HORIZON2020 Programme
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SCOPING DOCUMENTS

(1st round of prioritization)

Prioritized substance group: Bisphenols

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Scoping document on Substance group Bisphenols

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1. Introduction

HBM4EU has established Chemical Working Groups during the proposal phase for the nine prioritized substance groups that HBM4EU will work on in 2017 and 2018. Additional substance groups will be identified by late 2018 through the implementation of a refined prioritization strategy.

For each substance group, scoping documents are produced under Work package 4.4 of HBM4EU. The scoping document will contain a review of the available evidence, will list policy-related questions, identify knowledge gaps and propose research activities. Proposed activities will be fed into the framework of work packages and tasks of HBM4EU in a coordinated and harmonized manner, and will constitute the basis for the annual work plans. The scoping documents are the linkage between policy questions and the research to be undertaken (broken down for single substances) in order to answer those questions. This methodology will optimize work on the different substances, avoid redundancies, ensure coordination and facilitate the calculation of budgets for each WP. The scoping documents do not contain a comprehensive literature review per substance group but are intended to provide information for the WP leaders who will draft the Annual Work Plans.

For the selected substance groups the availability of (toxicology or human biomarker) data is variable. A scheme was therefore developed to classify the compounds within each substance group into categories A, B, C, D and E based on the availability of data to answer research questions (see further). In direct response to the key project goal of exploiting HBM data in policy making to positively impact on human health, the research activities for each substance group will generate knowledge on exposure trends and associated health effects. Throughout the course of the project, we will generate knowledge that will shift substances towards to a higher level of knowledge category.

For further information see www.hbm4eu.eu

2. Background Information

2.1 Hazardous properties

There is a large literature on the toxicity of bisphenol A including at low doses [reviewed in WHO and UNEP (2012), Gore et al. (2015), and Vandenberg (2014)]. Studies have indicated that it could be associated with increased risk for:

- Fetal development: miscarriages, decreased birth weight at term,
- Reproductive and sexual dysfunctions,

- Breast and prostate cancer or at least significant breast tissue remodelling. Studies have indicated that those effects were associated with gestational and neonatal exposure [Seachrist et al. (2016)].
- Altered immune system activity,
- Obesity and metabolic dysfunctions and diabetes in adults,
- Cardiovascular disease in adults
- Cognitive and behavioural development in young children.

Despite the wealth of studies, there are still controversies concerning the toxic effects of BPA. Those are related to some lack of reproducibility of the experimental studies possibly due to different designs. Different types of studies should be distinguished. Several studies (both experimental and human) have focused on perinatal exposure using different doses including low doses and monitoring a variety of outcomes [FitzGerald and Wilks (2014)]. In human there are several cohort studies associating perinatal exposure and child development. In addition, there are cross-sectional studies where associations were found between BPA exposure and metabolic and cardiovascular diseases. The latter studies have established association but cannot reveal a causal link between BPA and a toxic outcome. In conclusion, there is a real concern that BPA exposure could be linked to a variety of health outcomes in human, with different level of evidence depending on the outcome and the exposure period. Other Bisphenols, notably many BPA substitutes structurally similar to BPA, have been less studied although data suggest they are also oestrogenic, and likely to induce similar health effects [Rochester and Bolden (2015)].

BPA elicits a variety of endocrine disrupting effects targeting steroid hormones as well as thyroid hormones. Several studies have explored the mechanisms of endocrine disruption. Initial studies have indicated an interaction with the nuclear ER alpha estrogen receptor with a relatively low affinity. Further studies have indicated an interaction with other receptors such ERbeta, ERRgamma and GPR32. An unresolved question is which of those receptors is involved in the low dose fetal effects of BPA.

BPF, BPS, BPAF, along with Bisphenol Z (BPZ), Bisphenol E (BPE) and Bisphenol B (BPB) are suspected to be endocrine disrupting chemicals which are oestrogenic [Mesnage et al. (2017)]. BPB, BPE, BPF display anti-androgenic activities in some settings [Rosenmai et al. (2014)]. Moreover a study on BPS and BPAF exposure showed that it can modify the histology of zebra fish testes and ovaries and influence homeostasis of testosterone and oestradiol, and parental exposure to environmentally relevant concentration of BPAF results in delayed hatching of the offspring [Shi et al. (2015)]. BPS and BPF induce proliferation and migration of breast cancer cells via the oestrogen receptor dependent pathway in vitro [Kim et al (2017)].

2.1.1 Exposure characteristics

BPA is used in certain plastics, epoxy resins and thermal papers and is among the highest volume of chemicals produced world-wide. There is evidence that contamination can occur through different routes, including food, water, air and skin (particularly in occupational exposure of cashiers). BPA has a relatively short half-life (hours); it is conjugated and believed to be inactive in that form, but there is concern that it may be locally deconjugated at the tissue level. There is a clear advantage in measuring free and conjugated forms both to address the possibility of external contamination during the assay and to better assess the active form of the substance.

There is solid evidence that a large majority of the human population is exposed to BPA. Many biomonitoring studies are available for bisphenol A (BPA) but the majority of the studies have a single measurement of exposure. These studies are useful in estimating the exposure to BPA in a particular population and follow time trends but not for risk assessment. Studies with multiple biological samples (usually pregnancy cohorts) have shown that BPA has poor Intraclass Correlation Coefficient (ICC) and therefore a single biological measurement can cause exposure misclassification. Further, there is a lack of consensus on how to deal with multiple samples in estimating the correct exposure. In addition, not all countries in Europe have biomonitoring data available on BPA. In DEMOCOPHES[1], seventeen European countries participated, but BPA was added for a group of only 6 countries. BPA is analyzed in very few European birth cohorts in Germany, Norway, Spain and France [Casas et al. (2013)].

Bisphenol F (BPF), Bisphenol S (BPS), and Bisphenol AF (BPAF) are among the main substitutes of BPA in polycarbonate plastics and epoxy resins [Chen et al. (2016)].

2.1.2 Policy relevance

Regulatory measures have been taken at the EU level while additional measures have been taken in certain countries. In the EU, bisphenol A is regulated under REACH (1907/2006/EC). EU law regulates BPA in plastic materials and articles intended to come into contact with food [Commission Regulation (EU) No 10/2011], and the only EU restriction is for BPA in baby bottles [Commission Directive 2011/8/EU]. The EU is considering additional regulation of BPA in coatings and varnishes such as for the use of coatings in metal packaging and varnishes on screw caps. Additional measures have been taken in several countries. For example, France banned BPA in all food contact materials [French Law No 2012-1442], other countries like Denmark, Belgium and Sweden, banned it in those materials intended for children under 3.

Since 2017 BPA is on the Candidate List of substances of very high concern for Authorisation (SVHC candidates) as it is classified toxic for reproduction. Currently, France is preparing a dossier for the identification of BPA as a human ED-SVHC substance, and Germany for the identification as an environmental ED-SVHC substance.

There are also controversies between different agencies concerning the most protective Total Daily Intake (TDI). Furthermore, BPA is also present in thermal papers and exposure of cashiers has been assessed and led to a proposal for restriction and substitution. Different committees of ECHA have analysed the benefits and costs of restrictions and sent their conclusion to the European Commission. BPA regulation is actively debated across the world. BPS and BPF are the major BPA substituents with distinct industrial applications. Much less is known about their putative toxicity and their presence in human matrices, although initial studies have indicated that they may display toxic effects that are similar to BPA [Rochester and Bolden (2015), Auerbach et al. (2016)]. Other bisphenol compounds are also manufactured and little is known about their toxicity and diffusion at this stage.

2.1.3 Technical aspects

Although BPA (and to a much lesser extent BPS and BPF) have been assayed in several human biomonitoring studies there is a need to harmonize procedures for sample handling, storage and analytical methodologies. However, assays for conjugated and free substances should also be harmonized. The same holds true for other bisphenols.

Furthermore, external contamination during sample collection, handling and analysis is an important criteria during the evaluation of studies to be considered both for assigning reference values (HBM values) and risk assessment. For BPF and BPS, there are few biomonitoring studies available (see below) but there is a lack of literature for other bisphenols [Chen et al. (2016)].

2.1.4 Societal concern

In several countries and probably world-wide, BPA has been considered as the typical endocrine disruptor. In many cases, the societal concern towards EDCs is highly connected to the bisphenol

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[1] Demonstration Of A Study To Coordinate And Perform Human Biomonitoring On A European Scale – DEMOCOPHES (2010) http://www.eu-hbm.info/democophes

case and to the campaigns to regulate BPA. Therefore there is a lot of expectations in this field. It is important to fill the gaps and to attempt to address the uncertainties, because the bisphenol case appears to be emblematic of the EDC. It is also associated with the Di-ethylstilbestrol scandal which is well known by the EU population. Similarly to Di-ethylstilbestrol, BPA is considered as a threat for pregnant women, the fetus and young children. Whatever we achieve with bisphenols will actually be useful for all EDCs and for the role of public authorities in protecting pregnant women and the next generations.

3. Categorization of Substances

Table 1: Substances included in the substance group, listed according to availability of toxicology and human biomarker data, in category A, B, C, D, E substances (see general introduction)

Category	Abbreviation/ Acronym	Systematic name	CAS No.	Regulation
A	BPA	4,4'-isopropylidenediphenol	80-05-7	REACH Annex V; Annex XVII, Entry 66 PACT list entry 13/04/2017: Hazard assessment. Scope: ED. OSH Legislation: Consumer uses, Article service life, Widespread uses by professional workers, Formulation or re-packing, Uses at industrial sites, Manufacture, Signs at work, CAD, Young workers, Pregnant or breastfeeding workers. Environmental legislation: Classified Seveso Waste Directive Annex III Professional and consumer legislation: Cosmetics (EC) No 1223/2009 Annex II; Toy safety Directive Appendix C
C	BPS	4,4'-sulphonyldiphenol	80-09-1	CoRAP list PACT list entry 01/04/2015: Hazard assessment. Scope: ED. OSH Legislation: Article service life, Formulation or re-packing, Uses at

Category	Abbreviation/ Acronym	Systematic name	CAS No.	Regulation
				industrial sites, Manufacture.
	BPF	4,4'-methylenediphenol	620-92-8	REACH Annex III Inventory PACT list entry 01/10/2015: RMOA. Scope: ED. Under development OSH Legislation: CAD
C	BPB	4,4'-(1-methylpropylidene) bisphenol	77-40-7	REACH Annex III Inventory PACT list entry 07/03/2017: RMOA. Scope: ED. Under development OSH Legislation: CAD
	BPAF	4,4'-[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene] diphenol	1478-61-1	REACH Annex III Inventory PACT list entry 01/10/2015: RMOA. Scope: ED. Under development OSH Legislation: CAD Environmental legislation: Classified Seveso
	BPAP	4,4'-(1-Phenylethylidene)bisphenol	1571-75-1	REACH Annex III Inventory OSH Legislation: CAD Environmental legislation: Classified Seveso Waste Directive Annex III
	BPBP	2,2-bis(2-hydroxy-5-biphenylyl)propane	24038-68-4	-
	BPC	4,4'-isopropylidenedi-o-cresol	79-97-0	REACH Annex III Inventory
	BPCl2	4,4'-(dichlorovinylidene) diphenol	14868-03-2	REACH Annex III Inventory OSH Legislation: CAD
	BPE	4,4′-Ethylidenebisphenol	2081-08-5	-
	BPPH	4,4'-Dihydroxytetraphenyl-methane	1844-01-5	-

Category	Abbreviation/ Acronym	Systematic name	CAS No.	Regulation
	BPM	4,4'-(1,3-phenylene-bis(1-methylethylidene))bis-phenol	13595-25-0	CoRAP list PACT list entry 02/02/2017: Hazard assessment. Not ED. OSH Legislation: Article service life, Uses at industrial sites, Manufacture, Signs at work, CAD, Pregnant or breastfeeding workers. Environmental legislation: Classified Seveso Waste Directive Annex III
	BPP	4,4'-(1,4-Phenylenediisopropylidene) bisphenol	2167-51-3	REACH Annex III Inventory OSH Legislation: CAD
	BIS2	Bis(2-hydroxyphenyl)methane	2467-09-9	-
	DHDPE	p,p'-oxybisphenol	1965-09-9	REACH Pre-Registration process OSH Legislation: CAD, Young workers. Waste Directive Annex III
	BPFL	9,9-Bis(4-hydroxyphenyl)fluorene	3236-71-3	REACH Registration Dossier OSH Legislation: CAD Environmental legislation: Classified Seveso Waste Directive Annex III
	BPZ	4,4'-cyclohexylidenebisphenol	843-55-0	REACH Annex III Inventory OSH Legislation: CAD, Pregnant or breastfeeding workers. Environmental legislation: Classified Seveso
	BP4,4’	Biphenyl-4,4'-diol	92-88-6	REACH Registration Dossier OSH Legislation: Widespread uses by professional workers, Uses at industrial sites, CAD, Young workers. Environmental legislation: Classified Seveso Waste Directive Annex III

Category	Abbreviation/ Acronym	Systematic name	CAS No.	Regulation
				Professional and consumer legislation: Plastic contact with food (EU) No 10/2011 Annex I

4. Policy-related questions

There are several critical questions concerning bisphenols that need to be resolved. The first is whether different regulations in different countries lead to different internal exposure values and whether the increasingly frequent use of substituents has led to increased exposure and to the presence of mixtures of bisphenols in humans. The second is identify safety values taking into consideration the accumulating knowledge on Bisphenol toxicity particularly at low doses. A third question is whether substitutes are safer than BPA considering their hazardous properties and current and expected exposure to those compounds.

Specific policy-related questions are:

1. What is the current exposure of the EU population to BPA?
2. Do different regulatory controls across the EU concerning in particular BPA lead to different exposures?
3. Are bisphenols (BPA and substitutes) exposure levels of concern for health?
4. Is occupational exposure of cashiers a health concern?
5. What is the toxicity of BPA substitutes?
6. Are health risks age and gender dependent?
7. Can we find evidence for low-dose effects within mixtures?
8. How can HBM feed into assessment of the Tolerable Daily Intake (TDI) for BPA, as set by the European Food Safety Authority (EFSA)?
9. Is it important to eliminate legacy BPA from material cycles (i.e. waste till receipt rolls) when implementing a circular economy in order to protect human health?

5. Research Activities to be undertaken

Table 2: Listing of research activities to be carried out to answer the policy questions summed up in 1.3

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
1. What is the current exposure of the EU population to BPA?	BPA	Different types of studies could be considered to address the current exposure of the EU population to BPA: well characterized samples such as Cophes/Democophes, high quality national studies, studies including several samples per individual to account for intra-individual variability, studies with available or planned health outcomes. In the annex to table 2 following EU countries are listed to have HBM data on BPA: De, Be, Fr, At, Cz, Se,El and DEMOCOPHES countries . Age groups for	Inventorying available HBM data in EU ->WP7 Use already available biomonitoring data in Europe to: 1. Find out which countries lack HBM data 2. Evaluate the quality of the available data such that design of future biomonitoring studies can be improved accordingly, calculate exposure levels. -> WP8 , WP9, WP10

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
		which data are available differ among the countries.	To use already available biomonitoring data in Europe to define the minimum number of samples required per individual to estimate the correct exposure to BPA. -> WP10 To compare single samples vs multiple samples for exposure assessment -> WP9, WP13 To identify exposure pathways for BPA and its toxicokinetic characteristics. -> WP12
2. Do different regulatory controls across the EU concerning in particular BPA lead to different exposures?	BPA (Cat. A)	On 16 June 2017 ECHA[2] classified BPA as an endocrine disruptor and a substance of high concern. Specific countries such as France, Denmark and Sweden have already stricter bans in place ECHA[3], has recently updated the BPA entry to reflect an additional reason for inclusion due to its endocrine disrupting properties causing adverse effects to the environment.	Find out whether there are HBM data or suitable samples available before and after the ban in Fr, Se, Dk? If not design an appropriate study to analyse samples time trends-> WP7, WP8
3. Are bisphenols exposure levels of concern for health?	BPA (Cat. A) BPS, BPF (Cat. C)	KEMI[4] has identified a total of over 200 chemical substances that have a chemical structure similar to Bisphenol A and which may be found on the European market. According to results from data simulations, 37 of these substances may have endocrine disrupting properties like those identified for Bisphenol A. Only available in vitro/in vivo experimental settings in which BPA AOP have already been explored will be used to assess the effects of BPS and BPF.	To determine whether current or expected exposure levels of BPS and BPF are of concern for health in the general population and at the workplace? Derive health based HBM guidance values for the general population and for workers (WP5 / T5.2) and to identify the relationship to the environment and workplace. What is the evidence for low-dose effects? Analyse data from longitudinal cohort studies -> WP13

[2] https://echa.europa.eu/-/msc-unanimously-agrees-that-bisphenol-a-is-an-endocrine-disruptor
[3] https://echa.europa.eu/-/seven-new-substances-added-to-the-candidate-list-entry-for-bisphenol-a-updated-to-reflect-its-endocrine-disrupting-properties-for-the-environment
[4] https://www.kemi.se/en/news-from-the-swedish-chemicals-agency/2017/new-report-37-bisphenols-may-be-endocrine-disruptors/

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
			Do BPS and BPF act on the same AOPs as BPA? -> WP13 Targeted assessment of toxic effects of BPS/BPF as compared to BPA. Targets priority will be given to cancer, reproductive, hormonal, metabolic, immune and neurological effects. The linkage with effect biomarkers could be explored in human samples as well as mixture effects. -> WP13 / T13.1, WP14 / T14.3 and WP15 / T15.3. Urgently harmonize procedures for sample handling, storage and analytical methodologies for BPA, BPS and BPF to minimize external contamination. Encourage European countries to participate in inter-laboratory comparisons. -> WP9 To identify existing analytical methods allowing to monitor in human matrices BPA, BPS, BPF and possibly other BPs, as well as the necessary gaps to be fulfilled in terms of method development and validation. -> WP9, WP16 To identify exposure pathways for BPS, BPF (possibly other BPs) and their toxicokinetic characteristics. -> WP12 To identify effect biomarkers associated to bisphenol exposure and to determine whether those effect markers are common to all bisphenol compounds. -> WP14
4. Is occupatio	BPA (Cat. A)	A directive[5] was published on the restriction of BPA in thermal paper based on the recommendation of the SEAC.	To find out whether BPA occupational exposure of cashiers is a health concern. To

[5] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R2235&from=FR

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
nal exposure of cashiers a health concern?		Another directive[6] revised the OEL (Occupational Exposure Limit values) for BPA of 2mg/m3 TWA in occupational settings.	feed into the Commission decision on whether to ban BPA in till receipts, as recommended by ECHA's Committee for Socio-Economic Analysis (SEAC).-> WP8
5. What is the toxicity of BPA substitutes?	BPS, BPF (Cat. C)	BPS and BPF are the primary substitutes of BPA. Some countries have started the process to restrict BPS because of its toxicity profile. DG Grow and DG Santé recommend to monitor BPA as well as BPS and BPF, the most prominent substituents. Recent findings in the US[7] have shown that some people's exposure to BPF can meanwhile be higher than to BPA. CHEM Trust suggest to explore this evidence in Europe particularly in women of child-bearing age.	What is the toxicity of BPA substitutes? To identify effect biomarkers associated to bisphenol exposure and to determine whether those effect markers are common to all bisphenol compounds. -> WP14
6. Are health risks age and gender dependent?	BPA BPS, BPF (Cat. C) Other Bisphenols (Cat. C)	Most regulation and recommendation tend to focus on pregnant women and infants.	To determine age and gender specific health effects of BPA. -> WP9, WP10, WP13 To derive health based HBM guidance values and perform risk assessments for different age groups and sex. -> WP5 / T 5.2 & 5.3 To measure hormonal levels in new-borns exposed transplacentally and pubertal children due to environmental exposure to BPs. -> WP14
7. Can we find evidence for low-dose effects within mixtures?			To determine the effect of combined exposures to substance mixtures within the bisphenol family and with other families and whether this could impact health guidance (in food contamination, cosmetics, other plasticizers, etc.) -> WP15

[6] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017L0164&from=FR

[7] https://silentspring.org/blog/results-our-biomonitoring-study-are

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
			To identify effect biomarkers associated to bisphenol exposure and to determine whether those effect markers are common to all bisphenol compounds. -> WP14 To develop indicators for combined exposures. -> WP5 / T 5.4
8. How can HBM feed into assessment of the Tolerable Daily Intake (TDI) for BPA, as set by the European Food Safety Authority (EFSA)?	BPA (Cat. A) BPS, BPF Other Bisphenols (Cat. C)	In its 2015 re-evaluation of BPA exposure and toxicity, EFSA (European Food Safety Authority) used a more refined methodology than before supported by new data to review the Tolerable Daily Intake (TDI) for BPA from 50 to 4 µg/kg bw/day.	To derive EU-wide health based guidance values for BPA and other bisphenols (BPS and BPF). Find out how to feed this into an assessment of the TDI for BPA as set by EFSA. -> WP5 / T 5.2, To relate exposure pathways including food pathway for BPA, BPS, BPF (possibly other BPs) to HBM data. -> WP12 To determine whether different regulatory controls across EU MS lead to different exposures.
9. Is it important to eliminate legacy BPA from material cycles (i.e. waste till receipt rolls) when implementing a circular economy in order to protect	BPA (Cat. A)	As long term goal, it will be important to eliminate legacy BPA from material cycles (i.e. waste till receipt rolls) when implementing a circular economy in order to protect human health. CHEM Trust suggests policy proposals should be developed to extend the focus to the whole group of bisphenols.	It is not clear whether these questions can be tackled within HBM4EU: Gather data on environmental persistence and the fate of bisphenols to determine exposure risks to humans and ecosystems. Studies that investigate photo-degradation and microbial degradation would provide understanding of environmental transformation products and fate of bisphenols. Correlate environmental monitoring data with HBM4EU data -> WP12

Policy question	Substance	Available knowledge	Knowledge gaps and activities needed
human health?			

Annex to table 2: Listing of available knowledge related to policy questions

Substance	Available knowledge related to policy question
BPA	**Germany** 1995-2009,(20-29 yr.- urine & plasma): **[Koch et al. (2012)]** & 2003-2006 (GerES IV); (3-14 yr.- urine): **[Becker et al. (2009)]** (*rp*); **Belgium, Flanders** 2007-2012 (14–15 yr.): **[Geens et al. (2014)]** (*rp*) & 2011-2012 (DEMOCOPHES), (6-12yr., mothers, pregnant women- urine): **[Covaci et al. (2015) and 3XG (2013)]** & 2012-2015 (FLEHS 3), (50-65 yr.-urine): **[Steunpunt Milieu en Gezondheid (2015)]**; **Norway** 2012,(food & estimated dietary exposure in adults): **[Sakhi et al. (2014)]**; **Greece** 2009-2011, (mother-child pairs: 2yr., pregnant women- urine): **[Myridakis et al. (Oct. 2015)]** & 2011-2014, (children <18yr., adults- hair): **[Tzatzarakis et al. (2015)]** & 2012 (2.5-87 yr. Ẋ=49yr.- urine) **[Asimakopoulos et al. (Feb. 2014)]** & 2014, (adult males, anonymous individuals- urine, serum)- analytical method: **[Myridakis et al. (Feb 2015), Asimakopoulos and Thomaidis (2015) and Asimakopouloset al. (Jan. (2014)]** & 2014 (Developing foetus, neonates, infants, children and adults- plasma, urine) -continuous lifetime model: **[Saringiannis et al. (2014)]**; **Austria** 2008-2011, (mother- children pairs: 6-11yr., 25-50 yr.-urine): **[Hohenblum et al. (2012)]** & 2010-2012, (6-15 yr., 18-64 yr., 65-79 yr.-urine): **[Hartmann et al. (2016)]**; **Sweden** 2008-2009 (food, young women-serum): **[Gyllenhammar et al. (2012)]** & 2010-2011, (18-80 yr.-urine): **[Bjermo et al. (2013)]** & 2010-2013, (17-19 yrs.-urine)-time series:**[Jönsson et al. (2014)]** & 2011-2012 (DEMOCOPHES) (mother-child pairs: 6-11yr.,<45yr.-urine): **[Larsson et al. (2014)]** 1996-2011, (first-time mothers-blood serum): **[Gyllenhammar et al (2012) Tidstrend 1996-2011]** **Czech republic** 2015, (35.8±4.7 yr.-plasma, seminal plasma) analytical method: **[Vitku et al. (2015)]** & 2000-2006, (canned foodstuffs, migration)-analytical method: **[Poustka et al. (2007)]** & 1999-2000 (water samples & river sediments): **[Stachel et al. (2003)]**; **France** 2011, 2013 (Blood, urine, amniotic liquid, tissue extracts) - analytical method: **[Lacroix et al. (2011), Viguie et al. (2013) and Gayrard et al. (2013)]** & 2013-2016, (Mother-premature infants-human breast milk): **[Deceuninck et al. (2015)]** & 2003-2006, EDEN cohort (pregnant women-urine): **[Philippat et al. (2014)]** & 2011 ELFE cohort (pregnant women on delivery-urine) **[Dereumeaux et al. (March 2016) and Dereumeaux et al. (Dec. 2016)]**.
BPS	**Belgium, Flanders** 2012-2015 (FLEHS 3), (50-65 yr.-urine): **[Steunpunt Milieu en Gezondheid (2015)]** method development; **Sweden** 1996-2011, (first-time mothers-blood serum): **[Gyllenhammar et al (2012) Tidstrend 1996-2011]**; **France** 2013-2016 (Mother-premature infants-human breast milk): **[Deceuninck et al. (2015)]**;
BPF	**Sweden** 1996-2011, (first-time mothers-blood serum): **[Gyllenhammar et al (2012) Tidstrend 1996-2011]**; **Czech republic** 2000-2006, (canned foodstuffs, migration)-analytical method: **[Poustka et al. (2007)]** & 1999-2000 (water samples & river sediments): **[Stachel et al. (2003)]**; **France** 2013-2016 (Mother-premature infants-human breast milk): **[Deceuninck et al. (2015)]**;

Substance	Available knowledge related to policy question
BPB, BPAF, BPBP, BPC, BPCl2, BPE, BPPH, BPM, BPP, BIS2, DHDPE, BPFL, BPZ, BP4,4'	**France** 2013-2016 (Mother-premature infants-human breast milk): **[Deceuninck et al. (2015)]**;

rp = representative for the (respective) population

6. Results Report

In Year 2 (M18) a short overview of the results achieved within the HBM4EU programme shall be depicted here. Please, briefly state the main results answering the corresponding policy questions in a general understandably manner.

Table 3: Short overview of results of the activities carried out within HBM4EU to answer the policy questions with reference to corresponding deliverables

Policy Question No. (keyword)	Short Summary of Results
	If there is a Deliverable you extracted the results from, please mention it

7. References

1. Asimakopoulos, A. G., Wang, L., Thomaidis, N. S., Kannan, K. (2014) A multi-class bioanalytical methodology for the determination of bisphenol A diglycidyl ethers, p-hydroxybenzoic acid esters, benzophenone-type ultraviolet filters, triclosan, and triclocarban in human urine by liquid chromatography-tandem mass spectrometry. *Journal of Chromatography A,* 1324, 141-8. https://doi.org/10.1016/j.chroma.2013.11.031
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