Urinary levels of BPA among European women and major determinants of exposure

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Introduction to Bisphenols

Anthropic substances, characterized by 2 hydroxyphenolic functional groups.

Widely used in the plastic industry :
- Polycarbonate for food containers, plastic bottles, glasses, epoxy resins in cans and tins.
- Thermal papers, medical devices, clothes, etc.

HO—⬡—C(CH₃)₂—⬡—OH

HO $\quad$ OH

H₃C $\quad$ CH₃
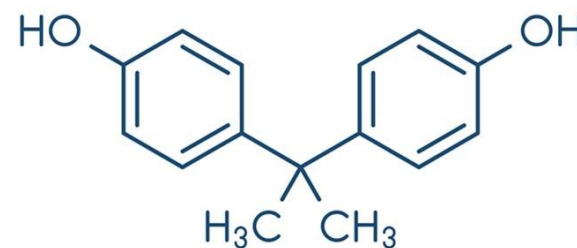
bisphenol A

Endocrine disruptor. Reproductive and developmental effects.
Increase the risk of breast cancer after gestational or neonatal exposure.

Under REACH regulation.
National regulations : Ban in baby bottles in France since 2011 and in food and drinks containers since 2015.

Initial objectives of the study

Opportunity to use existing European data to :

- **Describe the exposure distribution to bisphenols**

    Depending on specific criteria : sex; age group; geographical area, etc.

- **Identify major determinants of exposure to bisphenols**

    Depending on the variables analysed in European studies.

- **Determine Time trends of exposure to bisphenols**

    Depending on the availability of existing data

➡ Surveys identified and selected from the metadata overview from T7.1

Characteristics of eligible studies

| Characteristics of studies		Number of countries involved	Origin of the data set (HBM4EU Metadata ID)
Addressed population	General population	5	Austria (77), Belgium (1021), Finland (1003; 1024), Germany (1041), Israel (115)
	Mothers (in child pairs population)	6	Austria (142), Belgium (1057; 1061), Denmark (1056; 1059), Norway (1025), Spain (1038), Slovenia (1004)
	Pregnant women	8	Belgium (1057), Denmark (1056), France (1039; 1058), Greece (1058), Lithuania (1058), Norway (1058), Spain (1058), United Kingdom (1058)
	Other	1	Sweden (1042)
Geographical area	Northern Europe	6	Finland (1003; 1024), Lithuania (1058), Norway (1025; 1058), Sweden (1042), Denmark (1026; 1059), United Kingdom (1058)
	Western Europe	4	Austria (77; 142), Belgium (1021; 1057; 1061), France (1039; 1058), Germany (1041)
	Southern Europe	3	Greece (1058), Slovenia (1004), Spain (1038; 1058)
	Other	1	Israel (115)

Characteristics of eligible studies

Characteristics of studies		Number of countries involved	Origin of the data set (HBM4EU Metadata ID)
Coverage of study	International level	6	France (1058), Greece (1058), Lithuania (1058), Norway (1058), Spain (1058), United Kingdom (1058)
	National level	8	Austria (77; 142), Belgium (1061), Finland (1024), France (1039), Germany (1041), Israel (115), Norway (1025), Spain (1038),
	Regional level	5	Belgium (1021), Denmark (1026; 1056; 1059), Finland (1003), Slovenia (1004), Sweden (1042)
	Local level	1	Belgium (1057)
Urinary sampling method	Urine-spot	12	Austria (77), Belgium (1021; 1057), Finland (1003), France (1039; 1058), Greece (1058), Israel (115), Lithuania (1058), Norway (1058), Slovenia (1004), Spain (1058), Sweden (1042), United Kingdom (1058)
	Urine-morning	5	Austria (142), Belgium (1061), Denmark (1056; 1059), Norway (1025), Spain (1038)
	Urine-24h	2	Finland (1024), Germany (1041)
Urine dilution	Creatinine (only)	10	Austria (77; 142), Belgium (1061), Denmark (1059), Israel (115), France (1039; 1058), Greece (1058), Lithuania (1058), Norway (1058), Spain (1038; 1058), United Kingdom (1058)
	Specific gravity (only)	1	Sweden (1042)
	Creatinine & specific gravity	6	Belgium (1021; 1057), Denmark (1056), Finland (1003), Germany (1041), Norway (1025), Slovenia (1004)

Selection of European studies

Characteristics and availability of European existing data leads to focus on :

- Describtion of **Exposure distribution** and identification of **determinant of exposure**, not possible to determine time trends

- BPA, no data on BPF and BPS

- **Women**

- **General population**

- **Urinary levels**

- **Northern and Western areas**

21/11/2018

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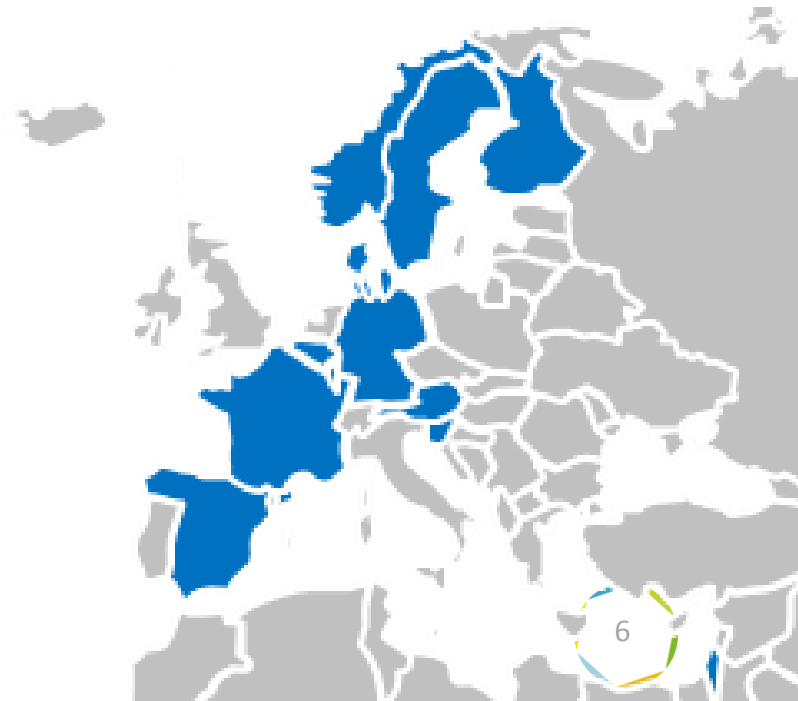
Inclusion criteria of HBM surveys

- **<u>Type of population</u>** : general population surveys or targeted on mother/newborn or mother/child pair's populations or in pregnant women

- **<u>Type of survey</u> :** prospective or cross-sectional, national or regional surveys

- **<u>Type of available data</u> :** Urinary BPA concentration, variables on potential determinants of BPA exposure levels (including individual characteristics and potential sources of exposure to BPA)

Exclusion criteria of HBM surveys

- Studies not on general population : clinical population, occupational studies, etc.

- Occupation that involves a BPA exposure wil not be considered as an exclusion criteria.

Identified data collections and status of response for participating at 15/11/2018

Study	Country	Coverage	Addressed population	Analysed samples	Approval to participate
PBAT	Austria	National level	General population	594	YES (single measurement data)
IBS	Israel	National level	General population	246	YES
IC-HBM	Austria	National level	Mother (child pairs population)	25	NO (sharing individual data is not possible)
RefLim2011	Finland	Regional level	Non-occupationally exposed people	121	Awaiting confirmation
SLO-DEMOCOPHES	Slovenia	Regional level	Mother (child pairs population)	141	YES
FLEHS3RefAdult	Belgium	Regional level	General population	194	Awaiting confirmation
FINRISK2012	Finland	National level	General population	399	YES
IES	Norway	National level	Mother (child pairs population)	48	YES
DEMOCOPHES-SPAIN	Spain	National level	Mother (child pairs population)	231	YES
ELFE	France	National level	Pregnant women	1764	YES
ESB	Germany	National level	General population	60	YES
BAMSE	Sweden	Regional level	Other (?)	100	No (BPA data not yet available)
OCC	Denmark	Regional level	Mother (child pairs population)	869	YES
3xG	Belgium	Local level	Pregnant women	150	Awaiting confirmation
HELIX	France, Greece, Lithuania, Norway, Spain, United Kingdom	International level	Pregnant women	1084	NO
DK-DEMOCOPHES	Denmark	Regional level	Mother (child pairs population)	145	YES
DEMOCOPHES_BE	Belgium	National level	Mother (child pairs population)	125	YES
DEMOCOPHES-LUXEMBOURG	Luxembourg	NB: study not initially present in the HBM4EU metadata overview			YES
DEMOCOPHES-SWEDEN	Sweden	NB: study not initially present in the HBM4EU metadata overview			YES
INMA	Spain	NB: study not initially present in the HBM4EU metadata overview			YES

Two possible statistical approachs

- **<u>Separated approach</u> :** compute separate estimates for each survey and combine them afterwards by some sort of weighted average

- **<u>Pooled approach</u> :** pool the data from each survey, adjust the survey weights and continue as if the combined sample was simply one larger sample

Variables to include

- **<u>Exposure variable</u> :** urinary conjugated BPA concentration

- **<u>Accompanying variables</u> :** all variables that may explain exposure levels of BPA in the studied population.
  - individual and socio-demographic characteristics (sex, age, country)
  - potential sources of exposure to BPA (lifestyle, household environment, dietary habits and other individual characteristics)

Number of determinants factors to assess and include in the statistical model will depend on the availability of variables in selected studies

Challenges within the study

- Pooling of data from studies focusing on pregnant women with data from studies on general population

- Dealing with European geographical representativeness (missing data from eastern area)

- Dealing with different sampling plans

- Dealing with different urinary sampling methods (morning urine, one spot urine or 24h urine)?

- Pooling data from studies which do not use the same urinary dilution assessment method?

Time schedule

June 2018 : Elaboration of the protocol

August-October 2018 : Identifying and inviting data collections to participate

November 2018-March 2019 : Data transfert procedures

April-May 2019 : Statistical analyses

June-September 2019 : Preparation of publication

Thank You

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