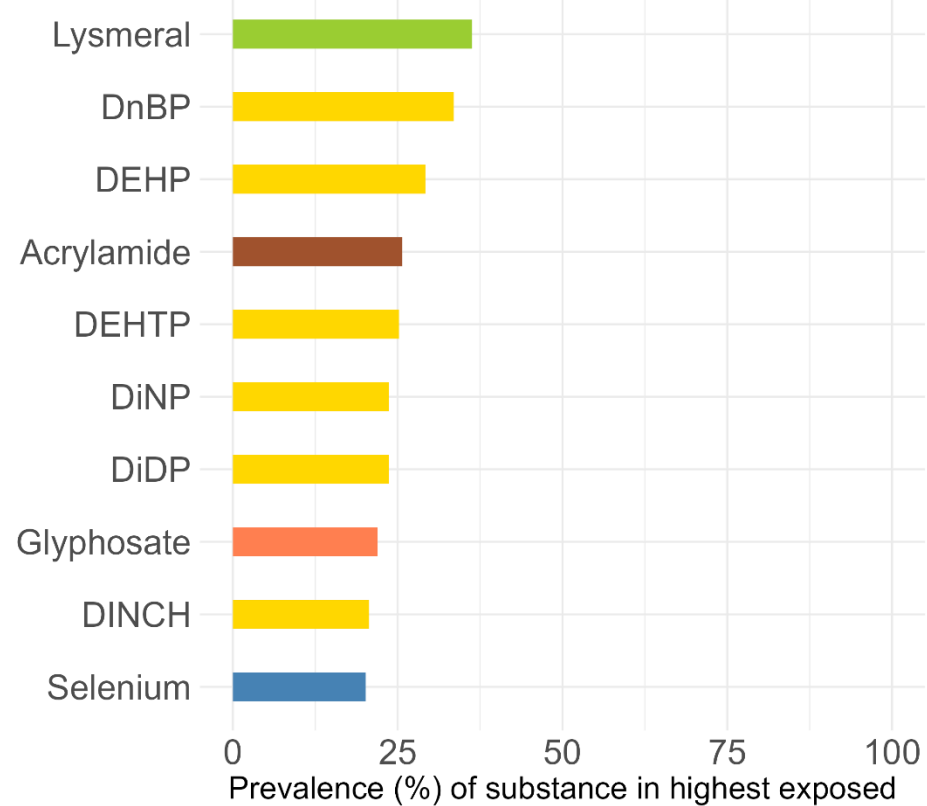

When it rains, it pours: substance mixtures

Drivers of 25% highest exposed individuals (children & adolescents) in P50 and P95

based on Median Exposure Load



based on P95 Exposure Load

phthalates and substitutes




fragrances




metals and metalloids



acrylamide



preservatives, biocides, solvents



pesticides

Lysmeral, acrylamide, phthalates, and selenium are important drivers of exposure burden in highest exposed individuals

Based on Willey et al. 2021

MnHexP – tracking down the exposure

Mono-n-Hexylphthalate (MnHexP)

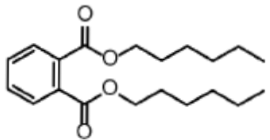


→ MnHexP in urine (children & adults)

PARC

→ „Rapid Response Mechanism“

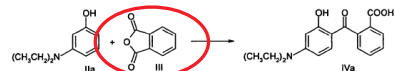
Di-n-Hexylphthalat
 → CLP: Repr 1B, H360 FD
 → SVHC, REACH Annex XIV
 → REACH: no registration



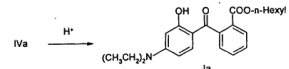
Evidence 1 BASF

→ The Patent

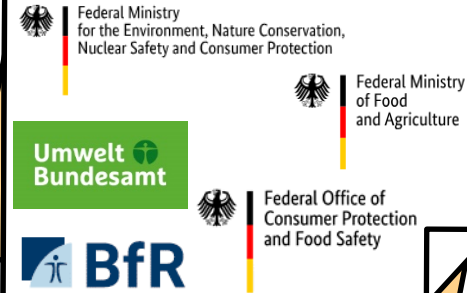
WO 2003/097578



II. anschließende Veresterung der in der 1. Stufe gebildeten 2-(4-N,N-Diethylamino-2-hydroxybenzoyl)benzoesäure der Formel IVa mit Hexanol. Gegenwart eines sauren Katalysators zum 2-(4-N,N-Diethylamino-2-hydroxybenzoyl)benzoesäure-n-Hexylester der Formel Ia.



Coordination Board

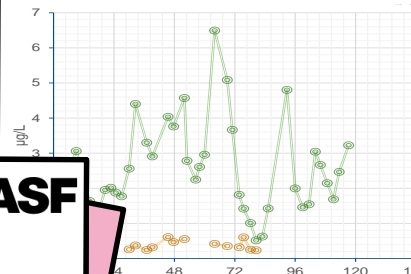


Evidence 2 → The Products

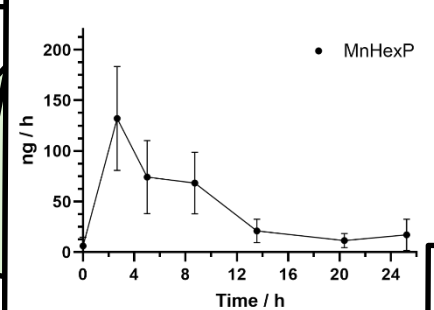


Clue 1 → The Self-experiment

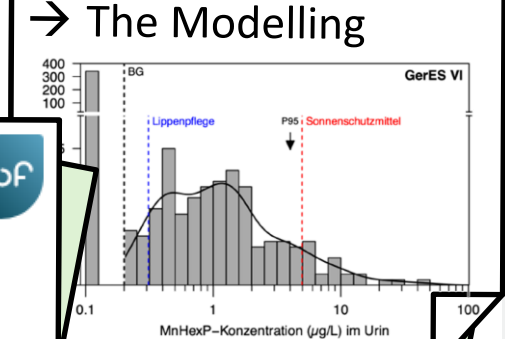
→ The Self-experiment



Clue 2 → The Kinetics study



Clue 3 → The Modelling



MnHexP – case solved!

**Mono-n-Hexylphthalate
(MnHexP)**



Conclusion

HBM data

- *are needed and used for regulatory decisions in Europe (binding regulation)*
- *are essential to raise awareness and inform citizens and their decisions*
- *reveal gaps in the regulatory system*
- *serve as early warning*

Outlook:

- *a sustainable HBM für Europe needed*
- *mixtures and the assessment of realistic exposure scenarios in humans need more efforts*

Aligned Studies

PFAS

Phthalates and substitutes

Bisphenols

Organophosphate flame retardants

Pesticides

Metals



Greetings from the HBM team at UBA (Section II 1.2)!



... and more!

Thank you for your attention!

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<https://www.hbm4eu.eu/>

<https://www.EU-PARC.eu>

<https://www.umweltprobenbank.de/en/documents>

