



science and policy
for a healthy future

How can HBM4EU
contribute to policy making
on phthalates and
bisphenols?

Policy context, legislation in
place and challenges ahead



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HBM4EU Priority Substances webpage

is://www.hbm4eu.eu/the-substances/



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SUBSTANCES

HBM4EU priority substances

In developing priorities for the first annual work plan, the consortium implemented an exercise to prioritise substances for action, taking into account both national and EU level policy needs for knowledge on chemical exposure and health outcomes. As a first step, substances for which knowledge is needed to support current EU policy making were identified through close dialogue with an EU Policy Board. Input from the national level was fed in through a Steering Committee, composed of national representatives and established to guide the preparation of this proposal.

An initial set of criteria was then produced, including such aspects as whether a substance is of concern to human health, whether there is evidence of human and/or environmental exposure at EU level and whether there are open policy questions. The financial and technical feasibility of monitoring the substances was also a criterion.

Substances proposed at both national and EU level were then systematically assessed against these criteria, based on information provided from both EU and national levels. This first prioritisation exercise resulted in the nine substance groupings that have been the focus of HBM4EU activities in 2017 and 2018.

The first list of HBM4EU priority substances includes:

- Aniline family
- Bisphenols
- Cadmium and chromium VI
- Chemical mixtures
- Emerging substances
- Flame retardants
- PAHs
- Per-/poly-fluorinated compounds
- Phthalates and Hexamoll® DINCH

The consortium compiled information on substance classification, policy-related research questions and research objectives for each substance, with the results captured in [scoping documents for the first list of priority substances](#). These scoping documents formed the basis for the development of activities for inclusion in the annual action plans for HBM4EU.

CALENDAR | NOV 2018

<< Nov 2018 >>

M	T	W	T	F	S	S
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5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

HIGHLIGHTS

The 41st Mycotoxin Workshop in Lisbon on May 6 – 8, 2019: The conference will be organized by the Lisbon School of Health Technology, Instituto Politécnico de Lisboa (ESTeSL-IPL) in collaboration with the Society for Mycotoxin Research and will take place at Lisbon School of Health Technology. [Please find the details here.](#)

INTERNAL WEBPAGES

<https://www.hbm4eu.eu/the-substances/>

1st list of priority substances

Substance	Exposure routes	Policy relevance
Phthalates and DINCH	Consumer products	REACH
Poly/per-fluorinated compounds	Consumer products, via environment, diet	REACH, Stockholm Convention, Food Contact Materials
Bisphenol A, S and F	Consumer products, diet	REACH, Legislation on FCM
Brominated and organophosphate flame retardants	Consumer products	REACH, Stockholm Convention
Poly aromatic hydrocarbons	Urban air	NEC Directive, Long Range Transboundary Air Pollution Convention, REACH
Cadmium and chromium VI	Occupational exposure, environmental exposure, diet, smoking (Ca)	REACH, Water Framework Directive, Drinking Water Directive
Aniline derivatives	Occupational exposure	REACH authorisation list
Mixtures	Multiple exposure routes	2012 Communication on combination effects, risk assessment of mixtures, pesticide residues legislation
Emerging substances	Multiple exposure routes	

Bisphenols

- Used in manufacture of plastic articles such as polyvinylchloride (PVC) and polycarbonate
- **Bisphenol A (BPA)** is the substance in the bisphenol group produced and used in the **highest volumes**
- Polycarbonate used in the manufacture of modern optical media,



- building and construction materials, automotive parts and domestic appliances
- BPA used in epoxy resins, e.g. beverage cans. Small amounts of the BPA migrate into food and beverages, resulting in **human exposure**
- Thermal papers, leading to **concerns regarding the exposure** of cashiers
- Some bisphenols are used as laboratory reagents

Bisphenols - Concerns

- June 2017, BPA was identified as having **endocrine disrupting properties** for human health by [ECHA's Member State Committee](#)
- **Toxic for reproduction**, BPA was already listed as a substance of **very high concern (SVHC)** on the [Candidate List](#) under [REACH](#)
- The identification of **BPA as a SVHC** generates **pressure for BPA to be substituted by other bisphenols** in the European Union (EU).
- Swedish Chemicals Agency identified over 200 other bisphenols with a chemical structure similar to BPA that can occur on the European market
- A number of other bisphenols have been registered under REACH

Bisphenols – Hazardous properties

- Existing literature on the toxicity of BPA, including at low doses (WHO and UNEP)
- Exposure to BPA could be associated with increased risk for:
 - Foetal development: miscarriages, decreased birth weight at term;
 - Reproductive and sexual dysfunctions;
 - Breast and prostate cancer or at least significant breast tissue remodelling, associated with gestational and neonatal exposure;
 - Altered immune system activity;
 - Obesity and metabolic dysfunctions and diabetes in adults;
 - Cardiovascular disease in adults; and
 - Cognitive and behavioural development in young children.

Bisphenols – Hazardous properties

- **Uncertainties** concerning the **toxic effects** of BPA --> lack of reproducibility of the experimental studies
- **BPA exposure** could be linked to a variety of **health outcomes in humans (more research is needed)**
- Concerns prompted industry to develop BPA substitutes
- Bisphenol F (BPF) is used in epoxy resins and thermal papers, bisphenol S (BPS) is used in epoxy resins, polycarbonate, polyethersulphone, thermal papers, phenolic resins and polyester resins
- **Less** is known about their **toxicity**
- Initial studies indicate they may cause **similar toxic effects** to BPA (see ECHA's Risk Assessment Committee [notes](#))

Bisphenols – Human exposure

- Solid evidence that a **large majority** of the human population is **exposed to BPA**
- Detected in urine and blood samples in all humans sampled
-> suggesting continuous exposure to low doses of it
- Many biomonitoring studies are available for BPA
- However, the majority of the studies have a single measurement of exposure:
 - useful in estimating the exposure to BPA in a particular population and follow time trends,
 - Not useful for risk assessment
- Not all European countries in Europe have biomonitoring data on BPA

Bisphenols – Legislative status in the EU

- Bisphenols manufactured or imported at volumes over one tonne a year must be registered under [REACH](#)
- **Specific measures** have been taken to **limit human exposure** to BPA at EU level
- BPA is on the [REACH Candidate List](#) of substances of very high concern for Authorisation
- Classified as **toxic for reproduction** and its **endocrine disrupting properties** which cause probable serious effects to **human health**
- The use of BPA in thermal papers is also [restricted under REACH](#) and will enter into effect in January 2020
- On the 7th Nov 2018, the Commission adopted a Communication outlining its commitment to work with Member States in the criteria to identify endocrine disruptors in the areas of pesticides and biocides ([COM\(2018\) 734](#))

Bisphenols – Legislative status in the EU

- A number of bisphenols have been or are being assessed under the [Community Rolling Action Plan](#) and under the [Public Activities Coordination Tool \(PACT\) List](#)
- BPA, BPS and 4,4'-dihydroxybiphenyl (BP4,4') are authorised for use in food contact materials in the EU under [Regulation 10/2011/EU](#), relating to plastic materials and articles intending to come into contact with foodstuffs.
- In January 2011, the European Commission adopted [Directive 2011/8/EU](#), prohibiting the use of BPA for the manufacture of polycarbonate infant feeding bottles.
- EFSA's work BPA in food contact materials available [EFSA webpages on BPA](#).

Bisphenols – Legislative status in the EU

- Bisphenols are subject to control under **health and safety legislation, environmental legislation and consumer legislation**, as a result of their classification under the [CLP Regulation](#)
- In 2014, the Scientific Committee on Occupational Exposure Limits (SCOEL) recommended an occupational exposure limit value of **2 mg/m³** over an 8 hour time weighted average for BPA ([SCOEL, 2014](#)).
- Due to uncertainties related to the short half-life of BPA no biological limit value (BLV) was proposed.
- A biological guidance value (BGV) of **7 µg/L** was recommended for the identification of potentially occupationally exposed from the occupationally non-exposed
- In 2017, [Directive 2017/164/EU](#) established an indicative occupational exposure limit value of **2 mg/m³** over 8 hours for BPA

Bisphenols – Legislative status in European countries

- Several countries have restrictions on the use of BPA in FCM, in pacifiers and teething rings
- Occupational exposure limits are also in place in different countries

Food contact materials, pacifiers and teething rings:

- France banned BPA in all food contact materials as of January 2015 ([French Law No 2012-1442](#)).
- Baby bottles made from BPA were banned in France under law No 2010-729 of 30 June 2010. [Law No 2012-1442 of 24 December 2012](#) then expanded the scope of the ban to include all food packaging, containers and utensils, as well as teething rings and soother shields
- In Denmark, [BPA has been prohibited in food contact materials intended to come into contact with children under three since 2010](#).
- From January 2013, Belgium banned the use of BPA in food contact materials intended for children less than three years old and in plastic articles like spoons and plates for the same age group
- In Austria, it is prohibited to manufacture pacifiers and teething rings with BPA or place them on the market, following Federal Law Gazette Part II, No.327/2011.
- From January 2013, Sweden banned BPA in varnish and coatings in food contact materials intended for 0-3 year olds.

Bisphenols – Occupational exposure

- Denmark has set an Occupational Exposure Limit (OEL) of 3 mg/m³ for BPA, based on the general national OEL for organic dust of 3 mg/m³
- In Germany, Switzerland, Finland and Austria the OELs is set at 5 mg/m³

Bisphenols – Critical questions

1. 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
2. Reflect on the implications that growing evidence regarding the toxicity of bisphenols at low doses might have for current toxicity references values
3. Are the substitutes being used to replace BPA safe, considering their hazardous properties and current and expected exposure

Bisphenols – Policy related questions

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?

Research activities are being carried out to answer the policy questions

Phthalates

- Phthalates (or phthalate esters) and the non-phthalate substitute Hexamoll® DINCH® are a **group of plasticizers** with a production volume of **millions of tons per year**
- Phthalates can cause a variety of adverse effects in humans and in laboratory animals such as **endocrine disrupting and reproductive effects**
- Some phthalates, such as di(2-ethylhexyl) phthalate (DEHP), butylbenzyl phthalate (BBzP), di-n-butyl phthalate (DnBP), and di-isobutyl phthalate (DiBP) induce the so-called **phthalate syndrome** already at low doses, which covers **different reproductive abnormalities** in male offspring of rats exposed during pregnancy
- **Not all phthalates** exhibit the **reprotoxic and developmental** effects and **not all have the same endocrine disrupting** potency
- It is assumed, that **similar adverse effects** are also caused in **humans**, since the effects of the **phthalate syndrome in rats have similarities** with the **observed testicular dysgenesis syndrome in humans**

Phthalates

- Less harmful plasticiser substitutes became available
 - di(2-propylheptyl) phthalate (DPHP) and Hexamoll[®] DINCH[®]
- DPHP is thought to have no anti-androgenic effects, but only minimal data is available
- Hexamoll[®] DINCH[®] was introduced into the market in 2002 as a substitute mainly for DEHP and DINP.
- Current available data suggests that Hexamoll[®] DINCH[®] has no reproductive effects and is not an endocrine disrupter, but nephrotoxic effects were observed in a subchronic feeding study in rats (EFSA, 2006)
- These effects relevant for the derivation of a TDI of 1 mg/kg BW .

Phthalates - Exposure

- Not chemically bound to the (plastic) materials, they can leach, migrate or evaporate into indoor air and atmosphere, foodstuff or other materials
- Exposure can be by ingestion, inhalation and dermal contact
- Simultaneous exposure to multiple phthalates leads to cumulative exposure which might exceed health-based guidance values and therefore pose a risk to the public health
- DEHP, DnBP, BBzP, DEMPP, DnPeP, DiPeP and DHNUP are **prohibited for use in cosmetics** in the European Union
- Consumer articles from outside EU (e.g. from Asia or USA) can contain phthalates since there is no such strict restriction for the use of phthalates

Phthalates – Societal concern

- Due to the **endocrine disrupting properties**, some phthalates have been **assigned use restrictions** in the late **1990s**
- Societal concern due to **their toxicity to reproduction** and presence in biological matrices of humans
- Greenpeace conducted several studies addressing phthalates in consumer products and the potential health effects emerging from its endocrine disrupting effects in the early **2000s**

Phthalates – Policy relevance

- DEHP, DnBP, DiBP, BBzP, DnPeP, DiPeP, DHNUP, DnHP and DMEP are classified as **reproductive toxicants category 1B** under Annex VI to CLP regulation ([EC 1272/2008](#))
- In 2017, also due to their reprotoxic properties, DEHP, BBzP, DnBP and DiBP, were identified as SVHC and included in the candidate list for the inclusion in [Annex XIV](#) of the REACH regulation
- Four of the nine above mentioned phthalates are already **regulated subject to authorisation** (DEHP, BBzP, DnBP and DiBP) since February 2015 ([Directive \(EU\) 2015/863](#))
- In April 2018, the EC proposed to expand the restriction of phthalates under [REACH](#) to DEHP, BBzP, DnBP, and DiBP
- In addition, DiNP, di-n-octyl phthalate (DnOP), DiDP are **restricted for all children's toys and childcare articles** that can be placed in children's mouth with a concentration limit of 0.1% by entry 52 of Annex XVII to REACH

Phthalates – Policy relevance

Major highlights of the proposed amendment and a comparison with entry 51 to Annex XVII of REACH are summarized in Table 1.

	WTO Document no. 18-1935 Draft Regulation to amend entry 51 to Annex XVII of REACH	Entry 51 to Annex XVII of REACH [4]
Scope (Plasticized Materials)	<ul style="list-style-type: none">– Toys and Childcare Articles– Articles	<ul style="list-style-type: none">– Toys and Childcare Articles
Phthalate	DEHP, DBP, BBP and DIBP	DEHP, DBP and BBP
Requirement	≤ 0.1% (individually or in combination)	≤ 0.1% (sum)
Effective Date	<ul style="list-style-type: none">– Potentially late 2018 for toys and childcare articles– Potentially early 2020 for articles	In force

Phthalates – Policy relevance

- Other product-specific legislation which regulate certain phthalates include:
 - Cosmetic Products' Regulation ([EC/1223/2009](#))
 - Regulation on plastic materials and articles intended to come into contact with food ([EC 935/2004](#) and [Directives 80/590/ECC & 89/109/ECC](#))
 - Regulation for Plastics Implementation Measure ([10/2011/EC](#))
- Certain phthalates have specific migration limits (SMLs):
 - DEHP with a SML of 1.5 mg/kg foodstuff, BBzP with an SML of 30 mg/kg foodstuff, DnBP with a SML of 0.3 mg/kg foodstuff and DiNP, DiDP and Hexamoll[®] DINCH[®]

Phthalates – Policy Questions

1. Which are the **most sensitive, reliable and cost effective methods** and biomarkers to measure phthalates and Hexamoll[®] DINCH[®]?
2. What is the extent of the **current exposure of the EU population** to the 16 phthalates (Cat A, B and C) and their substitute Hexamoll[®] DINCH[®]?
3. Do the **exposure levels differ** significantly between the countries?
4. What are the **main sources of exposure** and the **reasons for differences** in exposure (different regulations in different countries) to phthalates and Hexamoll[®] DINCH[®]?
5. What are the **high exposure groups**? (Is there a statistical significant and toxicological relevant difference in mean concentration between adults and children? [...] between occupational exposed and non-exposed adults? [...] between male and female?)
6. Are there **different time trends for unregulated** (DEP, DMP, DCHP, DPHP) and **regulated phthalates**(DEHP, BBzP, DnBP, DiBP, DinP, DnOP) and Hexamoll[®] DINCH[®]?
7. How **effective have the different mitigation steps** and regulations been phthalates?

7a) Had the **restriction under REACH the favourable impact**, that is a reduction of GM/median concentrations of the already restricted phthalates (DEHP, BBzP, DnBP, DiNP, DiDP, DnOP), especially for children from 2007 until today (2018-2021)?

Phthalates – Policy Questions

7b) Was the introduction of the **Authorisation obligation under REACH** effective **enough to protect European citizens**? Is there a sufficient decrease of the Cat. A substance levels subject to authorisation (GM/median) in the European population (general/children?) from year 2015 until today (2018-2021) (i.e. DEHP, DnBP, DiBP, BBzP)? Are there differences between countries?

7c) Had the **identification as SVHC already an impact** on the reduction of the phthalate exposure of the population (i.e. Did the exposure of a certain substance decline after the substance is identified as SVHC)?

8. **Is the exposure to phthalates and their substitutes of health-relevance** for the general population and vulnerable groups (inter alia children and pregnant women)? What part of the population has exposure levels exceeding the HBM guidance values -if existing-or TDI)?

9. Does the **health relevance** depend on **age and gender**?

10. Can **EU wide accepted HBM guidance values be derived for single substances** and for the **additively acting phthalates**?

11. How **can cumulative risks of phthalates** and other anti-androgenic substances be **assessed for their health relevance**? Are their additive effects relevant for regulation?

12. How can **HBM4EU results feed into the regulatory decisions** of ECHA and EFSA?

13. What is the **economic impact of phthalates and substitute exposure**?

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