



science and policy
for a healthy future

Phthalates and Hexamoll DINCH[®]

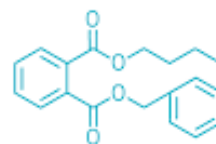
Currently available HBM-
evidence in Europe and
ongoing work in HBM4EU in
relation to identified policy

HBM4EU Workshop of Task 5.5 – Phased Action Plan

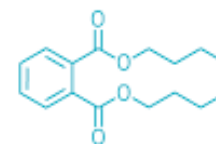
Brussels, 8 – 9 November 2018

Phthalates and DINCH – Priority Substance Group

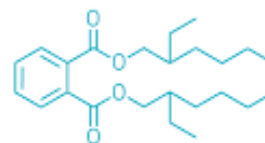
- Large group of substances used as plasticisers in variety of products



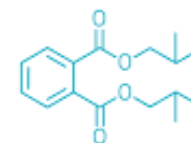
Butylbenzyl phthalate (BBP)



Di-n-butyl phthalate (DBP)



Di(2-ethylhexyl) phthalate (DEHP)



Diisobutyl phthalate (DIBP)

Source: cen.acs.org



- Many identified as toxic to reproduction and/or having endocrine disrupting properties

- High frequency of detection



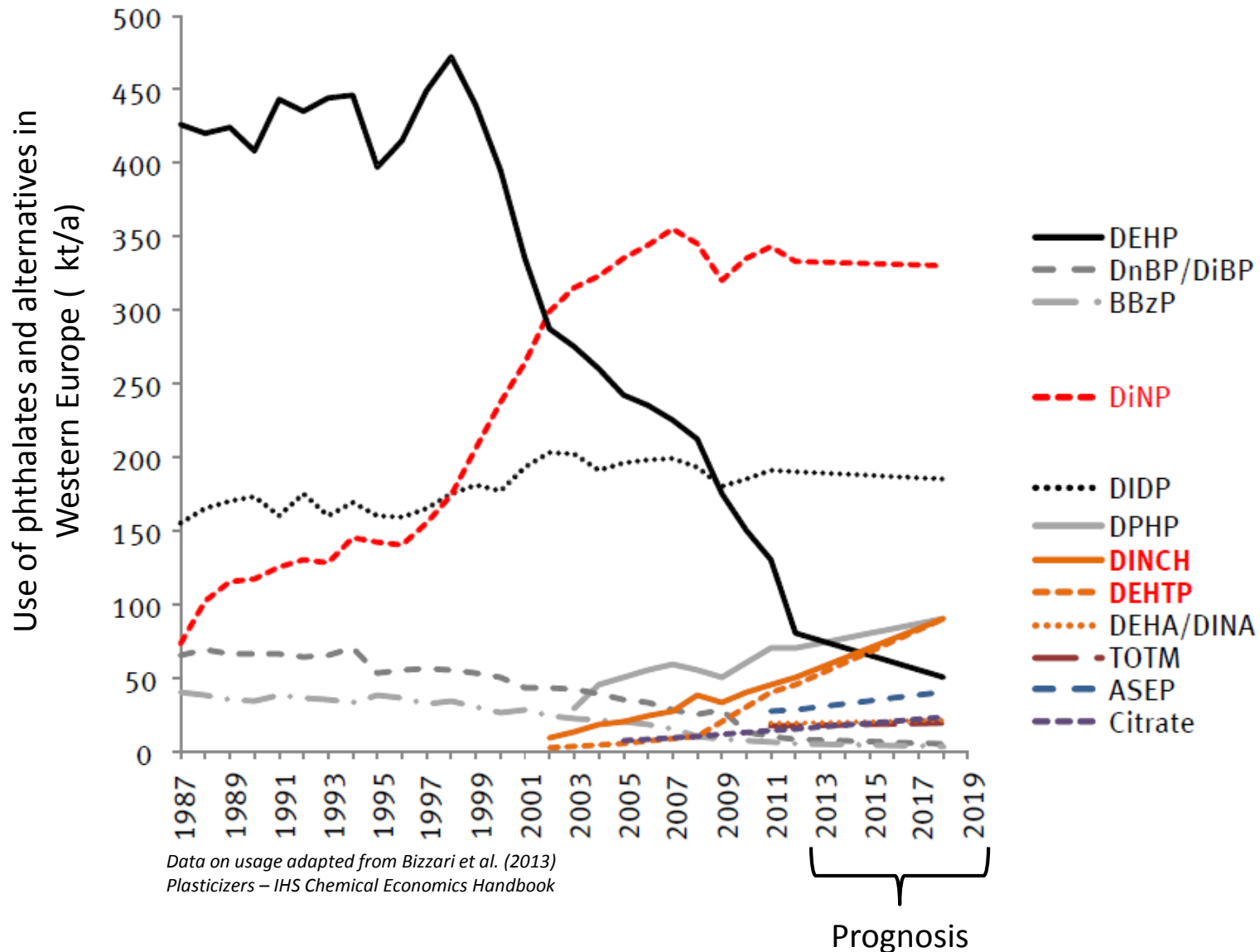
Phthalates and DINCH – Regulation

Substance	Substance of Very High Concern	Regulation
DEHP	Toxic for reproduction (Article 57c), Endocrine disrupting properties – human & environment (Article 57f)	REACH: Annex XIV & Annex XVII, Entry 51
BBzP	57c 57 f (human)	REACH: Annex XIV & Annex XVII, Entry 51
DnBP	57c 57 f (human)	REACH: Annex XIV & Annex XVII, Entry 51
DiBP	57c 57 f (human)	REACH: Annex XIV
DiNP	-	REACH: Annex XVII, Entry 52
DiDP	-	REACH: Annex XVII, Entry 52
DIDP	-	REACH: Annex XVII, Entry 52

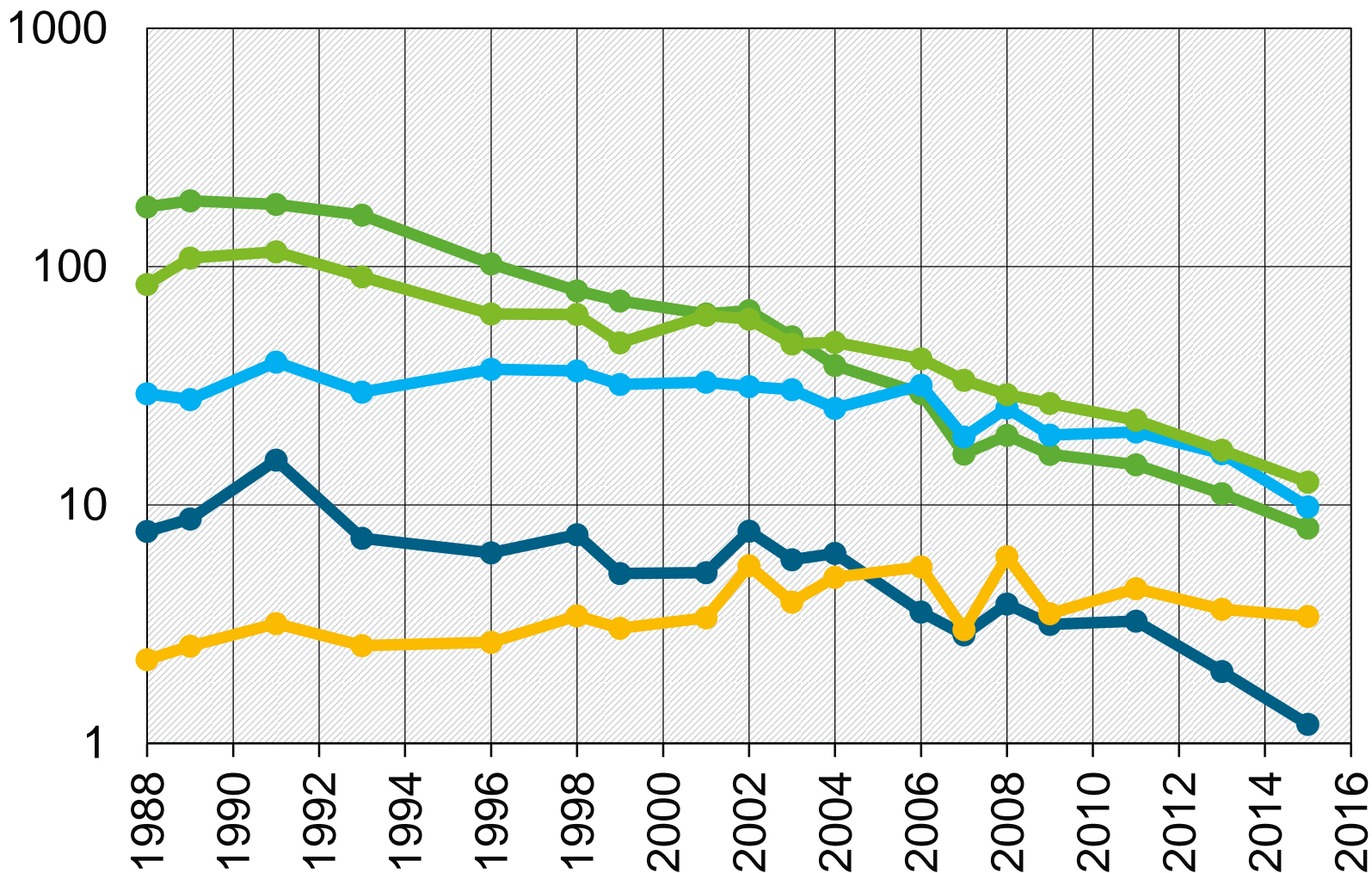
Phthalates and DINCH in Europe – DEMOCOPHES

- 16 countries measured metabolites of DEP, DiBP, DEHP, DnBP and BBzP in mother-child pairs (2011-2012)
- LOQs >80% for all metabolites
- Children higher exposed compared to mothers
- Few exceeded HBM-I/BE values
- Exposure differences in countries

Phthalates and DINCH– Change in usage



Phthalates and DINCH – Exposure trends Germany

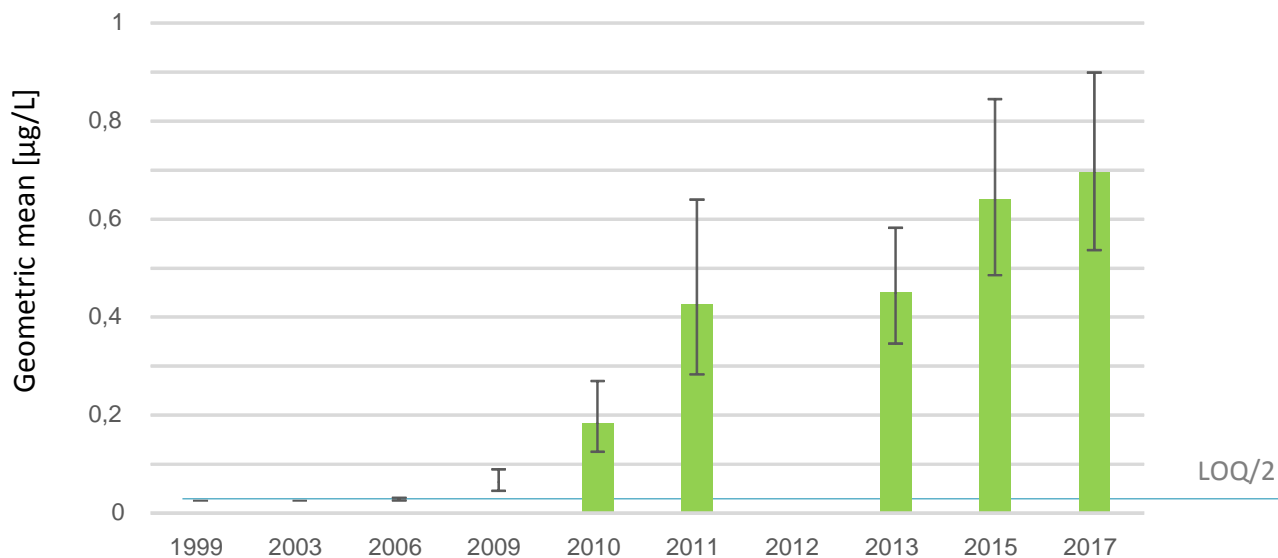


Metabolites of **DnBP**, **DEHP**, **BBzP**, **DiBP**, **DiNP**

Phthalates and DINCH – Exposure trends Germany

UNPUBLISHED DATA

OH-MINCH (DINCH)



Market introduction

High detection frequencies seen in Germany, Sweden, Portugal

Phthalates and DINCH – Exposure trends Germany

UNPUBLISHED DATA

DEHTP levels increase since 2009 continuously

DEHP, DnBP, DiBP
and BBzP where classifies as SVHC 2008

Detection rates of DPHP also increase.
This increase is closely related to the increase in consumption

Phthalates and DINCH – Exposure trends

- Downward trend for some phthalates indicated in Germany, Sweden, partly Denmark and Belgium (DnBP, DEHP), France
- Nevertheless, high detection frequencies in seen in studies of Denmark, France, Germany, Austria, Sweden
- Increasing trend indicated for alternatives: DINCH (Germany, Sweden) and DEHTP, DPHP (Germany)
- DCHP, DnPeP, DnOP are detected in very few samples at low concentrations (Austria, Denmark, Germany)

Phthalates and DINCH – Exposure trends & policies

- Extensive restrictions → still high detection frequencies (Austria, Germany, Denmark, France, Sweden)
 - HBM4EU: How is the current exposure (incl. Detection frequencies) from 2015 on for DEHP, DnBP, BBzP, DiBP (restriction proposal)
- Increasing trends for alternatives → in Germany already critical levels detected
 - HBM4EU: How is the current exposure for alternatives? Exposure sources (food contact materials: DINCH/DEHTP; sources for DPHP?)
 - HBM4EU: HBM HBGVs for alternatives
- Mixture issue between phthalates and also with other anti-androgenic substances
 - HBM4EU: mixture case study with other anti-androgenic compounds & sum HBM HBGVs for phthalates possible?

Phthalates and DINCH – Research Questions

Main research questions to be answered within HBM4EU

- What is the **current exposure** in Europe?
 - Are there **differences in countries**?
 - How **effective** have the **regulations** been?
 - Are there **high exposure groups**?
 - What are the exposure **sources**?
 - Exposures of **health relevance**? Is it depending on age? Sex? SES?
...?
- Focus also on **substitutes** due to increased use (DINCH, DPHP)
- Take into account the effects of **combined exposures**

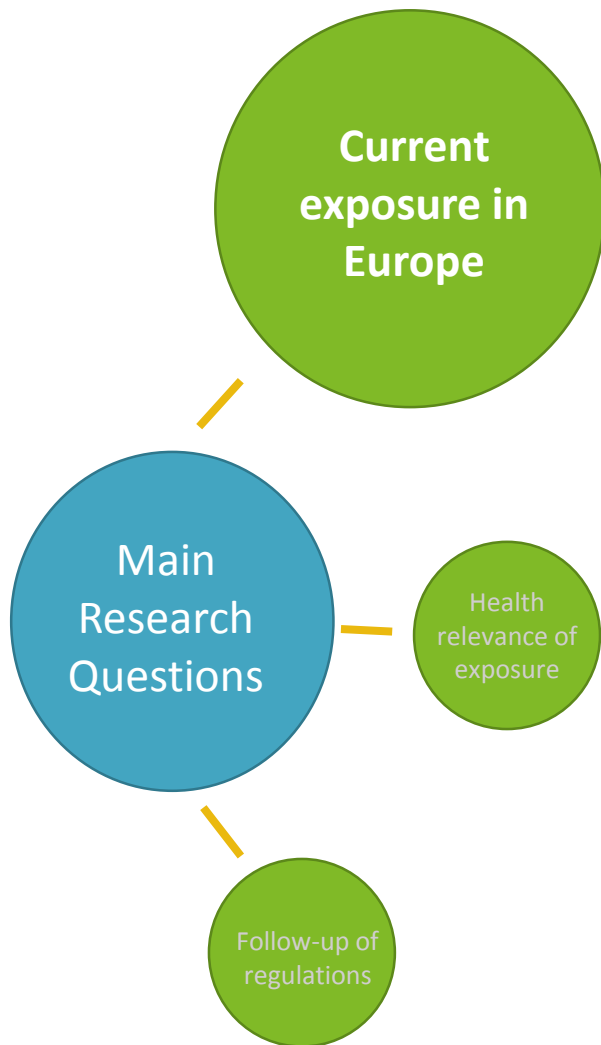


Phthalates and DINCH – Research in HBM4EU

Main research questions to be answered within HBM4EU

- **Current exposure** within Europe: WP8.1 **Alignment of studies** & exchange of **DEMOCOPHES samples** in WP7.4 & WP8.2
- **Follow-up of regulations** : WP10 will do **time trend analyses** with data set of Danish and German young adults to investigate the following substances: DEHP, BBzP, DEP, DnBP, DiNP, DiBP, DiDP, DMP, DnOP, DPHP, DnPeP, DCHP and DINCH
- **Health relevance** of exposure levels: WP5.2 develops **HBM-HBGVs** for 5 phthalates and DINCH
- Tackle the **mixture issue**: WP5.2 will elaborate if **sum HBM-HBGV** is possible & WP15.1 – **case studies**

Phthalates and DINCH – Results of HBM4EU



WP 7

- Gap analysis
- Strategy for exchange of human samples
- Material Transfer Agreements



WP 8

- Strategy developed based on gaps identified: EU-wide HBM measurement of phthalates in children and adolescents in biobanked samples & new sample collection



WP 9

- Exposure biomarkers & methods selected
- 22 candidate laboratories for phthalates & 9 for DINCH
- QA/QC results received of 16 participants

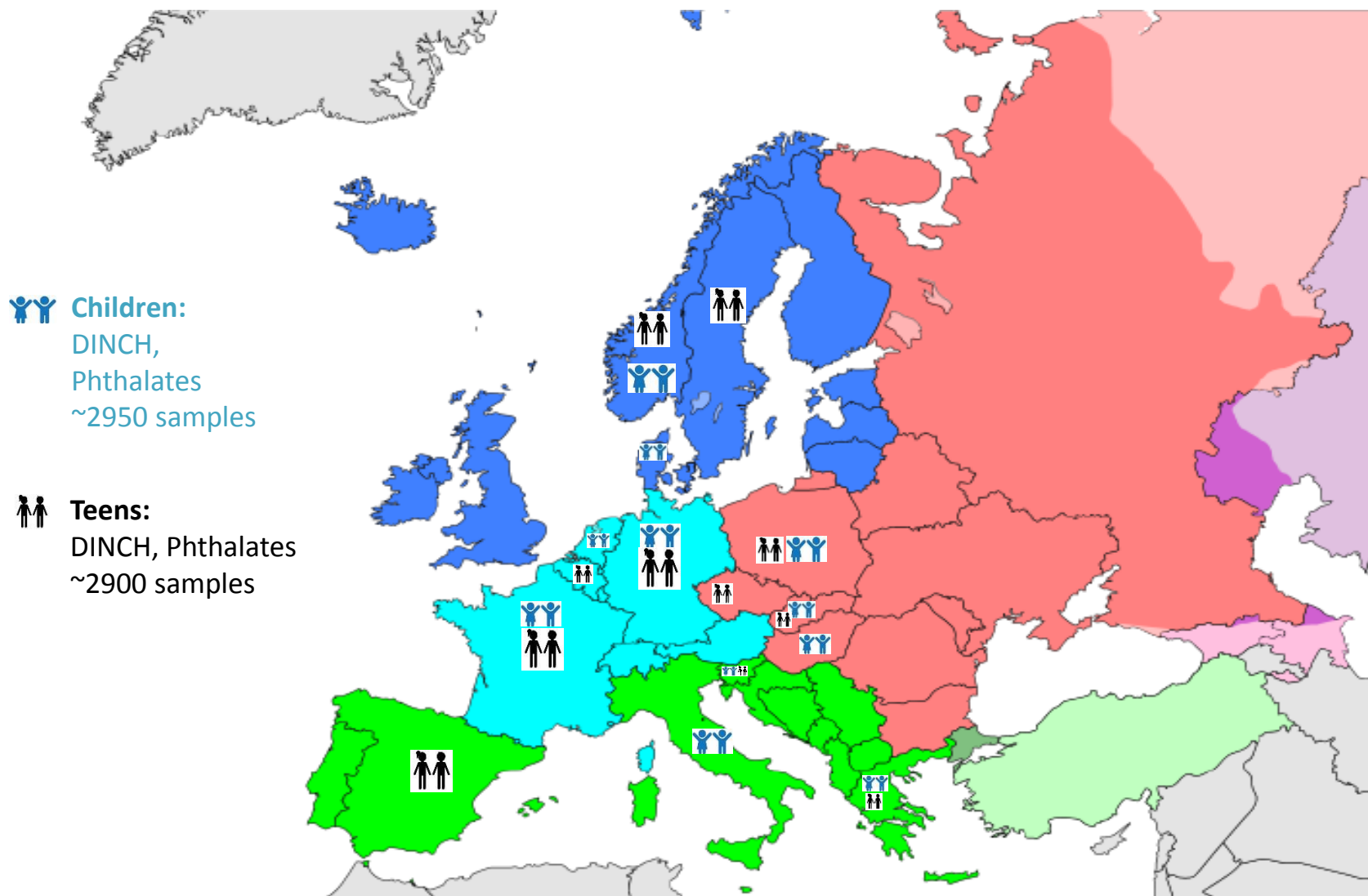


WP 10

- Statistical Analysis Plan developed
- 30 meta data sets from 12 countries integrated into HBM4EU repository



Phthalates and DINCH – Generating Data



United Nations geoscheme subregions of Europe:

■ Northern Europe ■ Western Europe ■ Eastern Europe ■ Southern Europe (source: https://en.wikipedia.org/wiki/United_Nations_geoscheme_for_Europe)

Phthalates and DINCH – Results of HBM4EU



WP 5

- HBM-HBGVs for DINCH & DEHP
- Drafts of HBM-HBGVs for DPHP & DnBP in national expert consultation



WP 14

- List of effect biomarkers for phthalates

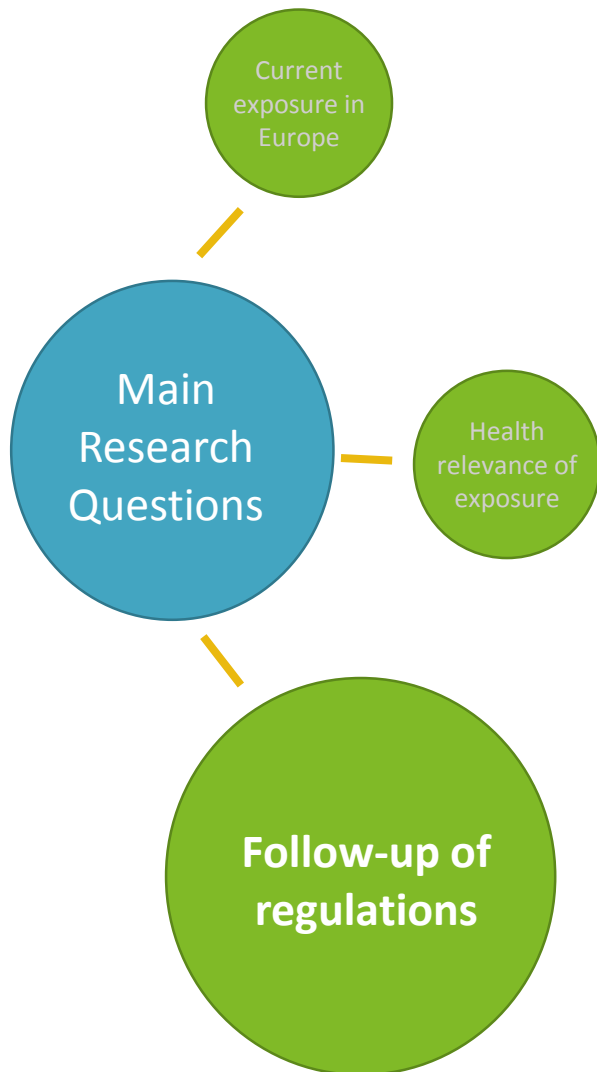


WP 15

- Study plan for case study to investigate anti-androgenic chemicals and male reproductive health (phthalates, bisphenols, PAHs, pesticides, ...)



Phthalates and DINCH – Results of HBM4EU



WP 5

- Overview of HBM in Risk Assessment and Health Impact Assessment
- Method for HBM-based indicators developed
- Case study at EU level for phthalates currently in phase 2 (bilateral consultations with stakeholders, scientist and policy makers)



WP 8

- Strategy developed based on gaps identified: will help to determine differences in countries, which might be due to different regulations

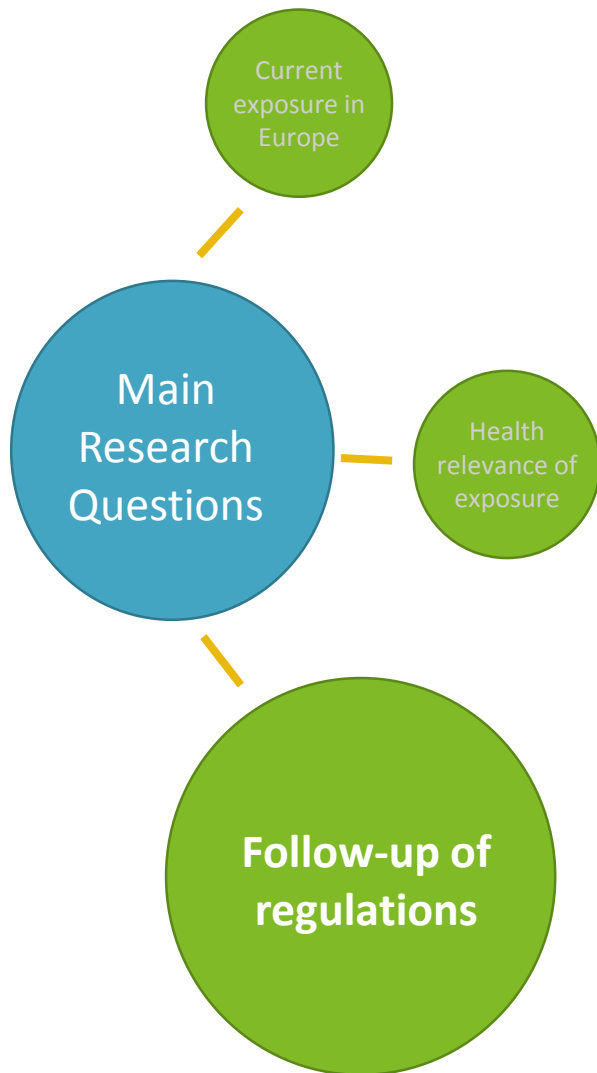


WP 10

- Protocol for time trend analyses in German and Danish young adults
- Protocol to derive European reference values



Phthalates and DINCH – Results of HBM4EU



WP 5

- Overview of HBM in Risk Assessment and Health Impact Assessment
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WP 8

- Strategy developed based on gaps identified: will help to determine differences in countries, which might be due to different regulations



WP 10

- Protocol for time trend analyses in German and Danish young adults
- Protocol to derive European reference values/exposure distributions



Phthalates and DINCH – Results of HBM4EU

- Derivation of HBM-HBGVs for DiBP and BBzP
- Assess whether HBM-HBGVs can be derived for mixtures (group of phthalates)
- Implement strategy and sampling scheme developed under 8.1 to obtain European exposure data
- Analyses of DINCH and phthalates in 3 time points to determine time trends
- Time trend analyses of phthalates and alternatives in German and Danish young adults to follow-up regulations
- Case study of anti-androgenic chemicals and male reproductive health starts to give more insight into mixture health effects

Working together towards

Good chemical policy for a healthy future!





science and policy
for a healthy future

Rosa Lange
Marike Kolossa

Thank you very
much for your
attention!



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